Evidence Reports of Kampo Treatment 2009: 320 Randomized Controlled Trials (EKAT 2009)

Task Force for Evidence Reports (ER-TF),
Special Committee for Evidence-based Medicine (EBM)
The Japan Society for Oriental Medicine (JSOM)

Edited by

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1 June 2009

ver. 1.3　2009.9.4

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Special Committee for Evidence-based Medicine (EBM)
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Executive Summary

The Special Committee for Evidence Based Medicine (EBM), established in June 2001 by the Japan Society for Oriental Medicine (JSOM), issued the "EBM in Kampo 2002, Interim Report" (*Nihon Toyo Igaku Zasshi* [*Japanese Journal of Oriental Medicine*] 2002: 53 (5), supplementary issue) in 2002, followed by "Evidence Reports of Kampo Treatment" (*Nihon Toyo Igaku Zasshi* [Kampo Medicine] 2005: 56, EBM supplementary issue) in 2005. These publications were intended to present the evidence from "good" studies, including randomized controlled trials (RCTs), of Kampo products published between 1986 and 2002. However, those studies had several weaknesses, such as lack of clear inclusion/exclusion criteria. Thus questions were raised by readers such as why particular articles had or had not been included.

Accordingly, the following improvements were made in the second phase, starting in 2005:

(1) Although all RCTs for the period 1986–2008 were reviewed, only some of these were included.
(2) The "systematic review" approach was adopted in literature search, and evidence appraisal was adopted to enhance comprehensiveness, accuracy, and transparency of the review.
(3) The structure of the abstracts included eight standard items, i.e., "objectives," "design," "setting," "participants," "intervention," "main outcome measures," "main results," and "conclusions", and four additional items, i.e., "from Kampo medicine perspective," "safety assessment in the article," "abstractor's comments," and "abstractor's name and date."
(4) Excluded references along with the reasons for their exclusion were listed.
(5) Because the main mission of the task force was to develop structured abstracts, recommendations were not made. Recommendations will be dealt with during the development of clinical practice guidelines (CPG) in the future.
(6) A system to enable feedback from readers through the internet and other media on the current reports was established.
(7) In order to have transparency and accountability, conflicts of interests (COI) of the members of the Task Force were disclosed.

This phase 2 report includes only RCTs of Kampo products (extract granules, tablets, and capsules, or pills, approved for sale as ethical Kampo prescriptions in Japan). It excludes studies of in-house formulations such as decoctions, since no quality control criteria have been established.

The data sources of searches were 1) the Cochrane Library (CENTRAL), 2) *Igaku Chuo Zasshi* (*Japana Centra Revuo Medicana* [*JCRM*], Ichushi) web, and 3) the database offered by the Japan Kampo Medicines Manufacturers Association (JKMA).

Structured abstracts were arranged in the order used in the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10).

The interim report published in 2007 lists 98 structured abstracts prepared from 116 references published between 1999 and 2005. "Evidence Reports of Kampo Treatment 2009: 320 Randomized Controlled Trials" (EKAT 2009)" in Japanese (http://www.jsom.or.jp/medical/ebm/er/index.html) contain structured abstracts of 320 RCTs and one meta-analysis of 385 references published between 1986 and 2008. It was in 1986 when the current quality control standard for Kampo formulations was established by request of the Ministry of Health and Welfare (MHW, currently the Ministry of Health, Labor and Welfare: MHLW).

This Report in English here covers 143 structured abstracts of 180 references published in the period 1999–2008. The English translation of the 178 structured abstracts on the base of references published 1986–1998 is under construction.

We would appreciate your comments on the contents, methodology, relevant references, and other matters. Please send your comments to ebm-er@jsom.or.jp. We will review and respond to them in the final report.

Lists of Structured Abstracts

Note: Original English titles assigned by authors were used in this list and the structured abstracts. When references had no English titles, the Task Force translated the original Japanese titles into English ones (*).

Abbreviations: C: Cochrane Library (CENTRAL), I: *Igaku Chuo Zasshi* (*Japana Centra Revuo Medicana*, Ichushi), N: Database Offered by Nikkankyo (the Japan Kampo Medicines Manufacturers Association), UC: Under Construction.

<<Structured Abstracts describing RCTs and the References Reporting Them>>

Infections (including Viral Hepatitis) (18 abstracts, 23 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
A09	Efficacy of keihito for diarrhea in children	keihito (啓脾湯)	Miyazaki R, Tomita H. A study of the efficacy of keihito for diarrhea in children*. *Kampo no Rinsho* (*Journal of Kampo Medicine*) 1996; 43: 217-23 (in Japanese).	quasi-RCT	N	UC
A16.2	Improvement effects on appetite and host defense in patients undergoing chemotherapy for pulmonary tuberculosis	hochuekkito (補中益気湯), hochuekkito (補中益気湯) ＋shosaikoto (小柴胡湯)	Watanabe A, Hasegawa S. Effect of combined Kampo medicines as adjuvant therapy for pulmonary tuberculosis*. *Nippon Iji Shinpo* (*Japan Medical Journal*) 1992; (3553): 76-7 (in Japanese).	RCT	N	UC
			Watanabe A, Takahashi N, Uchida Y, et al. Efficacy of hochuekkito as adjuvant therapy for pulmonary tuberculosis*. *JAMA* (*Japanese version*) 1992; 13 (6) suppl: 20-1 (in Japanese).		N	
A16.2	Efficacy for reducing hepatic dysfunction and improving *hiiqikyo* (*脾胃気虚*, splenogastric *qi* deficiency) in tuberculosis patients undergoing chemotherapy	hochuekkito (補中益気湯)	Nakanishi F. Experience with hochuekkito in the short-course intensified chemotherapy for pulmonary tuberculosis*. *Nikkei Medical* 1994; 23 (12): 24-5 (in Japanese).	RCT	N	UC
			Shijubo N, Nakanishi F. Experience with hochuekkito in the short-course intensified chemotherapy for pulmonary tuberculosis – the reducing effect on hepatic dysfunction occurring as an adverse drug reaction–*. *Kampo Igaku* (*Kampo Medicine*) 1993; 17: 241-3 (in Japanese).		N	
A49.0	To determine whether hochuekkito has efficacy in preventing colonization and infection with methicillin-resistant *Staphylococcus aureus* (MRSA).	hochuekkito (補中益気湯)	Seki T, Matsumoto T, Deguchi H, et al. Evaluation of the efficacy of hochuekkito in preventing MRSA colonization and infection*. *Kampo Igaku* (*Kampo Medicine*) 1999; 23: 196-7 (in Japanese).	RCT-envelope	I	40
A49.0	To determine whether hochuekkito can improve immune and nutritional status in immuno-compromised hosts.	hochuekkito (補中益気湯)	Suzuki J, Arata S, Sugiyama M. Improvement of immunity and nutrition by hochuekkito in immuno-compromised hosts – for the control of MRSA –*. *Progress in Medicine* 2002; 22: 1362-3 (in Japanese).	RCT	I	41
A49.8	To determine the efficacy and safety of triple therapy with proton pump inhibitor, antibiotic, and goshuyuto for *Helicobacter pylori* (*H. pylori*) infection.	goshuyuto (呉茱萸湯)	Higuchi K, Arakawa T, Ando K, et al. Eradication of Helicobacter pylori with a Chinese Herbal medicine without emergence of resistant colonies. *American Journal of Gastroenterology* 1999; 94: 1419-20.	RCT	C	42
B02.2	To determine whether hochuekkito has a preventive effect on postherpetic neuralgia (PHN).	hochuekkito (補中益気湯)	Taniguchi S, Kono T, Terai T. Preventive effect of hochuekkito on postherpetic neuralgia*. *Progress in Medicine* 2002; 22: 863-5 (in Japanese).	RCT	I	43
			Taniguchi S, Terai T, Kono T, et al. The effect of hochuekkito on postherpetic neuralgia*. *Hifu no Rinsho* (*Clinical Practice of Dermatology*) 1999; 41: 601-3 (in Japanese).		N	

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
B18.1	Therapeutic effect of shosaikoto combined with interferon (IFN) -beta therapy on chronic active hepatitis B	shosaikoto (小柴胡湯)	Sata M, Amagase H, Koga S, et al. Therapeutic effect of IFN-β (Feron) plus shosaikoto combination therapy on chronic active hepatitis B*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1994; 71: 814-20 (in Japanese).	RCT-envelope	I	UC
B18.1	Efficacy of shosaikoto on chronic hepatitis B	shosaikoto (小柴胡湯)	Sato S, Ishikawa K, Chiba T. Efficacy of Sho-saiko-to on chronic type B hepatitis. *Shokakika* (*Gastroenterology*) 1991; 15: 39-49 (in Japanese).	RCT-envelope	N	UC
B18.1	Efficacy and safety in children with HBe antigen-positive chronic hepatitis B	shosaikoto (小柴胡湯)	Shiraki K, Tanimoto K, Togashi T, et al. A study of the efficacy of shosaikoto in children with HBe antigen-positive chronic hepatitis B*. *Shonika Rinsho* (*Japanese Journal of Pediatrics*) 1991; 44: 2146-51 (in Japanese).	RCT	N	UC
			Shiraki K, Tanimoto K. Clinical Evaluation of the efficacy of TSUMURA Shosaikoto in children with chronic hepatitis B*. *Dai 7-kai Nihon Shoni Toyo Igaku Kenkyukai Koen Kiroku* (*Proceedings of the 7th meeting of the Japan Pediatric Society for Oriental Medicine*) 1991; 7: 18-22 (in Japanese).		N	
B18.2	Determination of efficacy and safety of shosaikoto for type C chronic liver diseases	shosaikoto (小柴胡湯)	Hatakeyama S, Ueki J, Ishizuka M, et al. Comparative study of ursodeoxycholic acid and Shosaikoto as treatment for chronic liver diseases type C. *Yakuri to Chiryo* (*Japanese Pharmacology & Therapeutics*) 1994; 22: 3295-305 (in Japanese).	RCT-envelope	I	UC
B18.2	Efficacy of shosaikoto combined with interferon for reducing adverse effects in patients with chronic hepatitis C	shosaikoto (小柴胡湯)	Nakajima O, Sone M. Interferon plus shosaikoto combination therapy for chronic hepatitis C (the first report) - effectiveness in reducing adverse effects of interferon-*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*). 1993; 70: 2994-3002 (in Japanese).	RCT-envelope	I	UC
B18.2	Efficacy and safety of shosaikoto in chronic hepatitis C after interferon therapy	shosaikoto (小柴胡湯)	Nakajima O, Sone M. Evaluation of the usefulness of shosaikoto in the treatment of chronic hepatitis C after interferon therapy - the second report-*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1998; 75: 1883-8 (in Japanese).	RCT	I	UC
			Sone M, Nakajima O. Evaluation of the usefulness of shosaikoto in the treatment of chronic hepatitis C after interferon therapy*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1995; 72: 3193-7 (in Japanese).		I	
B18.2	To confirm the efficacy of shosaikoto for interferon-resistant chronic hepatitis C.	shosaikoto (小柴胡湯)	Nakajima O, Sone M, Kurokawa K, et al. The Complemental treatment for chronic hepatitis C. *Kagaku Ryoho Kenkyusyo Kiyo* (*Bulletin of the Institute of Chemotherapy*) 2003; 34: 40-51 (text in Japanese with English abstract).	RCT-envelope	I	44
B18.2	To confirm the efficacy of shosaikoto for chronic hepatitis C.	shosaikoto (小柴胡湯)	Nakajima O, Sone M, Onishi H, et al. Preventive effect of shosaikoto on the progression of chronic hepatitis C to cirrhosis*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1999; 76: 176-84 (in Japanese).	RCT	I	45
B18.2	Efficacy of interferon plus shosaikoto combination therapy for chronic hepatitis C	shosaikoto (小柴胡湯)	Tanaka N, Matsuzaki Y, Osuga T, et al. A comparative study of IFN monotherapy versus IFN plus TJ-9 shosaikoto combination therapy in patients with chronic hepatitis C (interim report)*. *Progress in Medicine* 1993; 13: 2868-72 (in Japanese).	RCT-envelope	N	UC
B18.2	Efficacy for reducing adverse effects of interferon therapy in patients with chronic hepatitis C	maoto (麻黄湯) + keishito (桂枝湯) + kojinmatsu (紅参末)	Isai H. Efficacy of Kampo formulations for reducing adverse effects of interferon therapy in patients with chronic hepatitis C*. *Shindan to Chiryo (Diagnosis and Treatment)* 1996; 84: 1505-9 (in Japanese).	RCT	N	UC
B24.0	Efficacy and safety in the treatment of HIV infection	shosaikoto (小柴胡湯)	Fukue H, Hagiwara T, Yoshida S, et al. Efficacy of high-dose shosaikoto for HIV infection*. HIV Kansensha Hassho Yobo, Chiryo ni kansuru Kenkyuhan Heisei 7 Nendo Kenkyu Hokokusho (Research Report by the Study Group on Prevention and Treatment of HIV Infection) 1996: 203-10 (in Japanese).	DB-RCT	N	UC

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs) (28 abstracts, 34 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
C16.9	Improvement effect on host-immunity in patients undergoing postoperative adjuvant chemotherapy for gastric cancer	juzentaihoto (十全大補湯)	Konno H, Maruo Y, Baba S, et al. Improvement of host-immunity by Juzen-taiho-to in the postoperative adjuvant chemotherapy for patients with gastric cancer. *Biotherapy* 1997; 11: 193-9 (text in Japanese with English abstract).	RCT-envelope	N	UC
C16.9	Efficacy for reducing adverse effects and improving performance status (PS) in patients undergoing postoperative adjuvant chemotherapy for gastric cancer	ninjin'yoeito (人参養栄湯)	Sugimachi K. A study of the usefulness of ninjin'yoeito in the postoperative adjuvant chemotherapy for gastric cancer*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1995; 72: 454-8 (in Japanese).	RCT-envelope	I	UC
C16.9	Efficacy of juzentaihoto (TJ-48) combined with oral 5-FU as postoperative adjuvant chemotherapy in patients with surgically treated gastric cancer.	juzentaihoto (十全大補湯)	Yamada T. Randomized controlled trial of the efficacy of juzentaihoto (TJ-48) combined with oral 5-FU for gastric cancer*. *Progress in Medicine*. 2004; 24: 2746-7 (in Japanese)	RCT	N	46
C18.9	Efficacy for reducing adverse effects of tegafur in patients with colorectal cancer	juzentaihoto (十全大補湯)	Toda T, Matsuzaki K, Kawano T, et al. Preoperative and postoperative combination therapy with slow-release tegafur capsules and Juzen-taiho-to in patients with colorectal cancer - Tissue concentrations and thymidine phosphorylase activity -. *Gan no Rinsho* (*Japanese Journal of Cancer Clinics*) 1998; 33:317-23 (text in Japanese with English abstract).	RCT-envelope	N	UC
C18.9	Immunostimulation and suppression of liver metastasis in postoperative patients with colorectal cancer	shosaikoto (小柴胡湯)	Sasaki K, Takashima K, Kitagawa K, et al. Immunostimulation and suppression of liver metastasis by Kampo medicines in postoperative patients with colorectal cancer*. *Progress in Medicine* 1992; 12: 1652-5 (in Japanese).	RCT	N	UC
C18.9	Immunostimulation and improvement of nutritional status in postoperative patients with colorectal cancer	ninjin'yoeito (人参養栄湯)	Araki Y, Tanaka T, Ogata Y, et al. Immunological evaluation of the efficacy of Kampo prescription for postoperative patients with colorectal cancer*. *Shinyaku to Rinsho* (*Journal of New Remedies and Clinic*) 1992; 41: 1670-6 (in Japanese).	RCT-envelope	N	UC
C18.9	To determine the clinical efficacy of juzentaihoto for the prevention of postoperative recurrence of colorectal cancer.	juzentaihoto (十全大補湯)	Sasaki K, Ezoe E, Araya J, et al. Effects of Kampo medicine on the immune Functions in gastroenteric cancer patients. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2006; 15: 9-14 (in Japanese).	RCT	N	47
			Sasaki K, Takasaka H, Furuhata T, et al. Effect of Kampo medicine on cancer chemotherapy. *Geka Chiryo* (*Surgical Therapy*) 2007; 97: 504-10 (in Japanese).		N	
C20.0	To determine the effects of daikenchuto on intestinal obstruction following colorectal cancer surgery.	daikenchuto (大建中湯)	Takagi K, Nagata H, Horie T, et al. Effect of the preventive herbal therapy using Dai-kenchu-to on intestinal obstruction following curative resection for colorectal cancer: prospective, randomized study. *Kampo Kenkyu* (*Kampo Research*) 2007; (429): 270-1 (in Japanese).	RCT	I	48
C22.0	Efficacy for reducing adverse effects of anticancer drug for hepatocellular carcinoma	juzentaihoto (十全大補湯)	Nagatomo H, Shigehira M. Efficacy of TSUMURA Juzentaihoto for reducing the adverse effects of the anticancer drug cisplatin*. *Kampo Igaku* (*Kampo Medicine*) 1992; 16: 116-9 (in Japanese).	RCT	N	UC
C22.0	Preventive effect on the progression of cirrhosis to liver cancer	shosaikoto (小柴胡湯)	Ayukawa K, Sato T, Nagase S, et al. Preventive effect of shosaikoto on liver carcinogenesis*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1994; 71: 1874-6 (in Japanese).	quasi-RCT	I	UC
C34.9	Preventive effect on myelosuppression in patients undergoing chemotherapy for primary lung cancer	juzentaihoto (十全大補湯)	Yamagata T, Ajimura K, Yukawa S. Effect of juzentaihoto on myelosuppression during lung cancer chemotherapy*. *Therapeutic Research* 1998; 19: 705-8 (in Japanese).	RCT-envelope	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
C34.9	Preventive effect of hochuekkito on general malaise in patients undergoing chemotherapy for advanced primary lung cancer	hochuekkito (補中益気湯)	Inui H, Yamagata T, Minakata Y, et al. Prevention of side effects during lung cancer chemotherapy by Hochuekki-to. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 1993; 2: 56-60 (in Japanese).	RCT-envelope	N	UC
C34.9	To evaluate the efficacy of hochuekkito combined with clarithromycin (CAM) for improvement in the prognosis of lung cancer.	hochuekkito (補中益気湯)	Kato S, Kishiro I, Machida S, et al. Combined effects of hochu-ekki-to (Bu-Zhong-Yi-Qi-Tang) and clorithromycin on Lung Carcinoma. Kampo to Meneki-Arerugi (Kampo and Immuno-Allergy) 1999; 13: 83-8 (text in Japanese with English abstract).	RCT	N	49
C34.9	Efficacy of hochuekkito for the prevention and relief of symptoms related to chemotherapy for primary lung cancer	hochuekkito (補中益気湯)	Mori K, Saito Y, Tominaga K. Utility of hochu-ekki-to in general malaise accompanying lung cancer chemotherapy. *Biotherapy* 1992; 6: 624-7 (text in Japanese with English abstract).	RCT	I	UC
C50.9	Efficacy for reducing adverse effects and improving QOL in breast cancer patients undergoing postoperative chemotherapy	ninjin'yoeito (人参養栄湯) or hochuekkito (補中益気湯)	Nagao K, Nishimura R, Matsuda M, et al. Clinical evaluation of the combined effect of tegafur and hozai (traditional Chinese medicine)*. *Toho Igaku* (*Eastern Medicine*) 1998; 14: 63-71 (text in Japanese with English abstract).	RCT-envelope	N	UC
C50.9	Efficacy of supportive therapy for advanced breast cancer patients	juzentaihoto (十全大補湯)	Adachi I. Supporting therapy with Shi Quan Da Bu Tang in advanced breast cancer patients. *Biomedical Research* 1990; 11 suppl: 25-31.	RCT-envelope	N	UC
			Adachi I, Watanabe T, Chen JY, et al. Supportive therapy of oriental medicine for patients with advanced breast cancer. *Gan to Kagaku Ryoho* (*Japanese Journal of Cancer and Chemotherapy*) 1989; 16: 1538-43 (text in Japanese with English abstract).		C&I	
			Adachi I. Juzen-taiho-to as a supporting therapy in advanced breast cancer. *Biotherapy* 1989; 3: 782-8 (text in Japanese with English abstract).		I	
C57.9	Efficacy for relieving subjective symptoms and improving activities of daily living in patients following gynecologic cancer surgery	ninjin'yoeito (人参養栄湯)	Mizuno M, Yoshikawa H, Taketani Y, et al. Clinical effects of ninjin'yoeito on performance status (PS) and recovery of physical strength in patients following gynecologic cancer treatment – comparison with no-treatment controls–*. *Sanka to Fujinka* (*Obstetrics and Gynecology*) 1993; 60: 1533-45 (in Japanese).	RCT	I	UC
C57.9	Efficacy for reducing adverse effects of CAP chemotherapy	ninjin'yoeito (人参養栄湯) ＋hochuekkito (補中益気湯)	Hasegawa K, Fukunishi H, Kiyoshige K, et al. Clinical usefulness of Kampo medicines (Ninjin-yoei-to, Juzen-taiho-to) for side effects in gynecologic cancer chemotherapy – Effects on reducing side effects by CDDP in CAP therapy–. *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1994; 11: 181-7 (text in Japanese with English abstract).	RCT	N	UC
C57.9	Efficacy of ninjin'yoeito on subjective and objective symptoms and bone-marrow function during postoperative chemotherapy or radiotherapy in female patients with genital cancer*	ninjin'yoeito (人参養栄湯)	Yamamoto T, Fujita H, Okada H, et al. Clinical evaluation of the effects of ninjin'yoeito on subjective and objective symptoms and bone-marrow function during chemotherapy or radiotherapy in female patients with genital cancer*. *Oncology & Chemotherapy* 1994; 10: 126-34 (in Japanese).	RCT-envelope	N	UC
C57.9	To determine the efficacy of ninjin'yoeito for reducing myelosuppression due to chemotherapy for gynecologic cancer.	ninjin'yoeito (人参養栄湯)	Oda T. My prescription – clinical application of ninjin'yoeito in gynecologic cancer – a preventive effect on bone marrow suppression–*. *WE* 2004; 9: 5-6.	quasi-RCT	I	50
			Oda T, Ohnuki T, Kihara K, et al. A clinical study of a traditional Chinese herbal medicine, NINJIN-YOUEI TO in bone marrow suppression due to chemotherapy in gynecologic cancer. *Yamagata Kenritsu Byoin Igaku Zasshi* (*The Yamagata Journal of Medicine*) 2004; 38; 6-9 (in Japanese).		I	
C67.9	Effect of juzentaihoto on survival of patients undergoing adjuvant chemotherapy for bladder cancer	juzentaihoto (十全大補湯)	Fukui I, Gotoh S, Kihara K, et al. Adjuvant chemotherapy for invasive bladder cancer: multicenter study. *Nippon Hinyokika Gakkai Zasshi* (*Japanese Journal of Urology*) 1992; 83: 1633-9 (text in Japanese with English abstract).	RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
C68.9	Efficacy and safety of saireito for relieving the adverse urological effects of anticancer drugs	saireito (柴苓湯)	Ohkawa T, Ebisuno S, Watanabe T, et al. Clinical evaluations of Saireito, a herbal drug, for the side-effects of cancer chemotherapy in urological field. *Biotherapy* 1990; 4: 1445-60 (text in Japanese with English abstract).	RCT-envelope	I	UC
C80.0	Efficacy of juzentaihoto for reducing adverse effects and improving QOL in postoperative patients undergoing chemotherapy for gastric, colorectal, or breast cancer	juzentaihoto (十全大補湯)	Kosaka A, Kamiya T, Sumiyama M, et al. Usefulness of TSUMURA Juzentaihoto (TJ-48) for reducing adverse effects of anticancer drugs and improving QOL*. *Progress in Medicine* 1994; 14: 2259-64 (in Japanese).	RCT-envelope	N	UC
			Kosaka A, Hojyo M, Osaku M, et al. The value of TSUMURA Juzentaihoto (TJ-48) in reducing adverse effects of anticancer drugs from the perspective of QOL improvement*. *Progress in Medicine* 1993; 13: 1072-9 (in Japanese).		N	
C80.0	Efficacy and safety for reducing adverse reactions during cancer radiotherapy	juzentaihoto (十全大補湯)	Hashimoto S, Tanaka Y. Adverse reactions to cancer radiotherapy*. *Sanfujinka no Sekai* (*World of Obstetrics and Gynecology*) 1990; 42 suppl: 176-84 (in Japanese).	RCT-envelope	N	UC
			Tanaka Y, Hashimoto S. Effects of TSUMURA Juzentaihoto on various complaints occurring as adverse reactions during radiotherapy*. *JAMA* (*Japanese version*) 1988; (6) suppl: 70-1 (in Japanese).		N	
C80.0	Effect on the cell-mediated immunity of postoperative patients with esophageal, gastric, or colorectal cancer	juzentaihoto (十全大補湯)	Yamada T. Clinical study of Juzen-taiho-to administration for postoperative esophageal carcinoma, gastric carcinoma, and colorectal carcinoma – Influence of surgical intervention and postoperative chemotherapy on cell mediated immunity–. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1992; 9: 157-64 (text in Japanese with English abstract).	RCT-envelope	N	UC
C80.0	Clinical effects in patients undergoing chemotherapy (tegafur)	hochuekkito (補中益気湯), ninjin'yoeito (人参養栄湯)	Ohara T, Onda M, Futagawa S, et al. Clinical evaluation of the combined effect of Bu-Zhong-Yi-Qi-Tang (Japanese name, Hochu-ekki-to) or Ren-Shen-Yang-Rong-Tang (Japanese name, Ninjin-youei-to) and the anticancer drug tegafur. *Yakuri to Chiryo* (*Japanese Phamacology & Therapeutics*) 1993; 21: 4423-34 (in Japanese).	RCT-envelope	I	UC
C80.0	To determine whether preoperative administration of hochuekkito relieves surgical stress in patients with gastric or colorectal cancer.	hochuekkito (補中益気湯)	Saito S, Iwagaki H, Kobayashi N, et al. Effects of a Japanese herbal medicine (TJ-41) on surgical stress of patients with gastric and colorectal cancer*. *Nihon Rinsho Geka Gakkai Zasshi* (*Journal of Japan Surgical Association*) 2006; 67: 568-74 (in Japanese).	RCT	I	51
D25.9	To evaluate the anti-tumor effect of keishibukuryogan in patients with hysteromyoma/uterine adenomyosis.	keishibukuryogan (桂枝茯苓丸)	Yamamoto K, Hirano F, Ikoma N, et al. Efficacy of keishibukuryogan for hysteromyoma/uterine adenomyosis. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2003; 20: 135-7 (in Japanese).	RCT	I	52

Blood Diseases including Anaemia (14 abstracts, 17references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
D50.0	To evaluate the efficacy and safety of tokishakuyakusan for hypochromic anemia in patients with uterine myoma.	tokishakuyakusan (当帰芍薬散)	Akase T, Akase T, Onodera S, et al. A comparative study of the usefulness of tokishakuyakusan and an oral iron preparation in the treatment of hypochromic anemia in cases of uterine myoma. *Yakugaku Zasshi* (*Journal of the Pharmaceutical Society of Japan*) 2003; 123: 817-24.	RCT	C&I	53
D50.8	Efficacy of ninjin'yoeito for iron deficiency anemia due to menorrhagia	ninjin'yoeito (人参養栄湯)	Yanagihori A, Miyagi M, Hori M, et al. Efficacy of ninjin'yoeito for iron deficiency anemia*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1995; 72: 2605-8 (in Japanese).	RCT-envelope	I	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
D50.8	Combined effect of erythropoietin and ninjin'yoeito on anemia after autologous blood donation	ninjin'yoeito (人参養栄湯)	Aoe H, Takada K, Kawahara N, et al. Effectiveness of erythropoietin and ninjin'yoeito in preoperative autologous blood donation*. *Jikoketsu Yuketsu* (*Journal of Japanese Society of Autologous Blood Transfusion*) 1997; 10: 145-51 (in Japanese).	RCT	N	UC
D50.8	To evaluate the efficacy of juzentaihoto and ninjin'yoeito combined with an erythropoietin (EPO) preparation in preoperative autologous blood donation in cancer patients.	juzentaihoto (十全大補湯), ninjin'yoeito (人参養栄湯)	Aoe H, Sumida Y, Kawahara N, et al. Efficacy of an erythropoietin preparation and Kampo medicines in preoperative autologous blood donation in cancer patients*. *Jikoketsu Yuketsu* (*Journal of Japanese Society of Autologous Blood Transfusion*) 1999; 12: 100-4 (in Japansese).	RCT	N	54
D50.8	To evaluate the efficacy of using juzentaihoto to augment preoperative autologous blood donation in cancer patients.	juzentaihoto (十全大補湯)	Aoe H. Effect of Juzen-taiho-to on haematological recovery from predeposit autologous blood donation*. *Pharma Medica* 2007; 25: 11-4 (in Japanese).	RCT	I	55
			Aoe H, Matsuo T, Ebisutani M, et al. Effects of juzentaihoto (ten strong tonic herbs decoction) on presurgical autologous blood pooling in cancer patients*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2000; 17: 67-71 (in Japanese).		N	
			Aoe H, Ota M, Kawahara N, et al. Effects of juzentaihoto in preoperative autologous blood pooling*. *Rinsho Kensa* (*Journal of Medical Technology*) 2003; 47: 395-9 (in Japanese).		I	
D64.8	To evaluate the efficacy and safety of ninjin'yoeito for ribavirin-induced anemia.	ninjin'yoeito (人参養栄湯)	Motoo Y, Mouri H, Ohtsubo K, et al. Herbal medicine Ninjinyoeito ameliorates ribavirin-induced anemia in chronic hepatitis C: A randomized controlled trial. *World Journal of Gastroenterology* 2005; 11: 4013-7.	RCT	C	56
D69.6	Efficacy of goreisan for thrombocytopenia after cholecystectomy	goreisan (五苓散), shosaikoto (小柴胡湯)	Seki M. Efficacy of goreisan for preventing thrombocytopenia and activating vascular endothelial cells after cholecystectomy*. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1990; 7: 510-1 (in Japanese).	RCT	N	UC
D69.6	Effects of preoperative administration of shosaikoto on thrombocytopenia in gynecologic cancer patients receiving anti-cancer drugs	shosaikoto (小柴胡湯)	Mori T, Tauchi K, Yokoyama S, et al. Effects of Sho-saiko-to (Xiao-Chai-Hu-Tang) on thrombocytopenia bei therapy with anti-cancer drugs. *Sanfujinka Chiryo* (*Obstetrical and Gynecological Therapy*) 1992; 65: 102-5 (in Japanese).	RCT	N	UC
D70	Improvement in thrombocytopenia and leukopenia by kamikihito administration in patients receiving anti-cancer drugs	kamikihito (加味帰脾湯)	Inoue S, Kuwahara H, Kato Y, et al. Thrombopoietic and leukopoietic effects of a traditional Chinese herbal medicine, formula reverti lienalis compositae (Japanese name: *Kami-kihi-to TJ-137*) in cancer patients. *Biotherapy* 1998; 12: 1071-6 (text in Japanese with English abstract).	RCT-cross over	N	UC
D70	Effects of juzentaihoto on leukopenia in patients receiving cancer chemotherapy	juzentaihoto (十全大補湯)	Suzuki S, Abe R, Nomizu T, et al. Effect of juzentaihoto (TJ-48) on leukopenia in patients receiving cancer chemotherapy*. *Progress in Medicine* 1995; 15: 1968-71 (in Japanese).	RCT-envelope	I	UC
D70	Improvement in subjective symptoms and leukopenia by ninjin'yoeito administration in patients undergoing radiotherapy for thoracoabdominal tumors	ninjin'yoeito (人参養栄湯)	Okawa T, Hashimoto S, Sakamoto S, et al. Ninjin-Yoei-To in the treatment of leukopenia and symptoms associated with radiotherapy of malignant tumors. *Gan no Rinsho* (*Japanese Journal of Cancer Clinics*) 1995; 41: 41-51 (text in Japanese with English abstract).	RCT	I	UC
D72.8	Preventive effect of preoperative administration of shosaikoto on postoperative lymphopenia in female patients	shosaikoto (小柴胡湯)	Hatano T. Mitigation of postoperative lymphopenia and protection of T cells by preoperative administration of Xial-Chai-Hu-Tang. *Journal of Saitama Medical School* 1990; 17: 357-63 (text in Japanese with English abstract).	RCT	N	UC
D75.8	Effect of combined juzentaihoto during chemotherapy in patients with gynecologic cancers	juzentaihoto (十全大補湯)	Fujiwara M, Koumoto Y. Effect of juzentaihoto on myelosuppression due to chemotherapy for gynecologic malignant tumor*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 1998; 15: 86-9 (in Japanese).	RCT-cross over	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
D86.0	Effects of keishikajutsubuto on the levels of angiotensin-converting enzyme and lysozyme in sarcoidosis patients	keishikajutsubuto (桂枝加朮附湯)	Inagaki M, Nakazawa T, Michimata H, et al. Treatment experience with TSUMURA Keishikajutsubuto for pulmonary sarcoidosis*. *Wakan Iyaku Gakkaishi (Journal of Medical and Pharmaceutical Society for WAKAN-YAKU)* 1990; 7: 316-7 (in Japanese).	RCT	N	UC
			Inagaki M. Effectiveness of Kampo medicine in relieving complaints associated with chronic intractable diseases*. *Kampo Shinryo* 1993; 12: 1-3 (in Japanese).		N	

Metabolism and Endocrine Diseases (10 abstracts, 12 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
E11.9	Efficacy and safety of seishinrenshiin on improvement in glucose tolerance	seishinrenshiin (清心蓮子飲)	Azuma M, Motomiya M, Toyota T. Effects of Seishin-Renshi-In (TJ-111) on blood sugar levels of patients with non-insulin-dependent diabetes mellitus. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1994; 45: 339-44 (text in Japanese with English abstract).	RCT-envelope	N	UC
E22.9	To evaluate the efficacy of unkeito for reducing high luteinizing hormone (LH) levels and improving ovulation disorder.	unkeito (温経湯)	Ushiroyama T, Ikeda A, Sakai M, et al. Effects of Unkei-to, an herbal medicine, on endocrine function and ovulation in women with high basal level of luteinizing hormone secretion. *The Journal of Reproductive Medicine* 2001; 46: 451-6.	RCT-envelope	C	57
E28.2	To evaluate the efficacy of switching to unkeito from treatment based on the traditional diagnostic criterion “eight-principle pattern identification” in women with polycystic ovary syndrome (PCOS).	unkeito (温経湯), tokisyakuyakusan (当帰芍薬散), keishibukuryogan (桂枝茯苓丸)	Ushiroyama T, Hosotani T, Mori K, et al. Effects of switching to wen-jing-tang (unkei-to) from preceding herbal preparations selected by eight-principle pattern identification on endocrinological status and ovulatory induction in women with polycystic ovary syndrome. *The American Journal of Chinese Medicine* 2006; 34: 177-87.	RCT-envelope	C	58
E28.3	To evaluate the efficacy of unkeito for luteal phase deficiency.	unkeito (温経湯)	Ushiroyama T, Ikeda A, Higashio S, et al. Unkei-to for correcting luteal phase defects. *The Journal of Reproductive Medicine* 2003; 48: 729-34.	RCT-envelope	C	59
E66.9	To evaluate the anti-obesity effect of bofutsushosan extract granules in obese patients and the course of high-sensitivity C-reactive protein (HS-CRP) as an arteriosclerosis-promoting factor.	bofutsushosan (防風通聖散)	Namiki T. Basic and clinical investigation of the effect of Kampo medicines on arteriosclerosis*. *Uehara Kinen Seimei Kagaku Zaidan Kenkyu Hokokushu* (*Research Reports of Uehara Memorial Foundation*) 2007; 21: 60-3 (in Japanese).	RCT-envelope	I	60
E78.5	Efficacy and safety of daisaikoto combined with probucol in patients with hyperlipidemia	daisaikoto (大柴胡湯)	Takashima T, Ohmori K, Higuchi N, et al. Combination therapy with probucol and daisaikoto (a Kampo medicine) - Effects of daisaikoto on HDL metabolism -. *Domyaku Koka* (*The Journal of Japan Atherosclerosis Society*) 1993; 21: 47-52 (text in Japanese with English abstract).	RCT-envelope	N	UC
			Yamamoto K. A study of the hepatic triglyceride (TG)-lowering effects and antioxidant capacity of various Kampo preparations*. *Proceedings of the 4th Kampo Treatment Seminar at Kyoto University* 1995: 48-56 (in Japanese).	RCT-envelope	N	
E78.5	Efficacy and safety of daisaikoto in patients with hyperlipidemia	daisaikoto (大柴胡湯)	Sasaki J, Matsunaga A, Handa K, et al. Effect of daisaikoto on hyperlipidemia - comparison with clinofibrate -*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1991; 68: 3861-71 (in Japanese).	RCT	I	UC
E78.5	Efficacy and safety of daisaikoto combined with bezafibrate in patients with hyperlipidemia	daisaikoto (大柴胡湯)	Muramatsu N, Okayasu M. Clinical study on hyperlipidemia at bezafibrate and Da-chai-hu-tang (Dai-saiko-to) for the combination therapy. *Shigaku* (*Odontology*) 1993; 81: 94-9 (text in Japanese with English abstract).	RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
E78.5	Effects of daisaikoto on serum lipid level and cerebral circulation	daisaikoto (大柴胡湯)	Yamano S, Sawai F, Hashimoto T, et al. Comparative effects between Dai-Saiko-to and elastase on lipid metabolism and cerebral circulation in patients with hyperlipidemia. *Kampo to Saishin-chiryo* (*Kampo & The Newest Therapy*) 1995; 4: 309-13 (in Japanese).	RCT-envelope	N	UC
E87.8	Efficacy and safety of goreisan in the treatment of hyponatremia after surgery for cholelithiasis or gallbladder polyps	goreisan (五苓散), shosaikoto (小柴胡湯)	Seki M, Fujioka M, Hatano T, et al. Analysis of regulatory effects of Gorei-san on circulatory, metabolic and diuretic function - especially in relation to endothelial activation and increase of urinary 6-keto-prostaglandin $F_1\alpha$ level-. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1992; 42: 313-22 (text in Japanese with English abstract).	RCT	N	UC
			Takagi S. Mitigation of hyponatremia after operation for cholelithiasis or gallbladder polyp by preoperative administration of Wu-Ling-San. *Journal of Saitama Medical School* 1990; 17: 145-50 (text in Japanese with English abstract).		N	

Psychiatric/Behavioral Disorders (10 abstracts, 12 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
F01.9	Efficacy of chotosan in the treatment of vascular dementia	chotosan (釣藤散)	Shimada Y, Terasawa K, Yamamoto T, et al. A well-controlled study of Choto-san and placebo in the treatment of vascular dementia. *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1994; 11: 246-55.	RCT-envelope	I	UC
			Shimada Y, Terasawa K, Yamamoto T, et al. Efficacy of Choto-san on vascular dementia: A well, placebo-controlled study. *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1994; 11: 370-1 (in Japanese).		I	
F01.9	Efficacy of chotosan in the treatment of vascular dementia	chotosan (釣藤散)	Terasawa K, Shimada Y, Kita T, et al. Choto-san in the treatment of vascular dementia: A double blind, placebo-controlled study. *Phytomedicine* 1997; 4: 15-22.	DB-RCT	N	UC
			Terasawa K. Chotosan in the treatment of vascular dementia. *Pharma Medica* 2007; 25: 57-9 (in Japanese).		I	
F03	To evaluate the efficacy of hachimijiogan for dementia.	hachimijiogan (八味地黄丸)	Iwasaki K, Kanbayashi S, Chimura Y, et al. A randomized, double-blind, placebo-controlled clinical trial of the Chinese herbal medicine "Ba wei di huang wan" in the treatment of dementia. *Journal of the American Geriatrics Society* 2004; 52: 1518-21.	DB-RCT	C	61
F03	To evaluate the efficacy of chotosan for improvement of cognitive function and activities of daily living in dementia patients.	chotosan (釣藤散), goshajinkigan (牛車腎気丸)	Suzuki T, Futami S, Igari Y, et al. A Chinese herbal medicine, Choto-san, improves cognitive function and activities of daily living of patients with dementia: A double-blind, randomized, placebo-controlled study. *Journal of the American Geriatrics Society* 2005; 53: 2238-40.	DB-RCT	C	62
F03	To evaluate the efficacy and safety of yokukansan for treating behavioral disorders and improving activities of daily living in dementia patients.	yokukansan (抑肝散)	Iwasaki K, Satoh-Nakagawa T, Maruyama M, et al. A randomized, observer-blind, controlled trial of the traditional Chinese medicine Yi-gan san for improvement of behavioral and psychological symptoms and activities of daily living in dementia patients. *Journal of Clinical Psychiatry* 2005; 66: 248-52.	RCT	C	63
F41.9	To determine the efficacy of saibokuto as a potentiator of the anxiolytic and antidepressant effects of diazepam.	saibokuto (柴朴湯)	Ishida H, Otake T, Kurihara H, et al. Clinical study on augmentative effect of Saiboku-to for anxiolytic and antidepressive action of diazepam. *Pain Clinic*, 1999; 20: 395-9 (in Japanese).	RCT	N	64
F45.3	Efficacy for relieving discomfort in the throat	saibokuto (柴朴湯)	Yamagiwa M, Sakakura Y, Harada T, et al. Therapeutic response to various drugs in patients with continuous or periodic discomfort in the throat. *Jibiinkoka Rinsyo* (*Practica otologica*) 1990; 83: 1687-92 (text in Japanese with English abstract).	RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
F45.3	To determine the efficacy of lansoprazole in patients with pharyngolaryngeal paresthesia and acid reflux symptoms (compared with rikkunshito as a control).	rikkunshito (六君子湯)	Yamagiwa M, Fujita K. Effect of treatment using lansoprazole on patients with an abnormal sensation in the throat and concomitant heart burn. *Jibi to Rinsho* (*Otologia Fukuoka*) 2007; 53: 109-15 (text in Japanese with English abstract).	quasi-RCT	I	65
F45.9	Symptom-relieving effects in elderly patients with underlying chronic disease	hachimijiogan (八味地黄丸) ＋ kojinmatsu (紅参末)	Kaneko H, Nakanishi K, Murakami A, et al. Clinical evaluation of combination treatment of Hatimi-zio-gan and Red Ginseng Powder on unidentified clinical complaints - estimation of double blind comparative study in many hospitals -. *Therapeutic Research* 1989; 10: 4951-65 (in Japanese).	DB-RCT	I	UC
F52.2	Efficacy and safety of oral prostaglandin E1 in the treatment of erectile dysfunction	goshajinkigan (牛車腎気丸)	Sato Y, Horita H, Adachi N, et al. Effect of oral administration of prostaglandin E1 on erectile dysfunction. *British Journal of Urology* 1997; 80: 772-5.	quasi-RCT	N	UC

Nervous System Diseases (including Alzheimer's Disease) (9 abstracts, 10 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
G30.9	To evaluate the efficacy and safety of kihito for Alzheimer-type dementia.	kihito (帰脾湯), goshajinkigan (牛車腎気丸)	Higashi K, Rakugi H, Yu H, et al. Effect of kihito extract granules on cognitive function in patients with Alzheimer's-type dementia. *Geriatrics & Gerontology International* 2007; 7: 245-51.	RCT	I	66
G43.9	To evaluate the efficacy and safety of goshuyuto for treatment of migraine.	goshuyuto (呉茱萸湯)	Maruyama T. Goshuyu-to versus lomerizine hydrochloride in the prophylactic treatment of migraine headaches: an open crossover trial.. *Itami to Kampo* (*Pain and Kampo Medicine*) 2006; 16: 30-97 (text in Japanese with English abstract).	RCT-cross over	I	67
G47.0	Efficacy and safety of sansoninto for sedation	sansoninto (酸棗仁湯)	Matsushita M, Saito M, Katayama S, et al. Clinical evaluation of DS-4773 on sedative effect: a cross-over trial. *Yakuri to Chiryo* (*Japanese Pharmacology & Therapeutics*) 1994; 22: 2371-82 (in Japanese).	RCT-cross over	I	UC
G47.1	Effect of kakkonto on sleepiness after sleep deprivation	kakkonto (葛根湯)	Zhuang H.Y., Kim Y, Kurachi M, et al. Effect of Kakkon-to on sleepiness after sleep deprivation of normal young adults. *Shinkei Seishin Yakuri (Japanese journal of neuropsychopharmacology)* 1992; 14: 319-25 (text in Japanese with English abstract).	DB-RCT	I	UC
			Hagino H, Kim Y, Kurachi M, et al. Effect of Kakkon-to on sleepiness after sleep deprivation with quantitative EEG method. *Noha to Kindenzu* (*Japanese Journal of Electroencephalography and Electromyography*) 1995; 23: 361-7 (text in Japanese with English abstract).		N	
G47.9	Effectiveness of orengedokuto on sleep disorder in patients in the acute phase of psychotic disorders	orengedokuto (黄連解毒湯)	Yamada K, Kanba S, Ohnishi K, et al. Clinical effectiveness of Oren-Gedoku-To for sleep disorder associated with acute schizophrenia and other psychotic disorders. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1997; 47: 827-31 (text in Japanese with English abstract).	RCT-envelope	N	UC
G47.9	To evaluate the efficacy of yokukansankachimpihange for sleep disorders.	yokukansanka chimpihange (抑肝散加陳皮半夏), anchusan (安中散)	Aizawa R, Kanbayashi T, Saito Y, et al. Effects of Yoku-kan-san ka chimpi-hange on the sleep of normal healthy adult subjects. *Psychiatry and Clinical Neurosciences* 2002; 56: 303-4.	RCT-cross over	C&I	68
G51.3	Efficacy of shakuyakukanzoto for relieving facial spasm	shakuyakukanzoto (芍薬甘草湯)	Kimura H, Otake T, Ishikura H. Efficacy of shakuyakukanzoto for relieving facial spasm*. *Shindan to Chiryo* (*Diagnosis and Treatment*) 1991; 79: 2505-8 (in Japanese).	RCT	N	UC
G54.4	To evaluate the efficacy of goshajinkigan for treatment of lumbar (low back) and leg pain.	goshajinkigan (牛車腎気丸)	Sekine R, Watanabe H, Mimura M, et al. The effects of Gosha-jinki-gan on the low back pain and lower limb pain caused by the lumbar spine: A comparison of Gosha-jinki-gan with Benfotiamine. *Itami to Kampo* (*Pain and Kampo Medicine*) 2003; 13: 84-7 (in Japanese)	RCT-cross over	I	69

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
G62.9	To evaluate the potential use of sokeikakketsuto and shakuyakukanzoto in preventing peripheral nerve disorder in patients receiving taxol.	sokeikakketsuto (疎経活血湯)	Miyabe Y, Taniguchi C, Kawashima M, et al. Effect of Kampo medicines (sokeikakketsuto, shakuyakukanzoto) for taxol-caused peripheral nerve disorder – evaluation by current perception threshold measured by Neurometer®*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2006; 23: 65-8 (in Japanese).	RCT-cross over	N	70

Eye Diseases (4 abstracts, 5 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
H00.0	To evaluate the efficacy of hainosankyuto for internal hordeolum in the acute phase.	hainosankyuto (排膿散及湯)	Takama N, Fujiwara T. The Efficacy of hainou-san-kyu-to for internal hordeolum. *Ganka Rinsho Iho* (*Japanese Review of Clinical Ophthalmology*) 2006; 100: 9-11 (in Japanese).	RCT	I	71
H18.9	To determine the efficacy of goshajinkigan for corneal sensitivity, superficial keratitis, and tear secretion in patients with insulin-dependent (type 1) diabetes mellitus.	goshajinkigan (牛車腎気丸)	Nagaki Y, Hayasaka S, Hayasaka Y, et al. Effects of Goshajinkigan on corneal sensitivity, superficial punctate keratopathy and tear secretion in patients with insulin-dependent diabetes mellitus. *The American Journal of Chinese Medicine* 2003; 31: 103-9.	DB-RCT	C	72
			Nagaki Y. Effects of goshajinkigan on diabetic keratopathy*. *Kampo Igaku* (*Kampo Medicine*) 2004; 28: 63-5 (in Japanese).		N	
H25.9	To determine the efficacy of Kampo medicines for aqueous flare elevation after small-incision cataract surgery.	orengedokuto (黄連解毒湯), kakkonto (葛根湯), saireito (柴苓湯)	Ikeda N, Hayasaka S, Nagaki Y, et al. Effects of traditional Sino-Japanese herbal medicines on aqueous flare elevation after small-incision cataract surgery. *Journal of Ocular Pharmacology and Therapeutics* 2001; 17: 59-65.	RCT	C	73
H25.9	To determine the efficacy of Kampo medicines for aqueous flare elevation after complicated cataract surgery.	kakkonto (葛根湯), saireito (柴苓湯)	Ikeda N, Hayasaka S, Nagaki Y, et al. Effects of Kakkon-to and Sairei-to on aqueous flare elevation after complicated cataract surgery. *The American Journal of Chinese Medicine* 2002; 30: 347-53.	RCT	C	74

Ear Diseases (5 abstracts, 5 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
H65.0	To determine the efficacy of shoseiryuto combined with eppikajutsuto for otitis media with effusion (OME) in adults.	shoseiryuto (小青竜湯) + eppikajutsuto (越婢加朮湯)	Inoue H. Rapid effect of combination therapy with shoseiryuto and eppikajutsuto for acute otitis media with effusion in adults. *Jibi to Rinsho* (*Otologia Fukuoka*) 2001; 47: 361-6 (in Japanese).	quasi-RCT	I	75
H65.9	Efficacy of saireito for otitis media with effusion	saireito (柴苓湯)	Machii K, Ikezono T, Utasato S, et al. Comparative study of the efficacy of saireito monotherapy versus antiallergic agent plus carbocysteine combination therapy for otitis media with effusion*. *Kampo Igaku* (*Kampo Medicine*) 1992; 16: 200-3 (in Japanese).	RCT	N	UC
H65.9	Efficacy of saireito for otitis media with effusion	saireito (柴苓湯)	Sato H, Nakamura H, Honjo I, et al. Clinical evaluation of Tsumura-Saireito in children with otitis media with effusion - A comparative randomized controlled study of cepharanthine -. *Jibiinkoka Rinsyo* (*Practica otologica*) 1988; 81: 1383-7 (text in Japanese with English abstract).	RCT	N	UC
H93.1	Efficacy of saireito for tinnitus	saireito (柴苓湯)	Tanaka H. Efficacy of a Kampo preparation combined with tranquilizers in patients with tinnitus. *Jibiinkoka Rinsyo* (*Practica otologica*) 1996; suppl 89: 8 (in Japanese).	RCT-cross over	N	UC
H93.1	To determine the efficacy of chotosan for tinnitus.	chotosan (釣藤散)	Suzuki T. *Clinical efficacy of chotosan for tinnitus. Pathology and treatment of tinnitus and dizziness*. The 28th Chiba Symposium of Japanese Traditional Medicine Tokyo: Kudansha; 2001:8-20 (in Japanese).	RCT-cross over	I	76

Cardiovascular Diseases (12 abstracts, 15 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
I10	Efficacy of chotosan and orengedokuto for hypertension	chotosan (釣藤散), orengedokuto (黄連解毒湯)	Narumi J, Kohsaka S, Miyazawa S, et al. Evaluation of the Kampo monotreatment for hypertensive patients using ambulatory blood pressure monitor. *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1994; 11: 282-3 (in Japanese).	RCT	N	UC
			Narumi J, Kohsaka S, Miyazawa S, et al. Evaluation of the Kampo monotreatment for hypertensive patients using ambulatory blood pressure monitoring*. *Kampo Shinryo* 1996; 15: 34-5 (in Japanese).		N	
I10	Efficacy and safety of daisaikoto and chotosan in patients with essential hypertension	daisaikoto (大柴胡湯), chotosan (釣藤散)	Sasaki J, Matsunaga A, Kusuda M, et al. Efficacy of daisaikoto and chotosan in patients with essential hypertension*. *Rinsho to Kenkyu (Japanese Journal of Clinical and Experimental Medicine)* 1993; 70: 1965-75 (in Japanese).	RCT-envelope	I	UC
I10	Effects of daisaikoto and saikokaryukotsuboreito on serum lipid levels in patients with mild to moderate hypertension	daisaikoto (大柴胡湯), saikokaryukotsuboreito (柴胡加竜骨牡蠣湯)	Saku K, Hirata K, Zhang B, et al. Effects of Chinese herbal drugs on serum lipids, lipoproteins and apolipoproteins in mild to moderate essential hypertensive patients. *Journal of Human Hypertension* 1992; 6: 393-5.	RCT	C	UC
I10	To evaluate the efficacy and safety of orengedokuto in patients with hypertension symptoms.	orengedokuto (黄連解毒湯)	Arakawa K, Saruta T, Abe K, et al. Double-blind placebo-controlled trial of TSUMURA Orengedokuto (TJ-15) for the treatment of accessory symptoms of hypertension*. *Rinsyo to Kenkyu* (*Japanese Journal of Clinical and Experimental Study*) 2003; 80: 354-72 (in Japanese)	DB-RCT	I	77
			Arakawa K, Saruta T, Abe K, et al. Improvement of accessory symptoms of hypertension by TSUMURA Orengedokuto Extract, a four herbal drugs containing Kampo-Medicine Granules for ethical use: a double-blind, placebo-controlled study. *Phytomedicine* 2006; 13: 1-10.		C	
I51.9	Efficacy and safety of orengedokuto plus red ginseng combination therapy for relieving symptoms associated with hypertension	orengedokuto (黄連解毒湯) orengedokuto (黄連解毒湯)＋ kojinmatsu (紅参末)	Kaneko H, Nakanishi K, Murakami A, et al. Clinical evaluation of the effect of Ohrengedoku-Toh and Ohrengedoku-Toh - Red Ginseng mixture on chronic cardiovascular disorders in middle and aged patients. *The Ginseng Review* 1991; 12: 89-93 (text in Japanese with English abstract).	DB-RCT	N	UC
I63.9	Efficacy and safety of orengedokuto in the treatment of cerebral infarction	orengedokuto (黄連解毒湯)	Ito E, Takahashi A, Kuzuya F. Clinical effectiveness of TSUMURA Orengedokuto in the treatment of cerebral infarction*. *Geriatric Medicine* 1991; 29: 303-13 (in Japanese).	RCT-envelope	I	UC
I67.9	Efficacy and safety of hachimijiogan in patients with hypertension or cerebrovascular disease and their concomitant symptoms	hachimijiogan (八味地黄丸)	Ito K, Yamamoto H, Saibara T, et al. The usefulness of Kanebo Hachimijiogan in patients with hypertension or cerebrovascular disease (excluding acute phase symptoms) and their concomitant symptoms: a multicenter, double-blind, crossover study*. *Shindan to Chiryo* (*Diagnosis and Treatment*) 1988; 76: 1096-114 (in Japanese).	DB-RCT (cross over)	I	UC
I67.9	Efficacy and safety of orengedokuto for relieving psychiatric symptoms in patients with late effects of cerebrovascular disease	orengedokuto (黄連解毒湯)	Otomo E, Togi H, Kogure K, et al. Clinical usefulness of TSUMURA Orengedokuto for the treatment of cerebrovascular disease: a well-controlled study comparing TSUMURA Orengedokuto versus Ca hopantenate, using sealed envelopes for allocation*. *Geriatric Medicine* 1991; 29: 121-51 (in Japanese).	RCT-envelope	I	UC
I69.4	To evaluate the efficacy and safety of tokishakuyakusan for treatment of hypofunction and decreased independence in patients with sequelae of cerebrovascular disorder.	tokishakuyakusan (当帰芍薬散)	Shimada Y. Efficacy of tokishakuyakusan for hypofunction and decreased independence in patients with sequelae of cerebrovascular disorder*. *Kosei Rodo Kagaku Kenkyuhi Hojokin Choju Kagaku Kenkyu Jigyo Buntan Kenkyu Hokokusyo* (*Ministry of Health, Labour and Welfare, Science Research Grant, Comprehensive Studies on Science of Aging, working-group research report*) 2007: 22-30 (in Japanese)	RCT	N	78

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
I73.0	To evaluate the effectiveness of orengedokuto in improving peripheral circulation in Raynaud's phenomenon.	tokishakuyakusan (当帰芍薬散), orengedokuto (黄連解毒湯)	Akiyama Y, Ohno S, Asaoka T, et al. The combination therapy with sarpogrelate hydrochloride and Kampo medicine (oren-gedoku-to or toki-shakuyaku-san) for Raynaud's phenomenon. *Japanese Journal of Oriental Medicine* 2001; 51: 1101-8 (text in Japanese with English abstract).	quasi-RCT	N	79
I89.0	To evaluate the efficacy and safety of goshajinkigan in the treatment of lymphedema.	goshajinkigan (牛車腎気丸)	Abe Y. The efficacy of goshajinkigan against lymphedema*. *Kampo Igaku* (*Kampo Medicine*) 2002; 25: 284-7 (in Japanese).	RCT	I	80
			Abe Y, Kosugi I, Kasashima F, et al. Lymphedema and Kampo*. *Progress in Medicine* 2003; 23: 1538-9 (in Japanese).		N	
I95.1	To examine the safety and efficacy of goreisan in the treatment of orthostatic hypotension in patients with diabetes mellitus.	goreisan (五苓散)	Nakamura H, Nakamura T, Nakagawa S et al. Efficacy of goreisan in treatment of orthostatic hypotension in patients with diabetes mellitus*. *Diabetes Frontier* 2000; 11: 561-3 (in Japanese).	RCT-cross over	I	81

Respiratory Diseases (42 abstracts, 52 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
J00	Efficacy of Kampo treatment in patients with common cold syndrome associated with fever	kakkonto (葛根湯), maoto (麻黄湯), keimakakuhanto (桂麻各半湯), chikujountanto (竹ジョ温胆湯), shoseiryuto (小青竜湯), keishikashakuyakuto (桂枝加芍薬湯) , kososan (香蘇散)	Homma Y. Kampo treatment of patients with common cold syndrome associated with fever. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1995; 46: 285-91 (text in Japanese with English abstract).	RCT-envelope	N	UC
J00	Effect on the duration and resolution of symptoms and treatment efficacy in patients with common cold syndrome	maobushisaishinto (麻黄附子細辛湯)	Homma Y, Takaoka K, Yozawa H, et al. Effectiveness of Mao-bushi-saishin-to in treating common cold syndrome - controlled comparative study using the sealed envelope method -. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1996; 47: 245-52 (text in Japanese with English abstract).	RCT-envelope	I	UC
			Homma Y. Treatment of common cold by a Kampo medicine - Maobushisaishin-tou-. *Pharma Medica* 2007; 25: 19-21 (in Japanese).	RCT-envelope		
J00	To assess the efficacy and safety of shosaikoto in patients with common cold.	shosaikoto (小柴胡湯)	Kaji M, Kashiwagi S, Yamakido M, et al. A double-blind, placebo-controlled study of TSUMURA Shosaikoto (TJ-9) for common cold*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Study*) 2001; 78: 2252-68 (in Japanese).	DB-RCT	I	82
J00	To evaluate the efficacy and safety of bakumondoto for postinfectious cough.	bakumondoto (麦門冬湯)	Fujimori K, Suzuki E, Simojo F. Comparison between bakumondoto (mai men dong tang) and dextromethorphan hydrobromide in terms of effect on postinfectious cough: a pilot study. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 2000; 51: 725-32	RCT	I	83
J00	To compare the cough-improvement effect of maobushisaishinto and western drugs in patients with the common cold.	maobushisaishinto (麻黄附子細辛湯)	Nishizawa Y, Nagano F, Yamada M, et al. A randomized comparison of cough-improvement effects between mao-bushi-saishin-to and western drugs for cold in common patients with allergic cold syndrome. *Kampo to Meneki Arerugi* (*Kampo and Immuno-Allergy*) 2005; 18: 56-67 (text in Japanese with English abstract).	RCT	N	84

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
J10.1	To determine the effect of maoto in combination with oseltamivir on the duration of fever.	maoto (麻黄湯)	Kubo T, Nishimura H. Antipyretic effect of Mao-to, a Japanese herbal medicine, for treatment of type A influenza infection in children. *Phytomedicine* 2007; 14: 96-101.	RCT	C	85
			Kubo T. Effect of maoto for treatment of influenza in children. (from The 56th General Meeting of The Japan Society for Oriental Medicine, presentation C-41)*. Medicament News 2005 Sep 5; 1846: 15.		N	
J10.1	To evaluate the efficacy of maoto in combination with oseltamivir phosphate in treating influenza.	maoto (麻黄湯)	Kimoto H, Kuroki H. Efficacy of combined administration of oseltamivir phosphate and maoto in treating influenza*. *Kampo Igaku* (*Kampo Medicine*) 2005; 29: 166-9 (in Japanese).	quasi-RCT	I	86
			Kuroki H, Kimoto H. Successful treatment of combination therapy with oseltamivir and mao-to for influenza – 3rd report-. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 2006; 19: 17-25 (text in Japanese with English abstract).		N	
J10.1	To determine the efficacy of combined oseltamivir phosphate and maoto for the treatment of influenza.	maoto (麻黄湯)	Kuroki H, Kimoto H. Successful treatment of combination therapy with oseltamivir and mao-to for influenza – 3rd report-. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 2006; 19: 17-25 (text in Japanese with English abstract).	quasi-RCT	N	87
			Kimoto H, Kuroki H. The efficacy of combined oseltamivir phosphate and maoto for the treatment of influenza*. *Kampo Igaku* (*Kampo Medicine*) 2005; 29:166-9 (in Japanese).		I	
J10.1	To evaluate the efficacy and safety of maobushisaishinto as an adjuvant for influenza vaccination in the elderly.	maobushisaishinto (麻黄附子細辛湯)	Iwasaki K, Taguchi M, Cyong JC, et al. Effects of mao-bushi-saishin-to on influenza vaccination in elderly subjects; a randomized control study. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2004; 17: 97-103 (text in Japanese with English abstract)	RCT	N	88
			Iwasaki K. Influenza and Kampo in the elderly*. *TSUMURA Mail Magazine* 2008; Suppl: 22-3 (in Japanese)	RCT-envelope	N	
J20.0	To compare the efficacy of bakumondoto and tipepidine hibenzate as antitussive agents in patients with mycoplasmal bronchitis.	bakumondoto (麦門冬湯)	Watanabe N, Miyazawa T. Comparative study of the effect of bakumondoto and tipepidine hebinzate on cough in patients with mycoplasmal bronchitis. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2007; 21: 31-6 (in Japanese).	RCT-envelope	N	89
J30.1	Preventive effect and safety of preseasonal administration of shoseiryuto in patients with cedar pollen allergy (hay fever)	shoseiryuto (小青竜湯)	Ohya Y. Efficacy of preseasonal administration of shoseiryuto for cedar pollen alergy*. *Kampo Shinryo* 1991; 10: 42-8 (in Japanese).	RCT	N	UC
			Ohya Y. Kampo treatment for allergic diseases: from the perspective of a general hospital*. *Progress in Medicine* 1988; 8: 604-12 (in Japanese).		N	
J30.1	Effects of shoseiryuto and ryokankyomishingeninto on springtime nasal allergy	shoseiryuto (小青竜湯), ryokankyomishingeninto (苓甘姜味辛夏仁湯)	Mori H. Comparative study of Kampo preparations Sho-Seiryu-To and Ryokankyomishingenin-To for nasal allergy. *Therapeutic Research* 1996; 17: 3691-6 (text in Japanese with English abstract).	quasi-RCT	N	UC
J30.1	Effects of shoseiryuto and eppikajutsuto on springtime nasal allergy	shoseiryuto (小青竜湯), eppikajutsuto (越婢加朮湯)	Mori H, Shimazaki Y, Kurata H, et al. Comparative study of Kampo preparations Sho-Seiryu-To and Eppika-Jutsu-To for nasal allergy and allergic conjunctivitis. *Therapeutic Research* 1997; 18: 3093-9 (text in Japanese with English abstract).	quasi-RCT	N	UC
J30.1	Effects of shoseiryuto and daiseiryuto on springtime nasal allergy	shoseiryuto (小青竜湯), daiseiryuto (大青竜湯) [keishitogo-makyokansekito (桂枝湯合麻杏甘石湯)]	Mori H. Comparative study of Kampo preparations Sho-Seiryu-To and Dai-Seiryu-To for nasal allergy and allergic conjunctivitis. *Therapeutic Research* 1998; 19: 3299-307 (text in Japanese with English abstract).	quasi-RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
J30.1	To compare the efficacy of shoseiryuto and keimakakuhanto in treating springtime nasal allergy and allergic conjunctivitis.	shoseiryuto (小青竜湯) and keimakakuhanto (桂麻各半湯) [keisito+maoto (桂枝湯+麻黄湯)]	Mori H, Kurata H, Shimazaki Y, et al. Comparative study of Kampo preparations sho-sei-ryu-to and kei-ma-kakuhan-to for nasal allergy and allergic conjunctivitis in spring. *Therapeutic Research* 1999; 20: 2941-7 (text in Japanese with English abstract).	quasi-RCT	N	90
J30.1	To compare the effects of shoseiryuto and maobushisaishinto in treating springtime nasal allergy and allergic conjunctivitis.	shoseiryuto (小青竜湯), maobushisaishinto (麻黄附子細辛湯)	Yoshimoto T, Mori H, Kurata H, et al. Comparative study of Kampo preparations sho-sei-ryu-to and maoh-bushi-saisin-to for nasal allergy and allergic conjunctivitis in spring. *Therapeutic Research* 2002; 23: 2253-9 (text in Japanese with English abstract).	quasi-RCT	I	91
J30.1	To compare the effects of shoseiryuto and gokoto in subjects with nasal allergy and allergic conjunctivitis in spring.	shoseiryuto (小青竜湯), gokoto (五虎湯)	Shimazaki Y, Mori H, Kurata H, et al. Comparative study of Kampo preparations Sho-Sei-Ryu-To and Go-Ko-To for nasal allergy and allergic conjunctivitis in spring. *Therapeutic Research* 2001; 22: 2385-91 (text in Japanese with English abstract).	quasi-RCT	I	92
J30.3	Efficacy and safety of shoseiryuto in the treatment of perennial nasal allergy	shoseiryuto (小青竜湯)	Baba S, Takasaka T, Inamura N, et al. Double-blind clinical trial of Sho-seiryu-to (TJ-19) for perennial nasal allergy. *Jibiinkoka Rinsyo* (*Practica otologica*) 1995; 88: 389-405 (text in Japanese with English abstract).	DB-RCT	I	UC
J303	Efficacy and safety of maobushisaishinto in the treatment of perennial nasal allergy	maobushisaishinto (麻黄附子細辛湯)	Nakai Y, Ohashi Y, Esaki Y, et al. Clinical evaluation of maobushisaishinto for nasal allergy*. *Jibi-inkouka Tenbou* (*Oto-Rhino-Laryngology, Tokyo*) 1990; 33: 655-73 (in Japanese).	quasi-RCT	N	UC
J32.9	Effectiveness of shin'iseihaito and shigyakusan for chronic rhinitis and sinusitis	shin'iseihaito (辛夷清肺湯), shigyakusan (四逆散)	Sakurada T, Ikeda K, Takasaka T, et al. Clinical effectiveness of Kampo medicine for chronic rhinitis and sinusitis. *Jibiinkoka Rinsyo* (*Practica otologica*) 1992; 85: 1341-6 (text in Japanese with English abstract).	RCT-envelope	N	UC
J39.2	Efficacy of saibokuto for relieving complaints after thyroid or parathyroid surgery	saibokuto (柴朴湯)	Suzuki S, Furukawa H, Ami H, et al. Experience with TSUMURA Saibokuto (TJ-96) in patients who underwent thyroid or parathyroid surgery*. *Progress in Medicine* 1994; 14: 2254-8 (in Japanese).	RCT-envelope	I	UC
J39.2	Healing effect of saibokuto on mucositis induced by head-and-neck and mediastinal irradiation	saibokuto (柴朴湯)	Saito Y, Mitsuhashi N, Takahashi I, et al. Effect of TSUMURA Saiboku-to as an agent for healing damage in treatment of radiomucositis due to irradiation of the head and neck area and mediastinum. *Biotherapy* 1992; 6: 1899-906 (text in Japanese with English abstract).	RCT	N	UC
J40	To evaluate the efficacy and safety of shoseiryuto in the treatment of bronchitis.	shoseiryuto (小青竜湯)	Miyamoto T, Inoue H, Kitamura S, et al. Effect of TSUMURA Sho-seiryu-to (TJ-19) on bronchitis in a double-blind placebo-controlled study. Rinsho Iyaku (Journal of Clinical Therapeutics & Medicine) 2001; 17: 1189-214 (text in Japanese with English abstract).	DB-RCT	I	93
			Miyamoto T. Clinical effectiveness of Shosei-ryuto in bronchitis. *Pharma Medica* 2007; 25: 23-5 (in Japanese).		I	
J44.9	Effectiveness of bakumondoto as an expectorant	bakumondoto (麦門冬湯)	Sasaki H, Satou K, Sasaki M, et al. Usefulness of Bakumondo-to in senile chronic respiratory disease patients having difficulty in expectoration: comparison with bromhexine hydrochloride preparations. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 1993; 7: 139-45 (text in Japanese with English abstract).	RCT-envelope	N	UC
J44.9	To assess the efficacy of smoking cessation combined with administration of seihaito for chronic obstructive pulmonary disease (COPD).	seihaito (清肺湯)	Kato S, Matsuda T, Nakajima T, et al. Clinical significance of the combination therapy of smoking cessation and seihaito for chronic obstructive pulmonary disease. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2005; 14: 260-5 (in Japanese).	RCT-envelope	I	94
			Kato S, Oda K, Hasumi H, et al. The combined effect of smoking cessation and Seihai-to on airway clearance on COPD patients. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2006; 19: 26-35 (text in Japanese with English abstract).		N	

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
J44.9	To investigate the effect of hochuekkito on systemic inflammation in subjects with chronic obstructive pulmonary disease (COPD).	hochuekkito (補中益気湯)	Fukuchi Y, Tatsumi K. Utility evaluation of Kampo in the treatment of chronic obstructive pulmonary disease. *Kosei Rodosho Kagaku Kenkyuhi Hojokin Choju Kagaku Sogo Kenkyu Jigyo Sokatsu Kenkyusyo Hokokusyo* (*Ministry of Health, Labour and Welfare, Science Research Grant, Comprehensive Studies on Science of Aging, Summary report*), 2007:1-31 (in Japanese).	RCT-envelope	N	95
			Shinozuka N, Tatsumi K, Nakamura A, et al. Evaluation of systemic inflammation and utility of hochuekkito administration in subjects with COPD*. *Kosei Rodosho Kagaku Kenkyu Kenkyuhi Hojokin Nanchisei Shikkan Kokufuku Kenkyu Jigyo Kokyufuzen ni Kansuru Chosa Kenkyu Heisei 18 Nendo Kenkyu Hokokusho* (*Ministry of Health, Labour and Welfare, Science Research Grant, The Intractable Disease Treatment Research Project, Research report fiscal year 2006*) 2007:94-9 (in Japanese).	RCT-envelope	N	
			Shinozuka N, Tatsumi K, Nakamura A, et al. The traditional herbal medicine Hochuekkito improves systemic inflammation in patients with chronic obstructive pulmonary disease. *Journal of the American Geriatrics Society* 2007; 55: 313-4.	RCT	C	
J45.0	Development of saibokuto inhalation therapy, and to evaluate its efficacy in preventing attacks of aspirin-induced asthma.	saibokuto (柴朴湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive Effect of Japanese Herbal Medicine, Saiboku-to (Cai-Pu-Tang) on Brochospasms in Aspirin-induced Bronchial Asthmatic Patients. A Randomized, Double-blind Test. *Jibi-inkoka Tenbo* (*Oto-Rhino-Laryngology Tokyo*) 2001; 44: 5-13 (text in Japanese with English abstract).	DB-RCT	I	96
J45.0	To evaluate the efficacy of short-term inhaled saibokuto in suppressing airway constriction, and long-term inhaled saibokuto in alleviating psychological suffering.	saibokuto (柴朴湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive effect of Kampo medicine, Cai-pu-tang (Japanese name: Saiboku-to, TJ-96) on brochospasms in aspirin-induced bronchial asthmatic patients and decrease of chronic pain. Especially psychological pain. *Itami to Kampo* (*Pain and Kampo Medicine*) 2001; 11: 14-21 (text in Japanese with English abstract).	DB-RCT	I	97
J45.0	To investigate the clinical effect of saibokuto for the treatment of atopic asthma.	saibokuto (柴朴湯)	Urata Y, Yoshida S, Irie Y, et al. Treatment of asthma patients with herbal medicine TJ-96: a randamized controlled trial. *Respiratory Medicine* 2002; 96: 469-74.	RCT-cross over	C	98
J45.0	To assess the efficacy and safety of inhaled shimpito for the control of aspirin-induced asthma.	shinpito (神秘湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive effect of Chinese tracitional medicine, she-bi-tang (shinpi to) on bronchospasm in aspirin-indolerant bronchial asthmatic patients – a randomized, group-paralleled comparative trial –. *Jibi-inkoka Tenbo* (*Oto-rhino-laryngology Tokyo*) 2003; 46: 3-14 (text in Japanese with English abstract).	RCT	I	99
J45.0	To assess the efficacy and safety of inhaled shimpito therapy for improving asthma symptoms in patients with aspirin-induced asthma.	shinpito (神秘湯)	Nishizawa Y, Nishizawa Y, Goto GH, et al.A randomized, group-parallel comparative trial of the suppressiveeffect of Chinese traditional medicine, shen-mi-tang (shin-pi-to), compared to sodium oramolycate inhalation in improving subjective and objective symptoms in bronchial asthmatics. *Jibi-inkoka Tenbo* (*Oto-rhino-laryngology Tokyo*) 2004; 47: 20-7 (text in Japanese with English abstract).	RCT	I	100
J45.0	To investigate the effect of saibokuto inhalation therapy in improving quality of life (QOL) in patients with aspirin-intolerant asthma.	saibokuto (柴朴湯)	Nishizawa Y, Nishizawa Y, Goto HG. Chronic pain in intractable and chronic medical conditions -*. *Mansei Totsu* (*The Journal of the Japanese Society for the Study of Chronic Pain*) 2002; 21: 67-77 (text in Japanese with English abstract).	RCT	I	101

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
J45.9	Efficacy and safety of saibokuto in patients with steroid-dependent bronchial asthma	saibokuto (柴朴湯)	Egashira Y, Nagano H, et al. Results of a comparative clinical study of the effect of "TSUMURA Saiboku-to" (TJ-96) against steroid dependent bronchial asthma in 2 groups, a Saiboku-to administration group and a non-administration group, divided by the envelope method. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 1990; 4: 128-44 (text in Japanese with English abstract).	RCT-envelope	N	UC
			Egashira Y, Nagano H. A multicenter clinical trial of TJ-96 in patients with steroid-dependent bronchial asthema. A comparison of groups allocated by the envelope method. *Annals of the New York Academy of Science* 1993; 685: 580-3.		C	
J45.9	Efficacy and safety of saibokuto in the treatment of bronchial asthma in children	saibokuto (柴朴湯)	Ito S, Mikawa H. Clinical evaluation of Saibokutou in the treatment of children with bronchial asthma. *Kiso to Rinsho* (*The Clinical Report*) 1992; 26: 3993-8 (in Japanese).	RCT-envelope	I	UC
			Ito S, Mikawa H. Effect of "TSUMURA Saiboku-to" (TJ-96) on bronchial asthma in children. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 1990; 4: 115-25 (text in Japanese with English abstract).		N	
J45.9	Efficacy of shinpito for inhibiting exercise-induced asthma and relieving clinical symptoms in patients with moderate or worse bronchial asthma	shinpito (神秘湯)	Tubaki T, Ebisawa M, Akimoto K, et al. Effects of Shinpi-to (*Shenbi-tang*) on bronchial asthma. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 1994; 8: 65-71 (text in Japanese with English abstract).	RCT	N	UC
J45.9	To assess the efficacy and safety of inhaled saibokuto while reducing the amount of inhaled beclomethasone during the course of treatment for bronchial asthma.	saibokuto (柴朴湯)	Nishizawa Y, Nishizawa Y, Nagano F, et al. Sparing effect of saibokuto inhalation on inhaled beclomethasone dipropionate to halved of reduction of inhaled beclomethasone dipropinate-dose: well-controlled comparative study of saiboku-to-inhalation and sodium cromoglycate-inhalation. *Jibi-inkoka Tenbo* (*Oto-rhino-laryngology Tokyo*) 2002; 45: 8-15 (text in Japanese with English abstract).	RCT	I	102
J45.9	To compare the efficacy of the anxiolytic-like agent saibokuto with that of shoseiryuto in patients with bronchial asthma.	saibokuto (柴朴湯), shoseiryuto (小青竜湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Clinical effect of a Kampo medicine, chai-po-tang (Japanese name: saiboku-to) compared with xiao-quing-long tang (Japanese name: shoseiryu-to) in asthmatics with anxiety and depression due to asthmatic attacks. *Nihon Toyo Shinshin Igaku Kenkyu* (*Journal of Japanese Association of Oriental Psychosomatic Medicine*) 2003; 18: 11-7 (text in Japanese with English abstract).	RCT	I	103
J45.9	To assess the efficacy of the anxiolytic-like agent, saibokuto, in treating bronchial asthma.	saibokuto (柴朴湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Clinical effect of a Chinese tracitional herbal medicine, chai-po-tang (Japanese name: saiboku-to) compared with clotiazepam in patients with bronchial asthmatics and anxiery disorder in multicenter randomized, comparative trial. *Nihon Toyo Shinshin Igaku Kenkyu* (*Journal of Japanese Association of Oriental Psychosomatic Medicine)* 2002; 17: 20-7 (text in Japanese with English abstract).	RCT	I	104
J45.9	To evaluate the efficacy and safety of saibokuto in patients with asthma exacerbations based on anticipatory anxiety.	saibokuto (柴朴湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Clinical effect of chai-po-tang (Japanese name: saiboku-to), a Chinese tracitional herbal medicine, in patients with bronchial asthma and autonomic nerve dysfunction: a multicenter, randomized, double-blined, placebo-controlled study. *Nihon Toyo Shinshin Igaku Kenkyu* (*Journal of Japanese Association of Oriental and Psychosomatic Medicine*) 2004; 19:37-41 (text in Japanese with English abstract).	RCT	I	105
J69.0	To investigate whether hangekobokuto (banxia houp tang) improves cough reflex in elderly patients likely to have aspiration pneumonia.	hangekobokuto (半夏厚朴湯)	Iwasaki K, Cyong JC, Kitada S, et al. A traditional Chinese herbal medicine, banxia houp tang, improves cough reflex of patients with aspiration pneumonia. *Journal of the American Geriatrics Society* 2002; 50: 1751-2.	DB-RCT	N	106

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
J69.0	To evaluate whether hangekobokuto prevents aspiration pneumonia and pneumonia-related mortality in elderly people with dementia.	hangekobokuto (半夏厚朴湯)	Iwasaki K, Kato S, Monma Y, et al. A pilot study of banxia houpu tang, a traditional Chinese medicine, for reducing pneumonia risk in older adults with dementia. *Journal of the American Geriatrics Society* 2007; 55: 2035-40.	RCT	C	107
J98.8	To determine the efficacy, impact on recurrence rate, and medical cost efficiency of antibiotics plus Kampo combination therapy for bacterial respiratory infections.	juzentaihoto (十全大補湯), kakkonto (葛根湯), keishito (桂枝湯), kososan (香蘇散), shosaikoto (小柴胡湯), hochuekkito (補中益気湯)	Mikamo H, Tamaya T. Usefulness of Kampo medicine for the treatment of infections from the perspective of medical economics*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2007; 24: 105-8 (in Japanese).	RCT	I	108

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases (49 abstracts, 62 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
K11.7	Efficacy of ninjin'yoeito for improvement of xerostomia induced by oxybutynin hydrochloride	ninjin'yoeito (人参養栄湯)	Miyazaki Y, Yamada A, Saitou M. Effect of Ninjin-Youei-tou on xerostomia induced by oxybutynin hydrochloride. *Shinyaku to Rinsho* (*Journal of New Remedies and Clinics*) 1994; 43: 2613-7 (in Japanese).	RCT	N	UC
K11.7	To compare the efficacy of bakumondoto versus cevimeline hydrochloride hydrate (Evoxac) or nizatidine (Acinon) for treating dry mouth.	bakumondoto (麦門冬湯)	Umemoto M, Nin T, Miuchi S, et al. Treatment of human dry mouth using various medicines. *Jibiinkoka Rinsho* (*Practica otologica*) 2007; 100: 145-52 (text in Japanese with English abstract).	RCT	I	109
K12.1	Efficacy and safety of orento for treating stomatitis	orento (黄連湯)	Oka S. The effects of Oren-to on stomatitis. *Nihon Toyo Igaku Zasshi (Japanese Journal of Oriental Medicine)* 1995; 46: 439-45 (text in Japanese with English abstract).	RCT	N	UC
K14.6	To determine the efficacy of saibokuto compared with tranquilizer plus vitamin B complex combination therapy for patients with glossodynia.	saibokuto (柴朴湯)	Bessho K, Okubo Y, Hori S, et al. Effectiveness of Kampo medicine (Sai-Boku-To) in treatment of patients with glossdynia. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 1998; 86: 682-6.	RCT	C	110
			Yamada T, Bessho K, Murakami K, et al. Clinical evaluation of sai-boku-to (Kampo medicine) for glossodynia. *Shika Yakubutsu Ryoho* (*Oral Therapeutics and Pharmacology*) 1998; 17: 18-22 (text in Japanese with English abstract).		N	
			Yamada T, Bessho K. Clinical evaluation of sai-boku-to (Kampo medicine) for glossodynia. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 1999; 8: 261-5 (in Japanese).		I	
K21.0	To determine the preventive effect of rikkunshito on postoperative reflux esophagitis.	rikkunshito (六君子湯)	Mizuno S, Yamagiwa K, Iwata M, et al. Effect of early treatment with TSUMURA Rikkunshito on gastrointestinal symptoms after resection of gastric cancer – focusing on reflux esophagitis -*. *Progress in Medicine* 2001; 21: 1366-7 (in Japanese).	RCT	I	111
K21.0	To determine the efficacy of rikkunshito combined with a proton pump inhibitor (PPI) for treating gastroesophageal reflux disease (GERD).	rikkunshito (六君子湯)	Koide A. Effect and role of TJ-43: rikkun-shi-to from the aspects of endoscopic findings and QOL improvement in GERD patients. *Medical Tribune Online* (*Digestive Disease Week: DDW*) 2005: 6-7 (in Japanese).	RCT	N	112
K21.0	To determine the efficacy of hangekobokuto-combined treatment in patients with respiratory symptoms associated with refractory gastroesophageal reflux disease (GERD).	hangekobokuto (半夏厚朴湯)	Kato S, Nakajima T, Matsuda T, et al. The effectiveness of the traditional Kampo medicine, "banxia houpu tang (hangekobokuto)" to respiratory disturbance by esophageal reflux disease. *Kampo to Saishin-Chiryo* (*Kampo & the Newest Therapy*) 2005; 14: 333-8 (in Japanese).	RCT-envelope	I	113

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
K21.9	To determine the efficacy of TSUMURA Rikkunshito Extract Granules for treatment of non-erosive reflux disease (NERD) unresponsive to proton pump inhibitors (PPIs).	rikkunshito (六君子湯)	Koide A. Establishment of new treatment strategy for non-erosive reflux disease (endoscopy-negative gastroesophageal reflux disease) – potential of rikkunshito[*]. *MedicalQ* 2006; 187 (in Japanese).	RCT	N	114
K25.9	Efficacy of saikokeishito and shigyakusan for preventing recurrence of gastric ulcer	saikokeishito (柴胡桂枝湯)	Nakahara A, Kashimura H, Fukutomi H. Gastric ulcer - saikokeishito or shigyakusan monotherapy -[*]. *Nikkei Medical* (separate-volume supplement) 1988; 17: 20-1 (in Japanese).	RCT-envelope	N	UC
			Fukutomi H, Nakahara A. Traditional oriental therapy of the gastric ulcer. *Shokakika* (*Gastroenterology*) 1990; 12: 159-65 (in Japanese).		N	
K27.9	Usefulness of shigyakusan and saikokeishito as a maintenance therapy for peptic ulcer	shigyakusan (四逆散), saikokeishito (柴胡桂枝湯)	Watanabe H. A study of peptic ulcer maintenance therapy combined with Kampo medicines[*]. *Kampo Igaku* (*Kampo Medicine*) 1995; 19: 18-21 (in Japanese).	RCT	N	UC
K29.7	Efficacy and safety of rikkunshito and hangeshashinto for treating acute gastritis and acute exacerbation of chronic gastritis	rikkunshito (六君子湯), hangeshashinto (半夏瀉心湯)	Ohta Y, Nishioka M, Yamamoto Y, et al. Multicenter clinical evaluation of Kampo preparations for medical use in the treatment of gastritis (acute gastritis and acute exacerbation of chronic gastritis) - comparison with gefarnate as a control -[*]. *Shindan to Chiryo* (*Diagnosis and Treatment*) 1990; 78: 2935-46 (in Japanese).	RCT-envelope	N	UC
K29.7	Efficacy and safety of rikkunshito for treating gastritis (acute gastritis and acute exacerbation of chronic gastritis)	rikkunshito (六君子湯)	Miyoshi A, Kaneko E, Nakazawa S, et al. Clinical evaluation of TJ-43 TSUMURA Rikkunshito in the treatment of gastritis (acute gastritis and acute exacerbation of chronic gastritis) - multicenter comparative study using sodium azulene sulfonate as a control -[*]. *Shindan to Chiryo* (*Diagnosis and Treatment*) 1991; 79: 789-810 (in Japanese).	RCT-envelope	N	UC
K29.7	Efficacy and safety of rikkunshito for treating gastritis	rikkunshito (六君子湯)	Takemoto T, Matsuda K, Tada M, et al. Clinical evaluation of the efficacy of TJ-43 Tsumura Rikkunshi-To on gastritis with abdominal symptom - multicenter group study in comparison with cetraxate -. *Shokakika* (*Gastroenterology*) 1990; 12: 223-34 (text in Japanese with English abstract).	RCT-envelope	N	UC
K30	Efficacy and safety of rikkunshito for treating epigastric indefinite complaints complicated by depression	rikkunshito (六君子湯)	Kawamura S, Okita K, Tada M, et al. Clinical comparison of TSUMURA Rikkunshito and sulpiride in the treatment of indefinite complaints of epigastric distress - mainly the antidepressive effect and the improvement of gastric emptying -[*]. *Progress in Medicine* 1992; 12: 1156-62 (in Japanese).	RCT-envelope	N	UC
K30	Efficacy of rikkunshito for treating indefinite complaints of epigastric distress	rikkunshito (六君子湯)	Komatsuzaki O. Clinical effect of TSUMURA Rikkunshito on indefinite epigastric distress - comparison with a control agent, and assessment mainly based on the endoscopic findings and the histology of gastric mucosal biopsy specimens before and after the treatment -[*]. *Kampo Igaku* (*Kampo Medicine*) 1993; 17: 120-31 (in Japanese).	RCT-envelope	N	UC
K30	Efficacy of saireito for post-infectious dyspepsia in infants	saireito (柴苓湯)	Ito J, Ito Y, Asai M, et al. Efficacy of saireito (TSUMURA) for post-infectious dyspepsia in infants: comparison with intestinal regulators[*]. *Shonika Shinryo* (*Journal of Pediatric Practice*) 1992; 55: 2089-92 (in Japanese).	RCT	I	UC
K30	Efficacy of rikkunshito in dyspeptic patients	rikkunshito (六君子湯)	Tatsuta M, Iishi H. Effect of treatment with Liu-Jun-Zi-Tang (TJ-43) on gastric emptying and gastrointestinal symptoms in dyspeptic patients. *Alimentary Pharmacology and Therapeutics* 1993; 7: 459-62.	RCT	C	UC
K30	Efficacy and safety of rikkunshito for treating complaints of gastrointestinal disorders including chronic gastritis	rikkunshito (六君子湯)	Miyoshi A, Yachi A, Masamune O, et al. Clinical evaluation of TJ-43 TSUMURA Rikkunshito in the treatment of indefinite complaints of gastrointestinal disorders including chronic gastritis - a multicenter comparative study using cisapride as a control -[*]. *Progress in Medicine* 1991; 11: 1605-31 (in Japanese).	RCT-envelope	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
K30	To determine the efficacy of rikkunshito as an agent to improve symptoms before endoscopy in patients with upper abdominal symptoms and need for endoscopy of the upper gastrointestinal tract.	rikkunshito (六君子湯)	Yamaguchi T, Koide A. Usefulness of Rikkun-shi-to (TJ-43), a Chinese herbal medicine, for the treatment of gastro-esophageal reflux disease (GERD). *Medical Science Digest* 2007; 33: 748-52 (in Japanese).	RCT-envelope	N	115
			Koide A. Adoption of rikkunshito before endoscopy in patients with upper abdominal symptoms*. *Nikkei Medical* 2002; 31: 22-3 (in Japanese).		N	
			Koide A. The improvement of QOL by rikkunshito in patients with need for endoscopy*. *Medical Tribune* 2004: 45 (in Japanese)		N	
K30	To evaluate the efficacy and safety of TJ-43 TSUMURA Rikkunshi-to in patients with dyspepsia caused by dysfunction of the upper gastrointestinal tract.	rikkunshito (六君子湯)	Harasawa S, Miyoshi A, Miwa T, et al. Double-blind multicenter post-marketing clinical trial of TJ-43 TSUMURA Rikkunshi-to for the treatment of dysmotility-like dyspepsia. *Igaku no Ayumi* (*Journal of Clinical and Experimental Medicine*) 1998; 187: 207-29 (in Japanese).	DB-RCT	I	116
			Harasawa S. The role of rikkunshito against NUD (non-ulcer dyspepsia) – especially its efficacy in dysmotility-like NUD*. *Progress in Medicine* 1999; 19: 843-8 (in Japanese).		N	
K30.0	To determine the efficacy of TSUMURA Rikkunshito Extract Granules for stimulating gastrointestinal emptying in patients after pylorus-preserving gastrectomy (PPG).	rikkunshito (六君子湯)	Nishida T. Effect of rikkunshito on gastrointestinal function in patients after gastrectomy*. *Progress in Medicine* 2006; 26: 3224-5 (in Japanese).	RCT-cross over	N	117
K52.9	To determine the safety and efficacy of hangeshashinto (TJ-14) for CPT-11-induced diarrhea during combination chemotherapy with cisplatin (CDDP) plus irinotecan hydrochloride (CPT-11) for advanced non-small-cell lung cancer (NSCLC).	hangeshashinto (半夏瀉心湯)	Mori K, Kondo T, Kamiyama Y, et al. Preventive effect of Kampo medicine (Hangeshashin-to) against irinotecan-induced diarrhea in advanced non-small-cell lung cancer. *Cancer Chemotherapy and Pharmacology* 2003; 51: 403-6.	RCT-envelope	C	118
			Mori K, Hirose T, Machida S, et al. Kampo medicines for the prevention of irinotecan-induced diarrhea in advanced non-small cell lung cancer. Gan to Kagaku Ryoho (Japanese Journal of Cancer and Chemotherapy) 1998; 25: 1159-63 (text in Japanese with English abstract).		C	
			Mori K. Hangeshashin-to (Kampo medicined) in the prevention of irinotecan-induced diarrhea in advanced non-small cell lung cancer. *Progress in Medicine* 1999; 19: 886-90 (text in Japanese with English abstract).		N	
K56.0	Effects of daikenchuto on intestinal paralysis after surgery for colorectal cancer	daikenchuto (大建中湯)	Nagashima Y, Tanaka N, Furukawa K, et al. Effects of daikenchuto (TJ-100) on intestinal paralysis after surgery for colorectal cancer*. *Progress in Medicine* 1998; 18: 903-5 (in Japanese).	RCT	N	UC
K56.0	To determine the efficacy and safety of daikenchuto for improving intestinal peristalsis in patients with intestinal paralysis after surgery for abdominal aortic aneurysm (AAA).	daikenchuto (大建中湯)	Takagaki Y, Kawasaki S, Komai H, et al. The effect of Chinese hearb medicine (dai-kenchu-to) on paralytic ileus after repair of abdominal aortic aneurysm. *Nihon Rinsho Geka Gakkai Zasshi* (*Journal of Japan Surgical Association*) 2000; 61: 325-8 (text in Japanese with English abstract).	RCT	N	119
K56.5	Efficacy of daikenchuto in patients with adhesive ileus	daikenchuto (大建中湯)	Ohyabu H, Matsuda S, Kurisu S, et al. Evaluation of daikenchuto in patients with adhesive ileus in a randomized trial*. *Progress in Medicine* 1995; 15: 1954-8 (in Japanese).	RCT-envelope	I	UC
K58.9	Efficacy of saikokeishito and keishikashakuyakuto for irritable bowel syndrome (IBS)	saikokeishito (柴胡桂枝湯), keishikashakuyakuto (桂枝加芍薬湯)	Ishii F, Iizuka B, Nagasako K, et al. Evaluations of the therapeutic efficacy of saikokeishito (TJ-10) versus keishikashakuyakuto (TJ-60) for irritable bowel syndrome and saireito (TJ-114) for ulcerative colitis*. *Progress in Medicine* 1993; 13: 2893-900 (in Japanese).	RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
K58.9	Efficacy and safety of keishikashakuyakuto for irritable bowel syndrome	keishikashakuyakuto (桂枝加芍薬湯)	Sasaki D, Uehara A, Hiwatashi N, et al. Clinical efficacy of keishikashakuyakuto for irritable bowel syndrome - a multicenter, randomized, parallel-group clinical trial -*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine)* 1998; 75: 1136-52 (in Japanese).	DB-RCT	I	UC
K59.0	Efficacy of junchoto and mashiningan for atonic constipation in the elderly	junchoto (潤腸湯), mashiningan (麻子仁丸)	Ishioka T. Comparison of the efficacy of junchoto and mashiningan for atonic constipation in the elderly stratified by physical strength*. *Kampo no Rinsho* (*Journal of Kampo Medicine*) 1996; 43: 1431-7 (in Japanese).	RCT-cross over	N	UC
K59.0	Effects of daiokanzoto on constipation	daiokanzoto (大黄甘草湯)	Miyoshi A, Masamune O, Fukutomi H, et al. The clinical effect of TSUMURA Daio-Kanzo-To Extract Granules for ethical use (TJ-84) on constipation using double blind test. *Shokakika* (*Gastroenterology*) 1994; 18: 299-312 (text in Japanese with English abstract).	DB-RCT	I	UC
			Miyoshi A, Masamune O, Fukutomi H, et al. The clinical effect of TSUMURA Daio-Kanzo-to Extract Granules for ethical use (TJ-84) against the constipation based on the new standard. *Shokakika* (*Gastroenterology*) 1996; 22: 314-28 (text in Japanese with English abstract).		I	
			Harasawa S, Miyoshi A. Reevaluation of Kampo medicine in patients with constipation - efficacy of Daio-kanzo-to -. *Shokakigan* (*Japanese Journal of Cancer of the Digestive Organs*) 1996; 6: 271-7 (text in Japanese with English abstract).		I	
K59.0	To evaluate the efficacy and safety of kumibinroto for chronic constipation in elderly dialysis patients.	kumibinroto (九味檳榔湯)	Nishizawa Y, Nishizawa Y, Goto HG, et al. Prospective multicenter randomized group-parallelled study: effect of Chinese traditional herb medicine, jiu-wei-bing-lang-tang (Japanese name: kumi-binro-to) on constipation in elderly patients with renol dialysis. *Kampo Kenkyu* (*Kampo Research*) 2004; 388: 132-8 (in Japanese).	RCT	I	120
K70.9	Efficacy of Kampo medicines for alcoholic liver disease	shosaikoto (小柴胡湯), shosaikoto (小柴胡湯) ＋inchingoreisan (茵チン五苓散)	Takahashi H, Maruyama K. Clinical aspects of Kampo treatment for alcoholic liver disease. *Igaku no Ayumi* (*Journal of Clinical and Experimental Medicine*) 1993; 167: 811-4 (in Japanese).	RCT	N	UC
K73.2	Effiacy and safety of shosaikoto for chronic active hepatitis	shosaikoto (小柴胡湯)	Hirayama C, Okumura M, Tanikawa K, et al. A multicenter randomized controlled clinical trial of Sho-Saiko-To in chronic active hepatitis. *Gastroenterologia Japonica* 1989; 24: 715-9.	DB-RCT	C&I	UC
			Hirayama C, Okumura M, Tanikawa K, et al. A multicenter randomized controlled clinical trial of shosaiko-to in chronic active hepatitis. *Kan-Tan-Sui* 1990; 20: 751-9 (in Japanese).		I	
K73.2	Efficacy of shosaikoto for chronic active hepatitis	shosaikoto (小柴胡湯)	Hirayama C, Okumura M, Tanikawa K, et al. A multicenter randomized controlled clinical trial of Shosaiko-to in chronic active hepatitis. Analysis of serum enzyme activities. *Kan-Tan-Sui* 1992; 25: 551-8 (in Japanese).	DB-RCT	I	UC
K73.9	Efficacy and safety of saireito for chronic hepatitis	saireito (柴苓湯)	Sasaki D, Sudoh T, Kunikane M, et al. Usefulness of Kanebo Saireito Extract Fine Granules for chronic hepatitis - a comparative study (with randomization carried out using the sealed-envelope method) -*. *Progress in Medicine* 1989; 9: 2923-37 (in Japanese).	RCT-envelope	I	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
K73.9	To determine the efficacy of liver protectors for preventing carcinogenesis in patients with chronic hepatitis C.	shosaikoto (小柴胡湯), juzentaihoto (十全大補湯)	Tarao K. Prevention of HCC by anti-inflammatory agents in patients with chronic hepatitis C. *Rinsho Shokaki Naika* (*Clinical Gastroenterology*) 2007; 22: 961-9 (in Japanese).	RCT	N	121
			Tarao K, Shibuya A, Ohkawa S, et al. Prevention of hepatocarcinogenesis by anti-inflammatory therapy: is combination anti-inflammatory therapy targeting an ALT level of under 80 units effective for hepatitis C virus-related cirrhosis (Child A)?: comparison with monotherapy*. *Kanagawa Cancer Center – Nenpo* (*Annual Report*) 2003; 19: 92 (in Japanese).		N	
			Tarao K. Persistent inflammation and hepatocarcinogenesis in chronic hepatitis C and hepatitis C virus-related cirrhosis*. *Kanagawa Igakkai Zasshi* (*The Journal of the Kanagawa Medical Association*) 2008; 33: 115-8 (in Japanese).		N	
K74.6	To evaluate the hepatocellular carcinoma-preventive effect of juzentaihoto administered for liver cirrhosis.	juzentaihoto (十全大補湯)	Higuchi K, Watanabe A. Study on liver cancer-preventive effect of juzentaihoto in patients with liver cirrhosis*. *Methods in Kampo Pharmacology* 2000; 5: 29-33 (in Japanese).	RCT-envelope	N	122
K74.6	To evaluate the hepatocellular carcinoma-preventive effect of juzentaihoto administered for liver cirrhosis.	juzentaihoto (十全大補湯)	Higuchi K, Shimizu Y, Yasumura S, et al. Preventive effect of liver carcinogenesis by Juzen-Taiho-To in the patients with liver cirrhosis. *Kan-Tan-Sui* 2002; 44: 341-6 (in Japanese)	RCT-envelope	I	123
K75.9	Efficacy of shosaikoto for chronic non-A, non-B hepatitis in children	shosaikoto (小柴胡湯)	Tajiri H, Kozaiwa K, Sawada A, et al. Efficacy of shosaikoto for chronic non-A, non-B hepatitis in children (non-A, non-B hepatitis in children and shosaikoto)*. *Nihon Shoni Toyo Igaku Kenkyukai Kaishi*（*Journal of the Japan pediatric society for oriental medicine*） 1996; 12: 12-7 (in Japanese).	RCT-envelope	N	UC
K76.9	Efficacy of saikokeishito for liver dysfunction induced by chemotherapy for pulmonary tuberculosis	saikokeishito (柴胡桂枝湯)	Mizutani Y, Imai S, Watanabe H, et al. Saiko-Keishi-To on patients with pulmonary tuberculosis: effect on liver disfunction. *Donan Igakkaishi* (*Journal of the Medical Association of South Hokkaido*) 1994; 29: 247-9 (in Japanese).	RCT-envelope	N	UC
K80.2	Effects of shosaikoto, goreisan, and tokishakuyakusan on the sphincter of Oddi	goreisan (五苓散), tokishakuyakusan (当帰芍薬散), shosaikoto (小柴胡湯)	Seki M, Fujioka M, Hatano T, et al. Differences between the effects of Sho-saiko-to, Gorei-san, and Toki-shakuyaku-san on the sphincter of Oddi - An intraoperative cholangiomanometric study -. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1993; 43: 395-402 (text in Japanese with English abstract).	RCT	N	UC
K82.8	Efficacy of goreisan and tokishakuyakusan on urinary 6-keto-prostaglandin F1α level in patients with gallbladder stones or polyps	goreisan (五苓散), tokishakuyakusan (当帰芍薬散), shosaikoto (小柴胡湯)	Takagi S. Increase of urinary 6-keto-prostaglandin F1α level by preoperative administration of Gorei-san or Toki-shakuyaku-san to the patients of gallbladder stones or polyps. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1992; 9: 32-9 (text in Japanese with English abstract).	RCT	N	UC
K83.1	Efficacy of inchinkoto for improving the bilirubin reduction rate after biliary drainage in patients with obstructive jaundice.	inchinkoto (茵チン蒿湯)	Okabayashi T, Tanaka N, Orita K. The effect of a Kanpo medicine, Inchinko-to for the bilirubin reduction rate after biliary drainage on the patients with obstructive jaundice. *Nihon Rinsho Geka Gakkaishi* (*Journal of Japan Surgical Association*) 1998; 59: 2495-500 (text in Japanese with English abstract).	RCT-envelope	I	UC
K91.3	Efficacy and safety of daikenchuto for ileus	daikenchuto (大建中湯)	Kubo N, Uchida Y, Akiyoshi T, et al. Efficacy of daikenchuto for ileus - a multicenter study -*. *Progress in Medicine* 1995; 15: 1962-7 (in Japanese).	RCT-envelope	I	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
K91.3	To determine the efficacy of daikenchuto for the treatment of postoperative ileus and the improvement of postoperative conditions.	daikenchuto (大建中湯)	Itoh T, Yamakawa J, Mai M, et al. The effect of the herbal medicine Dai-kenchu-to on post-operative ileus. *The Journal of International Medical Research* 2002; 30: 428-32.	RCT	C	124
K91.8	Efficacy and safety of shosaikoto for postoperative liver dysfunction	shosaikoto (小柴胡湯)	Okabayashi T, Mimura H, Orita K. Usefulness of shosaikoto (TJ-9) in the treatment of postoperative liver dysfunction*. *Progress in Medicine* 1989; 9: 851-5 (in Japanese).	RCT-envelope	N	UC
K91.8	Effect of shosaikoto on postoperative liver dysfunction	shosaikoto (小柴胡湯)	Usuba A, Gao L. S., Motoki R. Effect of Sho-saiko-to (Xao-chai-hu-tang) on liver dysfunctions after surgery - the benefits of preoperative administration and the importance of diagnosis according to traditional Chinese logic -. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1992; 43: 1-12 (in Japanese).	RCT	N	UC
K91.9	To determine the effects of daikenchuto on gastrointestinal emptying and motility in patients after total gastrectomy with jejunal pouch interposition reconstruction.	daikenchuto (大建中湯)	Endo S, Nishida T, Nishikawa K, et al. Dai-kenchu-to, a Chinese herbal medicine, improves stasis of patients with total gastrectomy and jejunal pouch interposition. *American Journal of Surgery* 2006; 192: 9-13.	RCT-cross over	C	125
K92.9	Efficacy and safety of keishikashakuyakuto combined with acarbose	keishikashakuyakuto (桂枝加芍薬湯)	Hasebe K, Machida M, Yada M, et al. Clinical application of Keishi-ka-syakuyaku-to for abdominal symptoms caused by α-glucosidase inhibitor acarbose. *Kiso to Rinsho* (*The Clinical Report*) 1997; 31: 3179-86 (text in Japanese with English abstract).	quasi-RCT	I	UC
K92.9	To determine the clinical effect of rikkunshito on gastrointestinal adverse reactions induced by fluvoxamine, an antidepressant.	rikkunshito (六君子湯)	Oka T, Tamagawa Y, Hayashida S, et al. Rikkunshi-to atenuates adverse gastrointestinal symptoms induced by fluvoxamine. *Biopsychosocial Medicine* 2007; 1.	RCT	N	126

Skin Diseases (13 abstracts, 14 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
L20.8	Efficacy and safety of shosaikoto for treating atopic dermatitis and for withdrawing or tapering topical corticosteroids	shosaikoto (小柴胡湯)	Shimoda S, Hashizume S, Morita M, et al. Efficacy of TSUMURA Shosaikoto for atopic dermatitis*. *Hifuka ni okeru Kampo Chiryo no Genkyo* 1991; 2: 15-24 (in Japanese).	RCT	N	UC
L20.9	To assess the efficacy of hochuekkito for the treatment of atopic dermatitis.	hochuekkito (補中益気湯)	Furue M, Tanaka Y, Kobayashi H, et al. Efficacy of Kanebo Hochuekkito in patients with atopic dermatitis with "qi-kyo" – a multicenter, double-blind trial*. *Arerugi* (*Japanese Journal of Allergology*). 2005; 54: 1020 (in Japanese).	DB-RCT	N	127
L29.8	Efficacy and safety of orengedokuto and goshajinkigan for the treatment of senile pruritus	orengedokuto (黄連解毒湯), goshajinkigan (牛車腎気丸)	Ohkawara A, Furuya K, Kurisu Y, et al. Experience with orengedokuto (TJ-15) and goshajinkigan (TJ-107) for the treatment of senile pruritus*. *Nishinihon Hifuka* (*The Nishinihon Journal of Dermatology*) 1991; 53: 1234-41 (in Japanese).	RCT-envelope	I	UC
L29.8	Efficacy of tokiinshi combined with a bath preparation containing licorice extract in patients with senile xerosis	tokiinshi (当帰飲子)	Iida T, Nishiyama C, Suzuki H. The effects of Toki-Inshi and a bath preparation containing licorice extract on patients with senile pruritus. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1996; 47: 35-41 (text in Japanese with English abstract).	RCT	N	UC
L29.8	Efficacy of hachimijiogan for the treatment of senile pruritus	hachimijiogan (八味地黄丸)	Ishioka T, Aoi R. Comparative evaluation of hachimijiogan and ketotifen fumarate on senile pruritus*. *Shinyaku to Rinsho* (*Journal of New Remedies and Clinics*) 1992; 41: 2603-8 (in Japanese).	RCT-cross over	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
L29.8	Efficacy of rokumigan and hachimijiogan for the treatment of senile pruritus	hachimijiogan (八味地黄丸), rokumigan (六味丸)	Ishioka T. Comparative evaluation of Rokumigan and Hachimi-jiogan on senile pruritus. *Therapeutic Research* 1995; 16: 1497-504 (text in Japanese with English abstract).	RCT-cross over	N	UC
L29.9	Effect on itching due to eczema and other skin disorders	unseiin (温清飲)	Kusumoto M, Fujimura Y, Yamada H, et al. Evaluation of the effectiveness of various drugs for relieving itching due to eczema carried out by personnel in inpatient pharmacy practice: assessment based on "itching" score -*. *Iyaku Journal* (*Medicine and Drug Journal*) 1993; 29: 973-6 (in Japanese).	RCT	N	UC
L29.9	Efficacy of orengedokuto and tokiinshi for the treatment of pruritus	orengedokuto (黄連解毒湯) + tokiinshi (当帰飲子)	Ohkuma M. Treatment of pruritus by Chinese drugs. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1993; 10: 126-30 (text in Japanese with English abstract).	RCT	N	UC
L29.9	Efficacy of orengedokuto, tokiinshi, external application, and oral antihistamine monotherapy or combination therapy for the treatment of pruritus	orengedokuto (黄連解毒湯) + tokiinshi (当帰飲子)	Ohkuma M. Treatment of pruritus by Chinese drugs with external application and oral antihistamine. *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1994; 11: 302-3 (in Japanese).	RCT	N	UC
L30.9	Efficacy and safety of jumihaidokuto for the treatment of chronic eczema and atopic dermatitis	jumihaidokuto (十味敗毒湯)	Kobayashi K, Ohkawara A. Therapeutic effect of jumihaidokuto on chronic eczema and atopic dermatitis*. *Hifuka ni okeru Kampo Chiryo no Genkyo* 1994; 5: 25-34 (in Japanese).	RCT-envelope	N	UC
L40.9	Efficacy of saireito combined with topical steroid therapy for psoriasis	saireito (柴苓湯)	Kukita A, Harada S, Fujisawa R, et al. The clinical efficacy of the herb medicine, TJ-114 (Sairei-to), on the topical steroid therapy of psoriasis vulgaris. *Rinsho Iyaku* (*Journal of Clinical Therapeutics & Medicines*) 1991; 7: 927-36 (text in Japanese with English abstract).	RCT-envelope	I	UC
L50.9	Efficacy of kakkonto as an adjuvant for reducing adverse reactions to oxatomide	kakkonto (葛根湯)	Tanaka M. Effects of oxatomide on urticaria. *Yakuri to Chiryo (Japanese Pharmacology and Therapeutics)* 1991; 19:5029-31 (in Japanese).	RCT	N	UC
L70.0	Efficacy of jumihaidokuto and orengedokuto for the treatment of acne vulgaris	jumihaidokuto (十味敗毒湯), orengedokuto (黄連解毒湯)	Ohkuma M. Treatment of acne by Chinese drugs and external application. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1993; 10: 131-4 (text in Japanese with English abstract).	RCT	N	UC
			Ohkuma M. Treatment of acne by Chinese drugs and external application - comparison with oral antibiotics -. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1993; 44: 173-7 (in Japanese).		N	

Diseases of the musculoskeletal system and connective tissue (19 abstracts, 18 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
M06.90	Efficacy in the management of chronic rheumatoid arthritis	saireito (柴苓湯)	Matsuura M. Efficacy of saireito in the management of chronic rheumatoid arthritis (RA)*. *Modern Physician* 1994; 14: 403-8 (in Japanese).	RCT-envelope	I	UC
M06.90	Efficacy for reducing adverse effects of steroids in patients with chronic rheumatoid arthritis	jiinkokato (滋陰降火湯)	Matsuta K, Gu XP, Ito K, et al. Evaluation of jiinkokato and steroid combination therapy for chronic rheumatoid arthritis*. *Kampo Igaku* (*Kampo Medicine*) 1995; 19: 50-2 (in Japanese).	RCT	N	UC
M17.9	Efficacy for improving analgesic effects, QOL, and exercise capacity in patients with knee osteoarthritis	boiogito (防已黄耆湯) + shuchibushimatsu (修治附子末)	Nishizawa Y, Nishizawa Y, Amenomori Y, et al. A comparison of the analgesic effect of non-steroid anti-inflammatory drugs (NSAIDs alminoprofen) and those of a Chinese traditional herbal medicine, Boi-ogi-to and Shuchi-Bushi-Powder on osteoarthropathy of the knee joint in middle-aged and elderly patients with knee-joint osteoarthropathy. *Itami to Kampo* (*Pain and Kampo Medicine*) *1998; 8: 17-32* (*text in Japanese with English abstract*).	RCT	I	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
M17.9	To evaluate the efficacy of boiogitokashuchibushimatsu for gonarthrosis.	boiogitoka shuchibushimatsu (防已黄耆湯加修治附子末)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Therapeutic effect of boiogitokashuchibushimatsu on gonarthrosis: a 10-year prospective randomized controlled trial with loxoprofen sodium*. *Pharma Medica* 2007; 25: 15-21 (in Japanese).	RCT	I	128
M35.0	To evaluate the efficacy and safety of bakumondoto therapy for dryness associated with primary Sjögren's syndrome.	bakumondoto (麦門冬湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Long-term effects of traditional Chinese herbal medicine, mai-men-dong-tang (Japanese name: bakumondo-to) compared with bromhexine, hydrochloride on sicca syndrome, especially, salivary secretion in patients with primary Sjögren's syndrome: a multicenter, randomized well controlled group parallel comparative trial study with bromhexine. *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2002; 43: 62-6.	RCT	I	129
M35.0	To evaluate the efficacy and safety of bakumondoto therapy for salivary hyposecretion associated with primary Sjögren's syndrome.	bakumondoto (麦門冬湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Long-term effect of traditional Chinese herbal medicine, mai-men-don-tang on sicca syndrome, especially, salicary secretion in patients with primary Sjögren's syndrome: a multicenter, randomized well controlled group-pararell double-blined study. *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2004; 45: 66-74.	DB-RCT	N	130
M35.0	To evaluate the efficacy and safety of bakumondoto for treatment of secondary Sjögren's syndrome.	bakumondoto (麦門冬湯)	Nishizawa Y, Nishizawa Y, Goto GH, et al. The Multicenter randomized comparative study of kampo herbal medicine, mai-men-dong-tang (Japanese name Bakumondo-to) compared with bromhexine on salivary secretion in secondary Sjögren's syndrome. *Itami to Kampo* (*Pain and Kampo Medicine*) 2004; 14: 10-7 (text in Japanese with English abstract).	RCT	I	131
M35.0	To evaluate the efficacy and safety of bakumondoto for treatment of dryness associated with secondary Sjögren's syndrome.	bakumondoto (麦門冬湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Improving effect of Chinese herb medicine mai-men-dong- tang (Japanese name: bakumondo-to) comparative with sicca syndrome in especial salivary patients with secondary Sjögren's syndrome in multicenter, well controlled, long-term comparative study. *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2003; 44: 65-70.	RCT	N	132
M35.0	To evaluate the efficacy for Sjögren's syndrome.	bakumondoto (麦門冬湯), rokumigan (六味丸), hachimijiogan (八味地黄丸), hochuekkito (補中益気湯)	Ohno S. The effect of Kampo medicine on salivary secretion in Sjögren's syndrome. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2006; 15: 134-40 (in Japanese).	RCT	I	133
M48.02	To evaluate the efficacy of hachimijiogan, goshajinkigan, and shuchibushi powder for relief of residual symptoms after surgical treatment of cervical spinal stenosis.	hachimijiogan (八味地黄丸), goshajinkigan (牛車腎気丸), goshajinkigan (牛車腎気丸) + shuchibushimatsu (修治附子末)	Maeshima S, Katayama Y. Spine and spinal cord diseases 1. Traditional Chinese medicines for the spinal disorders. *Kampo to Saishin-Chiryo* (*Kampo & the Newest Therapy*) 2004; 13: 232-6 (in Japanese).	RCT	I	134
M48.06	Efficacy and safety of hachimijiogan for lumbar spinal stenosis	hachimijiogan (八味地黄丸)	Hayashi Y, Saito E, Takahashi O. Usefulness of hachimijiogan for lumbar spinal stenosis*. *Geriatric Medicine* 1994; 32: 585-91 (in Japanese).	quasi-RCT	N	UC
M48.06	To evaluate the efficacy of goshajinkigan and shuchibushi powder for relief of chronic low back pain associated with lumbar spinal stenosis.	goshajinkigan (牛車腎気丸), oshajinkigan (牛車腎気丸) + shuchibushimatsu (修治附子末)	Maeshima S, Katayama Y. Spine and spinal cord diseases 1. Traditional Chinese medicines for the spinal disorders. *Kampo to Saishin-Chiryo* (*Kampo & the Newest Therapy*) 2004; 13: 232-6.	RCT	I	135

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
M54.56	Clinical effect on acute lumbago (so-called strained back)	shakuyakukanzoto (芍薬甘草湯)	Tamakawa S, Ogawa H. The effect of Shakuyaku-kanzo-to and Goshakusan on lumbago. *Itami to Kampo* (*Pain and Kampo Medicine*) 1997; 7: 83-5 (text in Japanese with English abstract).	RCT	N	UC
M54.56	Effects on nonspecific lumbago in women during menopause	keishibukuryogan (桂枝茯苓丸), keishibukuryogan (桂枝茯苓丸) ＋ shuchibushimatsu (修治附子末)	Ohta H, Makita K. Lumbago - with emphasis on nonspecific lumbago, which obstetricians and gynecologists think is the most common form in women -*. *Chiryo* (*The Journal of Therapy*) 1995; 77: 1646-57 (in Japanese).	RCT	N	UC
M54.56	Efficacy and safety of goshajinkigan for lumbago in the elderly	goshajinkigan (牛車腎気丸)	Nakamura T, Souza ACA, Ouchi Y, et al. Effects of goshajinkigan on lumbago*. *Dai 4 Kai Tokyo Naika Kampo Kenkyukai Koen Naiyo Shu* 1989; 4: 24-9 (in Japanese).	RCT-envelope	N	UC
M62.59	To evaluate the efficacy of juzentaihoto combined with hachimijiogan in patients with disuse syndrome.	juzentaihoto (十全大補湯), hachimijiogan (八味地黄丸)	Wang XD, Yoshida K, Honda K, et al. Study of the immunoregulatory activity of the combination therapy with juzentaihoto and hachimijiogan in patients with disuse syndrome*. *Kampo Igaku* (*Kampo Medicine*) 2006; 30: 65-7 (in Japanese).	RCT-envelope	I	136
M81.1	Combined effect of keishibukuryogan and vitamin D3 on osteopenia in women during menopause	keishibukuryogan (桂枝茯苓丸)	Ohta H, Nemoto K. Effect of concurrent administration of active vitamin D_3 and TSUMURA Keishibukuryogan on osteopenia following oophorectomy*. *Kampo Igaku* (*Kampo Medicine*) 1989; 13: 173-9 (in Japanese).	RCT	N	UC
M81.1	Combined effect of keishibukuryogan or tokishakuyakusan and vitamin D3 on osteopenia in women during menopause	keishibukuryogan (桂枝茯苓丸), tokishakuyakusan (当帰芍薬散)	Ohta H, Nemoto K. Preventive effect of 1α-hydroxyvitamin D_3 plus Kampo medicine combination therapy on osteopenia following oophorectomy - comparison between keishibukuryogan and tokishakuyakusan -*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 1990; 7: 65-70 (in Japanese).	RCT	N	UC
M81.9	Positive effects on menopause index, bone mass, and anemia in postmenopausal women with osteoporosis	kamikihito (加味帰脾湯)	Kanai S. The effect of Kami-kihi-to on the maintenance of bone mass in patients with osteoporosis. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1998; 49: 59-66 (text in Japanese with English abstract).	quasi-RCT	N	UC

Genitourinary Tract Disorders (including Climacteric Disorders) (30 abstracts, 37 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
N02.8	Efficacy and safety of saireito in childhood IgA nephropathy with focal/minimal mesangial proliferation	saireito (柴苓湯)	Yoshikawa N, Ito H, Sakai T, et al. A prospective controlled study of Sairei-to in childhood IgA nephropathy with focal/minimal mesangial proliferation. *Nihon Jinzo Gakkaishi* (*The Japanese Journal of Nephrology*) 1997; 39: 503-6 (text in Japanese with English abstract).	RCT-envelope	C	UC
N02.8	Efficacy and safety of Kampo medicines for IgA nephropathy in adults	saireito (柴苓湯)	Saruta T, Konishi K. Efficacy of Kampo medicines for renal diseases - with emphasis on saireito -*. *21 Seiki no Iryo to Kampo* 1994: 157-65 (in Japanese).	RCT-envelope	N	UC
N04.9	Efficacy of initial steroid therapy with saireito for preventing relapse in childhood steroid-responsive nephrotic syndrome	saireito (柴苓湯)	Yoshikawa N, Ito H, Takekoshi Y, et al. Standard versus long-term prednisolone with Sairei-to for initial therapy in childhood steroid-responsive nephrotic syndrome: A prospective controlled study. *Nihon Jinzo Gakkaishi* (*The Japanese Journal of Nephrology*) 1998; 40: 587-90 (text in Japanese with English abstract).	RCT-envelope	C&I	UC
N20.9	Efficacy for promoting the spontaneous discharge of upper urinary tract stones after extracorporeal shock wave lithotripsy	choreitogoshimotsuto (猪苓湯合四物湯) ＋ shakuyakukanzoto(芍薬甘草湯)	Kinoshita H, Kanaya H, Yamamoto S, et al. Effects of Chinese herbal medicine in promoting the spontaneous discharge of upper urinary tract stones after ESWL. *Nishinihon Hinyokika* (*The Nishinihon Journal of Urology*) 1993; 55: 61-6 (text in Japanese with English abstract).	RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
N32.8	To evaluate the efficacy and safety of goshajinkigan and propiverine hydrochloride for overactive bladder.	goshajinkigan (牛車腎気丸)	Nishizawa Y., Nishizawa Y, Yoshioka H., et al. Efficacy and safety of Chinese traditional medicine, Niu-Che-Shwn-Qi-Wan (Japanese name: Goshajinki-gan) versus propiverine hydrochloride on health-related quality of life in patients with overactive bladder in prospective randomized comparative study. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2007; 16: 131-42 (in Japanese).	RCT	I	137
N39.0	Efficacy of shosaikoto for improving immunity in the elderly	shosaikoto (小柴胡湯)	Toba K. Role in host defense mechanisms and effect on the prognosis of urinary tract infections in elderly subjects: A trial of a Chinese drug formulation*. *Dai 8 Kai Tokyo Naika Kampo Kenkyukai Koen Naiyo Shu* 1993; 8: 31-42 (in Japanese).	RCT-envelope	N	UC
			Toba K. Role in host defense mechanisms and effect on prognosis of urinary tract infections in elderly subjects: A trial of a Chinese drug formulation. *Taisha* (*Metabolism and Disease*) 1992; 29 suppl: 350-4 (in Japanese).		N	
N39.9	Efficacy of choreito and choreitogoshimotsuto for relieving nonspecific lower urinary tract complaints	choreito (猪苓湯), choreitogoshimotsuto (猪苓湯合四物湯)	Ohkawa T, Ebisuno S, Watanabe T. Urological diseases and Kampo medicine*. *Dai 23 Kai Nihon Igakkai Sokai Sateraito Shinpojiumu Nihon Toyo Igakkai Rinsho Kampo Kenkyukai Koen Naiyo Shu* 1992: 22-39 (in Japanese).	RCT-envelope	N	UC
N39.9	Efficacy of choreito and hachimijiogan for relieving urinary frequency, voiding pain, and incomplete emptying in patients without organic urinary tract disease	hachimijiogan (八味地黄丸), choreito (猪苓湯)	Fuse H, Sakamoto M, Iwasaki M, et al. Effect of Chorei-to and Hachimi-jio-gan on unidentified complatints on urinary tract. *Hinyoki Geka* (*Japanese Journal of Urological Surgery*) 1995; 8: 603-9 (in Japanese).	RCT-envelope	N	UC
N39.9	To evaluate the effect of single-dose administration of maobushisaishinto on urine flow.	maobushisaishinto (麻黄附子細辛湯)	Aoki Y, Ueda K, Tsutani K, et al. The influence of formula Ma-huang-fu-zi-xi-Xin-Tang (Mao-bushi-saishin-to; Mbst) on the results of urodynamic studies. *Journal of Traditional Medicine* 2001; 18: 203-9.	RCT-cross over	I	138
N40	Efficacy and safety for treating atopic dermatitis and for withdrawing or tapering topical corticosteroids	hachimijiogan (八味地黄丸), choreito (猪苓湯)	Sakamoto Y, Iwasaki M, Kazama T, et al. Study of effects Hachimi-jio-gan and Chorei-to on prostatic hypertrophy. *Dai 13 Kai Hinyokika Kampo Kenkyukai Koen Shu* 1996: 7-14 (text in Japanese with English abstract).	RCT-envelope	N	UC
N41.1	Efficacy and safety of goshajinkigan in the treatment of chronic prostatitis	goshajinkigan (牛車腎気丸)	Horiba T, Kato S, Tanaka T, et al. Clinical validity of gosha-jinki-gan in the treatment of chronic prostatitis - open comparative study with gosha-jinki-gan vs ciprofloxacin -. *Gendai Toyo Igaku* (*The Journal of Traditional Sino-Japanese Medicine*) 1994; 15: 37-44 (in Japanese).	RCT-envelope	N	UC
N46	Positive effect on sperm profiles of male infertility patients	saikokaryukotsuboreito (柴胡加竜骨牡蛎湯), hochuekkito (補中益気湯)	Hiramatsu M, Maehara I, Takahashi M, et al. Treatment experience with saikokaryukotsuboreito and hochuekkito in male infertility patients*. *Kampo Igaku* (*Kampo Medicine*) 1993; 17: 246-8 (in Japanese).	RCT	N	UC
N46	Efficacy and safety of hochuekkito in the treatment of male infertility	hochuekkito (補中益気湯)	Kazama T. Male infertility*. *Current Therapy* 1988; 6: 1683-6 (in Japanese).	RCT-envelope	N	UC
N64.9	Efficacy of kamishoyosan in the treatment of mastitis	kamishoyosan (加味逍遙散), keishibukuryogan (桂枝茯苓丸)	Inoue M. Kampo treatment for mastitis - kamishoyosan -*. *Kampo Igaku* (*Kampo Medicine*) 1994; 18: 238-41 (in Japanese).	RCT-envelope	N	UC
N64.9	Efficacy of shigyakusan in the treatment of mastitis	shigyakusan (四逆散), keishibukuryogan (桂枝茯苓丸)	Inoue M. Kampo therapy for mastitis - shigyakusan -*. *Kampo Igaku* (*Kampo Medicine*) 1990; 14: 132-6 (in Japanese).	RCT-envelope	N	UC
N64.9	Efficacy of tsudosan in the treatment of mastitis	tsudosan (通導散), keishibukuryogan (桂枝茯苓丸)	Inoue M. Clinical study of effects of Tsu-do-san on mastitis. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1993; 43: 517-21 (in Japanese).	RCT-envelope	N	UC
N64.9	Efficacy of tokakujokito in the treatment of mastitis	tokakujokito (桃核承気湯), keishibukuryogan (桂枝茯苓丸)	Inoue M. Clinical studies on effects of Tokakujoki-to for fibro-cystic disease of the breast. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1992; 42: 415-8 (in Japanese).	RCT-envelope	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
N81.4	To evaluate the hachimijiogan-induced improvement in postoperative discomfort associated with surgery for uterine prolapse and quality of life (QOL).	hachimijiogan (八味地黄丸)	Oribe K, Nishida Y. Efficacy of hachimijiogan for discomfort after surgery for uterine prolapse. *Gekkan Kampo Ryoho* (*Monthly Journal of Kampo Medicine and Herbs*) 2006; 10: 282-8 (in Japanese).	RCT	N	139
N93.9	To evaluate the efficacy and safety of kyukikyogaito for menometrorrhagia.	kyukikyogaito (キュウ帰膠艾湯)	Iwabuchi S. Effect of kyuki-kyogai-to on stopping dysfunctional uterine bleeding – comparison with occidental hemostatic drugs -. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 2000; 50: 883-903 (text in Japanese with English abstract).	quasi-RCT	I	140
N94.6	Pain-relieving effect on dysmenorrhea	tokishakuyakusan (当帰芍薬散)	Kotani N, Oyama T, Sakai I, et al. Analgesic effect of a herbal medicine for treatment of primary dysmenorrhea - a double-blind study. *The American Journal of Chinese Medicine* 1997; 25: 205-12.	DB-RCT	C	UC
N95.1	Clinical effect of keishibukuryogan combined with autonomic modulator	keishibukuryogan (桂枝茯苓丸)	Tanaka E, Saito H, Hiroi M. Kampo treatment for nonspecific complaints in climacteric women - comparison of clinical efficacy of Kampo medicine alone versus Kampo medicine combined with tofisopam -*. *Kampo Shinryo* 1997; 16: 22-4 (in Japanese).	RCT	N	UC
N95.1	Clinical effect on climacteric disorders	tokishakuyakusan (当帰芍薬散), kojinmatsu (紅参末)	Samukawa K, Ogita S. Climacteric disorders and medicinal ginseng*. *Chiryogaku* (*Biomedicine & Therapeutics*) 1994; 28: 57-62 (in Japanese).	RCT-envelope	N	UC
N95.1	To compare hormone replacement therapy (HRT) and Kampo therapy as treatment of climacteric disorders.	Kampo therapy （keishibukuryogan (桂枝茯苓丸), kamishoyosan (加味逍遙散), goshajinkigan (牛車腎気丸), etc.）	Ota H. Positioning of Kampo therapy and hormone replacement therapy in treatment of climacteric disorders*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2001; 18: 21-9 (in Japanese).	RCT	I	141
N95.1	To compare the efficacy of Kampo therapy with that of hormone replacement therapy (HRT) for climacteric disorders and to compare the efficacy of three non-sho-based (非随証) Kampo medicines for gynecological disease.	tokishakuyakusan (当帰芍薬散), kamishoyosan (加味逍遙散), keishibukuryogan (桂枝茯苓丸)	Takamatsu K. Study of the usefulness of Kampo therapy for climacteric disorders – a randomized trial of three major Kampo medicines for treatment of gynecological disease–*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2006; 23: 35-42 (in Japanese).	quasi-RCT	I	142
		kamishoyosan (加味逍遙散), tokishakuyakusan (当帰芍薬散), keishibukuryogan (桂枝茯苓丸), juzentaihoto (十全大補湯)	Takamatsu K, Musha C, Okano H, et al. Study of usefulness of Kampo therapy for climacteric disorders*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2002; 19: 111-6 (in Japanese).		I	
		tokishakuyakusan (当帰芍薬散), kamishoyosan (加味逍遙散), keishibukuryogan (桂枝茯苓丸)	Takamatsu K. HRT and Kampo medicine*. *Nippon Konenki Igakkai Zasshi* (*The Journal of the Japan Menopause Society*) 2004; 12:155-7 (in Japanese).		N	
			Takamatsu K, Makita K, Tanabe K, et al. HRT and Kampo medicine*. *Rinsho Kensa* (*Journal of Medical Technology*) 2004; 48: 877-84 (in Japanese).		N	
			Takamatsu K, Tanabe K. Efficacy of Kampo medicine against climacteric disorders*. *Sanfujinka Chiryo* (*Obstetrical and Gynecological Therapy*) 2004; 89: 408-15 (in Japanese).		N	

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
N95.1	To investigate the equivalence between non-extracted keishibukuryogan and keishibukuryogan extract.	keishibukuryogan (桂枝茯苓丸)	Ogita Y, Fujimoto S, Ushiroyama T, et al. Efficacy of formulation TK-061 for various climacteric symptoms – comparison with Teikoku Keishibukuryogan Extract Granules*. *Rinsho Fujinka Sanka* (*Clinical Gynecology and Obstetrics*) 2002; 56: 799-810 (in Japanese).	RCT	I	143
			Ogita Y, Fujimoto S, Ushiroyama T, et al. Keishibukuryogan formulation TK-061 prepared with crude drug – verification of efficacy for various climacteric symptoms*. *Sanka to Fujinka* (*Obstetrics and Gynecology*) 2002; 69: 953-62 (in Japanese).		I	
N95.1	To evaluate the efficacy of unkeito for climacteric disorders with depressive symptoms.	unkeito (温経湯), tokishakuyakusan (当帰芍薬散)	Koike K, Ohno S, Takahashi N, et al. Efficacy of the herbal medicine Unkei-to as an adjunctive treatment to hormone replacement therapy for postmenopausal women with depressive symptoms. *Clinical Neuropharmacology* 2004; 27: 157-62.	RCT-cross over	C	144
N95.8	To compare the efficacy of keishibukuryogan and hormone replacement therapy (HRT) for relief of hot flashes and chills.	keishibukuryogan (桂枝茯苓丸)	Ushiroyama T, Ikeda A, Sakuma K, et al. Comparing the effects of estrogen and an herbal medicine on peripheral blood flow in post-menopausal women with hot flashes: hormone replacement therapy and Gui-zhi-fu-ling-wan, a Kampo medicine. *The American Journal of Chinese Medicine* 2005; 33: 259-67.	RCT	C	145
N95.8	To evaluate the usefulness of Kampo medicine for treatment of depressive patients refractory to hormone replacement therapy (HRT).	unkeito (温経湯), tokishakuyakusan (当帰芍薬散)	Matsuo A, Koike K, Hoshina Y, et al. Study of the efficacy of unkeito for depressive and anxiety symptoms during menopause that are refractory to hormone replacement therapy.* *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2005; 22: 70-4 (in Japanese).	RCT-cross over	I	146
			Koike K. A slight advantage of Kampo treatment for gynecological disease 4: Menopausal depressed mood and the herbal medicine Unkei-to. *Sanfujinka Chiryo* (*Obstetrical and Gynecological Therapy*) 2006; 92: 784-6 (in Japanese).		N	
N95.8	To compare the effects of unkeito and vitamin E on peripheral blood flow.	unkeito (温経湯)	Ushiroyama T, Sakuma K, Nosaka S. Comparison of effects of vitamin E and wen-jing-tang (unkei-to), an herbal medicine, on peripheral blood flow in post-menopausal women with chilly sensation in the lower extremities: a randomized prospective study. *The American Journal of Chinese Medicine* 2006; 34: 969-79.	RCT	C	147
N97.0	To compare the effects of clomiphene monotherapy with tokishakuyakusan and clomiphene combination therapy infrequent menses, anovular menstrual cycle, and amenorrhea	tokishakuyakusan (当帰芍薬散)	Yasui T, Irahara M, Aono T. Sutadies on the combination treatment with clomiphene citrate and Toki-shakuyaku-san. *Nippon Funin Gakkai Zasshi* (*Japanese Journal of Fertility and Sterility*) 1995; 40: 83-91 (in Japanese).	RCT-envelope	N	UC

Ante/Post-partum Diseases (10 abstracts, 11 references)

ICD-10	Research Question	Kampo Formula	*References*	Study Design	Source	Page No.
O20.0	To evaluate the efficacy of kyukikyogaito as a therapeutic drug for imminent abortion in patients with uterine hemorrhage.	kyukikyogaito (キュウ帰膠艾湯)	Ushiroyama T, Sakuma K, Nosaka S, et al. Clinical efficacy of kyukikyogaito for imminent abortion with uterine hemorrhage*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2006; 23: 100-3 (in Japanese).	RCT	I	148
O47.0	Usefulness of tokishakuyakusan combined with ritodrine hydrochloride in the management of threatened premature delivery	tokishakuyakusan (当帰芍薬散)	Mizuno M, Sato K, Mori T, et al. Clinical evaluation of TSUMURA Tokishakuyakusan and ritodrine hydrochloride combination therapy in the management of threatened premature delivery*. *Sanka to Fujinka* (*Obstetrics and Gynecology*) 1992; 59: 469-80 (in Japanese).	RCT-envelope	N	UC

ICD-10	Research Question	Kampo Formula	*References*	Study Design	Source	Page No.
O90.9	To evaluate the usefulness of kyukichoketsuin for control of puerperium.	kyukichoketsuin (キュウ帰調血飲)	Takushima Y, Inoguchi H, Study on usefulness of kyukichoketsuin for control of puerperium – comparison with methylergometrine maleate (1st report) -*. *Progress in Medicine* 2001; 21: 1535-42 (in Japanese).	quasi-RCT	I	149
O90.9	To evaluate the efficacy and safety of kyukichoketsuin for puerperal psychosomatic disorder.	kyukichoketsuin (キュウ帰調血飲)	Sakuma K, Ushiroyama T, Akise D, et al. Clinical efficacy of kyukichoketsuin for regulation of puerperal psychosomatic functions. *Sanfujinka no Shinpo* (*Advances in Obstetrics and Gynecology*) 2002; 54: 80-6 (text in Japanese with English abstract).	RCT-envelope	I	150
			Ushiroyama T, Sakuma K, Souen H, et al. Therapeutic effects of Kyuki-chouketsu-in in restoring postpartum physical condition. *The American Journal of Chinese Medicine* 2003; 31: 437-44.		C	
O90.9	To evaluate the clinical usefulness of kyukichoketsuin for "postpartum restoration"	kyukichoketsuin (キュウ帰調血飲)	Wada H, Wada K, Motoyama K. Usefulness in postpartum control by kyukichoketsuin. *Sanfujinka no Sekai* (*World of Obstetrics and Gynecology*) 2003; 55: 1057-61.	RCT	I	151
O90.9	To evaluate the clinical usefulness of kyukichoketsuin during puerperium.	kyukichoketsuin (キュウ帰調血飲)	Narimatsu A., Ito A., Usefulness of kyukichoketsuin during puerperium. *Rinsho Iyaku* (*Journal of Clinical Therapeutics & Medicine*) 2001; 17: 1329-35 (text in Japanese with English abstract).	RCT	I	152
O92.3	To evaluate the postpartum lactation-promoting effect and safety of kyukichoketsuin.	kyukichoketsuin (キュウ帰調血飲)	Ushiroyama T, Sakuma K, Souen H, et al. Xiong-gui-tiao-xue-yin (Kyuki-chouketsu-in), a traditional herbal medicine, stimulates lactation with increase in secretion of prolactin but not oxytocin in the postpartum period. *The American Journal of Chinese Medicine* 2007; 35: 195-202.	RCT-envelope	C	153
O92.5	To determine a Kampo medicine effective for relieving the feeling of lactation deficiency.	kakkonto (葛根湯), Juzentaihoto (十全大補湯), kyukichoketsuin (キュウ帰調血飲), and combination of these Kampo formulations	Kawakami S, Nishimura J, Umeki M, et al. Kampo therapy for feeling of lactation deficiency*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2003; 20: 140-3.	RCT	I	154
O99.0	To determine whether rikkunshito combined with oral iron can improve hemoglobin level and reduce adverse reactions associated with the administration of iron for anemia in pregnant women.	rikkunshito (六君子湯)	Fushiki H, Saeki A, Shiozaki A. Attempt to reduce adverse reactions associated with oral iron preparation for anemia in pregnancy by combination with rikkunshito (TJ-43)*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2003; 20: 138-9 (in Japanese).	RCT	I	155
O99.3	To confirm the efficacy of kyukichoketsuin for the "maternity blues."	kyukichoketsuin (キュウ帰調血飲)	Ushiroyama T, Sakuma K, Ueki M. Efficacy of the Kampo medicine Xiong-gui-tiao-xue-yin (Kyuki-chouketsu-in), a traditional herbal medicine, in the treatment of maternity blues syndrome in the postpartum period. *The American Journal of Chinese Medicine* 2005; 33: 117-26.	RCT-envelope	C	156

Symptoms and Signs (19 abstracts, 27 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
R05	To evaluate the efficacy of bakumondoto for persistent cough after infection in the elderly.	bakumondoto (麦門冬湯)	Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Beneficial effect of Chinese tracitional herbal medicine, Mai-Men-Don-Tang (Japanese name: bakumondo-to) on acute pain in patients with acute internalmedical disease: antitussive effect on elderly patients with post infectious persistent coughs, prospective, multicenter, randomized comparative trial between mai-men-dong-tang and forminoben hydrochloride. *Itami to Kampo* (*Pain and Kampo Medicine*) 2003; 12: 13-21 (text in Japanese with English abstract).	RCT	I	157

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
R11	Effects of a Kampo suppository preparation on vomiting in children	goreisan (五苓散)	Nishi K, Takata K, Asano S, et al. Effects of goreisan suppository on vomiting in children - comparison with domperidone suppository -*. *Nihon Byoin Yakuzaishikai Zasshi* (*Journal of Japanese Society of Hospital Pharmacists*) 1998; 34: 1173-6 (in Japanese).	quasi-RCT	N	UC
R11	To evaluate the efficacy and safety of goreisan for vomiting in young children.	goreisan (五苓散), hochuekkito (補中益気湯)	Yoshida M. Efficacy of goreisan suppository for vomiting in young children*. *Toyoigaku* (*Japanese Journal of Oriental Medicine*) 2000; 28: 36-8 (in Japanese).	DB-RCT	N	158
			Yoshida M, Mizuno T, Mizoguchi F, et al. Efficacy of goreisan suppositories for vomiting in young children (2nd report) – a double-blind study of the hochuekkito suppository–*. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1991; 7: 506-7 (in Japanese).		I	
			Yoshida M. Efficacy of goreisan suppository*. *Nihon Syoni Toyo Igakkaishi* (*The Japan Pediatric Society for Oriental Medicine*) 2003; 19: 13-7 (in Japanese).		I	
R22.4	Efficacy and safety of saireito for posttraumatic or postoperative swelling in the lower extremities	saireito (柴苓湯)	Igarashi I. Clinical study of traditional Chinese medicine therapy for post-operative or post-traumatic swelling in lower extremities. *Seikeigeka* (*Orthopedic Surgery*) 1993; 44: 127-31 (in Japanese).	RCT	N	UC
R25.2	Efficacy and safety of shakuyakukanzoto for preventing muscle cramps in diabetic patients	shakuyakukanzoto (芍薬甘草湯)	Yoshida M, Kitaoka H, Masui Y, et al. Effects of Shakuyaku-Kanzo-to on muscle cramp in diabetics. *Shinkei Chiryogaku* (*Neurological Therapeutics*) 1995; 12: 529-34 (in Japanese).	RCT-envelope	N	UC
R25.2	To evaluate the efficacy and safety of shakuyakukanzoto for relief of muscle cramp.	shakuyakukanzoto (芍薬甘草湯)	Kumada T, Kumada H, Yoshiba M, et al. Effects of shakuyaku-kanzo-to (Tsumura TJ-68) on muscle cramps accompanying cirrhosis in a placebo-controlled double-blined parallel study. *Rinsho Iyaku* (*Journal of Clinical Therapeutics and Medicine*) 1999; 15: 499-523 (text in Japanese with English abstract).	DB-RCT	I	159
		shakuyakukanzoto (芍薬甘草湯)	Kumada T, Kiriyama I, Sone Y, et al. EBM-based Kampo therapy for gastrointestinal diseases 3. Efficacy of shakuyakukanzoto for "muscle cramps in the calves" associated with hepatic cirrhosis*. *Nihon Toyo Igaku Zasshi* (*Kampo Medicine*) 2003; 54: 536-8 (in Japanese).		N	
R25.2	To evaluate the efficacy and safety of shakuyakukanzoto for muscle cramps in the calves.	goshajinkigan (牛車腎気丸), shakuyakukanzoto (芍薬甘草湯)	Nishizawa Y, Nishizawa Y, Amemori Y, et al. A randomized paralleled group comparison in multicenter cooperation: analgesic effect and safety with gosha-jinki-gan and shakuyaku-kanzo-to in the treatment of painful muscle cramps in patients with cirrhosis. *Itami to Kampo* (*Pain and Kampo Medicine*) 2000; 10: 13-8 (text in Japanese with English abstract).	RCT	I	160
R31	Efficacy and safety of kyukikyogaito and saireito for essential microscopic hematuria	kyukikyogaito (キュウ帰膠艾湯), saireito (柴苓湯)	Yoshikawa H, Ikeuchi T, Kai Y. Clinical effects of Kyuki-kyogai-to and Sairei-to for essential microscopic hematuria. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 1997; 6: 55-8 (in Japanese).	RCT	N	UC
R31	Clinical efficacy of saireito for essential hematuria	saireito (柴苓湯)	Suzuki Y, Machida T, Onodera S, et al. Clinical effects of Sairei-to for essential hematuria. *Hinyoki Geka* (*Japanese Journal of Urological Surgery*) 1994; 7: 325-7 (in Japanese).	RCT	I	UC
R39.8	Effects on anti-heat shock protein (HSP) 60 antibody	hachimijiogan (八味地黄丸), seishinrenshiin (清心レン子飲)	Sekiguchi Y, Miyai K, Noguchi K, et al. Study of effects of anti-heat shock protein 60 antibody by Ba wei di huang wan and Qing xin lian zi yin (II). *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1998; 15: 326-7 (in Japanese).	RCT-cross over	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
R51	Efficacy and safety of chotosan for relieving the accompanying symptoms and sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension	chotosan (釣藤散)	Matsushita S, Ueda S, Ouchi Y, et al. Usefulness of chotosan (TJ-47) for relieving the accompanying symptoms and sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension*. *Geriatric Medicine* 1995; 33: 1333-41 (in Japanese).	RCT-envelope	I	UC
R51	Efficacy and safety of chotosan for relieving headache in patients with spinal cord injury	chotosan (釣藤散)	Nishizawa Y, Nishizawa Y, Fushiki S. Analgesic effects on headache in patients with spinal cord injury. *Nippon Zutsu Gakkaishi* (*Japanese Journal of Headache*) 1997; 25: 23-6.	DB-RCT	I	UC
R51	Efficacy and safety of goshuyuto versus keishininjinto for relieving chronic headache	goshuyuto (呉茱萸湯), keishininjinto (桂枝人参湯)	Seki H, Okita N, Takase S, et al. Pain-relieving effect of goshuyuto on chronic headache: comparison with keishininjinto (with randomization carried out using the sealed-envelope method)*. *Pharma Medica* 1993; 11: 288-91 (in Japanese).	RCT-envelope	I	UC
			Seki H, Tateyama M, Sahara M, et al. Pain-relieving effect of goshuyuto on chronic headache: comparison with keishininjinto (with randomization using the sealed-envelope method)*. *Shinryo to Shinyaku* (*Medical Consultation & New Remedies*) 1991; 28: 573-6 (in Japanese).		I	
R51	To evaluate the efficacy of goshuyuto for relief of chronic headache and to evaluate the associated adverse drug reactions.	goshuyuto (呉茱萸湯)	Odaguchi H, Wakasugi A, Ito H, et al. The efficacy of goshuyuto, a typical Kampo (Japanese herbal medicine) formula, in preventing episodes of headache. *Current Medical Research and Opinion* 2006; 22: 1587-97.	DB-RCT	C	161
			Odaguchi H, Hanawa Y. Complementary alternative medicine in headache treatment*. *Igaku no Ayumi* (*Journal of Clinical and Experimental Medicine*) 2005; 215: 1137-40 (in Japanese).		N	
R52.9	To evaluate the efficacy and safety of shakuyakukanzoto and L-glutamine for paclitaxel-induced myalgia and arthralgia.	shakuyakukanzoto (芍薬甘草湯)	Hasegawa K, Mizutani Y, Kuramoto H, et al. The Effect of L-glutamine and shakuyaku-kanzo-to for paclitaxel-induced myalgia/arthralgia. *Gan to Kagaku Ryoho* (*Japanese Journal of Cancer and Chemotherapy*) 2002; 29: 569-74 (text in Japanese with English abstract).	RCT-cross over	I	162
R53	To evaluate the efficacy of hochuekkito for the elderly with weakness.	hochuekkito (補中益気湯)	Satoh N, Sakai S, Kogure T, et al. A randomized double blind placebo-controlled clinical trial of Hochuekkito, a traditional herbal medicine, in the treatment of elderly patients with weakness N of one and responder restricted design. *Phytomedicine* 2005; 12: 549-54.	DB-RCT	C	163
R60.0	Efficacy of goreisan and saireito for mild edema of the dorsum of the foot in the elderly	saireito (柴苓湯)	Ishioka T. Comparison of the efficacy of goreisan and saireito for mild edema of the dorsum of the foot in elderly subjects stratified by physical strength*. *Kampo no Rinsho* (*Journal of Kampo Medicine*) 1997; 44: 1091-5 (in Japanese).	RCT-cross over	N	UC
R60.9	To investigate the efficacy and safety of saireito on postoperative edema and inflammation after total hip arthroplasty (THA).	saireito (柴苓湯)	Kishida Y, Miki H, Nishii T, et al. Therapeutic effects of Saireito (TJ-114), a traditional Japanese herbal medicine, on postoperative edema and inflammation after total hip arthroplasty. *Phytomedicine* 2007; 14: 581-6.	RCT	C	164

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
R73.0	To evaluate the efficacy and safety of bofutsushosan in obese Japanese women with impaired glucose tolerance.	bofutsushosan (防風通聖散)	Hioki C, Yoshimoto K, Yoshida T. Efficacy of Bofu-tsusho-san, an oriental herbal medicine, in obese Japanese women with impaired glucose tolerance. *Clinical and Experimental Pharmacology and Physiology* 2004; 31: 614-9.	DB-RCT	C	165
			Hioki C, Yoshimoto K, Yoshida T. Efficacy of bofu-tsusho-san in obese Japanese women with IGT. *Rinsho Kampo Yakuri Kenkyukai Kaishi*, 2004; 100th Memorial Issue: 19-22.	DB-RCT	I	
			Hioki C. Efficacy of bofutsushosan in obese women with IGT*. *Pharma Medica* 2007; 25: 43-8.	DB-RCT	I	
			Hioki C, Arai M. Bofutsushosan use for obesity with IGT: search for scientific basis and development of effective therapy with Kampo medicine. *Journal of Traditional Medicines* 2007; 24: 115-27.	DB-RCT	N	

Post-anesthesia and Postoperative Pain (2 abstracts, 2 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
T88.5	Efficacy of goshuyuto and goreisan for post-spinal headache	goshuyuto (呉茱萸湯), goreisan (五苓散)	Otake T, Kato I, Saito S, et al. The prophylactic effect of "Gosyuyu-to" and "Gorei-san" for post-spinal headache. *Pain Clinic* 1991; 12: 648-52 (in Japanese).	RCT	N	UC
T88.8	Effects on pain and hyperhidrosis after thoracotomy	keishikajutsubuto (桂枝加朮附湯), keishikajutsubuto (桂枝加朮附湯) ＋ shakuyakukanzoto (芍薬甘草湯)	Isai H. Successful control of postoperative pain and hyperidrosis by Kampo medicine after thoracotomy for pulmonary disease. *Itami to Kampo* (*Pain and Kampo Medicine*) 1997; 7: 29-32 (text in Japanese with English abstract).	RCT	N	UC

Others (26 abstracts, 28 references)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
Z01.8	To evaluate the effect of bakumondoto on cytochrome p450 1A2, xanthine oxidase, and N-acetyltransferase 2 activities.	bakumondoto (麦門冬湯)	Saruwatari J, Hisaeda S, Higa Y, et al. The in-vivo effect of bakumondo-to (TJ-29), a traditional Japanese medicine used for treatment of chronic airway disease, on cytochrome P450 1A2, xanthine oxidase and N-acetyltransferase 2 activity in man. *Journal of Pharmacy and Pharmacology* 2004; 56: 1171-7.	RCT-cross over	C	166
Z01.8	To evaluate the effect of shoseiryuto on blood carbamazepine concentration.	shoseiryuto (小青竜湯)	Ohnishi N, Yonekawa Y, Fumihara T. et al. Studies on interactions between traditional herbal and Western medicines, II. Lack of pharmacokinetic interaction between Shoseiryu-to and carbamazepine in healthy volunteers. *TDM Kenkyu (Japanese Journal of Therapeutic Drug Monitoring)* 1999; 16: 399-404.	RCT-cross over	I	167
			Yonekawa Y, Ohnishi N, Kitano N, et al. Drug interaction with Kampo medicines (2): kinetic characteristics of carbamazepine combined with shoseiryuto in healthy volunteers. *TDM Kenkyu* (*Japanese Journal of Therapeutic Drug Monitoring*) 1999; 16: 191-2.		N	
Z01.8	To evaluate the effect of hachimijiogan on human central retinal artery.	hachimijiogan (八味地黄丸)	Isobe H, Yamamoto K, Cyong JC. Effects of Hachimi-jio-gan (Ba-wei-di-huang-wan) on blood flow in the human central retinal artery. *The American Journal of Chinese Medicine* 2003; 31: 425-35.	RCT-cross over	C	168
Z01.8	To assess the efficacy and safety of hochuekkito on antibody production after influenza vaccination.	hochuekkito (補中益気湯)	Hamazaki K, Sawazaki S, Itomura M, et al. No effect of a traditional Chinese medicine, Hochu-ekki-to, on antibody titer after influenza vaccination in man: a randomized, placebo-controlled, double-blind trial. *Phytomedicine* 2007; 14: 11-4.	DB-RCT	C	169

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
Z01.8	To evaluate the effect of maobushisaishinto on antibody titer after influenza vaccination.	maobushisaishinto (麻黄附子細辛湯)	Terashima Y, Hamazaki K, Itomura M, et al. Effect of a traditional Chinese medicine, maobushisaishinto, on the antibody titer after influenza vaccination: A randomized, placebo-controlled, double-blind trial. *Journal of Traditional Medicines* 2007; 24: 59-66.	DB-RCT	I	170
Z01.8	To elucidate the mechanism of bushirichuto activity in raising gut-regulated peptide levels.	bushirichuto (附子理中湯)	Sato Y, Katagiri F, Itoh H, et al. Bushi-richu-to Raises Calcitonin Gene-related Peptide, Substance P, Somatostatin, and Vasoactive Intestinal Polypeptides Levels in Human Plasma. *Journal of Health Science* 2007; 53: 615-21.	RCT-cross over	I	171
Z01.8	To examine effects of rokumigan on serum amino acid concentrations.	rokumigan (六味丸)	Takahashi H, Nakao R, Hirasaka K, et al. Effects of single administration of Rokumi-gan (TJ-87) on serum amino acid concentration of 6 healthy Japanese male volunteers. *Journal of Medical Investigation* 2007; 54: 91-8.	RCT-cross over	I	172
Z01.8	Interaction with the pharmacokinetics of acetaminophen	kakkonto (葛根湯)	Qi J, Toyoshima A, Honda Y, et al. Pharmacokinetic study on acetaminophen: interaction with a Chinese medicine.*Journal of Medical and Dental Sciences* 1997; 44: 31-5.	RCT-cross over	C	UC
Z01.8	Effects of kakkonto on the pharmacokinetics of phenacetin	kakkonto (葛根湯)	Shimakura K, Mineshita S, Sanaka M, et al. Effects of kakkonto on the pharmacokinetics of phenacetin in human serum and saliva*. *Rinsho Yakuri* (*Japanese Joournal of Clinical Phamacology and Therapeutics*) 1994; 25: 229-30 (in Japanese).	RCT-cross over	N	UC
Z01.8	Effects of saibokuto and saikokaryukotsuboreito on central nervous systems in humans	saibokuto (柴朴湯), saikokaryukotsuboreito (柴胡加竜骨牡蛎湯)	Fukushima M. Profiles of effects of traditional oriental herbal medicines on central nervous system in humans - assessment of Saiboku-to and Saiko-ka-ryukotsu-borei-to using EEG and pharmacokinetics of herbal medicine-derived ingredients as indices -. *Seishin Shinkeigaku Zasshi* (*Psychiatria et Neurologia Japonica*) 1997; 99: 355-69 (text in Japanese with English abstract).	RCT	N	UC
Z01.8	Effects on bioavailability of ofloxacin (OFLX) in healthy volunteers	shosaikoto (小柴胡湯), rikkunshito (六君子湯), saireito (柴苓湯)	Hasegawa T, Yamaki K, Nadai M, et al. Lack of effect of Chinese medicines on bioavailability of ofloxacin in healthy volunteers. *International Journal of Clinical Pharmacology and Therapeutics* 1994; 31: 57-61.	RCT-cross over	C	UC
Z01.8	Effects on prednisolone metabolism	shosaikoto (小柴胡湯), saibokuto (柴朴湯), saireito (柴苓湯)	Homma M, Oka K, Ikeshima K, et al. Different effects of traditional Chinese medicines containing similar herbal constituents on prednisolone pharmacokinetics. *Journal of Pharmacy and Pharmacology* 1995; 47: 687-92.	RCT-cross over	C	UC
	Effects on prednisolone metabolism		Niitsuma T, Fukuda T, Yamamoto S, et al. Effects of saibokuto and other *Saiko-zai* (Saiko-drugs) on prednisolone metabolism*. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 1993; 7: 43-52 (in Japanese).		N	
Z01.8	Effect of coadministered Kampo medicine on the pharmacokinetics of levofloxacin (Cravit)	hochuekkito (補中益気湯), rikkunshito (六君子湯), juzentaihoto (十全大補湯)	Hasegawa T, Yamaki K, Muraoka I, et al. Effects of traditional Chinese medicines on pharmacokinetics of levofloxacin. *Antimicrobial Agents and Chemotherapy* 1995; 39: 2135-37.	RCT-cross over	C	UC
Z03.8	Efficacy of shakuyakukanzoto for relieving pain during colonoscopy	shakuyakukanzoto (芍薬甘草湯)	Arai M, Sato H, Shirota F. An investigation into the relief of colonscopy pain provided by Shakuyaku-kanzo-to. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 1994; 44: 385-90 (text in Japanese with English abstract).	RCT	N	UC
Z03.8	Efficacy of shakuyakukanzoto for relieving pain and complaints during preparation for barium enema	shakuyakukanzoto (芍薬甘草湯)	Imazato S, Kai S, Koizumi K, et al. A clinical study of Shakuyaku-Kanzo-to (Kampo) as a preparation for double contrast barium enema. *Therapeutic Research* 1997; 18: 5505-10 (text in Japanese with English abstract).	RCT	N	UC

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
Z03.8	Efficacy of a new colon preparation using daiokanzoto	daiokanzoto (大黄甘草湯)	Yokota H, Kanazawa H, Kondo T, et al. New colon preparation using the Kampo herb method (Daio-kanzo-to). *Therapeutic Research* 1989; 10: 1637-43 (text in Japanese with English abstract).	RCT	N	UC
Z03.8	To evaluate the efficacy of shakuyakukanzoto combined with polyethylene glycol solution (PEG) in pretreatment for large bowel endoscopy.	shakuyakukanzoto (芍薬甘草湯)	Saida Y, Takase M, Okumura C, et al. Efficacy of combined use of shakuyakukanzoto in pretreatment for large bowel endoscopy – prospective randomized trial*. *Nihon Daicho Kensa Gakkai Zasshi* (*Journal of the Japan Society of Colon Examination*) 2003; 20: 34-7 (in Japanese).	RCT-envelope	I	173
Z03.8	To evaluate the efficacy of directly sprayed shakuyakukanzoto on large bowel spasm.	shakuyakukanzoto (芍薬甘草湯)	Ai M. Assessment of the antipasmodic effect of peppermint oil and shakuyaku-kanzon-to (TJ-68); a Chinese herbal medicine on the clonic wall. *Medical Tribune Online* (*Digestive Disease Week: DDW*) 2005: 10-1 (in Japanese).	RCT	N	174
Z03.8	To evaluate the efficacy of pretreatment with shakuyakukanzoto for upper gastrointestinal tract endoscopy.	shakuyakukanzoto (芍薬甘草湯)	Sugihara N. Effectiveness of shakuyaku-kanzo-to as a pretreatment for upper digestive tract endoscopic examination*. *Kampo Shinryo* 1999; 18: 17-9 (in Japanese).	quasi-RCT	N	175
Z03.8	To evaluate the efficacy of daikenchuto combined with polyethylene glycol solution (PG solution) in pretreatment for large bowel endoscopy.	daikenchuto (大建中湯)	Saida Y, Sumiyama Y, Nagao J, et al. Dai-kenchu-to, a herbal medicine, improves precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage: results of a prospective randomized controlled trial. *Digestive Endoscopy* 2005; 17: 50-3.	RCT-envelope	I	176
Z03.8	To evaluate the efficacy and safety of direct spraying of shakuyakukanzoto on the colonic mucosa for suppression of bowel movement during colonoscopy.	shakuyakukanzoto (芍薬甘草湯)	Ai M, Yamaguchi T, Odaka T, et al. Objective assessment of the antispasmodic effect of shakuyaku-kanzo-to (TJ-68), a Chinese herbal medicine, on the colonic wall by direct spraying during colonoscopy. *World Journal of Gastroenterology* 2006; 12: 760-4.	RCT	C	177
Z03.8	To evaluate the efficacy of shakuyakukanzoto solution in preparation for colonoscopy used with the water method of distension.	shakuyakukanzoto (芍薬甘草湯)	Mizukami T., Maruyama K., Yamauchi H., et al. Assessment of antispasmodic effect of herbal medicine, shyakuyakukanzoto (TJ-68) on colonoscopy – Using colonoscopy insertion technique “collapsing method” –. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2006; 15: 69-76 (in Japanese).	quasi-RCT	I	178
Z03.8	To determine the bowel cleansing effect of precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage solution (PG solution) combined with daikenchuto and mosapride.	daikenchuto (大建中湯)	Saida Y, Nagao J, Nakamura Y, et al. Dai-kenchu-to and mosapride in combination with precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage: results of a prospective randomized controlled trial. *Nihon Daicho Kensa Gakkai Zasshi* (*Journal of the Japan Society of Colon Examination*) 2005; 22: 145-8 (in Japanese).	RCT	I	179
Z03.8	To determine the effectiveness of daikenchuto in bowel preparation for barium enema X-ray study.	daikenchuto (大建中湯)	Arai J, Nakajima S, Fujinuma S, et al. A Comparative study of bowel preparation for barium enema using divided administrations of powdered magnesium citrate with mosapride or DAIKEN CHUTOU. *Nihon Daicho Kensa Gakkai Zasshi* (*Journal of the Japan Society of Colon Examination*) 2002; 19: 170-3 (in Japanese).	RCT	I	180
Z22.8	To evaluate the effects of hochuekkito on prevention of MRSA carriage, prevention of Pseudomonas aeruginosa carriage, prevention of infection development, neutrophil count, and C-reactive protein (CRP) value.	hochuekkito (補中益気湯)	Ueda T, Yamashita K, Nakamori Y, et al. Study of the MRSA carriage-preventing effect of hochuekkito (TJ-41): 1st report*. *Progress in Medicine* 1999; 19: 1000-3 (in Japanese).	RCT	N	181

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
Z31.1	Effect of ovarian stimulation by tokishakuyakusan (used during in vitro fertilization and embryo transfer (IVF-ET) cycles) on follicular growth, luteal function, pregnancy rate, and abortion rate	tokishakuyakusan (当帰芍薬散)	Fujii S, Fukushi Y, Yamaguchi E, et al. A study of the addition of tokishakuyakusan during in-vitro fertilization cycles*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 1997; 14: 121-5 (in Japanese).	RCT	N	UC

<<A Structured Abstract describing Meta-analysis and the Reference Reporting It>>

Ante/Post-partum Diseases (1 abstract, 1 reference)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
O90.8	To evaluate the efficacy of kyukichoketsuin (KCL) in puerperal care in comparison with methylergometrine maleate (MME).	kyukichoketsuin (キュウ帰調血飲)	Koinuma M, Narikawa H, Kamei M, et al. Meta-analysis on the usefulness in postpartum control by kyukichoketsuin with methylergometrine maleate as control. *Nihon Toyo Igaku Zasshi* (*Kampo Medicine*) 2006; 57: 45-55 (text in English with Japanese abstract).	Meta-analysis	I	183

Structured Abstracts

(320 abstracts describing RCTs)

□Each bibliographic item is followed by its ID No. from a particular searched database (CENTRAL ID, PubMed ID, or Ichushi web ID).

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Infections (including Viral Hepatitis)

Reference

Seki T, Matsumoto T, Deguchi H, et al. Evaluation of the efficacy of hochuekkito in preventing MRSA colonization and infection*. *Kampo Igaku* (*Kampo Medicine*) 1999; 23: 196-7 (in Japanese). Ichushi Web ID: 2000068588

1. Objectives

To determine whether hochuekkito has efficacy in preventing colonization and infection with methicillin-resistant *Staphylococcus aureus* (MRSA).

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Department of Traumatology and Critical Care Medicine, Dokkyo Medical University Koshigaya Hospital

4. Participants

Ninety-five patients admitted to the above hospital.

5. Intervention

Arm 1: treatment with hochuekkito (補中益気湯) (2.5 g, t.i.d.) per os (p.o.) or using a nasogastric tube; every day from the third day of hospitalization.
Arm 2: no treatment with hochuekkito.

6. Main outcome measures

From all patients, nasal, throat, and urine specimens were cultured for MRSA on the second hospital day, one week later, and then once a week. Sputum was also cultured from patients who underwent endotracheal intubation or tracheotomy and from those who were able to provide sputum. Similarly wound cultures were performed for patients with wound infection. When at least one culture of any specimen was positive for MRSA, the patient was considered to be MRSA-positive.

7. Main results

A total of 63 patients - 30 of 48 in arm 1 and 33 of 47 in arm 2 - withdrew from the study. Among these withdrawals, 25 patients in arm 1 and 32 in arm 2 were transferred to other wards or died, 3 received no hochuekkito, and 3 underwent no laboratory follow-up (cultures). Thus, 18 patients in arm 1 and 14 in arm 2 were examined and compared. The most common disease was trauma, followed by cerebrovascular disorder. There was no significant difference in MRSA positivity between arm 1 (8 of 18 patients) and arm 2 (9 of 14 patients). Among the trauma patients, however, there was a trend toward lower MRSA positivity in hochuekkito-treated patients (5 of 11 [45.5%] being positive), compared with hochuekkito-untreated patients (5 of 7 [71.4%] being positive). A similar trend toward lower MRSA positivity in hochuekkito-treated patients was found among patients who required mechanical ventilation.

8. Conclusions

It is suggested that administration of hochuekkito could prevent MRSA infection.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The authors deserve praise for conducting this RCT in an emergency care setting. Given the setting, it is not surprising that many patients (66%) withdrew from the study. But the authors' reasons for the withdrawals provide readers with very useful information. They also described gown use and hand washing by medical personnel and visitors, reflecting their consideration of bias and confounding factors. Unfortunately, this study included only a small number of patients. If it had employed a blinded, placebo-controlled design, the report would have been more reliable. The development of future studies is expected.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Infections (including Viral Hepatitis)

Reference

Suzuki J, Arata S, Sugiyama M. Improvement of immunity and nutrition by hochuekkito in immuno-compromised hosts – for the control of MRSA –*. *Progress in Medicine* 2002; 22: 1362-3 (in Japanese). Ichushi Web ID: 2002261757 MOL, MOL-Lib

1. Objectives

To determine whether hochuekkito (補中益気湯) can improve immune and nutritional status in immuno-compromised hosts.

2. Design

Randomized controlled trial (RCT).

3. Setting

Critical Care and Emergency Center, Yokohama City University Medical Center.

4. Participants

Twenty-six immuno-compromised patients who were admitted to the above center. Of these, 13 patients received hochuekkito or placebo for three weeks or longer.

5. Intervention

Arm 1: oral or enteral administration of hochuekkito (補中益気湯) (2.5 g t.i.d.) in 7 patients (all males; mean age 53.3±5.6 years).

Arm 2: administration of the same amount of lactose (placebo) in 6 patients (4 males and 2 females; mean age 53.0±7.7 years).

6. Main outcome measures

Serum albumin level and peripheral lymphocyte count (at baseline, 1, 2, 3, and 4 weeks after the start of the treatment).

Change in prognostic nutrition index (PNI=[albumin level]×10+[peripheral lymphocyte count]×0.005).

7. Main results

There was no significant difference between the two arms in serum albumin level and peripheral lymphocyte count. In placebo-treated patients, PNI increased 1 week after the start of treatment, but decreased in the following week, then increased again. PNI was significantly higher in hochuekkito-treated patients than in placebo-treated patients ($P<0.05$).

8. Conclusions

PNI value was significantly increased by hochuekkito treatment.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The authors deserve praise for attempting the RCT in an emergency care setting. Since PNI is a surrogate outcome measure, future trials focusing on outcomes that involve the presence or absence of infection and quantity of nutrition, as mentioned in the last part of the present results, are anticipated. Although the number of patients in this study is small, future studies are expected to be larger and confirmatory. In the results of this paper, MRSA infection was identified in 4 of 9 previously non-infected patients in the lactose arm and only 1 of 8 in the hochuekkito arm.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 1 May 2009, 8 August 2009.

Infections (including Viral Hepatitis)

Reference

Higuchi K, Arakawa T, Ando K, et al. Eradication of Helicobacter pylori with a Chinese herbal medicine without emergence of resistant colonies. *American Journal of Gastroenterology* 1999; 94: 1419-20. CENTRAL ID: CN-00162864, Pubmed ID: 10235237

1. Objectives

To determine the efficacy and safety of triple therapy with proton pump inhibitor, antibiotic, and goshuyuto (呉茱萸湯) for *Helicobacter pylori* (*H. pylori*) infection.

2. Design

Randomized controlled trial (RCT).

3. Setting

No description of the setting is available; the authors belong to the Third Department of Internal Medicine, Osaka City University Medical School.

4. Participants

Sixty-three patients infected with *H. pylori*.

5. Intervention

Arm 1: treatment with omeprazole (40 mg/day), amoxicillin (1,500 mg/day), and goshuyuto (呉茱萸湯) (7.5 g/day), n=32.
Arm 2: treatment with omeprazole (40 mg/day) and amoxicillin (1,500 mg/day), n=31.
The duration of treatment was 2 weeks.

6. Main outcome measures

Histologic evaluation of gastric biopsy specimen and rapid urease test were performed.
The outcomes were evaluated at 4 weeks after the treatment.

7. Main results

H. pylori eradication rates were 60% in the double therapy arm and 80% in the triple therapy arm. There was no emergence of goshuyuto- or amoxicillin-resistant bacteria even in cases where treatment failed to eradicate *H. pylori*.

8. Conclusions

The novel triple therapy containing goshuyuto improves the eradication rate without increasing incidences of adverse effects and treatment resistance by *H. pylori*. This therapy is a useful tool for eradicating *H. pylori*.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Side effects were similar in arm 1 (4 patients with diarrhea) and in arm 2 (4 patients with diarrhea and 1 with abdominal pain). No serious adverse effects were observed.

11. Abstractor's comments

In this study, goshuyuto was used differently from its original application of Kampo medicine. This article, as a Letter to the Editor, lacks adequate descriptions, so the submission as an original article is desired.

12. Abstractor and date

Arai M, 15 June 2007, 1 April 2008, 8 August 2009.

Infections (including Viral Hepatitis)

Reference

Taniguchi S, Kono T, Terai T. Preventive effect of hochuekkito on postherpetic neuralgia*. *Progress in Medicine* 2002; 22: 863-5 (in Japanese). Ichushi Web ID: 2002176936

1. Objectives

To determine whether hochuekkito (補中益気湯) has a preventive effect on postherpetic neuralgia (PHN).

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital (one department of dermatology).

4. Participants

Fifty-seven patients with acute-phase herpes zoster.

5. Intervention

Arm 1: oral administration of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules (2.5 mg t.i.d.) for 12 weeks (42 patients: 12 males and 30 females; mean age, 69.2 years).

Arm 2: no treatment with hochuekkito (補中益気湯) (15 patients: 5 males and 10 females; mean age, 66.9 years).

6. Main outcome measures

Pain intensity was evaluated by visual analogue scale (VAS) at baseline, and 12 and 24 weeks after the start of treatment. Obtained data are expressed as median (25 percentile, 75 percentile).

7. Main results

VAS score in the hochuekkito arm and control arm was respectively 7.1 (6.5, 7.4) and 6.9 (5.5, 7.9) at baseline, 4.1 (3.0, 5.4) and 3.5 (1.7, 5.1) at 12 weeks, 1.4 (0.5, 2.3) and 2.9 (1.7, 4.2) at 24 weeks. The ratio of VAS score at 24 weeks to that at baseline (rVAS) was significantly different between the hochuekkito arm (0.20 [0.09, 0.30]) and control arm (0.42 [0.33, 0.53]).

8. Conclusions

During the acute phase of herpes zoster, 12-week oral administration of hochuekkito significantly controlled PHN at 24 weeks. Hochuekkito therefore has a preventive effect on PHN.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

In one of the 42 hochuekkito-treated patients, transient stomach discomfort developed, which did not interfere with continuation of the treatment.

11. Abstractor's comments

Many patients suffer from PHN for years. This study provides valuable insight. Since similar results were described in "Taniguchi S, Terai T, Kono T, et al. The effect of hochuekkito on postherpetic neuralgia*. *Hifu no Rinsho* (*Clinical Practice of Dermatology*) 1999; 41: 601-3 (in Japanese)", I would include a comment on that finding in the present study. Although the authors found no between-group difference in age, affected area, number of days with symptoms, underlying disease, and concomitant medications, there was a between-group difference in the number of cases. This problem is related to the incidence of PHN, so an examination of the influence of incidence of PHN on the study results is needed. The outcomes of these studies are clinically relevant, and results of further studies are expected.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Infections (including Viral Hepatitis)

Reference

Nakajima O, Sone M, Kurokawa K, et al. The Complemental treatment for chronic hepatitis C. *Kagaku Ryoho Kenkyusyo Kiyo* (*Bulletin of the Institute of Chemotherapy*) 2003; 34: 40-51 (text in Japanese with English abstract). Ichushi Web ID: 2004188041

1. Objectives

To confirm the efficacy of shosaikoto (小柴胡湯) for interferon-resistant chronic hepatitis C.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

One university hospital and general hospitals.

4. Participants

One hundred patients with chronic active hepatitis C who completed interferon therapy.

5. Intervention

Arm 1: treatment with squalene 1500 mg/day.(n=33)
Arm 2: treatment with cepharanthine (1 mg/kg body weight per day). (n=33)
Arm 3: treatment with shosaikoto (小柴胡湯) 6.0 g/day. **(**n=34**)**
In all arms, study drugs were orally administered in three divided daily doses before meals for 5 years.

6. Main outcome measures

Levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), procollagen III peptide (PIIIP), type IV collagen, and hepatitis C virus (HCV)-RNA.

7. Main results

AST and ALT showed overall significant decreases, except for transient elevations after 6 and 30 months of treatment. Type IV collagen, PIIIP, and HCV-RNA also decreased significantly in all arms. No significant differences in these variables were observed among the three arms. AST and ALT were significantly decreased at 50 months in arm 3, but not in arms 1 and 2. Choline esterase (Ch-E) did not change in arm 3, but decreased significantly in arms 1 and 2. Type IV collagen and HCV-RNA decreased significantly in arm 3 and increased significantly in arms 1 and 2. Changes in PIIIP were similar to those of type IV collagen.

8. Conclusions

Shosaikoto is effective for the treatment of chronic hepatitis C and its efficacy is equivalent to that of squalene or cepharanthine.

9. From Kampo medicine perspective

One patient with "*in-sho* (陰証, yin pattern)" and "*kyo-sho* (虚証, deficiency pattern)" was excluded before the allocation, and the study was actually conducted in 99 patients.OK

10. Safety assessment in the article

None.

11. Abstractor's comments

This study confirmed the efficacy of shosaikoto for the treatment of chronic hepatitis C.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Infections (including Viral Hepatitis)

Reference

Nakajima O, Sone M, Onishi H, et al. Preventive effect of shosaikoto on the progression of chronic hepatitis C to cirrhosis*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1999; 76: 176-84 (in Japanese). Ichushi Web ID: 1999207089 MOL, MOL-Lib

1. Objectives

To confirm the efficacy of shosaikoto (小柴胡湯) for chronic hepatitis C.

2. Design

Randomized controlled trial (RCT).

3. Setting

Multiple general hospitals.

4. Participants

Ninety-nine patients with chronic active hepatitis C who completed interferon therapy.

5. Intervention

Arm 1: oral administration of Kanebo Shosaikoto (小柴胡湯) Extract Fine Granules 6 g/day, t.i.d.(n=49)
Arm 2: oral administration of one of the commonly used liver protectors.(n=50)
Patients were followed for 50 months in both arms.

6. Main outcome measures

Level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), choline esterase (Ch-E), procollagen III peptide (PIIIP), type IV collagen, and hepatitis C virus (HCV)-RNA.

7. Main results

AST and ALT were significantly decreased at 50 months in arm 1, but not in arm 2. Ch-E did not change in arm 1, but decreased significantly in arm 2. Type IV collagen and HCV-RNA decreased significantly in arm 1, and increased significantly in arm 2. Changes in PIIIP were similar to those of type IV collagen.

8. Conclusions

Shosaikoto is effective for the treatment of chronic hepatitis C, and its prevention of the progression to cirrhosis is implied.

9. From Kampo medicine perspective

Patients with "*in-sho* (陰証, yin pattern)" and "*kyo-sho* (虚証, deficiency pattern)" were excluded before the allocation.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study confirmed the efficacy of shosaikoto for the treatment of chronic hepatitis C.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Yamada T. Randomized controlled trial of the efficacy of juzentaihoto (TJ-48) combined with oral 5-FU for gastric cancer*. *Progress in Medicine*. 2004; 24: 2746-7 (in Japanese)

1. Objectives

To evaluate the efficacy of juzentaihoto (十全大補湯; TJ-48) combined with oral 5-FU as postoperative adjuvant chemotherapy in patients with surgically treated gastric cancer.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Fifteen hospitals associated with Gifu University.

4. Participants

Ninety-four patients with surgically treated gastric cancer satisfying the following 8 criteria were included: (1) curability A or B; (2) no serious complications; (3) no preoperative treatment; (4) no double or multiple cancer; (5) WBC ≥3,000/mm^3, Plt ≥70,000/mm^3, total protein ≥ 6.0g/dL, AST/ALT ≤60 IU/L, and urinary protein (-), before the start of chemotherapy; (6) no possibility of pregnancy; (7) performance status of grade 0 or 1; (8) receipt of consent to participate in the study from patient or family member.

5. Intervention

Arm 1: monotherapy group; continuous treatment with 5-FU tablets (200 mg/day) for 2 years starting 2 weeks after surgery; 51 patients.

Arm 2: combination therapy group; continuous treatment with 5-FU tablets (200 mg/day) combined with TSUMURA Juzentaihoto (十全大補湯) Extract Granules (TJ-48; 7.5 g/day) for 2 years starting 2 weeks after surgery; 43 patients.

6. Main outcome measures

Five-year survival rate, 5-year survival rate by clinical stage.

7. Main results

Five-year survival rate was 74.3% in arm 1 and 73.5% in arm 2, indicating no significant difference between arms. By clinical stage, patients with stage I or II had 2-year and 5-year survival rates of 92% and 90%, respectively, in arm 1 (n=42), and 91% and 83%, respectively, in arm 2 (n=35), indicating no significant difference between arms. In contrast, patients with stage III or IV had 2-year and 5-year survival rates of 22% and 0%, respectively, in arm 1 (n=9), and 87% and 25%, respectively, in arm 2 (n=8), with median survival of 35.1 months in arm 2 and 14.2 months in arm 1, demonstrating significantly extended survival of patients treated with juzentaihoto.

8. Conclusions

Combination of juzentaihoto with oral 5-FU was effective for patients with surgically treated stage III or IV gastric cancer.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The finding that the combination with juzentaihoto extends the postoperative survival of patients with surgically treated gastric cancer is clinically very impressive. The adverse drug reactions (ADRs) associated with this anticancer treatment are also of interest. Also, some information on study design (such as blinding) is lacking, making further evaluation difficult. Publication of the original paper is awaited.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

References

Sasaki K, Ezoe E, Araya J, et al. Effects of Kampo medicine on the immune Functions in gastrointestinal gastroenteric cancer patients– utility from the perspective of immunity. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2006; 15: 9-14 (in Japanese).
Sasaki K, Takasaka H, Furuhata T, et al. Effect of Kampo medicine on the cancer chemotherapy of cancer. *Geka Chiryo* (*Surgical Therapy*) 2007; 97: 504-10 (in Japanese). MOL, MOL-Lib

1. Objectives

To determine the clinical efficacy of juzentaihoto (十全大補湯) for the prevention of postoperative recurrence of colorectal cancer.

2. Design

Randomized controlled trial (RCT).

3. Setting

The First Department of Surgery of Sapporo Medical University and other institutions (their names, unspecified).

4. Participants

One hundred and sixty-eight patients (mean age, 65 years) with stage II or III colorectal cancer who received curative resection and adjuvant chemotherapy between July 2001 and March 2005.

5. Intervention

Arm 1: treatment with oral 5-FU and juzentaihoto (十全大補湯) (manufacturer, not specified) 7.5 g/day, n=86.
Arm 2: treatment with oral 5-FU, n=82.

6. Main outcome measures

Recurrence rate, time to recurrence, and survival time.

7. Main results

Mean postoperative follow-up was 38.6 months. Recurrence rate for patients with stage II disease was slightly, though not significantly, more favorable in arm 1 (6.9%) than in arm 2 (14.0%). Mean times to recurrence were 18.2 months in arm 1 and 16.9 months in arm 2. The 3-year recurrence-free survival rate was slightly, though not significantly, better in arm 1: 92.2% in arm 1 and 85.9% in arm 2 for patients with stage II disease, and 67.5% and 62.9%, respectively, for patients with stage III disease.

8. Conclusions

Juzentaihoto may have a metastasis-suppressive effect, but since these are interim reports, the follow-up is still ongoing.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

These two papers are interim reports on a multicenter clinical study that evaluated the clinical efficacy of juzentaihoto for the prevention of postoperative recurrence of colorectal cancer. The data from slightly less than 100 patients in each arm were analyzed. At this point, no clear difference is observed between the juentaihoto-treated arm and the control arm, although the outcomes tend to be slightly more favorable in the former. A final report is anticipated. This abstract summarized mainly data from the second, recently published, paper mentioned above.

12. Abstractor and date

Oikawa T, 31 December 2008, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Takagi K, Nagata H, Horie T, et al. Effect of the preventive herbal therapy using Dai-kenchu-to on intestinal obstruction following curative resection for colorectal cancer: prospective, randomized study. *Kampo Kenkyu* (*Kampo Research*) 2007; (429): 270-1 (in Japanese). Ichushi Web ID: 2008028028

1. Objectives

To determine the effects of daikenchuto (大建中湯) on intestinal obstruction following colorectal cancer surgery.

2. Design

Randomized controlled trial (RCT).

3. Setting

Second Department of Surgery, Dokkyo University School of Medicine.

4. Participants

One hundred and seventy-five patients who underwent surgery for colorectal cancer (cecal colon [n=119] or rectal [n=56] cancer).

5. Intervention

Arm 1: treatment with daikenchuto (大建中湯) (manufacturer, not specified) 27 g/day (n=86).
Arm 2: no treatment (n=87).

6. Main outcome measures

The percentage of patients who postsurgically developed each of the following: ileus, abdominal pain, abdominal distention, and irregular bowel movements.

7. Main results

The between-arm difference in the percentage of patients who developed ileus in arms 1 (1.16%) and 2 (5.75%) or who experienced abdominal distension in arms 1 (2.33%) and 2 (6.90%) was not significant.
A significantly smaller percentage of patients in arm 1 developed abdominal pain (1.16% *vs* 9.20% [for arm 2]; *P*=0.042) or experienced irregular bowel movements (3.49% *vs* 13.79% [for arm 2]; *P*=0.033).

8. Conclusions

Daikenchuto extract fine granules did not prevent ileus following colorectal cancer surgery, but did result in the reduction of postoperative abdominal pain and irregular bowel movements.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The description of the study method in the present paper is extremely inadequate, and the protocol itself is problematic. Details, such as duration of treatment with daikenchuto extract fine granules, outpatient or inpatient setting, length of follow-up, and definitions of abdominal pain, abdominal distention, or irregular bowel movement are not given. Significant results would have been obtained if the authors had defined these specifics. Therefore, I recommend a rewrite of this paper after these details are clarified and the results are reviewed.

12. Abstractor and date

Hoshino E, 17 March 2009, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Kato S, Kishiro I, Machida S, et al. Combined effects of hochu-ekki-to (*Bu-Zhong-Yi-Qi-Tang*) and clorithromycin on Lung Carcinoma. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 1999; 13: 83-8 (text in Japanese with English abstract).

1. Objectives

To evaluate the efficacy of hochuekkito (補中益気湯) combined with clarithromycin (CAM) for improvement in the prognosis of lung cancer.

2. Design

Randomized controlled trial (RCT).

3. Setting

A university hospital (Department of Internal Medicine, Dokkyo Medical University Hospital).

4. Participants

Thirty-five patients with primary lung cancer lesions that responded to chemotherapy or radiotherapy either partially or completely (21 males, 14 females; mean age, 63.2±6.7 years; performance status [P.S.] 0-2; baseline clinical stage Ia [n=5], Ib [n=21], and II [n=9]; squamous cell carcinoma [n=14], adenocarcinoma [n=21]).

5. Intervention

Arm 1: combination therapy group; 400 mg/day of CAM + 7.5 g/day of hochuekkito (補中益気湯) extract granules administered to 17 patients (10 males, 7 females; mean size reduction of the primary lesion, 62.8 ± 11.2%).

Arm 2: monotherapy group; 400 mg/day of CAM administered to 18 patients (11 males, 7 females; mean size reduction of the primary lesion, 66.7±8.6%).

6. Main outcome measures

Tumor markers, NK cell activity (at baseline, and 2 and 12 months after the start of treatment), and 1-year survival.

7. Main results

Serum levels of tumor markers were significantly elevated in both treatment groups compared with the control group**.** In patients surviving 1 year after the start of treatment, NK cell activity, representing immunoreactivity, was elevated in both treatment groups, and was significantly higher in the combination therapy group than the control group.

8. Conclusions

The combination (hochuekkito plus CAM) seems to be effective for maintaining the efficacy of chemotherapy and radiotherapy.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study deserves praise for attempting to conduct RCT targeting a difficult-to-treat pathology of lung cancer prognosis. Regrettably, however, it is unclear whether "the control group" mentioned here refers to the CAM monotherapy group or yet another group, or to a before-after comparison in the same group. Clarification of the study is expected.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

References

Oda T. My prescription – clinical application of ninjin'yoeito during chemotherapy for gynecologic cancer: the preventive effect on bone marrow suppression*. *WE* 2004; 9: 5-6 (in Japanese). Ichushi Web ID: 2006050757

Oda T, Ohnuki T, Kihara K, et al. A clinical study of a traditional Chinese herbal medicine, NINJIN-YOUEI-TO in bone marrow suppression due to chemotherapy in gynecologic cancer. *Yamagata Kenritsu Byoin Igaku Zasshi (The Yamagata Journal of Medicine)* 2004; 38; 6-9 (in Japanese). Ichushi Web ID: 2004222295

1. Objectives

To determine the efficacy of ninjin'yoeito (人参養栄湯) for reducing myelosuppression due to chemotherapy for gynecologic cancer.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

One hospital.

4. Participants

Eight patients who underwent surgery for gynecologic cancer (ovarian [n=6], uterine [n=1], or fallopian tube [n=1] cancer) and received granulocyte colony-stimulating factor (G-CSF) for neutropenia during the first cycle of chemotherapy (CAP: cyclophosphamide, Farmorubicin [epirubicin], cisplatin).

5. Intervention

Arm 1: treatment with Kanebo Ninjin'yoeito (人参養栄湯) Extract Fine Granules (7.5 g/day in two divided doses) continuously from 1 to 2 weeks prior to the start of the second cycle of chemotherapy (n=4).

Arm 2: no treatment with ninjin'yoeito (n=4).

6. Main outcome measures

The following measures during the second and third cycles of chemotherapy: nadir leukocyte and neutrophil counts, the length of time for neutrophil count to fall below 1,000/μL, total dose of G-CSF, duration of neutrophil counts under 1,000/μL, and nadir hemoglobin level and platelet count.

7. Main results

There were no significant between-arm differences in nadir leukocyte, neutrophil, and platelet counts or in the length of time for the neutrophil count to fall below 1,000/μL. Duration of neutrophil count under 1,000/μL tended to be shorter in arm 1 than in arm 2 during the second cycle, and became significantly shorter during the third cycle. Total dose of G-CSF tended to be lower in arm 1 than in arm 2 during the second cycle, and became significantly lower during the third cycle. Nadir hemoglobin level during the second cycle, compared with that during the first cycle, was significantly lower in arm 1, but not in arm 2.

8. Conclusions

It is strongly suggested that Kanebo Ninjin'yoeito Extract Fine Granules may exert neutropenia-preventing effects by inducing pluripotent stem cells to multiply and differentiate and by increasing the activity of G-CSF.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

Because of the small sample size (only four in each arm), it seems difficult to address the statistical significance of differences observed in this study. Furthermore, although G-CSF administration affects "total dose of G-CSF" and "duration of neutrophil counts under 1,000/μL," administration criteria for G-CSF are not described. Thus the data are not objective. The significant decrease in hemoglobin level in arm 1 may indicate that Kanebo Ninjin'yoeito Extract Fine Granules is effective against neutrophil suppression, but not against suppression of erythropoietic cells. It is necessary to include more patients and to investigate not only the efficacy, but also the adverse events induced by G-CSF.

12. Abstractor and date

Hoshino E, 15 March 2009, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Saito S, Iwagaki H, Kobayashi N, et al. Effects of a Japanese herbal medicine (TJ-41) on surgical stress of patients with gastric and colorectal cancer*. *Nihon Rinsho Geka Gakkai Zasshi* (*Journal of Japan Surgical Association*) 2006; 67: 568-74 (in Japanese). Ichushi Web ID: 2006114494

1. Objectives

To determine whether preoperative administration of hochuekkito (補中益気湯) relieves surgical stress in patients with gastric or colorectal cancer.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Department of Gastroenterological Surgery, Transplant and Surgical Oncology, Okayama University, and six other institutions.

4. Participants

Forty-eight patients who underwent surgery for gastric (n=10) or colorectal (n=38) cancer.

5. Intervention

Arm 1: treatment with TSUMURA Hochuekkito (補中益気湯) Extract Granules 2.5 g, t.i.d. for 1 week prior to surgery (n=22).

Arm 2: no preoperative treatment (n=26).

6. Main outcome measures

The levels of cortisol, soluble tumor necrosis factor receptor (sTNF-R), and soluble interleukin-2 receptor (sIL-2R) measured right before surgery and on postoperative day 1; total and differential white blood cell counts measured preoperatively and postoperatively at days 1 and 7; C-reactive protein level measured preoperatively and postoperatively at days 1, 3, and 7; postoperative course of body temperature and pulse rate; length of postoperative stay; the number of patients who received therapeutic antibiotics after surgery.

7. Main results

There were no significant between-arm differences in total and differential white blood cell counts, CRP level, and rates of increase in sTNF-R and sIL-2R from before to after surgery. The rate of increase in cortisol from before to after surgery was significantly lower in arm 1. The body temperature from postoperative day 6 was significantly lower in arm 1. The pulse rate on postoperative days 6 and 7 was significantly lower in arm 1. The number of patients who received therapeutic antibiotics after surgery was significantly smaller in arm 1 (3/22) than in arm 2 (11/22).

8. Conclusions

Preoperative administration of TSUMURA Hochuekkito Extract Granules reduces the response to surgical stress and may be helpful for accelerating postoperative recovery.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse events: no adverse drug reactions occurred in arm 1.

11. Abstractor's comments

The authors postulate that preoperative administration of hochuekkito improves quality of life, helps control body temperature and heart rate, and reduces therapeutic administration of antibiotics in patients during postoperative recovery, and thus may lead to reduction of medical costs. They also suggest that the mechanism underlying these effects may involve Kampo medicine-induced attenuation of the increase in cortisol blood level. The principle of this treatment is similar to that of "immunonutrition," which involves omega-3 fatty acids, arginine, and nucleic acids. These approaches attempt to reduce postoperative surgical complications by means of preoperative nutritional supplementation. Cancer patients before surgery are in a state of *qikyo* (気虚, qi deficiency) with various anxieties, and at the same time in a relatively mild state of *kekkyo* (血虚, blood deficiency) if they are operable. Hochuekkito and other comparable *hozai* (補剤; formulations with tonic effects) seem to be suitable for these patients. The investigation of hochuekkito combined with the immunonutritional approach and further elucidation of the mechanism are anticipated in the future.

12. Abstractor and date

Hoshino E, 15 March 2009, 8 August 2009.

Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Yamamoto K, Hirano F, Ikoma N, et al. Efficacy of keishibukuryogan for hysteromyoma/uterine adenomyosis*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2003; 20: 135-7 (in Japanese). Ichushi Web ID: 2004068783

1. Objectives

To evaluate the anti-tumor effect of keishibukuryogan (桂枝茯苓丸) in patients with hysteromyoma/uterine adenomyosis.

2. Design

Randomized controlled trial (RCT).

3. Setting

Single hospital (Department of Obstetrics and Gynecology, Sakai Hospital, Kinki University School of Medicine).

4. Participants

The 24 patients seen at the above institution and diagnosed with hysteromyoma or uterine adenomyosis were randomized into two arms: 1) the gonadotropin-releasing hormone (GnRH) analogue + keishibukuryogan arm (mean age, 45.9 years; mean tumor diameter, 35.7 mm) and 2) the GnRH analogue arm (mean age, 46.3 years; mean tumor diameter, 34.1 mm).

5. Intervention

Arm 1: subcutaneous injection of a GnRH analogue (1.88 mg) once monthly for 4 consecutive months + oral administration of a sachet of TSUMURA Keishibukuryogan (桂枝茯苓丸) Extract Granules (2.5 g) t.i.d (before meals) for 12 months (n=14) .

Arm 2: subcutaneous injection of a GnRH analogue (1.88 mg) once monthly for 4 consecutive months (n=10).

6. Main outcome measures

Tumor response was evaluated on a 3-point scale: tumor diameter reduction: remarkably effective, ≥50%; effective, >0 - 50%; not effective, 0%. Evaluation was performed at baseline, 4, 8, and 12 months after intervention.

7. Main results

Four months after treatment, complete response was achieved in 42.9% (6/14) of arm 1 and 10% (1/10) of arm 2, showing that GnRH + keishibukuryogan tended to have a higher anti-tumor effect although there were no between-group differences in tumor size reduction 8 or 12 months after treatment. Analysis limited to hysteromyoma revealed that 4-month treatment produced complete response in a significantly higher percentage of arm 1 (50%) than arm 2 (0%) (P=0.012). When the analysis was limited to the GnRH analogue leuprorelin, 4-month treatment produced a significantly higher complete response rate in arm 1 (62.5%) than in arm 2 (0%) (P=0.016). GnRH + keishibukuryogan exerted clinical efficacy in the short-term but not in the long-term (8 or 12 months after treatment).

8. Conclusion

Keishibukuryogan increases the efficacy of standard GnRH therapy for tumor size reduction in 4-month, short-term treatment.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

As the contents of this paper have also been described in several previous case reports and clinical studies, the present study provided additional supportive evidence. Nevertheless, the present results are not sufficient to conclude that the effect can be generalized beyond the study sample because of the small sample size, but it will serve as a helpful reference in determining the future direction of research. Although the measure of tumor response (use of a 3-point scale) was rather crude, further accumulation of cases may enable more reliable determination — for clinical practice — of mean tumor reduction and differences in tumor reduction with time after administration.

12. Abstractor and date

Ushiroyama T, 1 April 2008, 8 August 2009.

Blood Diseases including Anaemia

Reference

Akase T, Akase T, Onodera S, et al. A comparative study of the usefulness of tokishakuyakusan and an oral iron preparation in the treatment of hypochromic anemia in cases of uterine myoma. *Yakugaku Zasshi* (*Journal of the Pharmaceutical Society of Japan*) 2003; 123: 817-24. CENTRAL ID: CN-00457950, Pubmed ID: 14513774, Ichushi Web ID: 2004068366 J-STAGE

1. Objectives

To evaluate the efficacy and safety of tokishakuyakusan (当帰芍薬散) for hypochromic anemia in patients with uterine myoma.

2. Design

Randomized controlled trial (RCT).

3. Setting

A university hospital (Outpatient Department of Obstetrics and Gynecology, Kitasato University Hospital).

4. Participants

Twenty-three patients having hypochromic anemia associated with uterine myoma visiting the above institution between August 1999 and the end of January 2000. Mean age: 45.4±1.99 years in the tokishakuyakusan group; 42.9 ± 1.68 years in the oral iron preparation group. Range of blood hemoglobin concentration: 8 – 12 g/dL.

5. Intervention

Arm 1: oral administration of a sachet of TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules (2.5 g) t.i.d. (before meals) for 3 months.

Arm 2: oral administration of a tablet containing sodium ferrous citrate (50 mg) q.d or b.i.d. (after meals) for 3 months.

6. Main outcome measures

Laboratory: hematology (RBC, hemoglobin, hematocrit, etc.), blood chemistry (serum iron, ferritin concentration, etc.), blood coagulation function (PT, APTT), evaluated at baseline, and 4 and 8 weeks.after dosing. Improvement in subjective symptoms, including pallor, dizziness on standing up, and dizziness/vertigo, evaluated on a 5-point scale at baseline, and 4 and 8 weeks after dosing. Adverse drug reactions (ADRs): incidences of heartburn, nausea/vomiting, diarrhea, etc. during 8-week administration.

7. Main results

Although there was no between-group difference in blood profile, subjective symptoms such as cold, pallor, spoon nail, and dizziness/vertigo were significantly improved with tokishakuyakusan (P<0.05). In particular, cold was improved significantly efficiently in the tokishakuyakusan group (score at 8 weeks: 0.3±0.2 for tokishakuyakusan, 2.0±0.6 for oral iron; P<0.05). ADRs occurred in 80% of patients receiving the oral iron preparation (heartburn and nausea noted with the highest incidences of 46.7% each) but in no patients receiving tokishakuyakusan.

8. Conclusions

Three-month treatment with tokishakuyakusan is more effective in improving subjective symptoms and is safer than an oral iron preparation for mild to moderate anemia in women with uterine myoma.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

ADRs occurred in none of 10 patients receiving tokishakuyakusan, while in 12 (80%) of 15 patients receiving the oral iron preparation.

11. Abstractor's comments

If clinicians designed a noninvasive antianemic treatment plan for the present study population, i.e., patients with anemia (defined as blood hemoglobin concentration, 8–12 g/dL) and uterine myoma, the oral iron preparation would be the treatment of choice. However, in the present study, tokishakuyakusan had higher efficacy for subjective symptom improvement. In addition, tokishakuyakusan was clinically more efficacious and safer (i.e., had no ADRs). However, since tokishakuyakusan (unlike the oral iron preparation) did not improve the blood profile, a combination of these drugs might be more efficacious. A new research protocol to investigate the efficacy of Kampo formulations combined with oral iron to reduce the severity of anemia is expected in the future.

12. Abstractor and date

Ushiroyama T, 1 April 2008, 8 August 2009.

Blood Diseases including Anaemia

Reference

Aoe H, Sumida Y, Kawahara N, et al. Efficacy of an erythropoietin preparation and Kampo medicines in preoperative autologous blood donation in cancer patients*. *Jikoketsu Yuketsu* (*Journal of Japanese Society of Autologous Blood Transfusion*) 1999; 12: 100-4 (in Japanese). MOL, MOL-Lib

1. Objectives

To evaluate the efficacy of juzentaihoto (十全大補湯) and ninjin'yoeito (人参養栄湯) combined with an erythropoietin (EPO) preparation in preoperative autologous blood donation in cancer patients.

2. Design

Randomized controlled trial (RCT). Intravenous administration of an iron preparation to patients with hemoglobin concentration of ≥14 g/dL. Randomization of patients with hemoglobin concentration of <14 g/dL to receive intravenous iron preparation + Kampo formulation + EPO or intravenous iron preparation + EPO.

3. Setting

Single hospital (Department of Obstetrics and Gynecology, Japanese Red Cross Society Himeji Hospital).

4. Participants

Ninety patients with gynecologic malignant tumors who visited the above institution between January 1992 and the end of November 1997 and preoperatively donated 800 mL or more of autologous blood.

5. Intervention

Arm 1: intravenous administration of an iron preparation (240 mg weekly) from the day of the first donation through the day before the operation.

Arm 2: intravenous administration of an iron preparation (240 mg weekly) + intravenous drip infusion of 6000 units of EPO three times weekly, from the day of the first donation through the day before the operation.

Arm 3: intravenous administration of an iron preparation (240 mg weekly) + intravenous drip infusion of 6000 units of EPO three times weekly + oral administration of TSUMURA Juzentaihoto (十全大補湯) Extract Granules or Ninjin'yoeito (人参養栄湯) Extract Granules 2.5 g t.i.d (before meals), from the day of the first donation through the day before the operation.

6. Main outcome measures

Hematological profile: RBC count, hemoglobin, hematocrit, reticulocyte count, etc., measured before donation (before administration) and preoperatively (immediately after completion of administration).

Serum biochemical profile: total protein, albumin, and iron concentrations, determined before donation (before administration) and preoperatively (immediately after completion of administration).

Hemoglobin increment: pre-donation hemoglobin concentration × volume of donated blood/volume of circulating blood – (pre-donation hemoglobin concentration – preoperative hemoglobin volume).

7. Main results

The increase in reticulocyte count from the time of donation to the time of operation was larger in the Kampo group (n=36) and EPO group than in the iron group (n=15). The increase in hemoglobin level was larger in the EPO group (1.73±1.30 g/dL) than the iron group (0.92±0.70 g/dL), and significantly (P<0.05) larger in the Kampo group (2.33±1.11 g/dL) than the EPO group.

8. Conclusions

Combining a Kampo formulation with an iron preparation plus EPO enhances the clinical effectiveness of preoperatively donated autologous blood.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The finding that adding juzentaihoto or ninjin'yoeito to the preoperative donation management protocol enhances the increase in blood hemoglobin concentration suggests that the hematological profile of donated autologous blood is better after use of the combination than after use of only the iron preparation plus EPO. Thus, this finding is clinically significant. With the accumulation of more cases, a safety study is expected including an examination of the possibility that complementary medicines promote cancer cell growth.

12. Abstractor and date

Ushiroyama T, 1 April 2008, 8 August 2009.

Blood Diseases including Anaemia

Reference

Aoe H. Effect of Juzen-taiho-to on haematological recovery from predeposit autologous blood donation. *Pharma Medica* 2007; 25: 11-4. Ichushi Web ID: 2008070612 MOL, MOL-Lib

1. Objectives

To evaluate the efficacy of using juzentaihoto (十全大補湯) to augment preoperative autologous blood donation in cancer patients.

2. Design

Randomized controlled trial (RCT).

3. Setting

Not identified (but the abstractor infers a Department of Obstetrics and Gynecology in each of the following three facilities: Japanese Red Cross Society Himeji Hospital, Fukuyama City Hospital, and Chugoku Central Hospital).

4. Participants

One-hundred and twenty patients who visited the above institutions within the past 5 years and 2 months and donated 800 mL or more autologous blood before undergoing surgery for gynecologic malignant tumors. Patients receiving preoperative chemotherapy and patients with collagen disease were excluded.

5. Intervention

Arm 1: intravenous administration of an iron preparation (240 mg weekly) + intravenous drip infusion of 6000 units of EPO three times weekly, from the day of the first donation through the day before the operation in patients with pre-donation Hb value of < 14 g/dL, n=52.

Arm 2: intravenous administration of an iron preparation (240 mg weekly) + intravenous drip infusion of 6000 units of EPO three times weekly + oral administration of a sachet (2.5 g) of TSUMURA Juzentaihoto (十全大補湯) Extract Granules t.i.d (before meals), from the day of the first donation through the day before the operation in patients with pre-donation Hb value of < 14 g/dL, n=51.

Arm 3: intravenous administration of an iron preparation (240 mg weekly), n=17.

6. Main outcome measures

Hematological profile: RBC count, hemoglobin, hematocrit, reticulocyte count, etc., measured before donation (before administration) and preoperatively (immediately after completion of administration).

Serum biochemical profile: total protein, albumin, and iron concentrations, determined before donation (before administration) and preoperatively (immediately after completion of administration).

Hemoglobin increment: pre-donation hemoglobin concentration × volume of donation blood/volume of circulating blood – (pre-donation hemoglobin concentration – preoperative hemoglobin concentration).

7. Main results

Decrements in RBC count and hematocrit after donation were significantly smaller in the EPO combination groups than in the iron monotherapy group, and significantly smaller in the juzentaihoto and EPO combination group than in the EPO combination group (P<0.05). There was also a significant difference in hemoglobin increment between arms (P<0.05).

8. Conclusions

An iron preparation combined with EPO and additionally with juzentaihoto enhances the clinical efficacy of preoperatively donated autologous blood.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study demonstrated that adding juzentaihoto to the preoperative donation management protocol successfully suppresses reductions in RBC count and hematocrit after donation and enhances the increase in blood hemoglobin concentration. This suggests that the hematological profile of donated autologous blood is better after use of this combination than after use of only an iron preparation plus EPO. Thus, this finding is clinically significant. With the accumulation of more cases, a safety study, including an examination of the possibility that complementary medicines promote cancer cell growth, is expected. Similar papers by the first author include: Aoe H, Matsuo T, Ebisutani M, et al. Efficacy of using juzentaihoto to augment preoperative autologous blood donation in cancer patients*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2000; 17: 67-71 (in Japanese); Aoe H, Ota M*, Kawahara N, et al. Efficacy of using juzentaihoto to augment preoperative autologous blood donation*. *Rinsho Kensa* (*Journal of Medical Technology*) 2003; 47: 395-9 (in Japanese). Ichushi Web ID: 2003251978

12. Abstractor and date

Ushiroyama T, 19 December 2008, 8 August 2009.

Blood Diseases including Anaemia

Reference

Motoo Y, Mouri H, Ohtsubo K, et al. Herbal medicine Ninjinyoeito ameliorates ribavirin-induced anemia in chronic hepatitis C: a randomized controlled trial. *World Journal of Gastroenterology* 2005; 11: 4013-7. CENTRAL ID: CN-00522971, Pubmed ID: 15996025

1. Objectives

To evaluate the efficacy and safety of ninjin'yoeito (人参養栄湯) for ribavirin-induced anemia.

2. Design

Randomized controlled trial (RCT).

3. Setting

One university hospital.

4. Participants

Twenty-three chronic hepatitis C patients treated with interferon alpha-2b and ribavirin. Five of them withdrew from the study.

5. Intervention

Arm 1: designated "the control group" and treated with interferon alpha-2b (IFNα-2b) and ribavirin,n=13
Arm 2: designated "the NY group" and treated with IFNα-2b and ribavirin plus TSUMURA Ninjin'yoeito (人参養栄湯) Extract Granules (9 g, orally), n=10.

IFNα-2b was administered for a total of 24 weeks at a dose of 10 MU intramuscularly, 6 days per week for the first 2 weeks and 3 days per week for the following 22 weeks. Ribavirin was orally administered for 24 weeks at a dose of 800 mg/day (if the patient's body weight was ≥ 60 kg) or 600 mg/day (body weight < 60 kg).

6. Main outcome measures

Maximum increase in red blood cell count (maxΔRBC), maximum increase in hemoglobin level (maxΔHb) minimum hemoglobin level (min Hb), white blood cell count (WBC), platelet count (Plt), T-helper 1 cell (Th1) count, T-helper 2 cell (Th2) count, Th1/Th2, and glutathione peroxidase level in peripheral blood.

7. Main results

Peripheral maxΔHb and min Hb were significantly improved in the NY group (P=0.026 and P=0.079, respectively). No between-group differences were observed in maxΔRBC, WBC count, Plt count, Th1 count, Th2 count, Th1/Th2, and glutathione peroxidase level. Antiviral effects were not different, either.

8. Conclusions

Ninjin'yoeito is an effective and safe treatment for ribavirin-induced anemia.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse reactions specific to ninjin'yoeito were not observed.

11. Abstractor's comments

This study showed the efficacy of ninjin'yoeito for ribavirin-induced anemia. The authors speculated that the mechanism of action of this drug is the activation of undifferentiated erythroid cells and antioxidation.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Metabolism and Endocrine Diseases

Reference

Ushiroyama T, Ikeda A, Sakai M, et al. Effects of unkei-to, a herbal medicine, on endocrine function and ovulation in women with high basal level of luteinizing hormone secretion. *The Journal of Reproductive Medicine* 2001; 46: 451-6. CENTRAL ID: CN-00355871, Pubmed ID: 11396371

1. Objectives

To evaluate the efficacy of unkeito (温経湯) for reducing high luteinizing hormone (LH) levels and improving ovulation disorder.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

One hospital (Osaka Medical College Hospital), although not mentioned.

4. Participants

One-hundred patients with ovulation disorder and an LH level of ≥10 mIU/mL, aged 21 to 32 years. Of these 100 patients, 38 were diagnosed with polycystic ovarian syndrome (PCOS).

5. Intervention

Arm 1: oral administration of a sachet (2.5 g) of TSUMURA Unkeito (温経湯) Extract Granules (TJ-106) t.i.d, 30 min before meals, for 8 weeks, n=52.
Arm 2: clinical observation (without administration of placebo granules) for 8 weeks, n=48.

6. Main outcome measures

Comparison of plasma LH level.
Comparison of ovarian follicle size evaluated by ultrasonography.

7. Main results

Of 52 patients receiving unkeito, 34 showed decreased LH level, and 28 showed improved menstrual cycle regularity. In addition, ovulation was confirmed in 11 patients. Decreased LH level was significant in patients without PCOS.

8. Conclusions

Unkeito improves ovulation disorder by normalizing the high level of LH in patients with ovulation disorder. It also increases E2 hormone level in non-PCOS patients. Control patients remained unchanged. Thus, unkeito is an effective treatment for ovulation disorder.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is highly significant in that it demonstrated the ovulation disorder-improving effect of unkeito at the hormonal level. However, the underlying mechanism of this improvement is not explained. Further investigation to determine, for example, why some patients do not respond to unkeito, is awaited. Nevertheless, it can be concluded that unkeito contributes to normalization of the menstrual cycle and stimulation of ovulation.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Metabolism and Endocrine Diseases

Reference

Ushiroyama T, Hosotani T, Mori K, et al. Effects of switching to wen-jing-tang (unkei-to) from preceding herbal preparations selected by eight-principle pattern identification on endocrinological status and ovulatory induction in women with polycystic ovary syndrome. *The American Journal of Chinese Medicine* 2006; 34: 177-87. CENTRAL ID: CN-00563518, Pubmed ID: 16552830

1. Objectives

To evaluate the efficacy of switching to unkeito (温経湯) from treatment based on the traditional diagnostic criterion "eight-principle pattern identification" in women with polycystic ovary syndrome (PCOS).

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Department of Obstetrics and Gynecology, Osaka University Faculty of Medicine.

4. Participants

Sixty-four patients who visited the outpatient department and were diagnosed with PCOS between 1993 and 2004.

5. Intervention

Sixty-four patients were randomly assigned to one of 2 groups using the diagnostic criterion "*in-yo* (陰陽, yin and yang), *kyo-jitsu* (虚実, excess or deficiency), *hyo-ri* (表裏, interior and exterior), *kan-netsu* (寒熱, cold and heat)" to receive 8-week preliminary administration of either "keishibukuryogan (桂枝茯苓丸)" or "tokishakuyakusan (当帰芍薬散)." Then, 54 non-ovulating patients were further assigned via the RCT-envelope method to receive either a continuation of the same treatment (the continuous treatment group; n = 27) or unkeito (温経湯) (the unkeito group; n = 27) for 8 weeks.

Arm 1: continuous administration group (TSUMURA Keishibukuryogan Extract Granules 7.5 g or TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules 7.5 g), n = 27.

Arm 2: TSUMURA Unkeito (温経湯) Extract Granules 7.5 g/day group, n = 27.

6. Main outcome measures

Blood follicle stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) levels and ovulation status.

7. Main results

Switching to unkeito decreased blood LH level and significantly stimulated ovulation.

8. Conclusions

Unkeito has an ovulatory inductive effect, regardless of conventional "*sho*"(証, pattern/syndrome) identification.

9. From Kampo medicine perspective

Although eight-principle pattern identification is an important criterion for treatment selection, it was not used for the selection unkeito, which was found to stimulate ovulation. Traditional diagnosis based on clinical findings, pathology, and hematology can be an important guide to the selection of Kampo formulae.

10. Safety assessment in the article

No special problems noted.

11. Abstractor's comments

This paper indicates that switching to unkeito after treatment based on traditional "*sho*" identification improves outcome. The requirement for more objective criteria to make a Kampo diagnosis is extremely important. Other Kampo formulae beside keishibukuryogan and tokishakuyakusan should be considered to treat PCOS. It is of interest to determine whether monotherapy with unkeito would be more effective than monotherapy with other formulae. Future research is expected.

12. Abstractor and date

Nakata H, 10 January 2009, 8 August 2009.

Metabolism and Endocrine Diseases

Reference

Ushiroyama T, Ikeda A, Higashino S, et al. Unkei-to for correcting luteal phase defects. *The Journal of Reproductive Medicine* 2003; 48: 729-34. CENTRAL ID: CN-00458287, Pubmed ID: 14562640

1. Objectives

To evaluate the efficacy of unkeito (温経湯) for luteal phase deficiency.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Not mentioned (the authors belong to a clinic of the Department of Obstetrics and Gynecology, Osaka Medical College)

4. Participants

One-hundred and ninety-seven patients with a luteal phase of <10 days or a luteal-phase blood progesterone concentration of <10 ng/mL, who had not received hormone therapy for the past 12 months.

5. Intervention

Arm 1: oral administration of 2.5 g of TSUMURA Unkeito (温経湯) Extract Granules (TJ-106) t.i.d (daily dose 7.5 g), n=103.
Arm 2: untreated control group, n=94. (88 included for analysis)
(Note) During 2 to 8 days after ovulation, 5,000 IU of human chorionic gonadotropin (hCG) was injected three times in 71 of 103 patients in arm 1 and all 94 patients in arm 2.

6. Main outcome measures

Ovarian follicle size, endometrial thickness, and luteal function improvement rating (prolongation of luteal phase or elevation in progesterone value).

7. Main results

During days 14 to 18 of the menstrual cycle, most of the unkeito group showed significant improvement in both ovarian follicle size and endometrial thickness (83/103 patients in arm 1 vs. 13/88 patients in arm 2). Luteal functions were also significantly improved by unkeito treatment

8. Conclusions

Unkeito improves luteal phase defect.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned

11. Abstractor's comments

This paper is a follow-up of "Effects of unkeito, an herbal medicine, on endocrine function and ovulation in women with high basal level of luteinizing hormone secretion (*The Journal of Reproductive Medicine* 2001;46:451-6.) by Ushiroyama T, Ikeda A, Sakai M, et al." In addition to the previously reported efficacy of unkeito for ovulation disorder, the present paper reports its luteal phase-stabilizing effects including thickening of the endometrium and elevating progesterone value. Although the mechanism of action of unkeito remains unclear, this report provides further details of the effects of unkeito.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Metabolism and Endocrine Diseases

Reference

Namiki T. Basic and clinical investigation of the effect of Kampo medicines on arteriosclerosis*. *Uehara Kinen Seimei Kagaku Zaidan Kenkyu Hokokushu* (*Research Reports of Uehara Memorial Foundation*) 2007; 21: 60-3 (in Japanese). Ichushi Web ID: 2008156867

1. Objectives

To evaluate the anti-obesity effect of bofutsushosan (防風通聖散) extract granules in obese patients and the course of high-sensitivity C-reactive protein (HS-CRP) as an arteriosclerosis-promoting factor.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

The outpatient department of internal medicine at a general hospital.

4. Participants

Patients who were obese (body mass index [BMI] of 25 or greater), hypertensive (diastolic blood pressure of 90 mmHg or higher and/or a systolic blood pressure of 140 mmHg or higher), treatment-naïve or taking oral antihypertensives, and aged ≥20 to <80 years were included after giving written informed consent. Exclusion criteria were: 1) serious complications (cardiac disease, renal disease, malignancy, etc.); 2) use of medications that might affect the outcome of this trial; 3) pregnant, lactating, or likely to become pregnant; and 4) considered ineligible by the investigator.

5. Intervention

Arm 1: bofu group: conventional therapy plus oral administration of bofutsushosan (防風通聖散) extract granules (manufacturer, not specified) 7.5 mg/day before or between meals for 12 weeks in 25 patients (16 males and 9 females; mean age, 63.3±12.3 years).

Arm 2: control group: continuation of conventional therapy in 30 patients (19 males and 11 females; mean age, 64.2±10.3 years).

6. Main outcome measures

1) Body weight, BMI, blood pressure, pulse; 2) levels of fasting blood glucose, hemoglobin a1c (Hba1c), and insulin; 3) levels of total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride; 4) visceral fat (measured by computed tomography [CT]); and 5) blood biochemistry including HS-CRP level, hepatic and renal functions, and electrolyte levels. 1) to 3) were measured at weeks 0, 4, 12, and 24; 4) at weeks 0 and 24; and 5) at weeks 0, 4, 8, 12, and 24.

7. Main results

Body weight was reduced by 1.16 kg (–1.5%) (from 77.82±17.53 kg at week 0 to 76.63±17.66 kg at week 24) in the bofu group, in contrast to the reduction of 1.49 kg (–2.8%) (from 71.79±10.16 kg at week 0 to 70.30±10.36 kg at week 24) in the control group. But the between-group difference was not significant. BMI was decreased by 1.6% (from 30.62±5.81 at week 0 to 30.14±5.78 at week 24) in the bofu group and 2.1% (from 27.80±2.56 at week 0 to 27.22±2.79 at week 24) in the control group.

HS-CRP was 1199.00±1040.46 μg/dL at week 0, then gradually increased by 914.54 μg/dL to 2113.54±4524.08 μg/dL at week 24 in the control group, while it was 2918.17±4239.03 μg/dL at week 0, transiently increased to 5229.26±11066.85 μg/dL at week 4, then decreased to 2694.92±3606.66 μg/dL at week 24 (decrease of 223.25 μg/dL from the week 0 level) in the bofu group.

8. Conclusions

Although body weight and BMI were higher in the bofu group than in the control group, HS-CRP at week 24 was decreased in the bofu group and increased in the control group.

9. From Kampo medicine perspective

The anti-arteriosclerosis effect of keishibukuryogan is also described in this paper.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is an RCT that used HS-CRP as an outcome measure to evaluate arteriosclerosis. The study is very interesting in that it used a novel approach to assess a Kampo medicine. Although results on body weight and BMI were negative, further studies are expected to reveal some positive effects.

12. Abstractor and date

Tsuruoka K, 26 January 2009, 8 August 2009.

Psychiatric/Behavioral Disorders

Reference

Iwasaki K, Kanbayashi S, Chimura Y, et al. A randomized, double-blind, placebo-controlled clinical trial of the Chinese herbal medicine "Ba wei di huang wan" in the treatment of dementia. *Journal of the American Geriatrics Society* 2004; 52: 1518-21. CENTRAL ID: CN-00491098, Pubmed ID: 15341554

1. Objectives

To evaluate the efficacy of hachimijiogan (八味地黄丸) for dementia.

2. Design

Double-blinded randomized controlled trial (DB-RCT).

3. Setting

Single hospital (long-term care facility).

4. Participants

Thirty-three anticholinergic-untreated dementia patients with an MMSE score of 0 – 25.

5. Intervention

Arm 1: oral administration of Uchida Hachimijiogan (八味地黄丸) 2.0g t.i.d. after meals for 8 weeks (n=16).

Arm 2: oral administration of 2.0 g of honey-mixed black rice powder as placebo t.i.d.after meals for 8 weeks (n=17).

6. Main outcome measures

Mini-Mental State Examination (MMSE) score, Barthel Index, and internal carotid artery pulsatility index at baseline, 8 weeks after start of dosing, and 8 weeks after completion of dosing.

7. Main results

After 8 weeks of dosing, in arm 1, a significant improvement over baseline was observed in MMSE score, from 13.5±8.5 to 16.3±7.7, Barthel Index, from 61.8±34.6 to 78.9±21.1, and pulsatility index, from 2.5±1.7 to 1.9±0.5, whereas no changes were noted in these variables in arm 2. At 8 weeks after completion of dosing (16 weeks after start of dosing), MMSE score and Barthel Index of arm 1 returned to control (arm 2) levels.

8. Conclusions

Hachimijiogan improves cognitive function, activities of daily living, and internal carotid arterial blood flow in dementia patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

During the study period, no adverse drug reactions occurred in either group. After completion of dosing, a hospital change due for personal reasons, and urinary tract infections and upper respiratory tract infections occurred in 1 and 2 patients in arm 1, respectively.

11. Abstractor's comments

This study, which investigated the efficacy of hachimijiogan for preserving or restoring cognitive function and activities of daily living in elderly dementia patients in a double-blind RCT, provides high-quality evidence. At week 16, MMSE scores of the hachimijiogan group had a large standard deviation (SD), indicating wide inter-individual variation in dementia severity. Even in the placebo group, MMSE score and Barthel Index did not worsen, though the study population included patients with Alzheimer's disease, suggesting disease progression may have been slower in these very old patients (aged 83 to 85 years, on average). In addition, whether the hachimijiogan-induced improvement (a mean of 2.8 points) in the dementia score of the MMSE led to clinical improvement will require further investigation. It is recommended that investigation separate patients with cerebrovascular disorders from those with Alzheimer's disease. To further elucidate the efficacy of hachimijiogan, longer-term observation of a larger sample is expected.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Psychiatric/Behavioral Disorders

Reference

Suzuki T, Futami S, Igari Y, et al. A Chinese herbal medicine, choto-san, improves cognitive function and activities of daily living of patients with dementia: A double-blind, randomized, placebo-controlled study. *Journal of the American Geriatrics Society* 2005; 53: 2238-40. CENTRAL ID: CN-00554102, Pubmed ID: 16398922

1. Objectives

To evaluate the efficacy of chotosan (釣藤散) for improvement of cognitive function and activities of daily living in dementia patients.

2. Design

Double-blinded randomized controlled trial (DB-RCT).

3. Setting

Not mentioned (authors belong to Department of Geriatric Medicine, Nippon Medical School Hospital, and another hospital).

4. Participants

Thirty patients with mild or moderate dementia: 13, Alzheimer type dementia (MMSE[1] score 14 – 25) and 17, Alzheimer disease (MMSE score 10 – 21) or cerebrovascular disorders (MMSE score not indicated). All were included in the analysis population.

[1]MMSE: Mini-Mental State Examination

5. Intervention

Arm 1: oral administration of 2.5 g of TSUMURA Chotosan (釣藤散) Extract Granules t.i.d. before meals for 8 weeks (n=10).

Arm 2: oral administration of 2.5 g of TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules t.i.d. before meals for 8 weeks (n=10).

Arm 3: oral administration of 2.5 g of placebo t.i.d. before meals for 8 weeks (n = 10).

6. Main outcome measures

Cognitive function evaluated by the MMSE; activities of daily living, by Barthel Index (BI); and caregiver burden, by Zarit Caregiver Burden Scale (Z score).

7. Main results

In arm 1, a significant improvement over baseline was observed in MMSE score, from 15.5±4.0 to 17.5±4.9, and BI, from 67.5±34.6 to 71.5±35.8, whereas no such improvement was seen in arm 2 or 3. There was no significant difference in Z score among the 3 arms.

8. Conclusions

Chotosan improves cognitive function and activities of daily living in dementia patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned

11. Abstractor's comments

This study, which investigated the efficacy of chotosan and goshajinkigan for cognitive function and activities of daily living in elderly patients with dementia in a double-blind RCT, provides high-quality evidence. Although the sample size was small and no statistically significant difference between the arms was found, cognitive function and activities of daily living were significantly improved over baseline in the chotosan group. However, no baseline characteristics except for age and sex are indicated, the underlying disease is not mentioned, and MMSE scores of patients with cerebrovascular disorders are not given. Patient characteristics and each score should be provided. Furthermore, MMSE score in the chotosan group was improved over baseline, but the level after 8-week dosing was almost equal to that in the placebo group (presumably because there was a significant difference in MMSE score at baseline between 2 groups). A future investigation of the efficacy of chotosan for improving cognitive function and activities of daily living is expected with a larger sample size and for a longer period.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Psychiatric/Behavioral Disorders

Reference

Iwasaki K, Satoh-Nakagawa T, Maruyama M, et al. A randomized, observer-blind, controlled trial of the traditional Chinese medicine yi-gan san for improvement of behavioural and psychological symptoms and activities of daily living in dementia patients. *Journal of Clinical Psychiatry* 2005; 66: 248-52 CENTRAL ID: CN-00502716, Pubmed ID: 15705012

1. Objectives

To evaluate the efficacy and safety of yokukansan (抑肝散) for treating behavioral disorders and improving activities of daily living in dementia patients.

2. Design

Randomized controlled trial (RCT).

3. Setting

Three hospitals (long-term care facilities).

4. Participants

A total of 60 patients with dementia due to Alzheimer's disease, cerebrovascular disorder, or Lewy body disease, having a Mini-Mental State Examination (MMSE) score of <24 and a neuropsychiatric inventory (NPI) score of >6; of these, 52 patients were included for analysis.

5. Intervention

Arm 1: oral administration of 7.5 g/day of TSUMURA Yokukansan (抑肝散) Extract Granules in 3 divided doses before meals for 4 weeks (n=27).
Arm 2: untreated control group (n=25).

6. Main outcome measures

MMSE score, Barthel Index, and NPI score.

7. Main results

No changes were found in MMSE score in either group. Significant improvements (compared with baseline) were observed in Barthel Index, from 56.4±34.2 to 62.9±35.2, and NPI score, from 37.9±16.1 to 19.5±15.6, in arm 1. In NPI subscales for hallucination, anxiety/excitement, etc., significant improvements over baseline were noted in arm 1. Additional treatment with tiapride hydrochloride, a dopamine D_1 selective neuroleptic, was required in 11 patients in arm 2 but in none in arm 1.

8. Conclusions

Yokukansan is effective for improvement of behavioral disorders and activities of daily living in dementia patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Dizziness and impaired postural sway were reported in 6 patients (54.5%) treated with tiapride hydrochloride. Two patients (7.4%) who continued yokukansan after the end of the observation period became oversedated but recovered with a reduced dose.

11. Abstractor's comments

This study, which investigated the efficacy of yokukansan for cognitive function and activities of daily living in elderly dementia patients in an RCT, provides high-quality evidence. However, the same nurses who rated MMSE and NPI scores, and Barthel Index may also have administered yokukansan, suggesting the possibility of a lack of blinding, which may have affected evaluations. In future, the effects of yokukansan in dementia patients are expected to be studied over a longer term.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Psychiatric/Behavioral Disorders

Reference

Ishida H, Otake T, Kurihara H, *et al*. Clinical study on augmentative effect of Saiboku-to for anxiolytic and antidepressive action of diazepam. *Pain Clinic*, 1999; 20: 395-9 (in Japanese).

1. Objectives

To determine the efficacy of saibokuto (柴朴湯) as a potentiator of the anxiolytic and antidepressant effects of diazepam.

2. Design

Randomized controlled trial (RCT).

3. Setting

A single clinic (pain clinic).

4. Participants

Fifteen patients with chronic anxiety or depression were included for analysis.

5. Intervention

Arm 1: oral administration of 7.5 g/day of saibokuto (柴朴湯) extract granules (manufacturer, not specified; frequency, not specified) for 2 weeks followed by 6 mg/day of diazepam for 2 weeks. (n=7)

Arm 2: oral administration of 6 mg/day of diazepam for 2 weeks. (n=8)

6. Main outcome measures

Hamilton Rating Scale (HS) score, diazepam and desmethyldiazepam blood levels, motor nerve conduction velocity (MCV)

7. Main results

Mean HS scores were 11.0, 7.4, and 4.1 before and after saibokuto and after diazepam, respectively, in Arm 1, while 8.9 and 5.5, respectively, before and after diazepam in Arm 2. Significant improvement in HS score was observed after diazepam in both arms. No between-arm difference was seen in diazepam and desmethyldiazepam blood levels or MCV.

8. Conclusions

Administration of saibokuto followed by diazepam, compared with diazepam monotherapy, has at least an equal anxiolytic and antidepressant effect.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The study comparing diazepam monotherapy with saibokuto and subsequent diazepam for anxiolytic and antidepressant treatment in patients with anxiety neurosis in a randomized controlled trial provides a high quality of evidence. The statement concluding that administration of saibokuto was likely to be associated with clinical improvement of symptoms was in the Discussion, although not in the Results. Despite the small sample size, it is likely that the effect of diazepam was enhanced by prior saibokuto treatment, so studies with larger sample size are needed. A trend towards clinical improvement of symptoms in the saibokuto arm was presented as a conclusion in the Discussion, but the measures of clinical symptoms are not mentioned. Providing details of these measures would improve the quality of this study.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Psychiatric/Behavioral Disorders

Reference

Yamagiwa M, Fujita K. Effect of treatment using lansoprazole on patients with an abnormal sensation in the throat and concomitant heart burn. *Jibi to Rinsho* (*Otologia Fukuoka*) 2007; 53: 109-15 (text in Japanese with English abstract). Ichushi Web ID: 2007166411

1. Objectives

To determine the efficacy of lansoprazole in patients with pharyngolaryngeal paresthesia and acid reflux symptoms (compared with rikkunshito (六君子湯) as a control).

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Two institutions including Matsusaka Chuo General Hospital.

4. Participants

Eighty-six patients with pharyngolaryngeal paresthesia and acid reflux symptoms who presented to the participating institutions between May 2003 and November 2005.

5. Intervention

Arm 1: administration of TSUMURA Rikkunshito (六君子湯) Extract Granules 7.5 g/day for 2 weeks in 38 patients who started treatment on odd-numbered days.

Arm 2: administration of lansoprazole 15 mg/day for 2 weeks in 48 patients who started treatment on even-numbered days.

6. Main outcome measures

Pharyngolaryngeal discomfort and reflux symptoms.

7. Main results

Rates of excellent, moderate, mild, and no improvement in pharyngolaryngeal discomfort after 2 weeks of treatment were 29, 34, 11, and 26%, respectively, in arm 1 and 33, 27, 19, and 21%, respectively, in arm 2. The respective rates of improvement in heartburn/acid reflux symptoms were 57, 30, 3, and 10% in arm 1 and 89, 9, 0, and 2% in arm 2.

8. Conclusions

No conclusions were drawn from this data (the authors say they will publish a new paper describing the outcomes in detail for rikkunshito-treated patients).

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This paper describes the efficacy of lansoprazole (compared with rikkunshito as a control) in patients with pharyngolaryngeal paresthesia and acid reflux symptoms. But, since the two treatment arms were not compared, the analysis seems to be incomplete. As the authors say they will publish a new paper describing the outcomes in detail for rikkunshito-treated patients, a follow-up report is anticipated.

12. Abstractor and date

Oikawa T, 31 December 2008, 8 August 2009.

Nervous System Diseases (including Alzheimer's Disease)

Reference

Higashi K, Rakugi H, Yu H, et al. Effect of kihito extract granules on cognitive function in patients with Alzheimer's-type dementia. *Geriatrics & Gerontology International* 2007; 7: 245-51. Ichushi Web ID: 2008113647

1. Objectives

To evaluate the efficacy and safety of kihito (帰脾湯) for Alzheimer-type dementia.

2. Design

Randomized controlled trial (RCT).

3. Setting

Hanwa Daini Senboku Hospital.

4. Participants

Seventy-five elderly patients diagnosed with Alzheimer's disease according to DSM-IV criteria, with Hachinski ischemic score of ≤4 points and Mini-Mental State Examination (MMSE) score of 10–26 points. Patients with marked hypertension, diabetes, hypercholesterolemia, heart disease, renal failure, or depression, or MRI findings of marked cerebral infarction were excluded.

5. Intervention

Arm 1: no treatment, n=20.
Arm 2: oral administration of 2.5 g of TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules t.i.d. after meals for 3 months, n=24.
Arm 3: Oral administration of 2.5 g of TSUMURA Kihito (帰脾湯) Extract Granules t.i.d. after meals for 3 months, n=20.

6. Main outcome measures

MMSE score, activities of daily living (ADL) evaluated in all patients at baseline and 3 months. Brain blood flow measured by single photon emission computed tomography (SPECT) in 6 patients in arm 2 and 4 patients in arm 3 at baseline and 3 months (selection criteria for performing SPECT not indicated).

7. Main results

Of 75 participants, 64 were included in the analysis population. MMSE score in arm 3 was significantly improved from baseline at 3 months and was also significantly improved compared with arm 1 and arm 2. In particular, disorientation and attentiveness were markedly improved. There were no among-arm differences in ADL and between baseline and 3 months. SPECT revealed no obvious changes in brain blood flow.

8. Conclusions

Kihito is an effective treatment for Alzheimer-type dementia.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

One patient in arm 2 experienced diarrhea and 1 patient in arm 3 increased blood pressure, leading to discontinuation of treatment.

11. Abstractor's comments

This excellent clinical study investigated and demonstrated the efficacy of kihito for Alzheimer's dementia using a non-Kampo-treatment and goshajinkigan as controls. The authors selected goshajinkigan as a control because of its *onji*-free composition and the lack of reports showing an effect on cognitive function. However, since the efficacy of hachimijiogan, containing goshajinkigan ingredients other than gohitsu and shazenshi, for elderly dementia has already been reported (Iwasaki K, Kanbayashi S, Chimura Y, et al. A randomized, double-blind, placebo-controlled clinical trial of the Chinese herbal medicine "Ba wei di huang wan" in the treatment of dementia. *Journal of the American Geriatrics Society* 2004; 52: 1518-21.), goshajinkigan was considered inappropriate for a control, although the results showed significantly improved MMSE score only with kihito. Furthermore, although they attribute, in the discussion, the absence of a difference in brain blood flow to the small sample size, information on selection criteria for performing SPECT would be necessary. The number of dropouts in arm 1 should be indicated. Although these details were omitted, this clinical research demonstrated the efficacy of kihito for treatment of dementia, and investigation of the mechanism of action and long-term effect using a larger sample size is expected.

12. Abstractor and date

Goto H, 28 November 2008, 8 August 2009.

Nervous System Diseases (including Alzheimer's Disease)

Reference

Maruyama T. Goshuyu-to versus lomerizine hydrochloride in the prophylactic treatment of migraine headaches: an open crossover trial.. *Itami to Kampo* (*Pain and Kampo Medicine*) 2006; 16: 30-97 (text in Japanese with English abstract). Ichushi Web ID: 2006303125

1. Objectives

To evaluate the efficacy and safety of goshuyuto (呉茱萸湯) for treatment of migraine.

2. Design

A crossover randomized controlled trial (RCT-crossover).

3. Setting

No description of the setting is available; the authors belong to the Department of General Medicine, Iida Municipal Hospital.

4. Participants

Fourteen patients with at least a 1-year history of migraine and suffering a mean of 3 or more migraine attack events monthly.

5. Intervention

Arm 1: oral administration of TSUMURA Goshuyuto (呉茱萸湯) Extract Granules 2.5 g t.i.d. for 28 days (n=14).
Arm 2: oral administration of lomerizine hydrochloride 5 mg b.i.d. for 28 days (n=14).
With 2-week withdrawal between courses. Oral triptans to treat migraine attacks were allowed.

6. Main outcome measures

Frequency of migraine attacks, visual analogue scale (VAS) score, number of triptan oral tablets used, response to a triptan (time to relieve attacks), evaluated in the pretreatment period (28 days), course 1 (28 days), withdrawal period (14 days), course 2 (28 days), and final period (28 days).

7. Main results

Differences in measures of drug efficacy (i.e., frequency of migraine attacks, VAS peak value, and number of triptan oral tablets used) were greater in goshuyuto group than in lomerizine hydrochloride group.

8. Conclusions

Goshuyuto is more effective for migraine attacks than lomerizine hydrochloride.

9. From Kampo medicine perspective

As indications of goshuyuto, the following *shoe*s were identified: *genchimyaku* (弦遅脈, string-like, slow pulse), *katsuhakutai* (滑白苔, slippy white tongue coating), *shinsuion* (振水音, splashing sounds in the stomach), *shinkahikou* (心下痞鞕, stuffiness and rigidity below the heart), *shishikanrei* (四肢厥冷, reversal cold of the limbs) in 71.4, 57.1, 64.3, 85.7, and 100% of patients.

10. Safety assessment in the article

While 2 patients receiving lomerizine hydrochloride experienced sleepiness, none receiving goshuyuto experienced any adverse drug reactions.

11. Abstractor's comments

This excellent clinical study investigated the effect of goshuyuto on migraine using lomerizine hydrochloride as the control and demonstrated that it prevented migraine attacks. However, the author stated in the discussion of his paper that lomerizine hydrochloride used as the control was weaker than reported in previous clinical research. Therefore, it would be necessary to determine whether migraine was correctly diagnosed in participants and whether response to previous oral treatment with lomerizine hydrochloride was poor. Furthermore, in arm 2, goshuyuto was received in course 1, and the frequency and severity of migraine attack had not returned to baseline levels by the start of lomerizine in course 2, suggesting that the pace of withdrawal was too rapid. This may explain the stronger effect of goshuyuto in arm 1 (patients who received goshuyuto in course 2). Moreover, compliance with goshuyuto treatment (74%) was significantly lower than compliance with lomerizine hydrochloride treatment (93%), warranting improvement in future compliance. Nevertheless, this research demonstrated that goshuyuto prevented migraine, and further investigation of its efficacy is expected with various prescriptions.

12. Abstractor and date

Goto H, 17 November 2008, 8 August 2009.

Nervous System Diseases (including Alzheimer's Disease)

Reference

Aizawa R, Kanbayashi T, Saito Y, et al. Effects of yoku-kan-san-ka-chimpi-hange on the sleep of normal healthy adult subjects. *Psychiatry and Clinical Neurosciences* 2002; 56: 303-4 CENTRAL ID: CN-00444122, Pubmed ID: 12047606, Ichushi Web ID: 2003024669

1. Objectives

To evaluate the efficacy of yokukansankachimpihange (抑肝散加陳皮半夏) for sleep disorders.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

Not mentioned (probably the Akita Red Cross Hospital)

4. Participants

Of 20 normal healthy men receiving yokukansankachimpihange before the start of the study, 7 with sleep disorders favorably affected were selected for the study.

5. Intervention

Arm 1: oral administration of yokukansankachimpihange (抑肝散加陳皮半夏) extract (manufacturer, dosage, and dosing frequency unknown) for 3 days followed by 1-week withdrawal and then by oral administration of anchusan (安中散) extract for 3 days.

Arm 2: oral administration of anchusan (安中散) extract (manufacturer, dosage, and dosing frequency unknown) for 3 days followed by 1-week withdrawal and then by oral administration of yokukansankachimpihange (抑肝散加陳皮半夏) extract product for 3 days.

(The grouping method for the 7 subjects is not indicated).

6. Main outcome measures

Sleep time, sleep latency, sleep depth, and rapid eye movement (REM) sleep time.

7. Main results

Total sleep time was significantly prolonged in arm 1 (438±13 min *vs* 371±19 min in arm 2).

8. Conclusions

Yokukansankachimpihange increases sleep time.

9. From Kampo medicine perspective

Seven subjects responding to yokukansankachimpihange were selected for the double-blind study.

10. Safety assessment in the article

No adverse drug reactions occurred in either group.

11. Abstractor’s comments

This study, which investigated the efficacy of yokukansankachimpihange for sleep in a double-blind RCT, provides high-quality evidence. However, giving participants yokukansankachimpihange as pretreatment and using anchusan (which has a similar taste) as the control may have compromised blinding. Nevertheless, the research content is advantageous in that it involved objective evaluation of sleep using all-night polysomnography. Investigation with a larger sample size is expected.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Nervous System Diseases (including Alzheimer's Disease)

Reference

Sekine R, Watanabe H, Mimura M, et al. The effects of Gosha-jinki-gan on the low back pain and lower limb pain caused by the lumbar spine: A comparison of Gosha-jinki-gan with Benfotiamine. *Itami to Kampo* (*Pain and Kampo Medicine*) 2003; 13: 84-7 (text in Japanese with English abstract). Ichushi Web ID: 2006247217

1. Objectives

To evaluate the efficacy of goshajinkigan (牛車腎気丸) for treatment of lumbar (low back) and leg pain.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

One general hospital and one university hospital.

4. Participants

Twenty patients with lumbar degeneration (aged 60 years or older) with a chief complaint of low back and leg pain persisting over 6 months.

5. Intervention

Arm 1: oral administration of 7.5 g/day of goshajinkigan (牛車腎気丸) extract granules for 4 weeks, followed by oral administration of 75 mg/day of benfotiamine for 4 weeks (n=10).

Arm 2: oral administration of 75 mg/day of benfotiamine for 4 weeks, followed by oral administration of 7.5 g/day of goshajinkigan (牛車腎気丸) extract granules for 4 weeks (n=10).

In each group, one patient experienced gastrointestinal symptoms following administration of goshajinkigan (牛車腎気丸) and was excluded from the statistical analysis.

6. Main outcome measures

Subjective symptoms (low back pain at rest, low back pain with motion, leg pain at rest, leg pain with motion, leg numbness, and leg fatigue), and clinical laboratory tests (hematology, blood biochemistry, and urinalysis).

7. Main results

Subjective symptoms – low back pain at rest, low back pain with motion, and leg numbness – were significantly improved after administration of goshajinkigan, compared with benfotiamine.

8. Conclusions

Goshajinkigan is more effective than benfotiamie, a vitamine B1 derivative, in the treatment of lumbar (low back) and leg pain.

9. From Kampo medicine perspective

In each arm, 6 patients with *jinkyo* (腎虚, kidney deficiency) were included. No difference was observed in the efficacy between patients with and without *jinkyo*.

10. Safety assessment in the article

Of 20 patients receiving goshajinkigan, 2 experienced gastrointestinal symptoms, which led to discontinuation of treatment. Hematology/biochemistry tests and urinalysis revealed no abnormalities in either arm.

11. Abstractor's comments

This study suggests the efficacy of goshajinkigan for low back and leg pain. To confirm that efficacy is not influenced by the presence of *jinkyo*, a clinical trial with a larger sample size is recommended.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Nervous System Diseases (including Alzheimer's Disease)

Reference

Miyabe Y, Taniguchi C, Kawashima M, et al. Effect of Kampo medicines (sokeikakketsuto, shakuyakukanzoto) for taxol-caused peripheral nerve disorder – evaluation by current perception threshold measured by Neurometer®*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2006; 23: 65-8 (in Japanese).

1. Objectives

To evaluate the potential use of sokeikakketsuto (疎経活血湯) and shakuyakukanzoto (芍薬甘草湯) in preventing peripheral nerve disorder in patients receiving taxol.

2. Design

A randomized crossover controlled trial (RCT-crossover).

3. Setting

Department of Obstetrics and Gynecology, Hamamatsu University School of Medicine, University Hospital.

4. Participants

Seven patients who received monthly paclitaxel–carboplatin (TJ) as the initial anticancer therapy (18 cycles) for gynecological malignant tumors (ovarian cancer, uterine cervical cancer, and endometrial cancer) at the above facility between April 2002 and March 2005.

5. Intervention

Arm 1: monthly TJ + oral administration of Kampo medicines (sokeikakketsuto (疎経活血湯), shakuyakukanzoto (芍薬甘草湯)) (manufacturer unknown) before meals for 14 days before and after TJ therapy.

Arm 2: monthly TJ.

6. Main outcome measures

Current perception threshold (CPT) measured by Neurometer® (2000 Hz, 250 Hz, and 5 Hz) 7 days before and 7 days after the start of TJ therapy: CPT value.

7. Main results

The value (predose CPT – postdose CPT)/predose CPT × 100 (%) decreased after TJ therapy, indicating deteriorating perception without Kampo treatment but remained unchanged with Kampo treatment.

8. Conclusions

TJ therapy when combined with Kampo medicines (sokeikakketsuto, shakuyakukanzoto), but not TJ therapy alone, reduces the severity of peripheral nerve disorder.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Administration of medicines caused no adverse drug reactions.

11. Abstractor's comments

This is a valuable study verifying the efficacy of sokeikakketsuto and shakuyakukanzoto for peripheral nerve disorder, an occasional adverse reaction to anticancer drug treatment that is evaluated by current perception threshold measurement. However, considering the small sample size (7 subjects), individual characteristics may greatly affect and bias the results; thus, increased number of cases may change the results. It is also important to ensure symptoms are consistent and relief of actual symptoms is documented by measured values, warranting continued research efforts. Furthermore, logically, the effect of a Kampo medicine is not constant but depends on the physical status of the host in each cycle of anticancer therapy. Therefore, identification of the "*sho*" (証, pattern/syndrome) of each individual in each cycle is recommended to investigate the correlation between pathological analysis in Kampo medicine and the objective evaluation by current perception threshold used in this study. This may lead to proper usage of Kampo medicines and establishment of highly effective regimens in cancer treatment.

12. Abstractor and date

Ushiroyama T, 19 December 2008, 8 August 2009.

Eye Diseases

Reference

Takama N, Fujiwara T. The Efficacy of hainou-san-kyu-to for internal hordeolum. *Ganka Rinsho Iho* (*Japanese Review of Clinical Ophthalmology*) 2006; 100: 9-11 (in Japanese). Ichushi Web ID: 2006117653

1. Objectives

To evaluate the efficacy of hainosankyuto (排膿散及湯) for internal hordeolum in the acute phase.

2. Design

Randomized controlled trial (RCT).

3. Setting

Two hospitals.

4. Participants

Twenty-six patients with internal hordeolum not complicated with other ophthalmopathy or diabetes who received basic treatment with 4 doses of antibiotic eye-drops (0.3% ofloxacin) + steroid eye-drops (0.1% fluorometholone) per day.

5. Intervention

Arm 1: basic treatment +oral administration of 2.5 g of TSUMURA Hainosankyuto (排膿散及湯) Extract Granules t.i.d. before meals (n=16).
Arm 2: basic treatment alone (n=10).

6. Main outcome measures

Duration of treatment (in days) required to achieve improvement in subjective symptoms, need for adjunctive treatment.

7. Main results

Duration of treatment in days required to achieve symptom improvement was significantly shorter in arm 1 (2.2±0.9) than in arm 2 (5.5±4.1) (P<0.001). The number of subjects requiring adjunctive treatment was not significantly different in arm 1 (1/16; 6.3%) and arm 2 (3/10; 30%). One patient in arm 1 healed 3 days after the start of treatment but had a recurrence 4 days after treatment discontinuation.

8. Conclusions

TSUMURA Hainosankyuto Extract Granules induced proliferation and differentiation of pluripotent stem cells and activity of granulocyte colony stimulating factor, strongly suggesting its suppressive effect on neutropenia.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse events were observed in either arm.

11. Abstractor's comments

In western medicine, antibiotics are concomitantly used with anti-inflammatory drugs. Kampo medicine, which preceded the discovery of the antibiotics used in the modern medicine, targets pathogenic microorganisms by an entirely different mechanism.

12. Abstractor and date

Hoshino E, 15 March 2009, 8 August 2009.

Eye Diseases

Reference

Nagaki Y, Hayasaka S, Hayasaka Y, et al. Effects of goshajinkigan on corneal sensitivity, superficial punctate keratopathy and tear secretion in patients with insulin-dependent diabetes mellitus. *The American Journal of Chinese Medicine* 2003; 31: 103-9. CENTRAL ID: CN-00437062, Pubmed ID: 12723759

1. Objectives

To determine the efficacy of goshajinkigan (牛車腎気丸) for corneal sensitivity, superficial keratitis, and tear secretion in patients with insulin-dependent (type 1) diabetes mellitus.

2. Design

Double-blined randomized controlled trial (DB-RCT).

3. Setting

Toyama Medical and Pharmaceutical University Hospital (now Toyama University Hospital), Department of Ophthalmology.

4. Participants

Fifty patients with insulin-dependent diabetes mellitus complicated with keratopathy. Participants met the following selection criteria: (1) 5 years or longer duration of insulin dependence; (2) simple or preproliferative diabetic retinopathy; (3) diffuse superficial keratitis revealed by fluorescein staining; (4) no history of eye disease other than diabetic retinopathy; and (5) no treatment with eye drops in the past 3 months.

5. Intervention

Arm 1: treatment with TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules 2.5 g t.i.d. (30 minutes before meals) for 3 months in 25 patients (age 25.5±6.9 years; male:female = 10:15; 14 with simple retinopathy and 11 with proliferative retinopathy; disease duration 11.6±5.7; group A).

Arm 2: treatment with placebo granules (lactose granules not containing extract powder) 2.0 g t.i.d. (30 minutes before meals) for 3 months in 25 patients (age 26.6±5.2 years; male:female = 13:12; 14 with simple retinopathy and 11 with proliferative retinopathy; disease duration 11.6±5.7; group B).

Arm 3: treatment with goshajinkigan (牛車腎気丸) for 3 months in 25 healthy volunteers (age 26.2±5.4 years; male:female = 11:14; group C).

6. Main outcome measures

Corneal sensitivity, fluorescein staining score, and Schirmer score were evaluated before and after the treatment.

7. Main results

Corneal sensitivity significantly improved from the pre-treatment value of 2.47±1.1 to the post-treatment value of 2.03±0.63 in group A ($P<0.05$) but not in group B (2.36±1.35 and 2.33±1.02, respectively). Schirmer score markedly improved from the pre-treatment value of 9.3±3.5 to the post-treatment value of 11.0±3.3 in group A ($P<0.01$) but not in group B (9.0±3.8 and 9.0±4.0, respectively). Fluorescein staining score markedly improved from the pre-treatment value of 1.32±0.56 to the post-treatment value of 0.64±0.49 in group A ($P<0.01$) but not in group B (1.40±0.64 and 1.36±0.68, respectively). Corneal sensitivity, Schirmer score, and fluorescein staining score all remained within their normal ranges in group C.

8. Conclusions

Goshajinkigan improves reduced corneal sensitivity, increases tear secretion, and markedly repairs damage to the corneal surface, thereby improving keratopathy without affecting the progression of diabetes mellitus.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions were observed.

11. Abstractor's comments

This study was a double-blind RCT involving 50 diabetic patients (groups A and B). It is a well-designed clinical trial in which both prescribing physician and patients were blinded. I would include a comment on a similar article (Nagaki Y. Effects of goshajinkigan on diabetic keratopathy*. *Kampo Igaku* (*Kampo Medicine*) 2004; 28: 63-5 [in Japanese]) in the present study. If more details, such as data on withdrawals, had been described, intention-to-treat (ITT) analysis data and more reliable results could have been obtained. Further studies are expected to determine effects of goshajinkigan on ocular complications of type 2 diabetes mellitus as a lifestyle-related disease.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Eye Diseases

Reference

Ikeda N, Hayasaka S, Nagaki Y, et al. Effects of traditional Sino-Japanese herbal medicines on aqueous flare elevation after small-incision cataract surgery. *Journal of Ocular Pharmacology and Therapeutics* 2001; 17: 59-65. CENTRAL ID: CN-00347524, Pubmed ID: 11322638

1. Objectives

To determine the efficacy of Kampo medicines for aqueous flare elevation after small-incision cataract surgery.

2. Design

Randomized controlled trial (RCT).

3. Setting

Toyama Medical and Pharmaceutical University Hospital (now Toyama University Hospital) and an affiliated hospital.

4. Participants

Fifty-four patients undergoing surgery for age-related cataract. Patients with complications (such as diabetes mellitus and autoimmune disease), a history of uveitis, or use of anti-inflammatory drugs were excluded.

5. Intervention

Arm 1: no medication in 20 patients (8 males and 12 females; 9 right eyes and 11 left eyes; mean age, 73.1 years [48-85 years]) as a control group.

Arm 2: treatment with TSUMURA Orengedokuto (黄連解毒湯) Extract Granules 7.5 g/day for 3 days before surgery, on the day of surgery, and for 7 days after surgery in 14 patients (5 males and 9 females; 8 right eyes and 6 left eyes; mean age, 74.5 years [56-90 years]).

Arm 3: treatment with TSUMURA Kakkonto (葛根湯) Extract Granules7.5 g/day on the same schedule as arm 2 in 10 patients (3 males and 7 females; 6 right eyes and 4 left eyes; mean age, 75.5 years [68-83 years]).

Arm 4: treatment with TSUMURA Saireito (柴苓湯) Extract Granules 9.0 g/day on the same schedule as arm 2 in 10 patients (5 males and 5 females; 4 right eyes and 6 left eyes; mean age, 73.8 years [61-84 years]).

Cataract surgery in all patients was performed by a single surgeon according to a standard small-incision procedure.

6. Main outcome measures

Aqueous flare intensity (in photon counts/msec) was measured preoperatively and on postoperative days 1, 3, 5, and 7.

7. Main results

Preoperatively, no differences were observed in aqueous flare intensity among the groups. Aqueous flare intensity on postoperative days 1, 3, and 5 was significantly lower in the orengedokuto group ($P<0.05$) and kakkonto group ($P<0.01$) than in the control group. There was no difference between the saireito and control groups.

8. Conclusions

Orengedokuto and kakkonto reduce aqueous flare elevation after small-incision cataract surgery.

9. From Kampo medicine perspective

Evaluation of *sho* and selection of Kampo formulations for each patient were conducted at the Kampo medicine clinic (now Department of Japanese Oriental Medicine) in the above-mentioned university hospital.

10. Safety assessment in the article

No adverse drug reactions were observed.

11. Abstractor's comments

Aqueous flare intensity was used in this RCT as a measure of intraocular inflammation after cataract surgery. Since aqueous flare is a surrogate outcome, results from clinical trials examining other outcomes such as reduction of treatment duration and dosage of commonly used postoperative medication are anticipated. See the article "Ikeda N, Hayasaka S, Nagaki Y, et al. Effects of Kakkon-to and Sairei-to on aqueous flare elevation after complicated cataract surgery. *The American Journal of Chinese Medicine* 2002; 30: 347-53", as a follow-up of the present study.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Eye Diseases

Reference

Ikeda N, Hayasaka S, Nagaki Y, et al. Effects of kakkon-to and sairei-to on aqueous flare elevation after complicated cataract surgery. *The American Journal of Chinese Medicine* 2002; 30: 347-53. CENTRAL ID: CN-00434525, Pubmed ID: 12230023

1. Objectives

To determine the efficacy of Kampo medicines for aqueous flare elevation after complicated cataract surgery.

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital (one department of ophthalmology).

4. Participants

Twenty-seven patients with bilateral cataracts (54 eyes were eligible) associated with idiopathic or sarcoid uveitis. Of these patients, 5 were excluded from analysis.

5. Intervention

No Kampo formulation was administered in right eye surgeries. In left eye surgeries, one of the following Kampo formulations was administered for 3 days before surgery, on the day of surgery, and for 7 days after surgery.

Arm 1: treatment with TSUMURA Kakkonto (葛根湯) Extract Granules 2.5 g t.i.d. in 12 patients (mean age, 64.2 years [48-75 years]; 6 males and 6 females; 9 with idiopathic uveitis and 3 with sarcoid uveitis).

Arm 2: treatment with TSUMURA Saireito (柴苓湯) Extract Granules 3.0 g t.i.d. in 10 patients (mean age, 73.8 years [61-84 years]; 7 males and 8 females; 12 with idiopathic uveitis and 3 with sarcoid uveitis).

Cataract surgery in all patients was performed by a single surgeon following a standard procedure.

6. Main outcome measures

Aqueous flare intensity (in photon counts/msec) was measured preoperatively and on postoperative days 1, 3, 5, and 7.

7. Main results

Preoperatively, aqueous flare intensity was not different between the two groups. For right eyes, flare intensity was 99.1 in the kakkonto group and 89.6 in the saireito group on postoperative day 1, and then gradually decreased in both groups. For left eyes, compared with the untreated right eyes, aqueous flare intensity was significantly decreased in the kakkonto group on postoperative days 1, 3, and 5 ($P<0.001$ for each). In contrast, there was no difference between left and right eyes in the saireito group.

8. Conclusions

Kakkonto inhibits the elevation in aqueous flare intensity after complicated cataract surgery.

9. From Kampo medicine perspective

Evaluation of *sho* and selection of Kampo formulations for each patient were conducted at the Kampo medicine clinic（now Department of Japanese Oriental Medicine）in the above-mentioned university hospital.

10. Safety assessment in the article

No adverse drug reactions were observed.

11. Abstractor's comments

This study was conducted as a follow-up to the preceding study "Ikeda N, Hayasaka S, Nagaki Y, et al. Effects of traditional Sino-Japanese herbal medicines on aqueous flare elevation after small-incision cataract surgery. *Journal of Ocular Pharmacology and Therapeutics* 2001; 17: 59-65". Participants in the present study were different from those in the preceding study, and patients with both cataracts and uveitis were examined. Also, kakkonto, which had been more effective than orengedokuto in the preceding study, was used as a test Kampo drug. These studies were conducted by the same investigators and the blinding was not described in either article; suggesting that these might have been single-blind studies.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Ear Diseases

Reference

Inoue H. Rapid effect of combination therapy with shoseiryuto and eppikajutsuto for acute otitis media with effusion in adults*. *Jibi to Rinsho* (*Otologia Fukuoka*) 2001; 47: 361-6 (in Japanese). Ichushi Web ID: 2002064379

1. Objectives

To determine the efficacy of shoseiryuto (小青竜湯) combined with eppikajutsuto (越婢加朮湯) for otitis media with effusion (OME) in adults.

2. Design

A quasi-randomized controlled trial (quasi-RCT).

3. Setting

A clinic (otorhinolaryngology).

4. Participants

Thirty-four patients aged 16 years or older with acute OME.
Diagnostic criteria: eligible patients were those who complained chiefly of aural fullness, hearing loss, and autophony in the preceding three weeks at interview, and who had tympanic effusion evident under a binocular microscope.

5. Intervention

Arm 1: treatment with carbocisteine 500 mg t.i.d. and clarithromycin 200 mg b.i.d. (after meals).
(a total of 18 ears of 14 patients; 10 males and 4 females; aged 37.9±11.5 years).
Arm 2: treatment with shoseiryuto (小青竜湯) extract 1 pack t.i.d. and eppikajutsuto (越婢加朮湯) 1 pack t.i.d. (after meals).
(a total of 28 ears of 20 patients; 11 males and 9 females; aged 38.1±16.9 years).
Patients in both arms were treated for 7 days. If excellent or good response was obtained and subjective symptoms disappeared at 4 days, treatment was stopped at 4 days.

6. Main outcome measures

Main variables were symptoms (assessed on interview) and eardrum findings (under a microscope) at 4 and 7 days after the first visit. Symptoms were evaluated on a 4-point scale as follows: 'excellent response,' 'good response,' 'minimal response,' and 'no response.' Eardrums were checked primarily for tympanic effusion. Tympanogram was recorded at the first visit and 7 days later (or at 4 days in patients who showed improvement at that point).

7. Main results

'Excellent or good response' with normalization or improvement of the tympanogram and with disappearance of tympanic effusion was achieved in 38.9% of the control group (arm 1) *vs* 75.0% of the Kampo group (arm 2); the outcome was significantly better in the Kampo group (P=0.02, Wilcoxon rank sum test). In patients with abnormal tympanogram at the first visit, therapeutic response tended to be more pronounced in the Kampo group. Time to the onset of improvement of subjective ear symptoms was significantly shorter in arm 2 than arm 1 (P=0.05).

8. Conclusions

In acute OME in adults, combination therapy with shoseiryuto extract and eppikajutsuto extract results in rapid disappearance of the effusion and improvement of ear symptoms.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Nausea was observed in one patient in arm 2, while no adverse drug reactions occurred in arm 1.

11. Abstractor's comments

This report is clinically relevant. Since patients were randomly assigned to each arm, based on odd- or even chart number, this study was strictly a randomized clinical controlled trial (CCT), not an RCT, and is classified as a quasi-randomized trial. Results from larger rigorously-designed trials are awaited.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Ear Diseases

Reference

Suzuki T. *Clinical efficacy of chotosan for tinnitus. Pathology and treatment of tinnitus and dizziness*[*]. The 28th Chiba Symposium of Japanese Traditional Medicine Tokyo: Kudansha; 2001:8-20 (in Japanese). Ichushi Web ID: 2003129990

1. Objectives

To determine the efficacy of chotosan (釣藤散) for tinnitus.

2. Design

A crossover randomized controlled trial (RCT-crossover).

3. Setting

A community hospital (department of otorhinolaryngology).

4. Participants

Fifty-eight patients with tinnitus.

5. Intervention

Arm 1: oral administration of TSUMURA Chotosan (釣藤散) Extract Granules 2.5 g, t.i.d. for 4 weeks, followed by mecobalamin 0.5 mg, t.i.d. for 4 weeks (n=29).

Arm 2: oral administration of mecobalamin 0.5 mg, t.i.d. for 4 weeks, followed by TSUMURA Chotosan (釣藤散) Extract Granules 2.5 g, t.i.d. for 4 weeks (n=29).

6. Main outcome measures

The intensity (loudness level) and duration of tinnitus, and tinnitus-associated annoyance was evaluated on a 6-point scale (from 0 = disappearance to 5 = maximum) according to the diagnosis criteria established by a study group of the Japan Audiological Society. Scores of these three measures were summed before and after each treatment, and the degree of improvement was measured by reduction in the summed score from the pre-treatment value. 'Disappearance' was defined as reduction to zero, 'marked improvement' as reduction of 8 or more points, 'moderate improvement' as reduction of 4 to 7 points, 'mild improvement' as reduction of 1 to 3 points, 'no improvement' as no change in score, and 'worsening' as increase in score.

7. Main results

In the chotosan-first group (arm 1), scores were significantly reduced after 4 weeks of chotosan treatment, but significantly increased after the switch to mecobalamin treatment. In mecobalamin-first group (arm 2), scores did not change at 4 weeks, and significantly increased after the switch to chotosan treatment. The degree of improvement in tinnitus was significantly different between groups at 4 weeks, then similar at 8 weeks. Improvements were significant, as compared with the pre-treatment baseline values, in both groups. Tinnitus had disappeared in 5 ears, was markedly improved in 8 ears, and was moderately improved in 14 ears. Moderate-to-marked improvement was seen in 39.8% of ears and mild-to-marked improvement in 80.9%. There was no case of 'worsening' tinnitus. Regarding background factors, there were no between-group differences in sex, age, diagnosis, disease duration, side of diseased ear, and medical history. Chotosan showed significant efficacy for tinnitus with heaviness of head/ headache or shoulder stiffness, compared with other accompanying symptoms.

8. Conclusions

Chotosan is more effective than mecobalamin in improving tinnitus.

9. From Kampo medicine perspective

Although specific results were not provided, the author concluded that the treatment would be more effective when they took into account on the patient's condition.

10. Safety assessment in the article

Serious adverse drug reactions were not reported in either group.

11. Abstractor's comments

This study provided high-quality evidence that chotosan is efficacious for tinnitus, which is often difficult to treat. Chotosan tended to improve, though not significantly, Meniere's disease and tinnitus without hearing loss, but not C5dip-type sensorineural hearing loss. These points are helpful when the efficacy of chotosan is determined, and also provide useful insights in its mechanism. In addition, unlike previous reports showing that patients with shorter disease duration were more likely to respond, this study described striking improvement in some cases, such as 'marked improvement' in a patient with disease for 30–40 years and complete recovery in several patients with disease for 4–5 years. The problems of this study are as follows: 1) The presentation of the results is inconsistent. For example, results are presented on a patient basis at first, and then on an affected-ear basis. 2) The report is incomplete because results from a Kampo medicine perspective are not presented. And 3) there is no description of the randomization step or the method of assignment to arm 1 and arm 2. The randomization step may have been omitted because of the crossover design. Nevertheless, an accurate description is desired. However, the article presents future challenges, and further developments are expected.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008, 8 August 2009.

Cardiovascular Diseases

Reference

Arakawa K, Saruta T, Abe K, et al. Double-blind placebo-controlled trial of TSUMURA Orengedokuto (TJ-15) for the treatment of accessory symptoms of hypertension*. *Rinsyo to Kenkyu* (*Japanese Journal of Clinical and Experimental Study*) 2003; 80: 354-72 (in Japanese). Ichushi Web ID: 2003184342 MOL, MOL-Lib

1. Objectives

To evaluate the efficacy and safety of orengedokuto (黄連解毒湯) in patients with hypertension symptoms.

2. Design

Double-blind, randomized, controlled trial (DB-RCT).

3. Setting

A total of 116 university hospitals and community hospitals.

4. Participants

A total of 265 patients with hypertension who met the inclusion and exclusion criteria; 204 included and 61 not included for analysis.

5. Intervention

Arm 1: administration of TJ-15 (containing 0.25 g of TSUMURA Orengedokuto (黄連解毒湯) Extract Granules) capsules, 2 cap, t.i.d. (n=103).

Arm 2: administration of placebo capsules, 2 cap, t.i.d. (n=101).

Oral administration before each meal. Duration of treatment: 8 weeks.

6. Main outcome measures

Reduction in blood pressure was evaluated by comparing blood pressure measurements (systolic, diastolic, and mean) obtained after the run-in period and after the treatment period, and the antihypertensive effect was classified into 5 grades. Improvement in five major accessory symptoms – irritability (feeling irritated), anxiety, sleep disorder, hot flushes, and facial flushing – and other subjective symptoms – headache/heavy-headedness, shoulder stiffness, dizziness, and malaise – were graded from –3 to 3.

7. Main results

There was no significant difference in blood pressure decrease, or antihypertensive effect, between the TJ-15 group and placebo group. Significant efficacy against hot flushes and facial flushing was observed in the treatment group. Irritability, anxiety, and sleep disorder were also improved in the treatment group as compared with the placebo group. Scores of the other subjective symptoms improved significantly. There was no significant between-group difference in the overall safety rating.

8. Conclusions

This study demonstrated the efficacy and safety of orengedokuto for the treatment of hypertension symptoms.

9. From Kampo medicine perspective

The inclusion criteria were high blood pressure and presence of hypertension symptoms (irritability, anxiety, sleep disorder, hot flushes, and facial flushing) indicating orengedokuto "*sho* (pattern/syndrome)". Also 'patients with "*kan-sho*" (寒証, cold/yin pattern) or "*kyo-sho* (虚証, deficiency pattern)" in Kampo medicine' were excluded. Although "*sho*" is not fully equivalent to body-mass index (BMI), patients with thin physique were excluded from this study, resulting in the mean BMI of 24.3. Thus, the focus of this study was on the patients who were most likely to respond to and benefit from orengedokuto.

10. Safety assessment in the article

Adverse effects were observed in eight patients (6.3%) in the placebo group and 15 patients (11.5%) in the TJ-15 group. Nausea (n=2), abnormal laboratory data such as liver dysfunction (elevated liver enzymes) (n=7), and generalized rash (n=1) might be associated with orengedokuto.

11. Abstractor's comments

Orengedokuto, a typical Kampo medicine for hypertension, was reevaluated in this original article. This study targets the symptoms related to stress or hyper-activation of sympathetic nervous system such as anger, stress, anxiety, and fear. In this multicenter double-blind clinical trial, blood pressure tended to decrease, but did not significantly decrease, in response to treatment. However, significant improvement in some accessory symptoms is a milestone. Compared with benzodiazepine anxiolytics in a study of essential hypertension, Orengedokuto seemed to show more efficacy. However, simple comparison cannot be done owing to different criteria used in selecting study participants. This study suggests that treatment based on "*sho*" may be effective. Related article: "Arakawa K, Saruta T, Abe K, et al. Improvement of accessory symptoms of hypertension by TSUMURA Orengedokuto Extract, a four herbal drugs containing Kampo-Medicine Granules for ethical use: a double-blind, placebo-controlled study. *Phytomedicine* 2006; 13: 1-10. [CENTRAL ID: CN-00553637, Pubmed ID: 16360926]" This study is published in an English-language journal and has the same content.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008, 13 March 2009, 8 August 2009.

Cardiovascular Diseases

Reference

Shimada Y. Efficacy of tokishakuyakusan for hypofunction and decreased independence in patients with sequelae of cerebrovascular disorder*. *Kosei Rodo Kagaku Kenkyuhi Hojokin Choju Kagaku Kenkyu Jigyo Buntan Kenkyu Hokokusyo* (*Ministry of Health, Labour and Welfare, Science Research Grant, Comprehensive Studies on Science of Aging, working-group research report*) 2007: 22-30 (in Japanese).

1. Objectives

To evaluate the efficacy and safety of tokishakuyakusan (当帰芍薬散) for treatment of hypofunction and decreased independence in patients with sequelae of cerebrovascular disorder.

2. Design

Randomized controlled trial (RCT) (assigned by randomized allocation in 20 cases and chosen by the patient in 6 cases).

3. Setting

University hospital and community hospital.

4. Participants

Thirty-one patients with sequelae of cerebrovascular disorder.

5. Intervention

Arm 1: administration of 2.5 g t.i.d. of TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules between meals (n=16) (for 12 months**)**.

Arm 2: no administration of Kampo medicines (n=15).

6. Main outcome measures

The Stroke Impairment Assessment Set (SIAS), Functional Independence Measure (FIM), body weight and *oketsu* (瘀血, static blood), *qikyo* (気虚, qi deficiency), *qiutsu* (気鬱, qi movement stagnation) and *jinky*o (腎虚, kidney deficiency), evaluated on a 5-point scale at baseline and every 3 months thereafter.

7. Main results

Both SIAS and FIM scores remained at baseline levels in arm 1 but increased significantly in arm 2 at 12 months, resulting in a significant between-arm difference. In arm 2, stroke recurred at 9 or 12 months.

8. Conclusions

Tokishakuyakusan suppresses hypofunction and decreased independence in patients with sequelae of cerebrovascular disorder requiring an intermediate level of care.

9. From Kampo medicine perspective

At 12 months, *oketsu* and *jinkyo* significantly improved in arm 1, but *oketsu* remained unchanged and *jinkyo* worsened in arm 2, resulting in a significant between-arm difference. In contrast, there was no significant difference in *qikyo* and *qiutsu* between arms.

10. Safety assessment in the article

One patient in arm 1 felt numbness in hands and feet. Since the cause (tokishakuyakusan, amantadine hydrochloride, or captopril) was unclear, all these drugs were discontinued in this patient.

11. Abstractor's comments

In this valuable report about the 1-year follow-up of patients with sequelae of cerebrovascular disorder, tokishakuyakusan was shown to suppress the hypofunction and decreased independence observable in the control group at 12 months. Since the sample size is small (15 or 16 patients), a study with a larger sample size is expected in the future. Further exploration of Kampo medicines potentially able to improve this condition is also expected.

12. Abstractor and date

Namiki T, 12 March 2009, 8 August 2009.

Cardiovascular Diseases

Reference

Akiyama Y, Ohno S, Asaoka T, et al. The combination therapy with sarpogrelate hydrochloride and Kampo medicine (oren-gedoku-to or toki-shakuyaku-san) for Raynaud's phenomenon. *Japanese Journal of Oriental Medicine* 2001; 51: 1101-8 (text in Japanese with English abstract).

1. Objectives

To evaluate the effectiveness of orengedokuto (黄連解毒湯) in improving peripheral circulation in Raynaud's phenomenon.

2. Design

Quasi-RCT.

3. Setting

Two departments (Department of Rheumatology and Department of Oriental Medicine) in Saitama Medical School.

4. Participants

Twenty patients with Raynaud's phenomenon who consulted at the above two departments between October and March from 1994 to 1997 (3 men and 17 women).

5. Intervention

Arm 1: oral administration of sarpogrelate hydrochloride (100mg) in three divided doses after meals.
Arm 2: oral administration of sarpogrelate hydrochloride (100mg) in three divided doses after meals, and orengedokuto (黄連解毒湯) 2.5 g t.i.d. before meals.
Arm 3: oral administration of sarpogrelate hydrochloride (100 mg) in three divided doses after meals, and tokishakuyakusan (当帰芍薬散) 2.5 g t.i.d. before meals.

6. Main outcome measures

Raynaud's phenomenon – subjective symptoms (cold sensation, numbness, pain) and increase in skin temperature assessed by thermography (increase of more than 0.6°C in the mean temperature of all 10 fingertips of both hands) – were evaluated before and after 12-week treatment. The efficacy was compared among subjects with different "*sho*" (証, pattern/syndrome) (*jitsu -sho* [実証, excess pattern], *chukan -sho* [中間証, intermediate pattern], and *kyo -sho* [虚証,deficiency pattern]) in Kampo medicine.

7. Main results

After 12-week treatment, the combination with orengedokuto had significantly higher efficacy than sarpogrelate hydrochloride alone (90% *vs.* 52.5%; $P<0.02$), while the combination with tokishakuyakusan had similar efficacy to sarpogrelate hydrochloride alone. Skin temperature at the fingertips was significantly increased in arm 3 (1.8±1.9°C; $P<0.02$) compared with arm 1 (0.6±0.8°C), and also significantly elevated in arm 2 (4.1±2.1°C; $P<0.005$) compared with arm 3. Combination therapy with Kampo formulations was effective in patients with *jitsu-sho,* but not in patients with *kyo-sho*.

8. Conclusions

Orengedokuto combined with sarpogrelate hydrochloride has higher efficacy in the treatment of Raynaud's phenomenon. However, *kyo-sho* patients did not respond to this combination therapy and had higher incidence of adverse drug reactions (ADRs), suggesting the importance of prescriptions according to the patient's "*sho.*"

9. From Kampo medicine perspective

In this study, 72.7% of the subjects were regarded as *kyo-sho* type. No subject was identified as the so-called orengedokuto-*sho* type – having conditions that are expected to respond to orengedokuto therapy. In *kyo-sho* subjects, the efficacy of the orengedokuto combination therapy was similar to that of sarpogrelate hydrochloride monotherapy, and a higher dropout rate was observed because of ADRs from the bitherapy. Therefore we suggest that administration of sarpogrelate hydrochloride plus orengedokuto should be withheld from *kyo-sho* subjects.

10. Safety assessment in the article

ADRs of the orengedokuto combination occurred in *kyo-sho* patients, including nausea (n=2) and diarrhea (n=2), neither of which was serious. No serious ADRs due to the tokishakuyakusan combination were noted.

11. Abstractor's comments

Sarpogrelate hydrochloride in combination with orengedokuto, which has been reported to improve peripheral circulation, improved more efficiently peripheral circulation in Raynaud's phenomenon when compared with sarpogrelate hydrochloride monotherapy as positive control in this study. It is interesting that improvement was greater with this combination than with the tokishakuyakusan combination, even when more than 70% of subjects were *kyo-sho*. Further scientific evaluation with a larger number of subjects is awaited.

12. Abstractor and date

Ushiroyama T. 1 April 2008, 8 August 2009.

Cardiovascular Diseases

Reference

Abe Y. The efficacy of goshajinkigan against lymphedema*. *Kampo Igaku* (*Kampo Medicine*) 2002;25:284-7 (in Japanese). Ichushi Web ID: 2002140795

1. Objectives

To evaluate the efficacy and safety of goshajinkigan (牛車腎気丸) in the treatment of lymphedema.

2. Design

Randamized controlled trial (RCT).

3. Setting

One hospital (department of cardiovascular surgery).

4. Participants

A total of 80 patients with lymphedema of the upper limbs (n=40) and lower limbs (n=40).

5. Intervention

Arm 1: oral administration of TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules (TJ-107) 2.5g t.i.d for 1 month in combination with compression therapy (n=40).
Arm 2: compression therapy without administration for 1 month (n=40).

6. Main outcome measures

Percentage reduction in edema: reduction in limb circumference assessed between the first visit (baseline) and after 1-month treatment was divided by baseline limb circumference, and expressed in percentage.

7. Main results

For lymphedema of the upper limbs, there was significant percentage reduction in arm 1 (15±3.4%) compared with arm 2 (5.7±1.2%; $P<0.05$). For lymphedema of the lower limbs, the percentage reduction was also significant in arm 1 (17.5±2.8% *vs* 6.7±0.8% in Arm 2; $P<0.05$).

8. Conclusions

Edema was significantly reduced in both patients with lymphedema of the upper limbs and those with lymphedema of the lower limbs by TSUMURA Goshajinkigan Extract Granules (TJ-107).

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The indications for goshajinkigan are chronic nephritis, nephritic syndrome, low back pain, edema in the lower extremity, and oliguria. This RCT assessed the efficacy of goshajinkigan for the treatment of lymphedema secondary to surgical procedures. Secondary lymphedema is generally intractable in many cases despite combined treatments including lymph drainage massage, compression skin care, exercise therapy under compression, and administration of anticoagulants. It is very meaningful that goshajinkigan was shown to be efficacious. The problem is that this paper is published in a business periodical without peer review, and information on patients' background and so on is therefore insufficient. Also, since the efficacy of goshajinkigan plus compression was assessed, the effect of goshajinkigan alone will need to be evaluated by comparison with placebo and positive control drugs in the future.

Article related to this paper:
Abe Y, Kosugi I, Kasashima F, et al. Lymphedema and Kampo*. *Progress in Medicine* 2003; 23: 1538-9 (in Japanese). MOL, MOL-Lib
A report on the same result is shown.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008, 8 August 2009.

Cardiovascular Diseases

Reference

Nakamura H, Nakamura T, Nakagawa S et al. Efficacy of goreisan in treatment of orthostatic hypotension in patients with diabetes mellitus*. *Diabetes Frontier* 2000; 11: 561-3 (in Japanese). Ichushi Web ID: 2001041016 MOL, MOL-Lib

1. Objectives

To examine the safety and efficacy of goreisan (五苓散) in the treatment of orthostatic hypotension in patients with diabetes mellitus.

2. Design

Randomized controlled trial (crossover design) (RCT- crossover).

3. Setting

One internal medicine clinic.

4. Participants

Ten patients with diabetes mellitus (type 1, 2; type 2, 8) associated with orthostatic hypotension diagnosed according to McDowell's criteria.

5. Intervention

Arm 1: Kanebo Goreisan (五苓散) Extract Tablets (EKT-17) 18 tablets/day, for 1 month, n=10.
Arm 2: placebo 18 tablets/day, for 1 month, n=10.

6. Main outcome measures

Body weight, subjective symptoms, and response to orthostatic challenge (change in blood pressure, plasma adrenaline noradrenaline, and aldosterone concentrations, and plasma renin activity) were evaluated at baseline, and 1 and 2 months after the start of treatment; adverse drug reactions (ADRs) were checked during the study.

7. Main results

There was no difference in body weight between the goreisan and placebo groups. The subjective symptom of orthostatic dizziness improved in 9 of 10 patients in the goreisan group, whereas no change was reported in all 10 subjects in the placebo group. Results of orthostatic challenge: Before standing, no significant difference was found in blood pressure between at baseline and after administration of goreisan or placebo. After standing, systolic and diastolic pressures increased significantly in the goreisan group ($P<0.05$), while no significant change was observed in the placebo group. There were no changes in the concentration of adrenaline, noradrenaline, or aldosterone, nor in plasma renin activity at orthostatic challenge after administration of goreisan or placebo.

8. Conclusions

In diabetic patients with orthostatic hypotension, goreisan improved subjective symptoms and normalized the decrease in blood pressure on standing.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no observed adverse drug reactions.

11. Abstractor's comments

General indications for goreisan are edema, nausea, vomiting, dizziness in subjects with thirst and decreased urine output. Authors applied this to diabetic orthostatic hypotension, which is neuropathic and intractable/ resistant to therapies in most cases. Modern medicine can prevent the decline in blood pressure on standing; however, problems such as adverse increase in supine blood pressure remain. In contrast, goreisan causes no increase in supine blood pressure, suggesting this Kampo formulation as an ideal therapeutic agent for orthostatic hypotension in diabetic patients. It is very meaningful that this randomized controlled trial demonstrated that goreisan has efficacy.
It is thought that further investigation with increased case numbers and multicenter trials will improve the reliability of data.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Kaji M, Kashiwagi S, Yamakido M, et al. A double-blind, placebo-controlled study of TSUMURA Shosaikoto (TJ-9) for common cold*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Study*) 2001; 78: 2252-68 (in Japanese). Ichushi Web ID: 2002145787 MOL, MOL-Lib

1. Objectives

To assess the efficacy and safety of shosaikoto (小柴胡湯) in patients with common cold.

2. Design

Double-blind randomized controlled trial (DB-RCT)

3. Setting

From September 1995 until March 1999.
Ten university hospitals, 42 community and other hospitals, and 2 clinics.

4. Participants

Patients with persistent symptoms for more than 5 days after the onset of common cold, age from 25 to 75 years, and complaints of at least one of the following symptoms: oral discomfort (bitter taste, sticky sensation, dysgeusia), anorexia, or malaise.

5. Intervention

The placebo had similar appearance and properties. Concomitant drug use was basically prohibited, except for dimemorfan phosphate (Astomin tablets) after day 3.
Arm 1: TSUMURA Shosaikoto (小柴胡湯) Extract Granules (TJ-9) 2.5g t.i.d., n=131.
Arm 2: placebo 2.5 g t.i.d., n=119.
Duration of administration: 1 week or less

6. Main outcome measures

Global improvement rating (comprehensive evaluation based on improvement rating of each symptom and patient's impression), improvement rating of each symptom**]**, and safety evaluation.

7. Main results

At baseline, the patients allotted to arm 1 were not matched to those allotted to arm 2 in the severity of headache, and the amount and viscosity of sputum. General improvement was significantly better in arm 1 than in arm 2, with the percentage of patients rated 4 (improved) or 5 (markedly improved) on a 5-point scale being 64.1% and 43.7% in arm 1 and arm 2, respectively. Individual symptoms (throat pain and malaise at day 3-4, clearance of sputum, appetite, joint pain and muscular pain at the end of study) all were significantly better in arm 1.

8. Conclusions

For patients with persistent common cold associated with oral discomfort (bitter taste, sticky sensation, dysgeusia), decreased appetite, and/or malaise, shosaikoto is effective and useful.

9. From Kampo medicine perspective

Subject selection was made on the basis of persistent symptoms and discomfort in the mouth, which indicate "shosaikoto-*sho*"

10. Safety assessment in the article

Ten (7.4%) of 136 subjects in arm 1 and 15 (11.4%) of 132 subjects in arm 2) experienced adverse effects. However, there were no serious adverse drug reactions.

11. Abstractor's comments

This study is a large-scale DB-RCT on Kampo therapy fitted to "*sho*" in Kampo medicine.

12. Abstractor and date

Fujisawa M, 15 June2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Fujimori K, Suzuki E, Simojo F. Comparison between bakumondoto (mai men dong tang) and dextromethorphan hydrobromide in terms of effect on postinfectious cough: a pilot study. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 2001; 51: 725-32. Ichushi Web ID: 2001145417 CiNii

1. Objectives

To evaluate the efficacy and safety of bakumondoto (麦門冬湯) for postinfectious cough.

2. Design

Randomized controlled trial (RCT).

3. Setting

Department of Medicine, Niigata University Medical and Dental Hospital., and a general hospital (internal medicine department).

4. Participants

Non-smoking patients with postinfectious cough for whom other causes for cough were ruled out, n=25.

5. Intervention

Arm 1: administration of TSUMURA Bakumondoto (麦門冬湯) Extract Granules (TJ-29) 9g/day for 7 days, n=13.
Arm 2: administration of dextromethorphan hydrobromide 60mg/day for 7 days, n=12.

6. Main outcome measures

Cough scores (cough frequency and intensity) were self-assessed everyday on a scale ranging from 0 to 9.

7. Main results

Arm 1: the cough score of 5.4±1.7 at baseline decreased significantly to 1.5±1.3 on day 7.
Arm 2: the cough score of 4.1±2.0 at baseline decreased significantly to 1.8±1.3 on day 7.
The antitussive effect developed more rapidly in arm 1 than in arm 2.

8. Conclusions

Bakumondoto is effective for postinfectious cough in non-smoking patients, and the antitussive effect is prompt.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No serious adverse drug reactions were observed in either group.

11. Abstractor's comments

The cough in all patients resolved within 4 weeks. Dextromethorphan hydrobromide suppresses cough; however, it may adversely lead to delay in the healing process. Therefore, whether bakumondoto is effective for postinfectious cough in non-smoking patients should be studied by comparing arm 1 with an untreated/placebo control group (postinfectious cough in a natural course). As cough score is a subjective measure, assessment with objective measures is also necessary. In terms of Kampo medicine, postinfectious cough can be caused in a variety of pathologies ("*Shokanron*" [傷寒論]). There are different formulae for different pathologies. For some of these, bakumondoto is not effective.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nagano F, Yamada M, et al. A randomized comparison of cough-improvement effects between mao-bushi-saishin-to and western drugs for cold in common patients with allergic cold syndrome. *Kampo to Meneki Arerugi* (*Kampo and Immuno-Allergy*) 2005; 18: 56-67 (text in Japanese with English abstract).

1. Objectives

To compare the cough-improvement effect of maobushisaishinto (麻黄附子細辛湯) and western drugs in patients with the common cold.

2. Design

Randomized controlled trial (RCT).

3. Setting

Two hospitals and four clinics.

4. Participants

Patients with the common cold.

5. Intervention

The study duration was 15 years.
Arm 1: Tsumura Maobushisaishinto (麻黄附子細辛湯) Extract Granules (TJ-127), n=879.
Arm 2: Western drugs for the common cold, n=879.

6. Main outcome measures

Various subjective symptoms (i.e. fever, headache, chill etc.).

7. Main results

In various assessments, maobushisaishinto was more effective than western drugs.

8. Conclusions

Administration of maobushisaishinto was efficacious for the common cold syndrome.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

The methodology and the subjects in this randomized controlled trial were not described. "Cough-improvement effect" is mentioned only in the title, but not in the text. Considering the short time course of the common cold syndrome, it is unclear why the randomized controlled study has been conducted for the past 15 years and continues even now.

12. Abstractor and date

Fujisawa M, 22 February 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Kubo T, Nishimura H. Antipyretic effect of Mao-to, a Japanese herbal medicine, for treatment of type A influenza infection in children. *Phytomedicine* 2007; 14: 96-101. CENTRAL ID: CN-00577142, Pubmed ID: 17141491

1. Objectives

To determine the effect of maoto (麻黄湯) in combination with oseltamivir on the duration of fever.

2. Design

Randomized controlled trial (RCT) (partly).

3. Setting

A hospital screening patients from January to May 2004.

4. Participants

Children (aged 0–13 years; n=60) suffering from influenza-like illness with fever of ≥38°C.

5. Intervention

Oseltamivir 2 mg/kg b.i.d., TSUMURA Maoto (麻黄湯) Extract Granules 0.06 g/kg t.i.d
Influenza infection was screened with a rapid diagnosis test, and diagnosis was confirmed by isolation of the virus or viral detection using RT-PCR
Arm 1: oseltamivir; influenza A; n=18.
Arm 2: oseltamivir and maoto (麻黄湯); influenza A; n=14.
Arm 3: maoto (麻黄湯); influenza A; n=17.
(Influenza-positive patients [by the rapid test] were randomly assigned to arm 1 and arm 2. Arm 3 included influenza-positive patients under the age of 1 year, who did not meet the criteria for oseltamivir treatment, and influenza-negative patients aged 1 year or older. Patients [n=11] without confirmed influenza virus infections were excluded.)

6. Main outcome measures

Time to becoming afebrile after initiation of the treatment.

7. Main results

The median duration of fever was 24 h, 18 h, and 15 h in arm 1, 2, and 3, respectively. Using the Wilcoxon rank sum test, significant differences were observed in arm 2 ($P<0.05$) and 3 ($P<0.01$) when compared with arm 1.

8. Conclusions

Maoto effectively reduces the duration of fever in children with influenza. A future large-scale trial is expected to investigate the efficacy of maoto in treating influenza, with a double-blinded, randomized controlled manner.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no adverse events in any group.

11. Abstractor's comments

Comparison between arms 1 and 2 was performed in an RCT. The result of this trial is also reported in "Kubo T. The effect of maoto for treatment of influenza infection in children. (from Presentation C-41 of the Japan Society for Oriental Medicine, 56th Annual Meeting) *Medicament News* 2005 Sep 5; 1846: 15 (in Japanese)," in which mean values are used as representative values for each arm.

12. Abstractor and date

Fujisawa M, 22 February 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Kimoto H, Kuroki H. Efficacy of combined administration of oseltamivir phosphate and maoto in treating influenza. *Kampo Igaku* (*Kampo Medicine*) 2005; 29: 166-9 (in Japanese). Ichushi Web ID: 2005292428

1. Objectives

To evaluate the efficacy of maoto (麻黄湯) in combination with oseltamivir phosphate in treating influenza.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

An internal medicine clinic screening patients from January to March 2004.

4. Participants

Adult patients (n=37) positive for influenza (rapid diagnostic test), and having fever (≥38°C) within 48 hours of onset.

5. Intervention

Oseltamivir phosphate (75 mg b.i.d. for 5 days), TSUMURA Maoto (麻黄湯) Extract Granules 2.5 g t.i.d. for 3 days), and Western medicines (an antihistamine [cyproheptadine hydrochloride] with either a bronchodilator [clenbuterol hydrochloride] or expectorant [carbocysteine]) were administered for 3 days.
Arm 1: oseltamivir phosphate and maoto (麻黄湯), n=10.
Arm 2: oseltamivir phosphate and Western medicines, n=9.

6. Main outcome measures

Body temperature.
The magnitude and time course of symptoms such as appetite, fatigue, and dizziness/light-headedness.

7. Main results

All subjects studied were infected with influenza A. Patients in arm 1 tended to become afebrile 12 hours earlier than patients in arm 2. There were no significant between-group differences in anorexia, fatigue, and dizziness/light-headedness, though patients in arm 1 tended to improve more rapidly than patients in arm 2.

8. Conclusions

Compared with oseltamivir plus Western formulations, oseltamivir plus Kampo formulation (maoto) tended to shorten the duration of fever and allowed patients to maintain normal activity.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no adverse events in any group.

11. Abstractor's comments

From the evidence presented, efficacy against symptoms other than fever remains unclear.
This report seems to be an interim report. In the following paper "Kuroki H, Kimoto H. Successful treatment of combination therapy with oseltamivir and Mao-to for influenza – 3rd report. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2006; 19: 17-25 (text in Japanese with English abstract)," the number of participants was increased to 91 subjects, and the duration of fever above 38°C tended to be shorter in arm 1 (after combined treatment with maoto) compared to arm 2 (after combined treatment with Western formulations).

12. Abstractor and date

Fujisawa M. 15 June 2007, 1 April 2008, 9 March, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Kuroki H, Kimoto H. Successful treatment of combination therapy with oseltamivir and mao-to for influenza – 3rd report-. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-allergy*) 2006; 19: 17-25 (text in Japanese with English abstract).

1. Objectives

To determine the efficacy of combined oseltamivir phosphate and maoto (麻黄湯) for the treatment of influenza.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

February to March 2005.
One hospital and one clinic.

4. Participants

One hundred and seven children who presented within 48 hours of symptom onset, were febrile (body temperature, 38°C or higher), and were positive for influenza by the rapid diagnostic test.

5. Intervention

Oseltamivir phosphate was administered at a dose of 75 mg, b.i.d. for 5 days. TSUMURA Maoto (麻黄湯) Extract Granules were administered at a dose of 2.5 g, t.i.d. for 3 days.
Arm 1: treatment with oseltamivir phosphate + maoto (麻黄湯) (n=52).
Arm 2: treatment with oseltamivir phosphate alone (n=55).

6. Main outcome measures

Body temperature.
Time-course changes in each of the following symptoms such as anorexia, cough, rhinorrhea, and insomnia was evaluated on a 3-point scale.

7. Main results

Fever tended to resolve more rapidly in arm 1 than in arm 2. Scores for anorexia, cough, rhinorrhea, and insomnia tended to be lower in arm 1 than in arm 2.

8. Conclusions

Maoto could be administered safely and its combination with western medicine seemed to improve symptoms further. Maoto seems to be a viable treatment for influenza in children.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions occurred.

11. Abstractor's comments

This study follows up a comparative study of oseltamivir + maoto *vs.* oseltamivir + western medicine, which found a trend toward earlier resolution of fever in the oseltamivir + maoto group ("Kimoto H, Kuroki H. The efficacy of combined oseltamivir phosphate and maoto for the treatment of influenza*. *Kampo Igaku* [*Kampo Medicine*] 2005; 29:166-9 [in Japanese].[Ichushi Web ID: 2005292428]").

12. Abstractor and date

Fujisawa M, 8 March 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Iwasaki K, Taguchi M, Cyong JC, et al. Effect of Mao-bushi-saishin-to on influenza vaccination in elderly subjects: a randomized controlled study. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2004; 17: 97-103. (text in Japanese with English abstract)

1. Objectives

To evaluate the efficacy and safety of maobushisaishinto (麻黄附子細辛湯) as an adjuvant for influenza vaccination in the elderly.

2. Design

Randomized controlled trial (RCT).

3. Setting

Not documented.

4. Participants

Eighteen patients with antibody titers of <1:10 to two types of influenza A antigens (H1N1, H3N2) as measured using an hemagglutination inhibition (HI) assay.

5. Intervention

Arm 1: oral administration of TSUMURA Maobushisaishinto (麻黄附子細辛湯) Extract Granules ([TJ-127]), 7.5 g/day, from 7 days before influenza vaccination until 14 days after vaccination; n=10.

Arm 2: no administration of TJ-127; influenza vaccination only; n=8.

6. Main outcome measures

Rise in antibody titer from baseline was measured at 4 weeks after vaccination and the rate of rise was compared between arms.

7. Main results

There was no significant between-arm difference in anti-H1N1 antibody titer. Anti-H3N2 antibody titer increased on average 4.9-fold in arm 2 (when compared with baseline) and 57.3-fold in arm 1 which was significant (P<0.04) when compared with arm 2. During the observation period, 2 patients in arm 2 but none in arm 1 became infected with influenza A virus.

8. Conclusions

The rise in anti-H3N2 antibody titer (but not anti-H1N1 antibody titer) was significantly greater in arm 1 than arm 2, suggesting that maobushisaishinto enhances the anti-H3N2 antibody titer induced by influenza vaccination and enhances specific immunity.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Influenza infection complicated with infections such as pneumonia contributes substantially to mortality in the elderly. Therefore, boosting the production of anti-influenza virus antibody would have an important preventive effect and reduce the cost of influenza treatment. From these points of view, this study investigated whether administration of maobushisaishinto can increase antibody level, with the expectation that maobushisaishinto acts as an adjuvant of the humoral immune response in the elderly with low influenza-antibody level. This report focuses on strategies for the prevention of influenza in the elderly with low response to influenza vaccine. Further studies are needed to determine why only anti-H3N2 antibody titer is significantly increased compared with control group whereas no significant difference was observed in anti-H1N1 antibody, and whether maobushisaishinto can promote production of specific antibodies.

The small number of patients was a problem in this study. Further analyses with an increased number of cases are necessary. Also studies on other Kampo medicines with adjuvant effects in subjects with low antibody production against influenza virus, and on methods of administration, are awaited.

Related article: "Iwasaki K. Influenza and Kampo in the elderly*. *TSUMURA Mail Magazine* 2008; Suppl: 22-3 (in Japanese)"

The number of the participants is higher, i.e., 18 in arm 1 (the maobushisaishinto group) and 15 in arm 2 (the control group). The results were almost the same, revealing elevated anti-H3N2 antibody titer in arm 1.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008. 12 March 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Watanabe N, Miyazawa T. Comparative study of the effect of bakumondoto and tipepidine hebinzate on cough in patients with mycoplasmal bronchitis. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2007; 21: 31-6 (in Japanese).

1. Objectives

To compare the efficacy of bakumondoto (麦門冬湯) and tipepidine hibenzate as antitussive agents in patients with mycoplasmal bronchitis.

2. Design

Randomized controlled trial using envelopes for allocation (RCT-envelope).

3. Setting

An internal medicine department in a hospital (the authors belong to the Division of Respiratory and Infectious Diseases, Department of Internal Medicine, St. Marianna University School of Medicine).

4. Participants

Female patients with mycoplasmal bronchitis who exhibited no signs of pneumonia on chest radiographs, n=14.

5. Intervention

Arm 1: administration of azithromycin 500 mg for 3 days, Tsumura Bakumondoto (麦門冬湯) Extract Granules (TJ-29) 3.0 g t.i.d. for 2 weeks, n=6.
Arm 2: administration of azithromycin 500 mg for 3 days, tipepidine hibenzate 60 mg for 2 weeks, n=8.

6. Main outcome measures

Cough score, white blood cell count, erythrocyte sedimentation rate, and C-reactive protein (CRP) level.

7. Main results

In arm 1, cough score was significantly decreased on day 5 compared to day 1 after the first visit ($P<0.05$). In arm 2, cough score was significantly decreased on day 7 ($P>0.05$). The rate of cough score decline was significant on day 5 in arm 1 ($P<0.05$) and on day 11 in arm 2 ($P<0.05$) There were no significant differences in white blood cell count, erythrocyte sedimentation rate, and CRP level.

8. Conclusions

Combination therapy with azithromycin and bakumondoto or tipepidine hibenzate appears to be effective in the treatment of cough in patients with mycoplasmal bronchitis.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Persistent cough in mycoplasmal bronchitis is often difficult to treat. This interesting study evaluates the efficacy of bakumondoto in a randomized controlled trial. It is likely that allocation by the envelope method leads to difficulty in preserving randomization. This clinical trial investigates the efficacy of azithryomycin combined with bakumondoto or tipepidine hibenzate in treating cough in mycoplasmal bronchitis, but the investigation lacks a placebo-group as control. Furthermore, to determine the difference in efficacy between the two arms, post-administration cough scores must be compared between the two arms. In addition, some participants have persistent cough even after 2 weeks in both arms. Consideration of Kampo "*sho*" (証, pattern/syndrome) for bakumondoto is required for further studies. Future studies regarding these points, and also inclusion of male patients, are awaited.

12. Abstractor and date

Okabe T, 25 November 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Mori H, Kurata H, Shimazaki Y, et al. Comparative study of Kampo preparations sho-sei-ryu-to and kei-ma-kakuhan-to for nasal allergy and allergic conjunctivitis in spring. *Therapeutic Research* 1999; 20: 2941-7 (text in Japanese with English abstract). MOL, MOL-Lib

1. Objectives

To compare the efficacy of shoseiryuto (小青竜湯), and keimakakuhanto (桂麻各半湯) in treating springtime nasal allergy and allergic conjunctivitis.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

From 25 January 1999 until 10 April 1999.
One hospital and three clinics of internal medicine.

4. Participants

Eighty eight patients with springtime nasal allergy and allergic conjunctivitis. Of these patients, 65 were included for analysis.

5. Intervention

Arm 1: TSUMURA Shoseiryuto (小青竜湯) Extract Granules (TJ-19) 3.0 g, t.i.d. for 2 weeks, n=32.
Arm 2: keimakakuhanto (桂麻各半湯) 8.0 g/day in three divided doses (4.0 g of TSUMURA Keishito (桂枝湯) Extract Granules [TJ-45] + 4.0 g of TSUMURA Maoto (麻黄湯) Extract Granules [TJ-27]) for 2 weeks, n=33.

6. Main outcome measures

Improvement in each symptom and global improvement.

7. Main results

Efficacy (percent improvement in arm 1 and arm 2, respectively) was observed against sneezing (68.8% and 66.7%), rhinorrhea (56.3% and 63.6%), nasal sinus obstruction (40.6% and 30.3%), and periocular pruritus (46.9% and 54.5%); there was no significant difference in between-arm improvements.
As for global improvement, 62.5% and 60.6% of patients in arm 1 and arm 2, respectively, were rated "moderately-to-markedly improved," demonstrating no significant between-arm difference in efficacy.

8. Conclusions

Keimakakuhanto is as effective as shoseiryuto in treating springtime nasal allergy and allergic conjunctivitis.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

In the shoseiryuto arm, two subjects reported dry mouth, one reported gastric distension, and one reported stomach discomfort leading to discontinued administration; and in the keimakakuhanto arm, one reported dry mouth and one discontinued administration because of nausea.

11. Abstractor's comments

As of 1999, no definite evidenced-based medicine (EBM) approach had been used to study the efficacy of Kampo formulations in treating springtime nasal allergy and allergic conjunctivitis. This paper presents a comparative study of the efficacies of two Kampo medicines, and further placebo-controlled analysis is awaited.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Yoshimoto T, Mori H, Kurata H, et al. Comparative study of Kampo preparations sho-sei-ryu-to and maoh-bushi-saisin-to for nasal allergy and allergic conjunctivitis in spring. *Therapeutic Research* 2002; 23: 2253-9 (text in Japanese with English abstract). Ichushi Web ID: 2003161479 MOL, MOL-Lib

1. Objectives

To compare the effects of shoseiryuto (小青竜湯) and maobushisaishinto (麻黄附子細辛湯) in treating springtime nasal allergy and allergic conjunctivitis.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Five clinics of internal medicine.

4. Participants

Of the patients who visited the above-mentioned clinics for the first time with springtime nasal allergy and allergic conjunctivitis (allergic rhinitis), 66 having previously diagnosed pollen hypersensitivity/pollinosis or newly diagnosed rhinitis with increased eosinophils in nasal discharge and elevated IgE level were enrolled. Exclusion criteria were: "*kyo-sho* (虚証, deficiency pattern)," sinusitis, nose disorders such as nasal septal deviation, conjunctivitis other than allergic conjunctivitis, pregnancy, and refusal to take Kampo medicines.

5. Intervention

Arm 1: TSUMURA Shoseiryuto (小青竜湯) Extract Granules (TJ-019) 3.0 g t.i.d., n=34.
Arm 2: TSUMURA Maobushisaishinto (麻黄附子細辛湯) Extract Granules (TJ-127) 2.5 g t.i.d., n=32.
Concomitant drug use was prohibited, with the exception of Intal eye drops or nasal spray for severe and intolerable symptoms.

6. Main outcome measures

Symptom improvement: Each of nose and eye symptoms after 2-week administration was rated on a 5-point scale (markedly improved, moderately improved, slightly improved, unchanged, and aggravated).
Global improvement: The severity of illness (nose and eye symptoms) after 2-week administration, compared with that before treatment, was rated on a 5-point scale (as maobushisaishinto acts rapidly, change in the symptoms was recorded beginning one week after the initiation of treatment.)
Overall safety: Adverse drug reactions after 2-week administration were evaluated on a 5-point scale.
Usefulness: The global improvement combined with overall safety was assessed on a 5-point scale (very useful, useful, slightly useful, indiscernible, and useless).

7. Main results

Slight-to-marked (or moderate-to-marked) improvement was seen in each of the following symptoms: sneezing (41.2% and 59.4% in arms 1 and 2, respectively), rhinorrhea (47.1% and 53.1%), nasal obstruction (58.8% and 37.5%), periocular pruritus (35.3% and 45.2%), lacrimation (23.5% and 19.4%), and ocular discharge (11.8% and 9.7%). The chi-square test and Mann-Whitney *U* test revealed no significant differences in improvement of any symptoms between the two arms. Also, there was no significant difference between the arms in global improvement (slight-to-marked global improvement in 67.6% and 71.9% for arms 1 and 2, respectively, and moderate-to-marked global improvement, 52.9% and 53.1%). As for usefulness, interventions were assessed to be "useful or very useful" in 50% for arm 1 and 50% for arm 2, with no significant between-arm difference.

8. Conclusions

Maobushisaishinto is suggested to be as effective as shoseiryuto in treating springtime nasal allergy and allergic conjunctivitis.

9. From Kampo medicine perspective

Maobushisaishinto is more suitable than shoseiryuto for treating subjects with "*kyo-sho*," who are frail or elderly.

10. Safety assessment in the article

No adverse drug reactions were observed in either arm.

11. Abstractor's comments

This study followed a RCT of shoseiryuto for nasal allergy and allergic conjunctivitis in spring (*Jibiinkoka Rinsyo* [*Practica otologica*] 1995; 88: 389-405 [in Japanese]), and uses the same outcome measures. However, patients were allocated sequentially and not properly randomized, making this study a clinical controlled trial (CCT: quasi-RCT). Results with no significant differences in this study provide a new therapeutic option for springtime nasal allergy and allergic conjunctivitis, and can be regarded as clinically meaningful.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Shimazaki Y, Mori H, Kurata H, et al. Comparative study of Kampo preparations Sho-Sei-Ryu-To and Go-Ko-To for nasal allergy and allergic conjunctivitis in spring. *Therapeutic Research* 2001; 22: 2385-91 (text in Japanese with English abstract). Ichushi Web ID: 2002138087 MOL, MOL-Lib

1. Objectives

To compare the effects of shoseiryuto (小青竜湯) and gokoto (五虎湯) in subjects with nasal allergy and allergic conjunctivitis in spring.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

One hospital and four clinics.

4. Participants

Patients with nasal allergy and allergic conjunctivitis in spring who had increased nasal eosinophil count and high IgE level, n=116.

5. Intervention

Patients who visited the setting of this study for the first time between 31 January 2000 and 10 April 2000 were recruited. Patients with severe symptoms were treated with Intal (sodium cromoglicate) nasal drops and eye drops. Assessments were done after two weeks of administration of one of the following.
Arm 1: Tsumura Gokoto (五虎湯) Extraction Granules 2.5 g, t.i.d., n=58.
Arm 2: Tsumura Shoseiryuto (小青竜湯) Extraction Granules 3.0 g, t.i.d., n=58.

6. Main outcome measures

Nasal symptoms: sneezing, discharge, and obstruction. Ocular symptoms: eyelid itching, tearing, eye discharge, and orbital pain.

7. Main results

Ten subjects in arm 1 and 17 in arm 2 who stopped visiting hospital/clinic and 1 subject in arm 1 who discontinued drug administration because of adverse effect were excluded. Though not significantly different between arms, the efficacy rates were higher in arm 2 for all outcome measures except eye discharge and orbital pain, which were higher in arm 1.

8. Conclusions

There was no significant between-arm difference in treatment usefulness, with usefulness in 70.8% of arm 1 and 80.5% of arm 2 was characterized as moderate or more than moderate.

9. From Kampo medicine perspective

Subjects with *kyosho* (虚証, deficiency pattern） were excluded because shoseiryuto and gokoto are used to treat subjects with *jitsusho* (実証, excess pattern) or *chukansho* (中間証).

10. Safety assessment in the article

Adverse effects included dry mouth (n=5), abdominal pain (n=1), hard stool (n=1), palpitation (n=1, excluded from analysis) in arm 1, and dry mouth (n=1) and constipation (n=1) in arm 2.

11. Abstractor's comments

The authors also compare Kampo drugs for allergic rhinitis or nasal allergy and allergic conjunctivitis in spring in several previous papers, which should be read together.

12. Abstractor and date

Fujisawa M, 15 January 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Miyamoto T, Inoue H, Kitamura S, et al. Effect of TSUMURA Sho-seiryu-to (TJ-19) on bronchitis in a double-blind placebo-controlled study. *Rinsho Iyaku* (*Journal of Clinical Therapeutics & Medicine)* 2001; 17: 1189-214 (text in Japanese with English abstract). Ichushi Web ID: 2002029631

1. Objectives

To evaluate the efficacy and safety of shoseiryuto (小青竜湯) in the treatment of bronchitis.

2. Design

Randomized controlled trial (RCT).

3. Setting

Seventeen university hospitals, forty-two hospitals, and three clinics.
From December 1994 until March 1999.

4. Participants

Patients aged 16 to <65 years with mild to moderate bronchitis, and evaluable symptoms (any of watery sputum, rales/rhonchi, and cough).

5. Intervention

The concomitant use of other drugs was prohibited with the exception of dimemorfan phosphate (Astomin) after day 4.
Arm 1: TSUMURA Shoseiryuto (小青竜湯) Extract Granules (TJ-19) 3.0 g t.i.d. for 7 days, n=101.
Arm 2: placebo 3.0 g t.i.d. for 7 days, n=91.

6. Main outcome measures

Global improvement (rate), improvement of bronchitis symptoms (such as cough and sputum), and safety.

7. Main results

At the end of treatment, there was a trend toward higher percentage of patients with moderate-to-marked global improvement in arm 1, compared with arm 2 (57.4% in arm 1 *vs* 42.9% in arm 2; *P*=0.06. No significant difference was observed at day 3 or 4. As for improvement of each symptom, ease of raising sputum, properties of sputum (purulent, viscous, etc.), and disturbance in activities of daily living, was significantly better in arm 1 at days 3-4. At the end of treatment, there was significant improvement in frequency of coughing, intensity of coughing, ease of raising sputum, and activities of daily living, and a tendency toward improvement in sneezing and nasal obstruction in arm 1.

8. Conclusions

Shoseiryuto was effective for bronchitis with mild symptoms.

9. From Kampo medicine perspective

Inclusion criteria of patients with watery sputum, rales/rhonchi, and/or cough were chosen to adopt the "*sho* (証, pattern/syndrome)" for shoseiryuto in Kampo medicine. Further subgroup analyses in patients without physical frailty and those with cough and watery sputum showed a significantly higher rate of global improvement in arm 1 than arm 2.

10. Safety assessment in the article

The incidence of adverse effects was 6.7% (7 cases) in arm 1 and 9.9% (9 cases) in arm 2, with no significant difference. No serious adverse effects were found.

11. Abstractor's comments

This is a large-scale double-blind RCT involving the subjects with shoseiryuto-*sho* in Kampo medicine.
Also, in another article "Miyamoto T. Clinical effectiveness of Shosei-ryuto in bronchitis. *Pharma Medica* 2007; 25: 23-5 (in Japanese). [Ichushi Web ID: 2008035989]", the efficacy of shoseiryuto is shown for mild to moderate bronchitis in patients who have watery sputum, rales/rhonchi, and/or cough.

12. Abstractor and date

Fujisawa M, 15 June 2007, 22 February 2009, 8 August 2009.

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Respiratory Diseases (including Influenza and Rhinitis)

Reference

Kato S, Matsuda T, Nakajima T, et al. Clinical significance of the combination therapy of smoking cessation and seihaito for chronic obstructive pulmonary disease. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2005; 14: 260-5 (in Japanese). Ichushi Web ID: 2005292823

Kato S, Oda K, Hasumi H, et al. The combined effect of smoking cessation and Seihai-to on airway clearance on COPD patients. *Kampo to Meneki-Arerugi* (*Kampo and Immuno-Allergy*) 2006; 19: 26-35 (text in Japanese with English abstract).

1. Objectives

To assess the efficacy of smoking cessation combined with administration of seihaito (清肺湯) for chronic obstructive pulmonary disease (COPD).

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT- envelope)

3. Setting

Two university hospitals.

4. Participants

Patients with GOLD stage 0, 1, or 2 COPD who had stopped smoking, but whose respiratory symptoms (cough, sputum, and dyspnea) were still present one month after smoking cessation, n=31.

5. Intervention

Arm 1: smoking cessation and administration of TSUMURA Seihaito (清肺湯) Extract Granules 9.0 g/day, for 24 months, n=16.

Arm 2: smoking cessation only, for 24 months, n=15.

6. Main outcome measures

Respiratory symptoms.

Chest radiography and chest CT findings (emphysema, organizing pneumonia, bronchial obstruction by sputum).

7. Main results

Respiratory symptoms were significantly improved in arm 1 compared with arm 2 for 1 to 6 months; however, no significant difference was found after 12 months. The imaging findings were significantly improved in arm 1 at 24 months.

8. Conclusions

Administration of seihaito for 6 months improves clinical symptoms, and administration for 24 months is necessary for improvement in imaging findings.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Dyspnea can be evaluated objectively by respiratory function testing and measurement of blood oxygen saturation, therefore use of these tests in the follow up period is desired.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including influenza and rhinitis)

Reference

Fukuchi Y, Tatsumi K. Utility evaluation of Kampo in the treatment of chronic obstructive pulmonary disease. *Kosei Rodosho Kagaku Kenkyuhi Hojokin Choju Kagaku Sogo Kenkyu Jigyo Sokatsu Kenkyusyo Hokokusyo* (*Ministry of Health, Labour and Welfare, Science Research Grant, Comprehensive Studies on Science of Aging, Summary report*), 2007:1-31 (in Japanese).

1. Objectives

To investigate the effect of hochuekkito (補中益気湯) on systemic inflammation in subjects with chronic obstructive pulmonary disease (COPD).

2. Design

Randomized controlled trial (envelope method) (RCT-envelope).

3. Setting

Twelve university hospitals and thirteen hospitals.

4. Participants

Clinically stable patients who fulfilled the diagnostic criteria of the Japan Respiratory Society Guidelines for COPD, n=71.

5. Intervention

Assessments were done after 6 months of treatment.

Arm 1: conventional treatments with Tsumura Hochuekkito (補中益気湯) Extract Granules (TJ-41), 2.5 g, b.i.d. or t.i.d., n=34.

Arm 2: control: continued conventional treatments, n=37.

6. Main outcome measures

Subjective symptoms: SGRQ (St. George's Respiratory Questionnaire), symptoms related to *ki-kyo*, incidence of common cold (assessed using patients' diaries), and frequency of exacerbations (defined on the basis of Anthonisen's criteria and requirement for systemic administration of steroids).

Objective measurements: body mass index (BMI), change in body weight, respiratory function, blood gas analysis, markers of nutrition status (prealbumin, leptin, and adiponectin), and markers of inflammation (high sensitivity C-reactive protein [hsCRP], TNF-α, and IL-6).

7. Main results

SGRQ subjective symptom score was significantly improved in arm 1. Also, incidence of the common cold and frequency of exacerbation were significantly less in arm 1 than in arm 2. There was no significant change in body weight in both arms during 6 months of observation. Prealbumin, a marker of nutritional status, increased significantly only in arm 1. Leptin level remained unchanged after administration of hochuekkito. The markers of systemic inflammation (hsCRP, TNF-α, and IL-6) were negatively correlated with severity of COPD (represented by FEV_1% predicted). In arm 1, hsCRP and TNF-α decreased significantly, but IL-6 remained unchanged. Concentration of adiponectin, secreted by adipocytes and suggested to be involved in the development of arteriosclerosis, was negatively correlated with BMI and significantly increased after treatment with hochuekkito.

8. Conclusions

Administration of hochuekkito improved systemic inflammation and nutritional status in subjects with COPD, and decreased COPD exacerbation and incidence of the common cold.

9. From Kampo medicine perspective

Among the symptoms related to *qikyo* (気虚, qi deficiency), physical lassitude, morale, fatigability, susceptibility to the common cold, and appetite improved.

10. Safety assessment in the article

There were no safety issues.

11. Abstractor's comments

There is an interim report of this study, "Shinozuka N, Tatsumi K, Nakamura A, et al. Evaluation of systemic inflammation and utility of hochuekkito administration in subjects with COPD*. *Kosei Rodosho Kagaku Kenkyu Kenkyuhi Hojokin Nanchisei Shikkan Kokufuku Kenkyu Jigyo Kokyufuzen ni Kansuru Chosa Kenkyu Heisei 18 Nendo Kenkyu Hokokusho* [*Ministry of Health, Labour and Welfare, Science Research Grant, The Intractable Disease Treatment Research Project, Research report fiscal year 2006*] 2007:94-9 (in Japanese)." The objective measurements data in the interim report were summarized and published in "Shinozuka N, Tatsumi K, Nakamura A, et al. The traditional herbal medicine hochuekkito improves systemic inflammation in patients with chronic obstructive pulmonary disease. *Journal of the American Geriatrics Society* 2007; 55: 313-4. [CENTRAL ID: CN-00578499, Pubmed ID: 17302677]" Weight loss as well as airflow limitation in subjects with COPD is an independent prognostic factor, and awareness is growing that COPD is a systemic inflammatory disease.

12. Abstractor and date

Fujisawa M, 22 February 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive Effect of Japanese Herbal Medicine, Saiboku-to (Cai-Pu-Tang) on Brochospasms in Aspirin-induced Bronchial Asthmatic Patients. A Randomized, Double-blind Test. *Jibi-inkoka Tenbo* (*Oto-Rhino-Laryngology Tokyo*) 2001; 44: 5-13 (text in Japanese with English abstract). Ichushi Web ID: 2002025794

1. Objectives

Development of saibokuto (柴朴湯) inhalation therapy, and to evaluate its efficacy in preventing attacks of aspirin-induced asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

Two clinics.

4. Participants

Patients with aspirin-induced asthma in whom the threshold dose of L-lysine-aspirin for provoking an asthma attack was determined by inhalation, n=74.

5. Intervention

Saibokuto inhalant: TSUMURA Saibokuto (柴朴湯) Extract Granules (TJ-96) were dissolved in injectable saline, sonicated for 90 minutes, and filtered through a Millipore sterile 0.22-micron filter. After adjustment to a concentration of 100 μg/mL, 5 mL of the inhalant was inhaled three times a day.
Arm 1: inhalation of saibokuto (柴朴湯) inhalant for 6 months, n=35.
Arm 2: inhalation of saline for 6 months, n=39.

6. Main outcome measures

The efficacy and safety of inhaled saibokuto for reducing the frequency of asthma attacks.

7. Main results

Saibokuto inhalant was newly developed. Prolonged inhalant usage significantly reduced the frequency of asthma attacks (0.004 times/person/6 months in arm 1 *vs* 0.120 times/person/6 months in arm 2).

8. Conclusions

Inhalation, compared with oral administration, can increase the concentration of saibokuto in the lung to the same level as achieved in experiments *in vivo* and *in vitro*, resulting in suppression of the production and release of biologically active substances in bronchoalveolar lavage fluid, and thereby of asthma attacks.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse effects were observed in 7 cases (20.0%) in arm 1 and 7 cases (17.9%) in arm 2, none of which led to withdrawal from the study.

11. Abstractor's comments

The preparation of saibokuto inhalant (as described above) involved more than simply dissolving the extract granules in saline.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive effect of Kampo medicine, Cai-pu-tang (Japanese name: Saiboku-to, TJ-96) on brochospasms in aspirin-induced bronchial asthmatic patients and decrease of chronic pain. Especially psychological pain. *Itami to Kampo* (*Pain and Kampo Medicine*) 2001; 11: 14-21 (text in Japanese with English abstract). Ichushi Web ID: 2002261501

1. Objectives

To evaluate the efficacy of short-term inhaled saibokuto (柴朴湯) in suppressing airway constriction, and long-term inhaled saibokuto（柴朴湯）in alleviating psychological suffering.

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital and three clinics.

4. Participants

Thirty-two patients with aspirin-induced asthma.

5. Intervention

1) Suppression of airway constriction (assessed by inhaling lysine-aspirin after inhaling the following):

Arm 1: saibokuto (柴朴湯) inhalant.

Arm 2: injectable distilled water.

2) Alleviation of mental suffering by inhalation for a long period (cross-over design with 6 months on saibokuto (柴朴湯) and 6 months on distilled water), n=32.

6. Main outcome measures

Suppression of airway constriction (forced expiratory volume in one second; $FEV_{1.0}$), biologically active substances in bronchoalveolar lavage fluid (BALF) at 30 minutes after inhaling lysine-aspirin, chronic pain.

7. Main results

In the trial of long-term inhalation, significant improvements were observed in each QOL domain and also in global QOL scores (this global QOL assessment method was developed by the authors using a visual analog scale [VAS] to assess physical [QOL-P], mental/psychological [QOL-M], social activity [QOL-S], medical economics [QOL-E], therapeutic drug [QOL-D], and individual QOL [QOL-I] incorporated items measuring the perspectives of individuals [including his/her perspectives on philosophy, thoughts, ethics, generation, policy, religion, and so on], as well as face scale and modified health assessment questionnaires). In arm 1, decreased $FEV_{1.0}$ as well as increased production and release of leukotrienes in BALF due to lysine-aspirin inhalation were significantly suppressed. In arm 1, $FEV_{1.0}$ improved more than 135% in 18 cases (56.3%), more than 125% in 4 cases (12.5%), and more than 110% in 1 case (3.1%), whereas in arm 2, no cases improved more than 135% and 125%, and 2 cases improved more than 110%.

8. Conclusions

Inhaled saibokuto therapy improved QOL and respiratory function.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Dysguesia (or altered sensation of taste) was observed in 5 cases (15.6%) in arm 1 and in 2 cases (6.3%) in arm 2. Cacosmia (or imagining of unpleasant odors) was observed in 7 cases (21.9%) in arm 1 and in 4 cases (12.5%) in arm 2. None of these adverse effects caused withdrawal from the study.

11. Abstractor's comments

Although the "global QOL assessment method" developed by the authors is used as the index of mental suffering, there is no documentation validating the use of this method in this paper, which claims improvement in mental suffering. Despite the resemblance to "Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive Effect of Japanese Herbal Medicine, Saiboku-to (Cai-Pu-Tang) on Brochospasms in Aspirin-induced Bronchial Asthmatic Patients. A Randomized, Double-blind Test. *Jibi-inkoka Tenbo* (*Oto-Rhino-Laryngology Tokyo*) 2001; 44: 5-13 (text in Japanese with English abstract)", this report differs as follows: use of distilled water as solvent instead of saline, and use of a non-random cross-over design instead of a randomized design.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Urata Y, Yoshida S, Irie Y, et al. Treatment of asthma patients with herbal medicine TJ-96: a randomized controlled trial. *Respiratory Medicine* 2002; 96: 469-74. CENTRAL ID: CN-00390241, Pubmed ID: 12117049

1. Objectives

To investigate the clinical effect of saibokuto (柴朴湯) for the treatment of atopic asthma.

2. Design

Randomized controlled trial (cross over) (RCT-cross over).

3. Setting

One university hospital and one hospital.

4. Participants

Adult patients with atopic asthma, n=33.

5. Intervention

Cross-over design (administration of saibokuto (柴朴湯) or placebo [2.5 g, t.i.d.] for 4 weeks, and then, after a washout period of at least 4 weeks, patients crossed over to receive the alternative treatment), n=33.
Arm 1: TSUMURA Saibokuto (柴朴湯) Extract Granules (TJ-96).
Arm 2: placebo.

6. Main outcome measures

Clinical symptoms, respiratory function test, methacholine provocation testing, eosinophil counts in blood and sputum, and eosinophilic cationic protein (ECP) in blood and sputum.

7. Main results

Symptom score (which employed similar severity classification according to Guidelines for Asthma Prevention and Management 2004 [JGL 2004]) before treatment was 1.65±0.38 in arm 1 and 1.66±0.43 in arm 2. After treatment, it was significantly decreased in arm 1 (0.73±0.25 in arm 1 and 1.63±0.39 in arm 2, P=0.001). Forced expiratory volume in 1 second ($FEV_{1.0}$) improved slightly but not significantly in arm 1. Response to provocation challenge with methacholine was significantly better in arm 1. Significant decreases in eosinophil counts and ECP in blood and sputum but not neutrophil counts were observed in arm 1.

8. Conclusions

Saibokuto improves clinical symptoms in patients with atopic asthma. Although $FEV_{1.0}$ and FVC were unaffected, saibokuto was able to attenuate eosinophilic inflammation.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

This is an RCT of Kampo treatment for asthma assessed using a respiratory function test.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive effect of Chinese tracitional medicine, she-bi-tang (shinpi to) on bronchospasm in aspirin-indolerant bronchial asthmatic patients – a randomized, group-paralleled comparative trial –. *Jibi-inkoka Tenbo* (*Oto-rhino-laryngology Tokyo*) 2003; 46: 3-14 (in Japanese). Ichushi Web ID: 2004041278

1. Objectives

To assess the efficacy and safety of inhaled shimpito (神秘湯) for the control of aspirin-induced asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

Several clinics and others, Osaka prefecture.

4. Participants

Patients with histories of aspirin-induced asthma, whose threshold levels of inhaled lysine-aspirin are determined, n=114.

5. Intervention

Arm 1: inhalation of TSUMURA Shimpito (神秘湯) Extract Granules, 500 μg in four divided doses, n=53.
Arm 2: inhalation of cromoglycate, 5 mg q.i.d., n=61.
Duration of the study was 1 year.

6. Main outcome measures

The effect was evaluated by assessing 1) leukotrienes levels in bronchoalveolar lavage (BAL) fluid, 2) forced expiratory volume in 1 second ($FEV_{1.0}$) after lysine-aspirin inhalation, and 3) frequency of asthma attacks (or exacerbations).

7. Main results

The decrease in $FEV_{1.0}$ after lysine-aspirin inhalation was significantly greater in arm 1 than arm 2. Also, the frequency of asthma attacks and leukotriene levels in BAL fluid were decreased in arm 1 relative to arm 2.

8. Conclusions

Inhaled shimpito is more efficacious than inhaled cromoglycate for the management of aspirin-induced asthma.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

The frequency of both abnormal laboratory findings and adverse reactions were higher in arm 2 than in arm 1 (number of cases are unclear because the results were omitted in this paper).

11. Abstractor's comments

Despite the term "multicenter, randomized" in the title, the method of randomization is not described, and the facilities where this clinical trial was actually performed (not the research institute) are unspecified. This paper does not state the number of withdrawals and analyzed cases during the 1-year follow-up of 114 subjects. Might it mean no withdrawals during the 1-year treatment period? Aspirin-induced asthma comprises 4-10% of all asthma cases. Inhaled corticosteroids are the most commonly used asthma medications. This study implies the greater efficacy of inhaled shimpito therapy in the management of asthma when compared with that of inhaled cromoglycate therapy. Further studies are awaited to assess whether oral administration of shimpito also provides similar efficacy when used by subjects with the appropriate "*sho*."

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Goto GH, et al. A randomized, group-parallel comparative trial of the suppressiveeffect of Chinese traditional medicine, shen-mi-tang (shin-pi-to), compared to sodium oramolycate inhalation in improving subjective and objective symptoms in bronchial asthmatics. *Jibi-inkoka Tenbo* (*Oto-rhino-laryngology Tokyo*) 2004; 47: 20-7 (text in Japanese with English abstract).
Ichushi Web ID: 2005016956

1. Objectives

To assess the efficacy and safety of inhaled shimpito (神秘湯) therapy for improving asthma symptoms in patients with aspirin-induced asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

Several clinics and other health care facilities, Osaka prefecture.

4. Participants

Patients with aspirin-induced asthma, whose thresholds for induction of asthma (attacks) have been determined, n=161.

5. Intervention

Arm 1: inhalation of shimpito (神秘湯), 500 μg in four divided doses, n=81.
Arm 2: inhalation of cromoglycate, 5 mg q.i.d., n=80.
Duration of the study was 3 years.

6. Main outcome measures

1) Frequency of asthma attacks (or exacerbations), 2) improvement in health-related QOL, 3) improvement in chronic pain, 4) leukotriene level in bronchoalveolar lavage (BAL) fluid

7. Main results

In arm 1, frequency of asthma attacks and leukotriene level in BAL fluid were significantly reduced, and QOL and chronic pain were significantly improved when compared with arm 2.

8. Conclusions

Inhaled shimpito therapy suppressed production of leukotrienes, prevented exacerbation of aspirin-induced asthma, alleviated chronic pain, and improved QOL.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Fewer cases and subjects had abnormal laboratory findings and adverse reactions in arm 1 than in arm 2.

11. Abstractor's comments

The authors do not specify the medical facilities where this clinical trial (described as multicenter trial) actually took place. In this prospective, randomized study, the number of withdrawals and cases analyzed during the 3-year period of observation for 161 enrolled subjects is not stated. It is unclear whether there were any withdrawals during this period. Aspirin-induced asthma comprises 4-10% of all cases of asthma. Inhaled corticosteroids are the most common medications used for asthma therapy. This study implies that inhaled shimpito therapy is more efficacious in the management of asthma than inhaled cromoglycate therapy. In patients with aspirin-induced asthma, health-related QOL is generally not good because of limitation on the use of nonsteroidal anti-inflammatory drugs (NSAIDs) for pain and inflammation. However, shimpito can improve these symptoms. Further studies are awaited to assess whether oral administration of shimpito also has similar efficacy when used in subjects with the appropriate "*sho*."

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Goto HG et al. Chronic pain in intractable and chronic internal diseases[*]. *Mansei Totsu* (*The Journal of the Japanese Society for the Study of Chronic Pain*), 2002; 21: 67-77 (text in Japanese with English abstract). Ichushi Web ID: 2003126703 MOL, MOL-Lib

1. Objectives

To investigate the effect of saibokuto (柴朴湯) inhalation therapy in improving quality of life (QOL) in patients with aspirin-intolerant asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital and two clinics.

4. Participants

Patients with aspirin-intolerant asthma, n=214.

5. Intervention

The study duration was 3 years. For saibokuto (柴朴湯) inhalation, 500 μg of saibokuto was packed into capsules comparable to those used for sodium cromoglycate (DSCG) inhalation.
Arm 1: saibokuto (柴朴湯) (the manufacturer not identified), 500 μg q.i.d. inhalation, n=105.
Arm 2: DSCG 20 mg q.i.d. inhalation, n=109.

6. Main outcome measures

Subjective symptoms, various tests, chronic pain, and QOL were assessed using a visual analog "total disease-related symptoms" scale developed by the authors, and face rating scores.

7. Main results

Saibokuto inhalation improved various endpoints.

8. Conclusions

Symptom-related QOL of patients with exacerbated aspirin-intolerant asthma was improved.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

The incidence of adverse effects was higher in arm 1, however, there was no significant difference in the number of cases. These results were omitted from the original article.

11. Abstractor's comments

This RCT resembles two other RCTs of saibokuto inhalation therapy, "Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive Effect of Japanese Herbal Medicine, Saiboku-to (Cai-Pu-Tang) on Brochospasms in Aspirin-induced Bronchial Asthmatic Patients. A Randomized, Double-blind Test. *Jibi-inkoka Tenbo* (*Oto-Rhino-Laryngology Tokyo*) 2001; 44: 5-13 (text in Japanese with English abstract)" and "Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Suppressive effect of Kampo medicine, Cai-pu-tang (Japanese name: Saiboku-to, TJ-96) on brochospasms in aspirin-induced bronchial asthmatic patients and decrease of chronic pain. Especially psychological pain. *Itami to Kampo* (*Pain and Kampo Medicine*) 2001; 11: 14-21 (text in Japanese with English abstract)". The only difference between these studies is the method of administering the inhalant: inhalation of saibokuto dissolved in distilled water or saline, or as a powder using a spinhaler as mentioned in this paper. Inhalation of powder should further improve QOL because powder increases accessibility. Common to these three papers is their complicated format, poorly-described rationale, and omission of results, which makes understanding the contents more difficult.

12. Abstractor and date

Fujisawa M, 22 February 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Nagano F, et al. Sparing effect of saibokuto inhalation on inhaled beclomethasone dipropionate to halved of reduction of inhaled beclomethasone dipropinate-dose: well-controlled comparative study of saiboku-to-inhalation and sodium cromoglycate-inhalation. *Jibi-inkoka Tenbo* (*Oto-rhino-laryngology Tokyo*) 2002; 45: 8-15 (text in Japanese with English abstract).
Ichushi Web ID: 2003036732

1. Objectives

To assess the efficacy and safety of inhaled saibokuto (柴朴湯) while reducing the amount of inhaled beclomethasone during the course of treatment for bronchial asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

Several clinics and others, Osaka prefecture.

4. Participants

Patients with stable bronchial asthma whose peak expiratory flow rate was maintained at more than 70% of normal for 6 months by the use of inhaled beclomethoasone (800 μg/day) , n=94.

5. Intervention

Amount of inhaled beclomethasone was reduced from 800 μg/day to 400 μg/day at 4 weeks before the intervention.
Arm 1: inhaled saibokuto (柴朴湯), 500 μg q.i.d., n=49.
Arm 2: inhaled cromoglycate, 20 mg q.i.d., n=45.
Duration of the study was 12 months.

6. Main outcome measures

1) Intensity of subjective symptoms (visual analogue scale), 2) peak expiratory flow (respiratory function test), 3) frequency of the use of β_2-agonist, 4) cytokine levels in bronchial lavage fluid, 5) nitric oxide (NO) concentrations in expired air, and so on.

7. Main results

In arm 1, subjective symptoms and respiratory function were significantly improved, and compared to arm 2, patients in arm 1 had significantly reduced frequency of β_2-agonist use, NO concentration in expired air, and cytokine levels in bronchial lavage fluid. Less than 10% decrease in the peak expiratory flow rate occurred in 67.3% of arm 1 and 13.3% of arm 2.

8. Conclusions

Inhaled saibokuto therapy was suggested to maintain the efficacy of inhaled beclomethasone as treatment for bronchial asthma despite dosage reduction.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse effects occurred in 11 cases (22.4%) in arm 1, and in 8 cases (17.8%) in arm 2.

11. Abstractor's comments

Although they mention a multicenter study, the authors cite only one research institute, and do not specify the facilities where the clinical trials were actually conducted. The number of withdrawals during the 1-year follow-up and the percentage of the 94 enrolled patients who were actually included for analysis were not stated. Perhaps no one withdrew during the 1 year of treatment. Inhaled saibokuto therapy is assumed to be efficient compared to inhaled cromoglycate. All participants in this study should be considered adult patients with mild asthma. In terms of Kampo medicine, bronchial asthma presents a variety of "*sho* (証, pattern/syndrome)." Previous studies demonstrated that oral administration of saibokuto shows only limited clinical efficiency for those who do not have "*sho*" for saibokuto.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Clinical effect of a Kampo medicine, chai-po-tang (Japanese name: saiboku-to) compared with xiao-quing-long tang (Japanese name: shoseiryu-to) in asthmatics with anxiety and depression due to asthmatic attacks. *Nihon Toyo Shinshin Igaku Kenkyu* (*Journal of Japanese Association of Oriental Psychosomatic Medicine*) 2003; 18: 11-7 (text in Japanese with English abstract). Ichushi Web ID: 2006192016

1. Objectives

To compare the efficacy of the anxiolytic-like agent saibokuto (柴朴湯) with that of shoseiryuto (小青竜湯) in patients with bronchial asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

The setting of this study is unstated; the authors of this paper work in clinics and are specialists in allergy and respiratory medicine.

4. Participants

Patients with bronchial asthma who fulfilled one of the following criteria were included (n=139): comprehensive asthma inventory score ≥20, both state trait anxiety inventory (STAI) I and II scores ≥ 41 in men and ≥ 42 in women, or self-rating depression scale (SDS) ≥ 40.

5. Intervention

Arm 1: TSUMURA Saibokuto (柴朴湯) Extract Granules 5.0 g/day in three divided doses (in capsule form) administered between meals for 24 weeks, n=71.

Arm 2: TSUMURA Shoseiryuto (小青竜湯) Extract Granules 5.0 g/day in three divided doses (in capsule form) administered between meals for 24 weeks, n=68.

6. Main outcome measures

Scores on various types of mental and psychological tests, subjective symptoms, bronchoalveolar lavage (BAL) fluid levels of hormones of the hypothalamo-pituitary-adrenal system, the assessment of suffering from chronic and intractable medical diseases, improvement in global symptoms (rated on a scale from 1 [markedly improved] to 5 [worsened], taking into account disease-related symptoms and the development of adverse reactions).

7. Main results

Various types of psychological tests, subjective symptoms, BAL fluid findings, levels of hormones of the hypothalamo-pituitary-adrenal system, chronic and intractable medical diseases, and global symptom scores showed significantly greater improvement in arm 1 than arm 2. The conditions of 66.2% of subjects in arm 1 and 7.3% in arm 2 were improved or better at the end of the study.

8. Conclusions

Saibokuto is more effective than shoseiryuto in asthma patients with anxiety symptoms.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Although the authors do not offer a detailed description, adverse effects were observed in 2 cases (2.8%) and 5 cases (7.4%) in arm 1 and 2, respectively. Abnormal laboratory findings were noted in 2 cases (2.8%) in arm 1 and 6 cases (8.8%) in arm 2.

11. Abstractor's comments

Using a double-blind randomized controlled design, this study provides high-quality evidence that saibokuto and shoseiryuto are effective for asthma in patients with anxiety symptoms. As the authors refer to development of adverse reactions, the number of withdrawals and the reasons for withdrawal should have been included to make this report even better. Accumulation of the detailed comparative information about these two Kampo drugs will clarify understanding of how both drugs work.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Clinical effect of a Chinese tracitional herbal medicine, chai-po-tang (Japanese name: saiboku-to) compared with clotiazepam in patients with bronchial asthmatics and anxiery disorder in multicenter randomized, comparative trial. *Nihon Toyo Shinshin Igaku Kenkyu* (*Journal of Japanese Association of Oriental Psychosomatic Medicine)* 2002; 17: 20-7 (text in Japanese with English abstract). Ichushi Web ID: 2006192005

1. Objectives

To assess the efficacy of the anxiolytic-like agent, saibokuto (柴朴湯), in treating bronchial asthma.

2. Design

Randomized controlled trial (RCT).

3. Setting

The setting of this study is unstated; the authors of this paper work in clinics, and are specialists in allergic and respiratory medicine.

4. Participants

Patients with bronchial asthma who fulfill one of the following criteria were included (n=107): comprehensive asthma inventory score ≥ 20, both state trait anxiety inventory (STAI) I and II scores ≥ 41 in men and ≥ 42 in women, or self-rating depression scale (SDS) ≥ 40.

5. Intervention

Arm 1: administration of TSUMURA Saibokuto (柴朴湯) Extract Granules 2.5 g t.i.d. before meals for 3 years, n=51.

Arm 2: administration of clotiazepam 15-30 mg/day (mean 23.9 mg/day) t.i.d. before meals for 3 years, n=56.

6. Main outcome measures

Clinical effects, scores various types of mental and psychological tests, airway hyperreactivity, bronchoalveolar lavage (BAL) fluid, improvement in global symptoms (as assessed by a combination of the preceding measures and the development of adverse reactions indicating worsening).

7. Main results

Scores on various types of psychological tests, airway hyperreactivity, BAL fluid findings, and global symptoms showed significantly greater improvement in subjects in arm 1 than those in arm 2. The conditions of 68.6% of subjects in arm 1 and 21.3% of subjects in arm 2 were improved or better.

8. Conclusions

Saibokuto is significantly more effective than clotiazepam in reducing the severity of asthma symptoms in asthma patients with anxiety symptoms.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

In arm 1, there were no adverse reactions or abnormal laboratory findings. In arm 2, there were 13 cases (23.2%) including cases of drowsiness and poor concentration.

11. Abstractor's comments

Using a double-blind randomized controlled design, this study provides high-quality evidence that saibokuto is effective for asthma in patients with anxiety symptoms. Withdrawal from the study is not documented in this paper, nor has it been stated whether bronchoscopy was performed in all cases. In the Results section, the authors often use the phrase "results omitted" and do not show the data. Because the results here indicate the efficacy of saibokuto for asthma patients with anxiety symptoms, these data should have been disclosed to further validate its efficacy. However this remains a well-designed study investigating the psychological and organic pathology of asthma and evaluating the long-term efficacy of a Kampo medicine. Further studies including other Kampo formulae are desired.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Clinical effect of Chai-to-tang (Japanese name: Saiboku-to), a Chinese traditional herbal medicine, in patients with bronchial asthma and autonomic nerve dysfunction: A multicenter, randomized, double-blind, placebo-controlled study. *Nihon Toyo Shinshin Igaku Kenkyu* (*Journal of Japanese Association of Oriental Psychosomatic Medicine*) 2004; 19: 37-41 (text in Japanese with English abstract). Ichushi Web ID: 2006203751

1. Objectives

To evaluate the efficacy and safety of saibokuto (柴朴湯) in patients with asthma exacerbations based on anticipatory anxiety.

2. Design

Randomized controlled trial (RCT).

3. Setting

The setting of this study is unstated; the authors of this paper work in clinics, and are specialists in allergic and respiratory medicine.

4. Participants Shimazaki Y, Mori H, Kurata H, et al. Comparative study of Kampo preparations

Patients with bronchial asthma who fulfill one of the following criteria were included (among 174 subjects participated, data from 172 subjects were analyzed): comprehensive asthma inventory score ≥ 20, both state trait anxiety inventory (STAI) I and II scores ≥ 41 in men and ≥ 42 in women, or self-rating depression scale (SDS) ≥ 40.

5. Intervention

Arm 1: Administration of TSUMURA Saibokuto (柴朴湯) Extract Granules 5.0 g/day three times a day before meals for 6 months, n=87.

Arm 2: Administration of lactose 5.0 g/day three times a day before meals for 6 months, n=85.

Each drug was given in indistinguishable capsule.

6. Main outcome measures

Assessment of improvement in objective and subjective symptoms concerning bronchial asthma, various types of mental and psychological tests, assessment of autonomic dysfunction, bronchoalveolar lavage (BAL) fluid, numbers of inflammatory cells in bronchial mucosa biopsy, frequency of asthma exacerbations, levels of hypothalamic, pituitary, and adrenal cortex hormones, assessment of chronic pain, and others.

7. Main results

Autonomic dysfunction, clinical symptoms, and BAL fluid analysis were significantly improved in arm 1 compared to arm 2. In arm 1, the number of subjects with asthma exacerbations decreased from 87 to 14 and the mean duration of asthma exacerbation decreased from 31.5 to 3.1 days, while both indices were increased in arm 2 (descriptions of the results in the text were imprecise).

8. Conclusions

Saibokuto is effective in improving asthma symptoms and psychiatric symptoms in patients with autonomic dysfunction due to asthma.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no differences between the two arms in the incidences of adverse effects and abnormal laboratory data (no precise description in the paper).

11. Abstractor's comments

As the authors' notes in the Discussion section, this is the first clinical trial in the world to evaluate the effect of saibokuto in patients with bronchial asthma in a randomized, double-blind, controlled design. Following up a number of subjects in detail in multicenter analysis should have required substantial efforts. Declaration of the missing details such as 1) the number of withdrawals during 6 months of observation, 2) the number of subjects who underwent bronchoscopy, and 3) precise data omitted in the Result section, would be effective in making the efficacy of saibokuto widely accepted. Accumulation of such detailed studies may lead to elucidation of the action mechanisms and the efficacy of Kampo medicine, and more similar studies are awaited.

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 1 May 2009, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Iwasaki K, Cyong JC, Kitada S, et al. A traditional Chinese herbal medicine, banxia houp tang, improves cough reflex of patients with aspiration pneumonia. *Journal of American Geriatrics Society* 2002; 50: 1751-2.

1. Objectives

To investigate whether hangekobokuto (半夏厚朴湯; banxia houp tang) improves cough reflex in elderly patients likely to have aspiration pneumonia.

2. Design

Randomized controlled trial (RCT).

3. Setting

University of Tokyo and Tohoku University, and their related facilities.

4. Participants

Elderly patients (mean age, 78) with cerebral atrophy and lacunar infarcts, who had at least one episode of aspiration pneumonia, n=16.

5. Intervention

Arm 1: hangekobokuto (半夏厚朴湯) extract (granules) 1.5 g t.i.d. orally for 4 weeks (n=7).
Arm 2: placebo (lactose) 1.5 g t.i.d. orally for 4 weeks (n=9)

6. Main outcome measures

Subjects inhaled nebulized citric acid solution (0.3-360 mg/mL) delivered by an ultrasonic nebulizer, and the cough threshold was defined as the concentration of citric acid at which subjects coughed at least five times.

7. Main results

In arm 1, the cough threshold decreased from 59.5 to 15.7. In arm 2, the values were 47.5 and remained unchanged.

8. Conclusions

The result suggests that hangekobokuto improves the (impaired) cough reflex in the elderly with an increased risk for aspiration pneumonia.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

It has been reported that angiotensin-converting enzyme inhibitor (ACE-I) improves silent aspiration, and that capsaisin improves cough reflex. This study suggests that hangekobokuto also affects the attenuated cough reflex in older patients with cerebral atrophy and lacunar infarcts. Larger RCTs to confirm its efficacy are awaited.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Iwasaki K, Kato S, Monma Y, et al. A pilot study of banxia houpu tang, a traditional Chinese medicine, for reducing pneumonia risk in older adults with dementia. *Journal of the American Geriatrics Society* 2007; 55: 2035-40. CENTRAL ID: CN-00620232, Pubmed ID: 17944889

1. Objectives

To evaluate whether hangekobokuto (半夏厚朴湯) prevents aspiration pneumonia and pneumonia-related mortality in elderly people with dementia.

2. Design

Randomized controlled trial (RCT).

3. Setting

Two hospitals (the authors belong to Tohoku University, Dokkyo University, and two hospitals).

4. Participants

Elderly subjects with dementia, n=95.

5. Intervention

Arm 1: Tsumura Hangekobokuto (半夏厚朴湯) Extract Granules 2.5 g t.i.d. (body weight ≥50 kg) or 2.5 g b.i.d. (body weight <50 kg) for 12 months, n=47.

Arm 2: placebo (lactose) 1.0 g t.i.d. (body weight ≥50 kg) or 1.0 g b.i.d. (body weight <50 kg) for 12 months, n=48.

6. Main outcome measures

The occurrence of pneumonia, and mortality due to pneumonia.

7. Main results

Data from 92 of the 95 subjects were analyzed. One of four patients who developed pneumonia in arm 1 died as a result, whereas 6 of 14 patients who developed pneumonia in arm 2 died as a result. There was a significant decrease in pneumonia onset in arm 1 compared to arm 2 (P<0.008). Mortality related to pneumonia tended to be less in arm 1 than in arm 2 (P=0.05).

8. Conclusions

Treatment with hangekobokuto reduced the risk of pneumonia and pneumonia-related mortality in elderly patients with dementia.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The findings of this well-designed randomized controlled study suggest the efficacy of hangekobokuto in preventing aspiration pneumonia in elderly people with dementia. In addition, hangekobokuto administration tended to improve activities of daily living such as self-feeding and to reduce the number of febrile days. Further studies to assess these points are expected.

12. Abstractor and date

Okabe T, 25 November 2008, 8 August 2009.

Respiratory Diseases (including Influenza and Rhinitis)

Reference

Mikamo H, Tamaya T. Usefulness of Kampo medicine for the treatment of infections from the perspective of medical economics*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2007; 24: 105-8 (in Japanese). Ichushi Web ID: 2008050180

1. Objectives

To determine the efficacy, impact on recurrence rate, and medical cost efficiency of antibiotics plus Kampo combination therapy for bacterial respiratory infections.

2. Design

Randomized controlled trial (RCT).

3. Setting

Obstetrics and Gynecology, Gifu University Hospital.

4. Participants

One hundred and sixteen patients diagnosed with acute bacterial respiratory infection.

5. Intervention

Arm 1: antibiotics alone group: treatment with levofloxacin for 5–10 days, n=51.
Arm 2: antibiotics + Kampo group A: treatment with levofloxacin for 5–10 days + juzentaihoto (十全大補湯) or hochuekkito (補中益気湯) for 5–10 days, n=37.
Arm 3: antibiotics + Kampo group B: treatment with levofloxacin for 5–10 days + kakkonto (葛根湯) or keishito (桂枝湯) or kososan (香蘇散) or 1–2 days + juzentaihoto (十全大補湯) or hochuekkito (補中益気湯) for 3–6 days, n=28.
None of the manufacturers of Kampo medicines used were specified.

6. Main outcome measures

Response rate, rate of recurrence within 7 days, and total medical cost.

7. Main results

The response rates were 96.1% in arm 1, 97.3% in arm 2, and 96.4% in arm 3; no statistically significant differences were observed. The recurrence rates were 3.9% in arm 1, 2.7% in arm 2, and 0% in arm 3; there were no significant between-group differences, although the rates were lower in arms 2 and 3. High recurrence rates were observed in cases of atypical pneumonia, caused by atypical pneumonia-related organisms. Total medical costs were significantly higher in arms 2 and 3, whereas for patients with recurrence, total costs tended to be reduced in these two arms.

8. Conclusions

Antibiotics plus Kampo combination therapy reduces the recurrence of bacterial respiratory infections. In patients infected with atypical pneumonia and prone to frequent recurrence, Kampo-combined therapy might reduce the total medical cost.

9. From Kampo medicine perspective

The drugs used in the intervention groups were selected on the basis of common applications: ephedra formulations such as kakkonto, are used to help generate body heat and sweat during the acute phase; shosaikoto is used for immune enhancement during the subacute phase; and *hozai* (補剤, formulations with tonic effects) such as hochuekkito and juzentaihoto are used during the recovery phase.

10. Safety assessment in the article

None.

11. Abstractor's comments

This is a very interesting RCT evaluating total medical cost as an outcome. We guess from the setting that all the participants were women. Inclusion of background factors (such as gender, age, and underlying disease) as well as standard criteria with which to evaluate outcomes (such as response and recurrence rates) would have helped readers understand the results. Also, using more uniform regimens in the intervention groups would have increased the value of the results. Further studies are anticipated to provide more data.

12. Abstractor and date

Tsuruoka K, 6 February 2009, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Umemoto M, Nin T, Miuchi S, et al. Treatment of human dry mouth using various medicines. *Jibiinkoka Rinsho* (*Practica otologica*) 2007; 100: 145-52 (text in Japanese with English abstract). Ichushi Web ID: 2007135958

1. Objectives

To compare the efficacy of bakumondoto (麦門冬湯) versus cevimeline hydrochloride hydrate (Evoxac) or nizatidine (Acinon) for treating dry mouth.

2. Design

Randomized controlled trial (RCT).

3. Setting

Gustatory Outpatient Clinic, Department of Otolaryngology, Hyogo College of Medicine.

4. Participants

One hundred patients with dry mouth (13 males and 87 females; mean age, 69.0 years). Patients with a basal salivary secretion rate of 3 mL/10 min or lower and a chewing-gum-stimulated salivary secretion rate of 10 mL/10 min or lower were included in the study. Exclusion criteria were Sjögren syndrome, diabetes mellitus, use of oral antihistamine or antipsychotic, asthma, ischemic heart disease, epilepsy, prostatic hyperplasia, and glaucoma.

5. Intervention

Arm 1: treatment with bakumondoto (麦門冬湯) (manufacturer, not specified) 3.0 g t.i.d. for 90 days in 24 patients (4 males and 20 females; mean age, 67.4 years), as the bakumondoto (麦門冬湯) group.

Arm 2: treatment with cevimeline hydrochloride hydrate 30 mg t.i.d. for 90 days in 42 patients (3 males and 39 females; mean age, 72.0 years), as the cevimeline group.

Arm 3: treatment with nizatidine 150 mg b.i.d. for 90 days in 34 patients (6 males and 29 females; mean age, 66.0 years), as the nizatidine group.

6. Main outcome measures

The basal rate and chewing-gum-stimulated salivary secretion rate after 90 days of treatment. Subjective symptoms were assessed using a questionnaire on a 4-point scale (“improvement”, “mild improvement”, “no change”, or “worsening”).

7. Main results

The rate of basal salivary secretion increased from 1.0±0.2 mL/10 min to 1.3±0.2 mL/10 min after treatment with bakumondoto, from 1.1±0.1 mL/10 min to 1.6±0.2 mL/10 min after treatment with cevimeline, and from 1.1±0.2 mL/10 min to 2.4±0.3 mL/10 min after treatment with nizatidine. The rate increases in the cevimeline and nizatidine groups were significant ($P<0.001$). The change in the rate of chewing-gum-stimulated salivary secretion after treatment with cevimeline and nizatidine were similarly significant ($P<0.001$). Both the basal rate and chewing-gum-stimulated salivary secretion rate were significantly different between the bakumondoto- and the nizatidine-treated groups (both $P<0.01$) but not between the bakumondoto- and the cevimeline-treated groups. Treatment with cevimeline or nizatidine led to “improvement” in subjective symptoms in 50–57% of patients and “improvement” or “mild improvement” in 85.7% of cevimeline-treated patients and 74.2% of nizatidine-treated patients. In contrast, only 4% of bakumondoto-treated patients noted “improvement”.

8. Conclusions

Cevimeline hydrochloride hydrate and nizatidine but not bakumondoto significantly increased both basal and stimulated salivary secretions and relieved subjective symptoms in patients with dry mouth.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No patients reported “worsening” of symptoms. No adverse drug reactions occurred.

11. Abstractor’s comments

This is a well-designed and well-conducted RCT. The authors speculate that saponins in ginseng, a component of bakumondoto, activate salivary cells by increasing cell membrane permeability. According to their discussion, increase in cell membrane permeability alone does not directly increase the amount of saliva. This was suggested by the fact that dry mouth in most subjects in this trial was due to age-related atrophy and impairment of salivary gland cells. Further studies are expected.

12. Abstractor and date

Tsuruoka K, 12 February 2009, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Bessho K, Okubo Y, Hori S, et al. Effectiveness of Kampo medicine (Sai-Boku-To) in treatment of patients with glossodynia. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 1998; 86: 682-6. CENTRAL ID: CN-00158400, Pubmed ID: 9868725

1. Objectives

To determine the efficacy of saibokuto (柴朴湯) compared with tranquilizer plus vitamin B complex combination therapy for patients with glossodynia.

2. Design

Randomized controlled trial (RCT).

3. Setting

Department of Oral and Maxillofacial Surgery Kyoto University Hospital.

4. Participants

Two hundred patients with glossodynia.

5. Intervention

Arm 1: treatment with TSUMURA Saibokuto (柴朴湯) Extract Granules, 2.5g, t.i.d. for 3 months. (n=100)
Arm 2: treatment with diazepam, 2mg, t.i.d. plus vitamin B complex formulation, 1 tablets, t.i.d. for 3 months. (n=100)

6. Main outcome measures

Each of the subjective symptoms (pain, burning sensation, and unpleasant feeling) was evaluated on a 10-point scale. 'Excellent response' was defined as disappearance of all symptoms, 'good response' as improvement of pain, and 'no response' as no improvement of pain.

7. Main results

In arm 1, the percentage of excellent and good responses was 70% at 1 month, 85% at 2 months, and 92% at 3 months after the start of treatment. These values in arm 2 were 74%, 71%, and 69%, respectively ($P<0.05$). Pain relief was experienced in a significantly higher percentage in arm 1 than in arm 2 at 3 months ($P<0.01$).

8. Conclusions

It is suggested that saibokuto (in particular, the three-month treatment) is more effective against glossodynia than the diazepam plus vitamin B complex formulation.

9. From Kampo medicine perspective

The discussion contains some speculations.

10. Safety assessment in the article

Mild anorexia and diarrhea were reported, respectively, in 3 and 1 patient receiving saibokuto, and severe sleepiness was reported in 33 patients receiving diazepam.

11. Abstractor's comments

This study suggests that saibokuto monotherapy (for 3 months) is more effective against glossodynia than the combination therapy (tranquilizer plus vitamin B complex). Also, saibokuto treatment is safe, as indicated by the low frequency of adverse effects and the possibility of long-term treatment. Results similar to those of this paper were published in the following two papers: "Yamada T, Bessho K, Murakami K, et al. Clinical evaluation of Sai-boku-to (Kampo medicine) for glossodynia. *Shika Yakubutsu Ryoho* (*Oral Therapeutics and Pharmacology*) 1998; 17: 18-22 (text in Japanese with English abstract) [MOL, MOL-Lib]" and "Yamada T, Bessho K. Clinical evaluation of Sai-boku-to (Kampo medicine) for glossodynia. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 1999; 8: 261-5. [Ichushi Web ID: 2000085045]" Although the sample size of the study described in the above two papers was about half that in the present study, the results were very similar.

12. Abstractor and date

Okabe T, 17 September 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Mizuno S, Yamagiwa K, Iwata M, et al. Effect of early treatment with TSUMURA Rikkunshito on gastrointestinal symptoms after resection of gastric cancer – focusing on reflux esophagitis -*. *Progress in Medicine* 2001; 21: 1366-7 (in Japanese). Ichushi Web ID: 2001269379 MOL, MOL-Lib

1. Objectives

To determine the preventive effect of rikkunshito (六君子湯) on postoperative reflux esophagitis.

2. Design

Randomized controlled trial (RCT).

3. Setting

No description of the setting is available; the authors belong to the First Department of Surgery, Mie University School of Medicine.

4. Participants

Forty-six patients who underwent resection of stage I to II gastric cancer.

5. Intervention

Arm 1: treatment with TSUMURA Rikkunshito (六君子湯) Extract Granules, 7.5 g/day, every day from the start of postoperative oral intake in 25 patients.
Arm 2: no treatment in 21 patients.

6. Main outcome measures

1) Gastrointestinal symptoms including heartburn, dysphagia, nausea/vomiting, dyspepsia, and anorexia; 2) endoscopic findings based on the Los Angeles classification; and 3) mean length of postoperative hospital stay.

7. Main results

At postoperative week 2, gastrointestinal symptoms were observed in 7 untreated patients (33%) and 4 rikkunshito-treated patients (16%). All the symptoms occurred less commonly in the treated patients than in the untreated patients. At postoperative week 4, reflux symptoms and heavy stomach were each seen in only 1 (4%) patient in arm1, whereas reflux symptoms, heartburn, dyspepsia, and anorexia developed in 3 (14%), 1 (5%), 1 (5%), and 2 (10%), respectively, in arm 2. As for endoscopic findings at postoperative week 3, there were grade A in 2 patients (10%) and grade B in 1 (5%) in arm 2, but grade A in only 1 (5%) in arm 1. At postoperative week 6, grade A esophagitis was observed in 1 patient (5%) in arm 2, and none in arm 1. Mean length of postoperative hospital stay was not significantly different between the two arms (47 ± 13 days [arm 2] *vs* 39±13 days [arm 1]), but a reduction of hospital days was noted.

8. Conclusions

Rikkunshito is highly effective not only for the treatment of reflux esophagitis after gastric cancer surgery, but also for the prevention of this disease.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

Studies 1 and 2 are described in the article. Study 1 was conducted to examine the therapeutic effect of rikkunshito on postoperative reflux esophagitis. Rikkunshito at a daily dose of 7.5 g was administered between meals every day from the onset of symptoms in 7 patients with stage I-II gastric cancer. The authors reported that symptoms disappeared in most patients at week 4. But since Study 1 had no control group and provided no details such as evaluation criteria, it was excluded from this structured abstract. Only part of Study 2 was included. In Study 2, 'randomization into two groups' was reported, but the details were not clear. Also, other details, such as statistical procedures and methods of assessing subjective symptoms, were not provided. This study is clinically valuable, but most of the article, which is published in a conference record, lacks adequate descriptions. Thus, submission as an original article is desired.

12. Abstractor and date

Arai M, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Koide A. Effect and role of TJ-43: rikkun-shi-to from the aspects of endoscopic findings and QOL improvement in GERD patients. *Medical Tribune Online* (*Digestive Disease Week: DDW*) 2005: 6-7 (in Japanese).

1. Objectives

To determine the efficacy of rikkunshito (六君子湯) combined with a proton pump inhibitor (PPI) for treating gastroesophageal reflux disease (GERD).

2. Design

Randomized controlled trial (RCT).

3. Setting

One general hospital.

4. Participants

Fifty-six patients with gastroesophageal reflux disease.

5. Intervention

Arm 1: oral administration of omeprazole (20 mg), as the PPI alone group.
Arm 2: oral administration of omeprazole (20 mg) plus TSUMURA Rikkunshito (六君子湯) Extract Granules (7.5 g), as the PPI + rikkunshito (六君子湯) group.

6. Main outcome measures

Endoscopic healing rates of reflux esophagitis and Gastrointestinal Symptom Rating Scale (GSRS) scores. The follow-up was scheduled at 8 weeks.

7. Main results

The endoscopic healing rates of reflux esophagitis at 8 weeks were not significantly different between the two groups. The PPI + rikkunshito group achieved significantly better scores on the following three GSRS domains: overall gastrointestinal symptoms, reflux, and abdominal pain.

8. Conclusions

Rikkunshito combined with PPI improves the quality of life (QOL) in GERD patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

Rikkunshito-combined therapy resulted in further improvement of QOL in GERD patients, especially in those with endoscopy-negative GERD (non-erosive reflux disease: NERD). On this basis, the authors concluded that PPI + rikkunshito is effective for "the improvement of QOL, particularly in NERD patients who are unlikely to respond to PPI."

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Kato S, Nakajima T, Matsuda T, et al. The effectiveness of the traditional Kampo medicine, "banxia houpu tang (hangekobokuto)" to respiratory disturbance by esophageal reflux disease. *Kampo to Saishin-Chiryo* (*Kampo & the Newest Therapy*) 2005; 14: 333-8 (in Japanese). Ichushi Web ID: 2006091322

1. Objectives

To determine the efficacy of hangekobokuto (半夏厚朴湯)-combined treatment in patients with respiratory symptoms associated with refractory gastroesophageal reflux disease (GERD).

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

No description of the setting is available; the authors belong to the Department of Cardiology and Pneumology, Dokkyo Medical University.

4. Participants

Nineteen GERD patients whose digestive symptoms but not respiratory symptoms (including cough, sputum, throat discomfort, and mild dyspnea) were relieved by conventional western medical treatments. All patients had no history of smoking or respiratory disease.

5. Intervention

Arm 1: treatment with TSUMURA Hangekobokuto (半夏厚朴湯) Extract Granules (7.5 g/day) in 10 patients.
Arm 2: no treatment in 9 patients.
In arm 1, hangekobokuto (半夏厚朴湯) was administered in addition to the usual western medical treatment for 6 months, and then hangekobokuto (半夏厚朴湯) was discontinued. The course of respiratory symptoms was examined for a total of 12 months in both the hangekobokuto (半夏厚朴湯)-combined and no-treatment arms.

6. Main outcome measures

Cough, sputum, throat discomfort, and mild dyspnea.

7. Main results

The degree of improvement was evaluated on a 5-point scale. Respiratory symptoms were significantly improved after a month of treatment in arm 1, compared with arm 2 ($P<0.01$). This effect persisted up to 6 months after start of combined treatment ($P<0.01$) and 6 months after discontinuation of hangekobokuto ($P<0.01$).

8. Conclusions

Hangekobokuto relieves respiratory symptoms, including cough, sputum, throat discomfort, and mild dyspnea, that are unresponsive to western medical treatments in GERD patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

Respiratory or ear-nose-throat symptoms are reported to occur in 30–50% of GERD patients, depending on the literature. Western medical treatments combine proton pump inhibitors, H_2 blockers, or stomachics, with theophylline formulations, expectorants, antitussives, erythromycin antibiotics, or inhaled steroids. In some patients, however, these treatments fail to improve these symptoms. This study can be praised for examining these clinically difficult-to-treat patients. The study method has several problems including failure to measure inter-subject variability of GERD scores evaluated according to the Los Angeles classification, small sample size, and lack of a safety and adverse drug reactions assessment.

12. Abstractor and date

Arai M, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Koide A. Establishment of new treatment strategy for non-erosive reflux disease (endoscopy-negative gastroesophageal reflux disease) – potential of rikkunshito*. *MedicalQ* 2006; 187 (in Japanese).

1. Objectives

To determine the efficacy of TSUMURA Rikkunshito (六君子湯) Extract Granules for treatment of non-erosive reflux disease (NERD) unresponsive to proton pump inhibitors (PPIs).

2. Design

Randomized controlled trial (RCT).

3. Setting

No description of the setting is available; the author belongs to a clinic.

4. Participants

One hundred and eighteen patients with PPI-unresponsive NERD.

5. Intervention

Arm 1: treatment with omeprazole (200 mg), as the PPI alone group, n=37.
Arm 2: treatment with TSUMURA Rikkunshito (六君子湯) Extract Granules (7.5 g), as the rikkunshito alone group, n=39.
Arm 3: treatment with omeprazole (200 mg) and TSUMURA Rikkunshito (六君子湯) Extract Granules (7.5 g), as the PPI + rikkunshito (六君子湯) group, n=42.
The duration of treatment was 4 weeks in all arms.

6. Main outcome measures

Gastrointestinal Symptom Rating Scale (GSRS) score (which includes ratings of overall gastrointestinal symptoms, reflux, abdominal pain, and dyspepsia).

7. Main results

Scores of overall gastrointestinal symptoms and reflux were significantly more improved in arm 3 than in arms 1 and 2; the scores in arms 1 and 2 were similar. The abdominal pain score was similarly improved in all three arms. Dyspepsia score was significantly more improved in arms 2 and 3 than in arm 1, but the scores in arms 2 and 3 were similar.

8. Conclusions

TSUMURA Rikkunshito Extract Granules is effective for relieving clinical symptoms of NERD.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study deserves praise for conducting a RCT using TSUMURA Rikkunshito Extract Granules as a study drug in patients with treatment-unresponsive NERD. Unfortunately, the mechanism was not discussed, and endoscopic findings and other features were not mentioned. Publication of the latter is expected in the future.

12. Abstractor and date

Kogure T, 26 January 2009, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Yamaguchi T, Koide A. Usefulness of Rikkun-shi-to (TJ-43), a Chinese herbal medicine, for the treatment of gastro-esophageal reflux disease (GERD). *Medical Science Digest* 2007; 33: 748-52 (in Japanese).

1. Objectives

To determine the efficacy of rikkunshito (六君子湯) as an agent to improve symptoms before endoscopy in patients with upper abdominal symptoms and need for endoscopy of the upper gastrointestinal tract.

2. Design

Randomized controlled trial using envelopes for allocation (RCT-envelope).

3. Setting

None; the authors are members of the Department of Medical Oncology, Graduate School of Medicine, Chiba University.

4. Participants

One hundred and twenty patients with upper abdominal symptoms and need for upper gastrointestinal endoscopy.

5. Intervention

Arm 1: treatment with H_2-receptor blocker (H2RB; ranitidine 150 mg; n=39).
Arm 2: treatment with proton pump inhibitor (PPI; omeprazole 20 mg; n=40).
Arm 3: treatment with TSUMURA Rikkunshito (六君子湯) Extract Granules 7.5 g (n=41).
The duration of treatment was not specified (the administration was continued until the upper gastrointestinal endoscopy was performed).

6. Main outcome measures

Acid reflux (heartburn, reflux), abdominal pains (epigastric pain, hunger, and nausea), dyspepsia (borborygmus, abdominal distention, eructation, and flatus), diarrhea (diarrhea, loose stool, and rectal urgency), and constipation (constipation, hard stool, feeling of incomplete evacuation).

7. Main results

Overall, gastrointestinal symptoms associated with impaired quality of life (QOL) were significantly improved after the treatment in all arms; the improvement was significantly greater in arm 3 than in arms 1 and 2. Also improved were acid reflux associated with impaired QOL in arm 1, acid reflux and abdominal pains associated with impaired QOL in arm 2, and acid reflux, abdominal pains, and dyspepsia associated with impaired QOL in arm 3. Significantly greater improvements were found for acid reflux in arm 3 than in arm 1; for abdominal pains in arms 2 and 3 than in arm 1; for dyspepsia in arm 3 than in arms 1 and 2. Considering only patients with reflux esophagitis, gastrointestinal symptoms were also significantly improved by treatment in all arms. Acid reflux improved in arm 1, and acid reflux, abdominal pains, and dyspepsia improved in arms 2 and 3. H2RB, PPI, and rikkunshito had similar effectiveness.

8. Conclusions

The efficacy of rikkunshito as a pre-endoscopic medication, even as monotherapy, is comparable to that of other gastric acid secretion inhibitors in patients with upper abdominal symptoms and need for upper gastrointestinal endoscopy.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is considered to be a follow-up to the following studies: 1) Koide A. Adoption of rikkunshito before endoscopy in patients with upper abdominal symptoms*. *Nikkei Medical* 2002; 31: 22-3 and 2) Koide A. The improvement of QOL by rikkunshito in patients with need for endoscopy*. *Medical Tribune* 2004: 45 (in Japanese). This clinically valuable study showed that the efficacy of rikkunshito against upper abdominal symptoms including gastroesophageal reflux disease is comparable to that of other gastric acid secretion inhibitors. The present study also deserves praise for assessing each clinical symptom objectively using the GSRS (Gastrointestinal Symptom Rating Scale). The cost-effectiveness of rikkunshito is mentioned without detail in the conclusion of this paper, but it is addressed more completely in paper 2). The present paper provides very interesting insights, but its first half is too general. Therefore, publication as an original article is desired.

12. Abstractor and date

Arai M, 20 January 2009, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Harasawa S, Miyoshi A, Miwa T, et al. Double-blind multicenter post-marketing clinical trial of TJ-43 TSUMURA Rikkunshi-to for the treatment of dysmotility-like dyspepsia. *Igaku no Ayumi* (*Journal of Clinical and Experimental Medicine*) 1998; 187: 207-29 (in Japanese). Ichushi Web ID: 1999085057

1. Objectives

To evaluate the efficacy and safety of TJ-43 TSUMURA Rikkunshito (六君子湯) in patients with dyspepsia caused by dysfunction of the upper gastrointestinal tract.

2. Design

Double-blind, randomized, controlled trial (DB-RCT).

3. Setting

A total of 54 institutions.

4. Participants

Patients (30–80 years old) with a chief complaint of persistent or intermittent (for more than 4 weeks) dysmotility-like dyspepsia, characterized by anorexia (or poor appetite), gastric distress, and heavy stomach feeling (presumably due to dysfunction of the upper gastrointestinal tract), and indicating "*kyo-sho* (deficiency pattern/syndrome)" by gastroptosis, physical weakness, etc.

5. Intervention

Arm 1: oral administration of TSUMURA Rikkunshito (六君子湯) Extract Granules (TJ-43) 2.5 g t.i.d. before or between meals for 2 weeks (n=147).

Arm 2: oral administration of low-dose (1:4 dilution) TSUMURA Rikkunshito (六君子湯) Extract Granules 2.5 g t.i.d. before or between meals for 2 weeks (n=133).

6. Main outcome measures

Five symptoms associated with dysmotility-like dyspepsia (anorexia, abdominal distension, stomach discomfort, heavy stomach feeling, and nausea).

Three symptoms associated with ulcer-like dyspepsia (upper abdominal/epigastric pain, heartburn or pyrosis, and eructation).

7. Main results

A total of 235 subjects (TJ-43 group, n=118; low-dose group, n=117) were included for analysis. Dysmobility-like dyspepsia symptoms were improved in 59.3% of the TJ-43 group and 40.2% of the low-dose group; overall symptoms including ulcer-like dyspepsia symptoms were also improved in 60.2% of the TJ-43 group and 41.0% of the low-dose group. These indicate that efficacy is significantly higher in the TJ-43 group. Furthermore, a significantly higher percentage of the TJ-43 group than the low-dose group (58.8% versus 39.3%) deemed the treatment useful.

8. Conclusions

The safety and effectiveness of TJ-43 was validated for the treatment of dysmotility-like dyspepsia in this double-blind study. We therefore conclude that TJ-43 Rikkunshi-to is clinically useful.

9. From Kampo medicine perspective

In this study, the inclusion criteria were "*kyo-sho* (虚証, deficiency pattern)" symptoms (i.e., decreased tone of abdominal wall, subjective/objective splashing sound, gastroptosis tendency, and mental/physical weakness) and the exclusion criteria were "*jitsu-sho* (実証, excess pattern)" symptoms (i.e., mental and physical strength, massive and muscular body, and reddish face).

10. Safety assessment in the article

Safety problems were detected in 2 cases in the TJ-43 group (diarrhea, elevated GOT) and 2 in the low-dose group (diarrhea, elevated GOT/GPT). Adverse effects (defined as symptoms undeniably caused by the drug) occurred in 7 of the TJ-43 group and 7 of the low dose group. None were serious.

11. Abstractor's comments

There is a similar report by Harasawa: "The role of rikkunshito against NUD (non-ulcer dyspepsia) – especially its efficacy in dysmotility-like NUD*. *Progress in Medicine* 1999; 19: 843-8 (in Japanese)." Use of low-dose TH-43 in the control group and use of Kampo diagnostic considerations when selecting the inclusion and exclusion criteria are appreciated. Improvement in "*kyo-sho*" symptoms is demonstrated.

12. Abstractor and date

Arai M, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Nishida T. Effect of rikkunshito on gastrointestinal function in patients after gastrectomy*. *Progress in Medicine* 2006; 26: 3224-5 (in Japanese). MOL, MOL-Lib

1. Objectives

To determine the efficacy of TSUMURA Rikkunshito Extract (六君子湯) Granules for stimulating gastrointestinal emptying in patients after pylorus-preserving gastrectomy (PPG).

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

Not indicated (the author belongs to a university hospital).

4. Participants

Eleven patients after PPG.

5. Intervention

Arm 1: no treatment for 4 weeks followed by treatment with TSUMURA Rikkunshito (六君子湯) Extract Granules (2.5 g t.i.d.) for 4 weeks, n=5.
Arm 2: treatment with TSUMURA Rikkunshito (六君子湯) Extract Granules (2.5 g t.i.d.) for 4 weeks followed by no treatment for 4 weeks, n=6.

6. Main outcome measures

Gastrointestinal Quality of Life Index (GIQLI) and rate of gastric retention as shown by gastric emptying scintigraphy.

7. Main results

Although no significant difference was observed in GIQLI, 8 patients preferred to continue the rikkunshito treatment.
Scintigraphy showed reduced rate of gastric retention of solids (but not of liquids) in patients treated with TSUMURA Rikkunshito Extract Granules.

8. Conclusions

TSUMURA Rikkunshito Extract Granules delays gastric emptying of solids in patients after PPG.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This trial is of high clinical interest, since it made objective evaluations based on gastric-emptying scintigraphy of solids and liquids separately. However, some questions about the design (including the randomization step) remain. So-called "between-group comparisons" will be desirable in the future.

12. Abstractor and date

Kogure T, 26 January 2009, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Mori K, Kondo T, Kamiyama Y, et al. Preventive effect of Kampo medicine (Hangeshashin-to) against irinotecan-induced diarrhea in advanced non-small-cell lung cancer. *Cancer Chemotherapy and Pharmacology* 2003; 51: 403-6. CENTRAL ID: CN-00437238, Pubmed ID: 12687289

1. Objectives

To determine the safety and efficacy of hangeshashinto (半夏瀉心湯) (TJ-14) for CPT-11-induced diarrhea during combination chemotherapy with cisplatin (CDDP) plus irinotecan hydrochloride (CPT-11) for advanced non-small-cell lung cancer (NSCLC).

2. Design

Randomized controlled trial using envelopes for allocation (RCT-envelope).

3. Setting

One hospital; the authors belong to the Department of Respiratory Disease, Tochigi Cancer Center.

4. Participants

From among inpatients with NSCLC who received dual therapy with CDDP plus CPT-11 from November 1993 through December 1996, forty one patients who met the following selection criteria were enrolled: 1) treatment-naïve with unresectable NSCLC (stage III, IV); 2) performance status 0 to 2; 3) preserved major organ function; 4) 75 years or younger; and 5) informed consent. Patients with serious complications, diarrhea, severe pleural effusion, or symptomatic cerebral metastasis were excluded from the study.

5. Intervention

Arm 1: treatment with TSUMURA Hangeshashinto (半夏瀉心湯) Extract Granules (TJ-14) 2.5 g t.i.d. before meals in 18 patients.

Arm 2: no treatment in 23 patients.

In the arm 1, hangeshashinto was administered every day from at least 3 days before through 21 days or more after the start of chemotherapy.

6. Main outcome measures

Stool properties and frequency of defecation, presence and severity of abdominal pain associated with defecation, presence or absence of bowel movements at night and bloody diarrhea.

7. Main results

The onset and the highest daily frequency of diarrhea were respectively recorded at 6.3 and 9.2 days after the start of chemotherapy in arm 1, and at 5.9 and 9.0 days in arm 2. During the first cycle of chemotherapy, the severity of diarrhea was significantly improved and the incidence of grade 3 or higher diarrhea was lower in arm 1 than in arm 2. The number of diarrhea episodes and the duration (in days) of diarrhea were not significantly different between the two arms.

8. Conclusions

Hangeshashinto is effective for preventing and relieving CPT-11-induced diarrhea in advanced NSCLC.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Mild constipation was reported in 2 hangeshashinto-treated patients. Other significant adverse effects were not observed.

11. Abstractor's comments

This clinical study indicated that the concomitant use of hangeshashinto is effective for diarrhea, which can occur during chemotherapy containing CPT-11. This study lacked a placebo control group and was not double-blinded. In a study using Kampo medicines as a control, it is difficult to prepare the placebo because Kampo medicines have specific textures and smells. Nonetheless, double-blind design should be considered in order to improve the quality of study. Similar results as this were reported in "Mori K, Hirose T, Machida S, et al. Kampo medicines for the prevention of irinotecan-induced diarrhea in advanced non-small cell lung cancer. *Gan to Kagaku Ryoho* (*Japanese Journal of Cancer and Chemotherapy*) 1998; 25: 1159-63 (text in Japanese with English abstract) [CENTRAL ID; CN-00153138, Pubmed ID: 9679578] [MOL, MOL-Lib]" and "Mori K. Hangeshashin-to (Kampo medicined) in the prevention of irinotecan-induced diarrhea in advanced non-small cell lung cancer. *Progress in Medicine* 1999; 19: 886-90 (text in Japanese with English abstract)."

12. Abstractor and date

Arai M, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Takagaki Y, Kawasaki S, Komai H, et al. The effect of Chinese hearb medicine (dai-kenchu-to) on paralytic ileus after repair of abdominal aortic aneurysm. *Nihon Rinsho Geka Gakkai Zasshi* (*Journal of Japan Surgical Association*) 2000; 61: 325-8 (text in Japanese with English abstract). J-STAGE

1. Objectives

To determine the efficacy and safety of daikenchuto (大建中湯) for improving intestinal peristalsis in patients with intestinal paralysis after surgery for abdominal aortic aneurysm (AAA).

2. Design

Randomized controlled trial (RCT).

3. Setting

No description of the setting is available (the authors are cardiovascular surgeons at community or university hospitals).

4. Participants

Twenty-one patients who underwent elective surgery for non-ruptured infrarenal AAA during the same time period.

5. Intervention

Arm 1: treatment with infusion of daikenchuto (大建中湯) dissolved in lukewarm water (5 g/20 mL) through a gastric tube, followed by clipping of the tube for 30 minutes, three times daily from the first postoperative day, in 7 patients.

Arm 2: treatment with infusion of lukewarm water (20 mL) in the same manner as arm 1 in 7 patients, as a control group.

Arm 3: treatment with infusion of lukewarm water (20 mL) and intravenous panthenol (100 mg/day) in 7 patients.

6. Main outcome measures

Degree of abdominal distension, and presence or absence of bowel sounds, passage of flatus, and small bowel gas on the abdominal X-ray.

7. Main results

Bowel sounds were heard immediately after the infusion of the study drug in all patients of arm 1, but not in any patient of arms 2 and 3. Time to the first passage of flatus after surgery was 3.1±0.8 days in arm 1, 5.1±1.3 days in arm 2, and 3.7±0.8 days in arm 3; significantly earlier passage of flatus was observed in arms 1 and 3 ($P<0.05$), but there was no significant difference in time to first passage of flatus between these two arms. Small bowel gas disappeared at 3.3±1.4 days after surgery in arm 1, at 6.1±1.2 days in arm 2, and at 6.3±2.8 days in arm 3; the gas disappeared significantly earlier in arm 1 than in arms 2 and 3 ($P<0.05$). No patients developed symptoms of ileus due to decreased intestinal peristalsis after resumption of oral intake.

8. Conclusions

Oral daikenchuto is effective for improving decreased intestinal peristalsis after surgery for non-ruptured AAA.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse drug reactions associated with daikenchuto treatment were not reported.

11. Abstractor's comments

AAA is caused by arteriosclerosis and common in the elderly, for whom elective surgery is indicated and achieves good outcome. In such cases, early ambulation and early resumption of oral intake are important for the prevention of early postoperative delirium. Administration of daikenchuto promotes significantly earlier recovery of intestinal peristalsis and is therefore clinically useful. Although three arms were compared in this study, other studies commonly compare just two arms - daikenchuto and panthenol as a standard treatment. This study was also limited by the small number of patients in each group. Thus, a review of the study design and number of subjects will be needed.

12. Abstractor and date

Arai M, 8 March 2007, 30 October 2007, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Nishizawa Y, Nishizawa Y, Goto HG, et al. Prospective multicenter randomized group-parallelled study: effect of Chinese traditional herb medicine, jiu-wei-bing-lang-tang (Japanese name: kumi-binro-to) on constipation in elderly patients with renol dialysis. *Kampo Kenkyu* (*Kampo Research*) 2004; 388: 132-8 (in Japanese). Ichushi Web ID: 2004202082

1. Objectives

To evaluate the efficacy and safety of kumibinroto (九味檳榔湯) for chronic constipation in elderly dialysis patients.

2. Design

Randomized controlled trial (RCT).

3. Setting

Clinics and other services (Osaka, Japan).

4. Participants

Three-hundred and eighteen patients who were 75 years or older and on dialysis were enrolled during 15 years.

5. Intervention

Arm 1: treatment with Kotaro Kumibinroto (九味檳榔湯) Extract Fine Granules 2g, t.i.d., n=160.
Arm 2: treatment with magnesium laxative 2.0 g/day in three divided doses, n=158.
Duration of the study was 9 months.

6. Main outcome measures

Number of urges to have bowel movements and dosage of the laxatives (Western medicines) combined with the study drug.

7. Main results

Both the number of urges to have bowel movements and the dosage of the combined laxatives were significantly more improved in arm 1 than in arm 2. Symptoms associated with bowel movements were also significantly improved.

8. Conclusions

Kumibinroto was more effective than magnesium laxative for improving the number of bowel movements and the dosage of the combined laxatives in elderly dialysis patients with chronic constipation.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Fewer adverse effects were reported in arm 1 than in arm 2 (data not shown). There were no abnormal examination findings.

11. Abstractor's comments

Although the word "multicenter" was mentioned in this article, none of the actual clinics, in contradistinction to research laboratories where this clinical trial was conducted, was specified. The authors conducted a 9-month, prospective, randomized study in 318 patients over a long period (15 years). Unfortunately, neither the number of withdrawals from the study nor the number of subjects included in the analysis was reported. Kumibinroto does not have a potent laxative effect. This study suggested that kumibinroto, combined with western laxatives, is more effective and safer than magnesium laxative for chronic constipation in elderly dialysis patients. Magnesium laxative, however, needs to be carefully administered and may cause hypermagnesemia in patients with renal impairment. Therefore, this type of laxative is usually avoided in patients undergoing hemodialysis. Regarding this point, the types and dosage of the western laxatives combined with the study drug are to be reported.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Tarao K. Prevention of HCC by anti-inflammatory agents in patients with chronic hepatitis C. *Rinsho Shokaki Naika* (*Clinical Gastroenterology*) 2007; 22: 961-9 (in Japanese).

1. Objectives

To determine the efficacy of liver protectors for preventing carcinogenesis in patients with chronic hepatitis C.

2. Design

Randomized controlled trial (RCT).

3. Setting

None (the author belongs to a specialized hospital).

4. Participants

One hundred and fifty-six patients with hepatitis C virus-related cirrhosis (stage Child A).

5. Intervention

Arm 1: target alanine aminotransferase (ALT) level ≤80; monotherapy with Stronger Neo-Minophagen C (SNMC; 40–100 mL, two or three times per week), ursodeoxycholic acid (UDCA), shosaikoto (小柴胡湯), or juzentaihoto (十全大補湯) (manufacturers, not specified) was administered. When the target level was not achieved in 2–3 months, dual therapy with SNMC + UDCA, UDCA + juzentaihoto (十全大補湯), or UDCA + shosaikoto (小柴胡湯) was administered. If the target level was still not achieved, triple therapy with SNMC + UDCA + shosaikoto (小柴胡湯) or SNMC + UDCA + juzentaihoto (十全大補湯) was administered. The choice of the therapy in each patient was not described, n=78.

Arm 2: monotherapy with UDCA, SNMC, shosaikoto (小柴胡湯), or juzentaihoto (十全大補湯) was administered; the choice of the drug was based on the ALT-lowering effect. Details, including the drug used, dose, and the number of patients who received each drug, were not available, n=50.

6. Main outcome measures

Incidence of liver cancer.

7. Main results

The incidence of liver cancer was lower in arm 1 than in arm 2.

8. Conclusions

Therapy consisting of combined Kampo medicines for liver protection is effective for suppressing carcinogenesis in patients with chronic hepatitis C.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study reports an effective treatment for suppressing carcinogenesis in patients with chronic hepatitis C. But since the specific design was not described and details (such as the choice of the therapy or the number of patients who received each drug in arm 2) were unclear, we cannot decide which of the treatments resulted in response. Studies employing easy-to-understand designs are desired.

The interim reports of this study are:

Tarao K, Shibuya A, Ohkawa S, et al. Prevention of hepatocarcinogenesis by anti-inflammatory therapy: is combination anti-inflammatory therapy targeting an ALT level of under 80 units effective for hepatitis C virus-related cirrhosis (Child A)?: comparison with monotherapy*. *Kanagawa Cancer Center – Nenpo* (*Annual Report*) 2003; 19: 92 (in Japanese).

Tarao K. Persistent inflammation and hepatocarcinogenesis in chronic hepatitis C and hepatitis C virus-related cirrhosis*. *Kanagawa Igakkai Zasshi* (*The Journal of the Kanagawa Medical Association*) 2008; 33: 115-8 (in Japanese).

12. Abstractor and date

Kogure T, 26 January 2009, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Higuchi K, Watanabe A. Study on liver cancer-preventive effect of juzentaihoto in patients with liver cirrhosis*. *Methods in Kampo Pharmacology* 2000; 5: 29-33 (in Japanese).

1. Objectives

To evaluate the hepatocellular carcinoma-preventive effect of juzentaihoto (十全大補湯) administered for liver cirrhosis.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

A university hospital (Department of Internal Medicine, Toyama Medical and Pharmaceutical University [now Toyama University Hospital]).

4. Participants

Seventy-two patients with liver cirrhosis due to hepatitis B or C virus (B, n=14; C, n=58). However, one patient who had liver cancer within half a year after entry into the study was excluded.

5. Intervention

Arm 1: juzentaihoto (十全大補湯)-treated group (B, n=8; C, n=18).
Arm 2: juzentaihoto (十全大補湯)-untreated group (B, n=6; C, n=39).

6. Main outcome measures

Cumulative survival curve by Kaplan-Meier method (log-rank test [Mantel-Cox]).
Cumulative hazard curve for hepatocellular carcinoma development by Kaplan-Meier method (log-rank test [Mantel-Cox]).
The threshold of liver cancer development was set at the time when liver cancer was first detected on imaging-based clinical diagnosis.

7. Main results

For overall liver cirrhosis, there was no significant difference in the cumulative survival curve between arms (chi-square=3.167, *P*=0.0751), but juzentaihoto-treated patients tended to have a more favorable prognosis. For overall liver cirrhosis, the cumulative hazard curve for hepatocellular carcinoma development showed the risk was significantly lower in the juzentaihoto-treated group than in juzentaihoto-untreated group (chi-square=5.832, *P*=0.0157). Analysis limited to liver cirrhosis type C also revealed significantly lower risk in the juzentaihoto-treated group (chi-square=4.197, *P*=0.0405).

8. Conclusions

It is suggested that administration of juzentaihoto prevents hepatocellular carcinoma from developing in patients with liver cirrhosis.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is valuable, since hepatocellular carcinoma frequently develops as a result of underlying hepatitis virus infection. Using sealed envelopes for allocation, this study is regarded as a randomized controlled trial. Information on the method of juzentaihoto administration and blinding may have made this report clinically more meaningful.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Higuchi K, Shimizu Y, Yasumura S, et al. Preventive effect of liver carcinogenesis by Juzen-Taiho-To in the patients with liver cirrhosis. *Kan-Tan-Sui* 2002; 44: 341-6 (in Japanese) Ichushi Web ID: 2002240679

1. Objectives

To evaluate the hepatocellular carcinoma-preventive effect of juzentaihoto (十全大補湯) administered for liver cirrhosis.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

A university hospital (Department of Internal Medicine, Toyama Medical and Pharmaceutical University [now Toyama University Hospital]).

4. Participants

Fifty-two patients with liver cirrhosis due to hepatitis B or C virus. However, patients who had liver cancer within a year after entry into the study and those who received shosaikoto or interferon were excluded.

5. Intervention

Arm 1: juzentaihoto (十全大補湯)-treated (type B, n=8; type C, n=15; type B + type C, n=1).
Arm 2: juzentaihoto (十全大補湯)-untreated (type B, n=5; type C, n=22; type B + type C, n=1).

6. Main outcome measures

Cumulative survival curves were drawn by the Kaplan-Meier method (with difference between curves analyzed by the log-rank test [Mantel-Cox test], Bleslow Gehan-Wilcoxon test, and Peto-Peto-Wilcoxon test). Cumulative hazard curves for hepatocellular carcinoma development were drawn by the Kaplan-Meier method (with difference between curves analyzed by the log-rank test [Mantel-Cox test], Bleslow Gehan-Wilcoxon test, and Peto-Peto-Wilcoxon test). The threshold of liver cancer development was set when liver cancer was first detected on imaging-based clinical diagnosis.

7. Main results

For all liver cirrhosis, the cumulative survival curve showed that vital prognosis was significantly more favorable in arm 1 than arm 2, with chi-square values of 4.066, 6.467, and 5.217 (P=0.0438, 0.0190, and 0.0224) by the log-rank test (Mantel-Cox test), Bleslow Gehan-Wilcoxon test, and Peto-Peto-Wilcoxon test, respectively. Analysis of the cumulative survival curve limited to patients with liver cirrhosis type C showed a tendency toward more favorable vital prognosis in arm 1, but no significant between-group difference. For all liver cirrhosis, the cumulative hazard curve for hepatocellular carcinoma development showed significantly lower incidence of hepatocellular carcinoma in arm 1 than in arm 2, with chi-square values of 5.265, 5.578, and 5.921 (P=0.0218, 0.0182, and 0.0150) by these tests, respectively. Analysis limited to liver cirrhosis type C revealed significantly lower incidence of hepatocellular carcinoma in arm 1 by the Bleslow Gehan-Wilcoxon test and Peto-Peto-Wilcoxon test (chi-square=4.659, 4.483, respectively; P=0.0309, 0.0342, respectively).

8. Conclusions

It is suggested that in liver cirrhosis, administration of juzentaihoto prevents hepatocellular carcinoma development.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is valuable since hepatocellular carcinoma frequently develops from underlying hepatitis virus infections. This study seems to be similar to the study published in *Methods in Kampo Pharmacology* (2000; 5: 29-33). There were fewer participants in the present study because stricter exclusion criteria were followed: liver cancer development within a year *vs* half a year in the previous study, and shosaikoto or interferon not permitted. Furthermore, use of diverse statistical tests made the results more meaningful, particularly clinically. Use of a placebo and blinding may have made the results more reliable.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Itoh T, Yamakawa J, Mai M, et al. The effect of the herbal medicine dai-kenchu-to on post-operative ileus. *The Journal of International Medical Research* 2002; 30: 428-32. CENTRAL ID: CN-00410068, Pubmed ID: 12235926

1. Objectives

To determine the efficacy of daikenchuto (大建中湯) for the treatment of postoperative ileus and the improvement of postoperative conditions.

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital (Cancer Research Institute of Kanazawa University)

4. Participants

Out of 154 abdominal surgery patients, 24 developed postoperative ileus were enrolled.

5. Intervention

Arm 1: treatment with daikenchuto (大建中湯) 15.0 g in 13 patients.
Arm 2: treatment with placebo (the same quantity and frequency of doses as arm 1) in 11 patients.
The study drugs were administered orally for 14 days.

6. Main outcome measures

Frequency of surgery for ileus and recurrence of ileus.

7. Main results

Surgery for postoperative ileus could be avoided significantly more frequently in the daikenchuto arm than in the placebo arm. In addition, daikenchuto tended to decrease, though not significantly, the recurrence rate of ileus.

8. Conclusions

Daikenchuto is a cost-effective and noninvasive therapeutic agent for postoperative ileus after abdominal surgery and has no adverse effects.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This RCT examined the efficacy of daikenchuto for postoperative ileus. This seems to be clinically relevant after abdominal surgery since the treatment for postoperative ileus is not established. Although mentioned in the conclusion, the safety and cost effectiveness of daikenchuto treatment were not described in the main text. It might have been better to mention those outcomes, and examine the dependence of these differences on subjects' underlying diseases or surgical procedures.

12. Abstractor and date

Arai M, 20 February 2007, 30 October 2007, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Endo S, Nishida T, Nishikawa K, et al. Dai-kenchu-to, a Chinese herbal medicine, improves stasis of patients with total gastrectomy and jejunal pouch interposition. *American Journal of Surgery* 2006; 192: 9-13. CENTRAL ID: CN-00556925, Pubmed ID: 16769267

1. Objectives

To determine the effects of daikenchuto (大建中湯) on gastrointestinal emptying and motility in patients after total gastrectomy with jejunal pouch interposition reconstruction.

2. Design

Randomized crossover controlled trial (RCT-cross over).

3. Setting

Osaka University Hospital.

4. Participants

Seventeen patients who underwent total gastrectomy with jejunal pouch interposition reconstruction for gastric cancer (mean age, 62 years).

5. Intervention

Arm 1: treatment with daikenchuto (大建中湯) (manufacturer, not specified) 5 g t.i.d. before meals for 2 weeks followed by no treatment for 2 weeks (n=10).

Arm 2: no treatment for 2 weeks followed by treatment with daikenchuto (大建中湯) (manufacturer, not specified) 5 g t.i.d. before meals for 2 weeks (n=7).

6. Main outcome measures

Gastrointestinal symptoms, emptying, motility, and quality of life (QOL) (using Visick grading scale with modification).

7. Main results

Daikenchuto significantly relieved postprandial stasis-related symptoms including upper abdominal fullness, discomfort, and abdominal pain. Scintigraphy with ^{111}In- and ^{99m}Tc-labeled meals showed that daikenchuto significantly accelerated clearance of both the liquid (P<0.01) and solid (P=0.015) components of food from the jejunal pouch. Manometric assessment of pouch motility (contraction time in 6 patients found a significant increase from the pretreatment levels after daikenchuto treatment (P=0.028).

8. Conclusions

Daikenchuto accelerates gastrointestinal emptying and motility and improves QOL after total gastrectomy followed by jejunal pouch interposition reconstruction.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This paper reports the effects of daikenchuto on gastrointestinal emptying and motility in patients after total gastrectomy with jejunal pouch interposition reconstruction. The authors evaluated a small number of patients in a RCT crossover and obtained highly accurate results. They deserve high praise, especially for exploring not only subjective symptoms but also gastrointestinal emptying and motility measured by relatively invasive procedures.

12. Abstractor and date

Oikawa T, 31 December 2008, 8 August 2009.

Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Oka T, Tamagawa Y, Hayashida S, et al. Rikkunshi-to attenuates adverse gastrointestinal symptoms induced by fluvoxamine. *Biopsychosoc Medicine* [Internet]. 2007 November 15 [cited 2008 Dec 31]; 1: 21. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2204024 DOI: 10.1 186/1751-0759-1-21.

1. Objectives

To determine the clinical effect of rikkunshito (六君子湯) on gastrointestinal adverse reactions induced by fluvoxamine, an antidepressant.

2. Design

Randomized controlled trial (RCT).

3. Setting

University of Occupational and Environmental Health Hospital.

4. Participants

Fifty patients with depressive disorder (mean age, 40.2 years).

5. Intervention

Arm 1: treatment with fluvoxamine 150 mg/day (escalating from 50 mg/day) and TSUMURA Rikkunshito (六君子湯) Extract Granules 7.5 g/day for 8 weeks, n=25.
Arm 2: treatment with fluvoxamine 150 mg/day (escalating from 50 mg/day) alone for 8 weeks, n=25.

6. Main outcome measures

Gastrointestinal symptoms (assessed by Gastrointestinal Symptom Rating Scale [GSRS] score) and depressive symptoms (by Self-rating Depression Scale [SDS] score).

7. Main results

Overall gastrointestinal symptoms due to fluvoxamine treatment were significantly relieved to a greater extent in arm 1 (GSRS total score, 1.97±0.81) than in arm 2 (2.52±0.99). No significant between-arm difference was observed in post-treatment SDS score.

8. Conclusions

Rikkunshito reduces fluvoxamine-induced gastrointestinal adverse reactions, especially nausea, without affecting the antidepressant effect of fluvoxamine.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

During the treatment, adverse reactions occurred significantly less frequently in arm 1 (6 patients) than in arm 2 (13 patients). In particular, the frequency of nausea was significantly lower in arm 1 (3 patients) than in arm 2 (9 patients).

11. Abstractor's comments

This paper reports that rikkunshito reduced nausea and other gastrointestinal adverse reactions induced by selective serotonin reuptake inhibitors (SSRI), such as fluvoxamine. Although sample size was relatively small, this trial was well-designed and valuable since it showed the usefulness of Kampo medicines from the perspective of reducing the adverse reactions to western medicines.

12. Abstractor and date

Oikawa T, 31 December 2008, 8 August 2009.

Skin Diseases

Reference

Furue M, Tanaka Y, Kobayashi H, et al. Efficacy of Kanebo Hochuekkito in patients with atopic dermatitis with "*qikyo*" – a multicenter, double-blind trial*. *Arerugi* (*Japanese Journal of Allergology*). 2005; 54: 1020 (in Japanese). MOL, MOL-Lib

1. Objectives

To assess the efficacy of hochuekkito (補中益気湯) for the treatment of atopic dermatitis.

2. Design

Randomized controlled trial (RCT).

3. Setting

Three university hospitals.

4. Participants

Patients with atopic dermatitis and "*qikyo*" (気虚, qi deficiency), n=77.

5. Intervention

Arm 1: hochuekkito (補中益気湯) group. Oral administration of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules (KB-41) 7.5 g/day in two divided doses.(n=37)
Arm 2: placebo group. Oral administration of placebo 7.5 g/day in two divided doses.(n=40)
Duration of administration and observation was 24 weeks for both arms.

6. Main outcome measures

Skin lesion score (according to Japanese Dermatology Association criteria), and change in the dosage of topical steroid and topical tacrolimus hydrate used.

7. Main results

The dosage of topical steroid and topical tacrolimus hydrate was significantly less in arm 1 than arm 2. The reduction in skin lesion score in arm 1 indicated nonsignificant improvement in these lesions when compared with arm 2.

8. Conclusions

Hochuekkito was effective in decreasing the amount of topical corticosteroid and topical tacrolimus hydrate used by patients with atopic dermatitis.

9. From Kampo medicine perspective

"*Qikyo*" was one of the inclusion criteria for enrollment in this trial. Changes in "*qikyo*" scores were not significantly different between the two arms.

10. Safety assessment in the article

Although the authors mention that "safety (including biochemical tests) was assessed," the results of this assessment are not described.

11. Abstractor's comments

This paper provides objective data on the efficacy of hochuekkito as an adjunctive therapy for atopic dermatitis.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference
Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Therapeutic effect of boiogitokashuchibushimatsu on gonarthrosis: a 10-year prospective randomized controlled trial with loxoprofen sodium*. *Pharma Medica* 2007; 25: 15-21 (in Japanese). Ichushi Web ID: 2008070613 MOL, MOL-Lib

1. Objectives
To evaluate the efficacy of boiogitokashuchibushimatsu (防已黄耆湯加修治附子末) for gonarthrosis.

2. Design
Randomized controlled trial (RCT).

3. Setting
University hospital (Department of Pathology and Applied Neurobiology, Kyoto Prefectural University of Medicine; Pain Clinic, Department of Anesthesiology, Shiga University of Medical Science; and Graduate School of Pharmaceutical Sciences, Osaka University) and 4 other hospitals.

4. Participants
Two hundred eleven patients with gonarthrosis.

5. Intervention
Arm 1: administration of boiogitokashuchibushimatsu (防已黄耆湯加修治附子末) (manufacturer unknown) (n=110); age at completion, 81.5±3.4 years; male/female ratio, 8:102.
Arm 2: administration of loxoprofen (n=101); age at completion, 82.0±3.1 years; male/female ratio, 9:92.
Ten-year trial. Capsules were taken with 350 mL of water 30 min before meals.
No more details (e.g. dose, dose frequencies) were indicated in the original paper.

6. Main outcome measures
Exercise capacity (EC), range of motion of knee, various chronic pains (CP), health-related quality of life (Hr-QOL), adiponectin, leptin, and orexin levels, knee circumference, synovial fluid retention as assessed by ultrasound, degree of joint space narrowing as assessed by CT scan, (direct, indirect, total) medical expenses monitored over a 10-year period.

7. Main results
All EC parameters (continuous walking distance, continuous upslope walking distance, number of steps in continuous downslope walking) were larger in arm 1 than in arm 2 (P<0.001). All parameters used to evaluate activities of daily living (ADL) (pain in passive exercise, spontaneous pain, pain on pressure, patella ballottement/soft tissue swelling, local heat, etc.), various CP, and Hr-QOL were significantly improved in arm 1 compared with arm 2 (P<0.001).

8. Conclusions
The treatment significantly improves EC, ADL, CP, and Hr-QOL and lowers total medical expenses.

9. From Kampo medicine perspective
The *sho* (pattern/syndrome) concept was a criterion for inclusion. Although "gonarthrosis complying with the *sho* for boiogitokabushi" was used as a criterion, the *sho* concept was not defined. The authors appear to consider that all patients with gonarthrosis in the study satisfy the sho for boiogitokabushi. There was no *sho* concept as an exclusion criterion and no subgroup analyses according to *sho*.

10. Safety assessment in the article
A significantly larger number of adverse events occurred in arm 2 (P<0.001 for all items): gastric ulcer (0 event in arm 1 *vs*. 24 events in arm 2), eruption/sleepiness/stomach discomfort/oedema (11 events *vs*. 348 events), and laboratory abnormality (3 events *vs*. 417 events).

11. Abstractor's comments
The filling of capsules to make the investigational products indistinguishable from each other is necessary for double-blind study of Kampo medicine. However, the dose of loxoprofen is missing from this paper (misprint?). This study assumed that "patients with gonarthrosis satisfy the *sho* for boiogitokashuchibushi." This assumption should have been verified in a pilot study. However, it is extremely rare that a particular disease corresponds one-on-one to an effective Kampo treatment; the treatment of most diseases needs several Kampo medicines selected according to patient conditions. Furthermore, prolonged administration of drugs (including loxoprofen used as the control drug in this study) causing potentially fatal adverse reactions in the elderly such as gastric mucosal disorder is problematic. Also problematic is the therapeutic use of fixed doses for painful disease. Moreover, duration of the study was too long, given the nature of this disease and the old age of most subjects. Conclusion should be drawn in a shorter term.

12. Abstractor and date
Hoshino E, 15 March 2009, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Long-term effects of traditional Chinese herbal medicine, mai-men-dong-tang (Japanese name: bakumondo-to) compared with bromhexine, hydrochloride on sicca syndrome, especially, salivary secretion in patients with primary Sjögren's syndrome: a multicenter, randomized well controlled group parallel comparative trial study with bromhexine. *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2002; 43: 62-6. Ichushi Web ID: 2005101735

1. Objectives

To evaluate the efficacy and safety of bakumondoto (麦門冬湯) therapy for dryness associated with primary Sjögren's syndrome.

2. Design

Randomized controlled trial (RCT).

3. Setting

Not mentioned

4. Participants

One-hundred and six patients with primary Sjögren's syndrome.

5. Intervention

Arm 1: bakumondoto (麦門冬湯) extract granules 3 g t.i.d. for 1 year. (n=51)
Arm 2: bromhexine hydrochloride 4 g t.i.d. for 1 year. (n=54)

6. Main outcome measures

Dryness, amount of salivation/lacrimation, and inflammatory reaction.

7. Main results

Salivation was increased in both groups but was significantly increased in the bakumondoto group. Lacrimation was significantly increased only in the bakumondoto group. Dryness was also improved only in the bakumondoto group. The inflammatory reaction remained unchanged in both groups.

8. Conclusions

Bakumondoto is more effective than bromhexine hydrochloride and safe in the treatment of dryness associated with primary Sjögren's syndrome.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were fewer adverse drug reactions (ADRs) or laboratory abnormalities in the bakumondoto group than in the bromhexine hydrochloride group (the number of ADRs not specified).

11. Abstractor's comments

This study provides objective evidence for the efficacy of bakumondoto for relieving dryness associated with primary Sjögren's syndrome.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Long-term effect of traditional Chinese herbal medicine, mai-men-don-tang on sicca syndrome, especially, salicary secretion in patients with primary Sjögren's syndrome: a multicenter, randomized well controlled group-pararell double-blined study. *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2004; 45: 66-74.

1. Objectives

To evaluate the efficacy and safety of bakumondoto (麦門冬湯) therapy for salivary hyposecretion associated with primary Sjögren's syndrome.

2. Design

Randomized controlled trial (RCT).

3. Setting

Two clinics, three university hospitals, and one general hospital.

4. Participants

Two-hundred and twenty-nine patients with primary Sjögren's syndrome.

5. Intervention

Arm 1: bakumondoto (麦門冬湯) extract granules 3 g t.i.d. before meals for 6 months (n=115).
Arm 2: placebo 3 g t.i.d. before meals for 6 months (n=114).

6. Main outcome measures

Dryness, amounts of salivation/lacrimation, joint pain, amount of sputum, Raynaud's symptom, limb skin temperature, and inflammatory reaction.

7. Main results

Salivation was increased in the bakumondoto group but decreased in the placebo group. Subjective symptoms were improved in the bakumondoto group but remained unchanged or were aggravated in the placebo group. Inflammatory reaction improved significantly only in the bakumondoto group.

8. Conclusions

Bakumondoto is effective and safe for the relief of subjective symptoms and salivary hyposecretion associated with primary Sjögren's syndrome.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were fewer adverse drug reactions (ADRs) or laboratory abnormalities or fewer patients with ADRs or laboratory abnormalities in the bakumondoto group than in the bromhexine hydrochloride group. There were no serious ADRs or laboratory abnormalities leading to treatment discontinuation in either group (the number of events not specified).

11. Abstractor's comments

This study provides objective evidence for the efficacy of bakumondoto in the treatment of dryness associated with primary Sjögren's syndrome.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Nishizawa Y, Nishizawa Y, Goto GH, et al. The Multicenter randomized comparative study of kampo herbal medicine, mai-men-dong-tang (Japanese name Bakumondo-to) compared with bromhexine on salivary secretion in secondary Sjögren's syndrome. *Itami to Kampo* (*Pain and Kampo Medicine*) 2004; 14: 10-7 (text in Japanese with English abstract). Ichushi Web ID: 2006260917

1. Objectives

To evaluate the efficacy and safety of bakumondoto (麦門冬湯) for treatment of secondary Sjögren's syndrome.

2. Design

Randomized controlled trial (RCT).

3. Setting

Three clinics and 3 university hospitals.

4. Participants

Eight-hundred and forty-seven patients with secondary Sjögren's syndrome.

5. Intervention

Arm 1: bakumondoto (麦門冬湯) extract granules 3 g t.i.d. before meals for 1 year (n=424).
Arm 2: bromhexine hydrochloride 4 g t.i.d. before meals for 1 year (n=423).

6. Main outcome measures

Dryness, amounts of salivation/lacrimation, joint pain, amount of sputum, Raynaud's symptom, limb skin temperature.

7. Main results

The amount of salivation was increased in both arms but was significantly higher in the bakumondoto group. Among bakumondoto-treated patients, those with mild disease showed significantly larger increases, whereas those with severe disease showed larger percent increases. The amount of lacrimation was significantly increased only in the bakumondoto group. Only in the bakumondoto group, the following variables were also improved: dryness, Raynaud's symptom, joint pain, cough/amount of sputum, and lowered temperature of the limb skin.

8. Conclusions

Bakumondoto is more effective and safer than bromhexine hydrochloride and therefore beneficial for treatment of mouth dryness associated with secondary Sjögren's syndrome.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were fewer adverse drug reactions (ADRs) or laboratory abnormalities in the bakumondoto group than in the bromhexine hydrochloride group (the number of ADRs not indicated).

11. Abstractor's comments

This study provides objective evidence for the efficacy of bakumondoto for the treatment of dryness associated with secondary Sjögren's syndrome. In the text, the dose of bromhexine hydrochloride was indicated as 120 mg, instead of the correct dose of 12 mg.
This paper seems to include data from the preliminary clinical trial published in *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2003; 44: 65-70.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Improving effect of Chinese herb medicine mai-men-dong-tang (Japanese name: bakumondo-to) comparative with sicca syndrome in especial salivary patients with secondary Sjögren's syndrome in multicenter, well controlled, long-term comparative study. *Nihon Daekisen Gakkaishi* (*Journal of the Japan Salivary Gland Society*) 2003; 44: 65-70.

1. Objectives

To evaluate the efficacy and safety of bakumondoto (麦門冬湯) for treatment of dryness associated with secondary Sjögren's syndrome.

2. Design

Randomized controlled trial (RCT).

3. Setting

None.

4. Participants

Seven-hundred and fifty-six patients with secondary Sjögren's syndrome.

5. Intervention

Arm 1: bakumondoto (麦門冬湯) extract granules 3 g t.i.d. for 1 year (n=380).
Arm 2: bromhexine hydrochloride 4 g t.i.d. for 1 year (n=374).

6. Main outcome measures

Dryness, amounts of salivation/lacrimation, joint pain, amount of sputum, Raynaud's symptom.

7. Main results

The amount of salivation was increased in both arms, but it was significantly higher in the bakumondoto group. The amount of lacrimation was significantly increased only in the bakumondoto group. The following outcome measures were also improved only in the bakumondoto group: dryness, Raynaud's symptom, joint pain, and cough/amount of sputum. The inflammatory reaction remained unchanged in both groups.

8. Conclusions

Bakumondoto is more effective and safer than bromhexine hydrochloride and therefore useful for treating dryness associated with secondary Sjögren's syndrome.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were fewer adverse drug reactions (ADRs) or laboratory abnormalities in the bakumondoto group than in the bromhexine hydrochloride group (the number of ADRs not indicated).

11. Abstractor's comments

This study provides objective evidence for the efficacy of bakumondoto for treating dryness associated with secondary Sjogren's syndrome. The duration and dosage of bakumondoto treatment was correlated with the amount of salivation, suggesting a dose-dependent effect.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Ohno S. The effect of Kampo medicine on salivary secretion in Sjögren's syndrome. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2006; 15: 134-40 (in Japanese). Ichushi Web ID: 2006203175

1. Objectives

To evaluate the efficacy for Sjögren's syndrome.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Outpatient Department of Rheumatology, Samitama Medical University Hospital.

4. Participants

Sixty-four patients with Sjögren's syndrome.

5. Intervention

Arm 1: 4-week administration of 2.5 g t.i.d. of TSUMURA Hochuekkito (補中益気湯) Extract Granules (n=32; after 4 dropped out, 28 included for analysis).

Arm 2: 4-week administration of Kampo medicine extracts that affect salivary secretion (3 g t.i.d. of TSUMURA Bakumondoto (麦門冬湯) Extract Granules alone [n=23]; 3 g t.i.d. of TSUMURA Bakumondoto (麦門冬湯) Extract Granules + 2.5 g t.i.d. of TSUMURA Rokumigan (六味丸) Extract Granules [n=3]; 3 g t.i.d. of TSUMURA Bakumondoto (麦門冬湯) Extract Granules + 2.5 g t.i.d. of TSUMURA Hachimijiogan (八味地黄丸) Extract Granules [n=4]) according to *sho* (証, pattern/syndrome) (n=32; after 2 dropped out, 30 included for analysis).

6. Main outcome measures

Change in salivary secretion from pre- to post-administration, measured using a chewing gum test.

7. Main results

27 out of 30 patients in Arm 1 demonstrated increase in salivary secretion, with a significant increase in mean pre-treatment secretion of 8.2+1.2ml to post-treatment average of 12.0+1.4ml ($p<0.005$). There was no statistical significance between pre- and post-treatment secretions in Arm 2. The amount of increase in salivary secretions before and after the treatment in Arm 1 was significantly greater than Arm 2 ($p<0.005$).

8. Conclusions

A Kampo medicine with moisturizing effect (but not a medicine without this effect) increased the amount of salivary secretion.

9. From Kampo medicine perspective

Arm 1 used "bensho (弁証)" (Kampo diagnosis) to allocate patients, specifically "jinkyo" (腎虚, kidney deficiency) which included 3 or more of the following 6 symptoms: 1) heaviness of the back; 2) heaviness in the lower legs with pain in heels and lateral surface of the lower legs; 3) tinnitus/hearing loss; 4) loss of hair and hair luster; 5) looseness or loss of teeth; and 6) sexual dysfunction (impotence, nocturnal emission). Kampo formulations for Arm 1 were selected based on the status of jinkyo: 1) bakumondoto alone for negative jinkyo; 2) bakumondoto plus rokumigan for jinkyo without chills; and 3) bakumondoto plus hachimijiogan for jinkyo with chills.

10. Safety assessment in the article

None.

11. Abstractor's comments

This is an interesting quasi-randomized controlled trial that is plausible for its attempt in incorporating "sho" (証) diagnosis for selection of treatment. Results from the trial demonstrated that bakumondoto, moisturizing formuala, with other Kampo forumalations comibination effectively enhanced salivary secretion in patients with Sjögren's syndrome than hochuekkito which was used as a control. A total of three pattern of combinations of Kampo formulation(s) were established for Arm 1 based on various manifestations of jinkyo. 23 out of 30 patients (77%) in Arm 1 received bakumondoto only. Future studies with improved RCT design and comparison with placebo or Western drug as a control appear warranted.

12. Abstractor and date

Namiki T, 17 March 2009, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Maeshima S, Katayama Y. Spine and spinal cord diseases 1. Traditional Chinese medicines for the spinal disorders. *Kampo to Saishin-Chiryo* (*Kampo & the Newest Therapy*) 2004; 13: 232-6 (in Japanese). Ichushi Web ID: 2004301321

1. Objectives

To evaluate the efficacy of hachimijiogan (八味地黄丸), goshajinkigan (牛車腎気丸), and shuchibushi (修治附子) powder for relief of residual symptoms after surgical treatment of cervical spinal stenosis.

2. Design

Randomized controlled trial (RCT).

3. Setting

One university hospital.

4. Participants

Twenty-four patients with residual symptoms following surgical treatment of cervical spinal stenosis.

5. Intervention

Arm 1: 2-month administration of hachimijiogan (八味地黄丸).
Arm 2: 2-month administration of goshajinkigan (牛車腎気丸).
Arm 3: 2-month administration of goshajinkigan (牛車腎気丸) + 1.0 g of shuchibushi powder (修治附子末).

No between-arm difference was noted in operative effect. Administration started at postoperative 2 months in all arms.
No details in original paper.

6. Main outcome measures

Subjective symptoms (pain and paresthesia) evaluated on a visual analogue scale (VAS).

7. Main results

Pain was improved in 24.8%, 37.1%, and 45.5% of patients receiving hachimijiogan, goshajinkigan, and goshajinkigan + shuchibushi powder, respectively. The efficacy of goshajinkigan + shuchibushi powder was significantly higher than that of hachimijiogan. Paresthesia was improved in 21.4%, 24.2%, and 28.5%, respectively, showing no difference between arms.

8. Conclusions

Hachimijiogan, goshajinkigan, and goshajinkigan + shuchibushi powder were all effective for residual symptoms of surgically treated cervical spinal disease, with the highest efficacy achieved by goshajinkigan + shuchibushi powder.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions (ADRs) or withdrawals occurred (the number of ADRs not indicated).

11. Abstractor's comments

This study provides evidence that Kampo formulations can be a therapeutic option for residual symptoms of surgically treated cervical spinal diseases. Given the higher efficacy at higher doses of shuchibushi, the authors infer that shuchibushi acts on opioid receptors.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Maeshima S, Katayama Y. Spine and spinal cord diseases 1. Traditional Chinese medicines for the spinal disorders. *Kampo to Saishin-Chiryo* (*Kampo & the Newest Therapy*) 2004; 13: 232-6. Ichushi Web ID: 2004301321

1. Objectives

To evaluate the efficacy of goshajinkigan (牛車腎気丸) and shuchibushi powder (修治附子末) for relief of chronic low back pain associated with lumbar spinal stenosis.

2. Design

Randomized controlled trial (RCT).

3. Setting

One university hospital.

4. Participants

Eighty-nine patients with chronic low back pain associated with lumbar spinal stenosis for which surgery is not indicated.

5. Intervention

Arm 1: 3-month administration of western medicines including non-steroidal anti-inflammatory drugs (NSAIDs), prostaglandin E2, vitamin B12, and/or H2 blockers (n=29).
Arm 2: 3-month administration of goshajinkigan (牛車腎気丸) alone (n=30).
Arm 3: 3-month administration of goshajinkigan (牛車腎気丸) + 2.0 g of shuchibushi powder (修治附子末) (n=30).
No details indicated in the original paper.

6. Main outcome measures

Low back pain and lower limb paresthesia evaluated on a visual analogue scale (VAS).

7. Main results

Lower back pain score was decreased from 6.7, 6.5, and 6.8 to 3.5, 4.5, and 3.2 in arms 1, 2, and 3, respectively. Lower limb paresthesia score was decreased from 5.6, 5.7, and 5.9 to 4.2, 3.9, and 3.2, respectively. Thus, there were no significant between-arm differences in therapeutic effects.

8. Conclusions

Both oshajinkigan and shuchibushi powder were as effective as western medicines for the relief of chronic low back pain and lower limb paresthesia associated with lumbar spinal stenosis.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions (ADRs) or withdrawals occurred in either arm (the number of ADRs not indicated).

11. Abstractor's comments

This study is of clinical significance since it provides evidence that Kampo medicines can be a therapeutic option for lumbar spinal stenosis, expanding the range of therapeutic options.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Diseases of the musculoskeletal system and connective tissue

Reference

Wang XD, Yoshida K, Honda K, et al. Study of the immunoregulatory activity of the combination therapy with juzentaihoto and hachimijiogan in patients with disuse syndrome*. *Kampo Igaku* (*Kampo Medicine*) 2006; 30: 65-7 (in Japanese). Ichushi Web ID: 2006283912

1. Objectives

To evaluate the efficacy of juzentaihoto (十全大補湯) combined with hachimijiogan (八味地黄丸) in patients with disuse syndrome.

2. Design

Randomized controlled trial (envelope method) (RCT-envelope).

3. Setting

One community hospital.

4. Participants

Patients after a prolonged period of bed rest and tube feeding.

5. Intervention

Arm 1: Tsumura Juzentaihoto (十全大補湯) Extract Granules and Tsumura Hachimijiogan (八味地黄丸) Extract Granules 2.5 g b.i.d. each for 24 weeks, n=13.
Arm 2: No administration of Kampo drugs, n=15.

6. Main outcome measures

Laboratory tests: hemograms and urine tests performed at 0, 4, 8, 12, 16, 20, and 24 weeks.
CD4 count, CD8 count, CD4/CD8 ratio, neutrophil phagocytotic activity, levels of immunoglobulins (IgM, IgG, and IgA) examined at 0, 12, and 24 weeks.

7. Main results

CD4/CD8 ratio and CD4 count were significantly increased in arm 1 compared to arm 2 at 12 weeks; however, no significant difference was observed at 24 weeks. There were no significant between-arm differences in the results of other tests.

8. Conclusions

In many cases, CD4/CD8 ratio and CD4 count were elevated at 12 weeks of administration.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Immunoregulatory effect of the combination two Kampo drugs was assessed using lymphocyte surface markers CD4 and CD8. The finding of significant increases in CD4/CD8 ratio and CD4 count at 12 weeks, but not at 24 weeks, demands the conduct of further studies designed to reveal whether immune status was restored or regulated.

12. Abstractor and date

Namiki T, 12 March 2009, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Nishizawa Y, Nishizawa Y, Yoshioka H, et al. Efficacy and safety of Chinese traditional medicine, Niu-Che-Shwn-Qi-Wan (Japanese name: Goshajinki-gan) versus propiverine hydrochloride on health-related quality of life in patients with overactive bladder in prospective randomized comparative study. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2007; 16: 131-42 (in Japanese). Ichushi Web ID: 2007260946

1. Objectives

To evaluate the efficacy and safety of goshajinkigan (牛車腎気丸) and propiverine hydrochloride for overactive bladder.

2. Design

A randomized controlled trial (RCT).

3. Setting

Not mentioned (authors belong to Nishizawa Clinic, Department of Pathology and Applied Neurobiology, Kyoto Prefectural University of Medicine and Department of Anesthesiology, Shiga University of Medical Science).

4. Participants

Seven hundred and four patients with overactive bladder, aged 45 years or older, prospectively enrolled over a 10-year period (1997–2006).

5. Intervention

Arm 1: administration of goshajinkigan (牛車腎気丸) (manufacturer not specified), 4.5 g/day, for 1 year (n=352).
Arm 2: administration of propiverine hydrochloride, 60 mg/day, for 1 year (n=352).

6. Main outcome measures

Symptoms of overactive bladder (urge to urinate, daytime urinary frequency, nocturia, and urine leak).
Quality of life (pain, erection dysfunction, cold sensation, etc.).

7. Main results

Symptoms of overactive bladder were significantly more improved in arm 2 than in arm 1 during the first month after treatment initiation, but significantly more improved in arm 1 than arm 2 during the second and subsequent months. At the completion of the study, the other concomitant symptoms and quality of life (QOL) were also significantly more improved in arm 1 than in arm 2.

8. Conclusions

It was suggested that goshajinkigan is effective for overactive bladder.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Four and 375 events of adverse drug reactions occurred in arm 1 and arm 2, respectively.

11. Abstractor's comments

This 1-year prospective randomized controlled trial in 704 patients suggests the efficacy of goshajinkigan for overactive bladder. Its efficacy for concomitant symptoms and QOL was also suggested. However, there is no mention of the number patients who withdrew, the facility or facilities where this trial was actually conducted, and the method of randomization. Future studies considering these points are awaited.

12. Abstractor and date

Okabe T, 28 November 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Aoki Y, Ueda K, Tsutani K, et al. The influence of formula Ma-huang-fu-zi-xi-Xin-Tang (Mao-bushi-saishin-to; Mbst) on the results of urodynamic studies. *Journal of Traditional Medicine* 2001;18:203-9. Ichushi Web ID: 2002139756 CiNii

1. Objectives

To evaluate the effect of single-dose administration of maobushisaishinto (麻黄附子細辛湯) on urine flow.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

Department of Urology, Nagoya City University Medical School and associated facilities.

4. Participants

Thirteen young male volunteers (mean age: 38.0 years) and six elderly male volunteers (mean age: 64.5 years).

5. Intervention

Arm 1: administration of 2 capsules of Kotaro Maobushisaishinto (麻黄附子細辛湯) in the 1st course followed by 2 capsules of placebo in the 2nd course, with 4-week withdrawal between courses.
Arm 2: administration conducted in the reverse order of arm 1.

6. Main outcome measures

Maximum urine flow rate at 3 hr after administration, mean urine flow rate, and voiding efficiency.

7. Main results

Regardless of the order of administration, no significant differences were observed in the maximum urine flow rate at 3 hr after administration, mean urine flow rate, or voiding efficiency between maobushisaishinto - and placebo-groups. There was no significant difference in the maximum urine flow rate, mean urine flow rate, or voiding efficiency between pre- and post-dose levels when treated with maobushisaishinto in the elderly.

8. Conclusions

It is suggested that single-dose administration of maobushisaishinto has no effect on urine flow in both young and old men.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

In elderly males with impaired urination due frequently to prostatic hyperplasia, ephedrine-containing formulations such as mao have been shown to aggravate the problem. This study concludes that single-dose administration of maobushisaishinto does not adversely affect urine flow in the elderly. However, since treatment with a Kampo formulation usually requires repeated administration for a certain period, the results of a clinical study with repeated administration will also need to be considered.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Oribe K, Nishida Y. Efficacy of hachimijiogan for discomfort after surgery for uterine prolapse. *Gekkan Kampo Ryoho* (*Monthly Journal of Kampo Medicine and Herbs*) 2006; 10: 282-8 (in Japanese).

1. Objectives

To evaluate the hachimijiogan (八味地黄丸)-induced improvement in postoperative discomfort associated with surgery for uterine prolapse and quality of life (QOL).

2. Design

A randomized controlled trial (RCT).

3. Setting

Department of Obstetrics and Gynecology, National Hospital Organization Oita Medical Center.

4. Participants

Nineteen patients with uterine prolapse who did not respond to hochuekkito and underwent vaginal radical operation for uterine prolapse at the above facility between December 2005 and March 2006.

5. Intervention

Arm 1: oral administration of TSUMURA Hachimijiogan (八味地黄丸)Extract Granules 2.5 g t.i.d. before meals, n=12.
Arm 2: no treatment, n=7.

6. Main outcome measures

Frequency of urination per day and mean residual urine volume at the start and 1 and 2 weeks after the start of hachimijiogan.

7. Main results

There was no significant difference in urination frequency. Residual urine volume was significantly decreased after hachimijiogan treatment for 1 week (21±2.3 mL *vs*. 13±4.2 mL, $P<0.05$) and 2 weeks (12±1.7 mL *vs*. 8.3±1.5 mL, $P<0.05$). In addition, 2 weeks of treatment with hachimijiogan decreased residual urine volume more significantly in patients with *shofukufujin* (小腹不仁, soft, weak lower abdomen) than in those without *fukusho* (腹証, abdominal pattern) (8.3±1.5 mL *vs*. 5.3±2.5 mL, $P<0.05$).

8. Conclusions

Hachimijiogan administered after surgery for uterine prolapse may accelerate tissue repair postoperatively, thereby improving patient QOL, particularly in patients with *shofukufujin.*

9. From Kampo medicine perspective

Traditionally, hochuekkito has been considered to be the effective treatment for uterine prolapse. However, because of a change in nutritional status, many women do not present conventional "*sho*", leaving room for reconsideration of the appropriate agent. Hachimijiogan is highly effective for decreasing residual urine volume after surgery for uterine prolapse and aiding recovery of the bladder and surrounding tissues.

10. Safety assessment in the article

No adverse drug reactions occurred after hachimijiogan treatment.

11. Abstractor's comments

This research raises questions about what Kampo medicine should be or how it should be utilized in an aging society. None of the existing treatments for genitourinary prolapse (including surgery, pessary insertion, and pharmacotherapy) are totally effective, raising concerns among clinicians. This research demonstrated that hachimijiogan is highly effective in decreasing postoperative residual urine volume particularly in patients with *shofukufujin*. Future research is desired to determine whether this clinical approach fusing western and oriental medicines can prevent recurrent uterine prolapse and how Kampo medicine can be used to treat uterine prolapse for *sho* of unclear *jinkyo* (腎虚, kidney deficiency).

12. Abstractor and date

Ushiroyama T. 12 December 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Iwabuchi S. Effect of kyuki-kyogai-to on stopping dysfunctional uterine bleeding – comparison with occidental hemostatic drugs -. *Nihon Toyo Igaku Zasshi* (*Japanese Journal of Oriental Medicine*) 2000; 50: 883-903 (text in Japanese with English abstract). Ichushi Web ID: 2000172969 CiNii

1. Objectives

To evaluate the efficacy and safety of kyukikyogaito (キュウ帰膠艾湯) for menometrorrhagia.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Obstetric and gynecologic practitioner, Yamagata.

4. Participants

The analysis population included 183 out of 200 randomized patients with menometrorrhagia.

5. Intervention

Arm 1: administration of 9.0 g of TSUMURA Kyukikyogaito (キュウ帰膠艾湯) Extract Granules for 7 days (n=100). Ninety-three patients were included for analysis.

Arm 2: administration of tranexamic acid (3 tablets of Transamin) and carbazochrome/VK mixture (3 tablets of Ophtharum K) for 7 days (n=100). Ninety patients were included for analysis.

6. Main outcome measures

Number of days from exploratory endometrial curettage to hemostasis.

7. Main results

The time to hemostasis was significantly shorter in arm 1 (4.29±1.54 days) than in arm 2 (5.45 ± 2.13 days). When response was determined by the criterion of 'hemostasis by day 7', the response rate was significantly higher (94.6%) in arm 1, compared with 72.2% in arm 2. By *sho* (証, pattern/syndrome), cases of hypofunction or intermediate function required significantly fewer days to hemostasis when receiving kyukikyogaito, whereas cases of hyperfunction showed no difference in the days to hemostasis between arms. By the appearance of the endometrium on imaging, cases of the proliferative phase or simple hyperplasia required significantly fewer days to hemostasis when receiving kyukikyogaito, whereas cases of stationary phase, atrophic phase and mixed proliferative/secretory phase or secretory phase showed no difference in the days to hemostasis between arms.

8. Conclusions

Kyukikyogaito is more effective for hemostasis in menometrorrhagia, compared with hemostatic drugs tranexamic acid and carbazochrome/VK mixture.

9. From Kampo medicine perspective

After, but not before, dosing, differential diagnosis of *sho* was made visually and by abdominal palpation, and it was concluded that kyukikyogaito is effective regardless of *sho*.

10. Safety assessment in the article

A 32-year-old patient complained of feeling bad after receiving 1 sachet of kyukikyogaito, and of stomach discomfort and nausea after receiving 2 sachets, and then discontinued the medicine after receiving 4 sachets and was switched to another drug.

11. Abstractor's comments

Various pathogenic mechanisms can cause menometrorrhagia in Kampo medicine, as in western medicine. Kyukikyogaito is a combination of a single medicine that acts on one of these mechanisms, called *shoninkyoson* (衝任虚損), and a hemostatic drug (*Kinkiyoryaku* [金匱要略]: synopsis of prescriptions of the golden chamber). Presence of both responders and non-responders to this combination suggests that the disease has a more than one pathogenesis. Although this study is a quasi-randomized controlled trial, in which patients were alternately randomized and placed in the order of visitation, a certain efficacy of kyukikyogaito for menometrorrhagia is suggested.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008. 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Ota H. Positioning of Kampo therapy and hormone replacement therapy in treatment of climacteric disorders*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2001; 18: 21-9 (in Japanese). Ichushi Web ID: 2002170744

1. Objectives

To compare hormone replacement therapy (HRT) and Kampo therapy as treatment of climacteric disorders.

2. Design

Randomized controlled trial (RCT).

3. Setting

None. The author belonged to the Department of Obstetrics and Gynecology, Tokyo Women's Medical University.

4. Participants

Ninety-six postmenopausal or ovariectomized patients with climacteric disorders.

5. Intervention

Arm 1: HRT (0.625 mg of conjugated estrogen and 2.5 or 5 mg of medroxyprogesterone acetate) (n=50).
Arm 2: Kampo therapy (keishibukuryogan (桂枝茯苓丸), n=19; kamishoyosan (加味逍遙散), n=11; goshajinkigan (牛車腎気丸), n=8; tokishakuyakusan (当帰芍薬散), n=2; tokakujokito (桃核承気湯), n=2; kihito (帰脾湯), n=2; nyoshinsan (女神散), n=2) (n=46).
No details indicated in the original paper.

6. Main outcome measures

Score on Keio modified menopause index, measured at baseline, 1, 6, and 12 months after the start of administration. Severity was defined as mild for 0–10 points, moderate for 10–20 points, and severe for 20–30 points, and response was defined as a change from severe to moderate, moderate to mild, or a score reduction by two-thirds in mild cases.

7. Main results

HRT improved the following 6 symptoms in 1 month: vasomotor manifestations; nervousness; low back and back pain; depression; insomnia; and headache. In contrast, Kampo therapy did not improve any symptoms in 1 month but improved the following 4 symptoms in 6 months: vasomotor manifestations; malaise; low back and back pain; and nervousness. Among Kampo medicines, only goshajinkigan was effective for low back and back pain.

8. Conclusions

The therapeutic effect of HRT is superior for hot flashes, perspiration, depression, and insomnia, whereas that of Kampo therapy is superior for malaise and chill.

9. From Kampo medicine perspective

The number of patients receiving keishibukuryogan (n=19), kamishoyosan (n=11), or tokishakuyakusan (n=2) was explained by the small number of cases with *kyo-sho* (虚証, deficiency pattern).

10. Safety assessment in the article

None.

11. Abstractor's comments

This paper outlines the characteristics of Kampo medicines and HRT. It recommends that Kampo medicine be administered in more responsive cases with specific symptoms. Subsequent publication of a study of individual Kampo medicines with more sensitive design is awaited.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Takamatsu K. Study of the usefulness of Kampo therapy for climacteric disorders – a randomized trial of three major Kampo medicines for treatment of gynecological disease–*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2006; 23: 35-42 (in Japanese). Ichushi Web ID: 2006288782

1. Objectives

To compare the efficacy of Kampo therapy with that of hormone replacement therapy (HRT) for climacteric disorders and to compare the efficacy of three non-*sho*-based (非随証) Kampo medicines for gynecological disease.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Departments of Obstetrics and Gynecology, Tokyo Women's Medical University (1) and Keio University Hospital (2).

4. Participants

(1) Seventy women receiving ambulatory treatment for climacteric disorders between November 2000 and January 2002.
(2) One hundred women receiving ambulatory treatment for climacteric disorders between January 1993 and December 2000.

5. Intervention

Comparison of clinical efficacy of HRT and Kampo medicine
Arm 1: administration of 2.5 g t.i.d. of TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules, TSUMURA Kamishoyosan (加味逍遙散) Extract Granules or TSUMURA Keishibukuryogan (桂枝茯苓丸) Extract Granules before meals for 4–8 weeks (n=70).
Arm 2: continuous coadministration of 0.625 mg t.i.d. of Premarin (conjugated equine estrogen) and 2.5 mg of Provera (medroxyprogesterone acetete) before meals for 4–8 weeks (n=110).
Evaluation of the efficacy of non- *sho*-based therapy with three major Kampo medicines for gynecological disease.
Arm 1: administration of 2.5 g t.i.d. of TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules before meals for 4–8 weeks (n=23).
Arm 2: administration of 2.5 g t.i.d. of TSUMURA Kamishoyosan (加味逍遙散) Extract Granules before meals for 4–8 weeks (n=23).
Arm 3: administration of 2.5 g t.i.d. of TSUMURA Keishibukuryogan (桂枝茯苓丸) Extract Granules before meals for 4–8 weeks (n=24).

6. Main outcome measures

Presence/absence and improvement of symptoms self-evaluated on a 4-point symptom severity scale using the Keio modified menopause index questionnaire.

7. Main results

Overall response rates for HRT and Kampo therapy were comparable (78.0% responders to HRT and 68.6% responders to Kampo therapy), although improvement was greater in patients receiving Kampo therapy (severity reduced by 2 or more points in 83.0% of patients receiving HRT and 21.4% of those receiving Kampo therapy). There was no difference in the percent who responded to the three non-*sho*-based therapies (65.2% were responders to tokishakuyakusan, 74.0% were responders to kamishoyosan, and 70.8% responders to keishibukuryogan). Kampo therapy was particularly effective for psychiatric manifestations including excitability, depression, irritation, anxiety, and brooding.

8. Conclusions

Using the same questionnaire, this study demonstrated that Kampo therapy has some effect on climacteric disorders, in particular, relieving subjective symptoms at almost the same rate as HRT and showing high efficacy against psychotic manifestations.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

In this paper, the rate of symptom improvement after Kampo therapy was approx. one-quarter that after HRT and the three Kampo medicines had comparable efficacy, showing that non-*sho*-based Kampo therapy for "climacteric disorders" is limited. Thus, this study is valuable in that it supports the importance of the *zuisho* (随証, based on pattern) approach to Kampo therapy in the treatment of climacteric disorders. Similar papers have been published by the first author including: 1) Takamatsu K, Musha C, Okano H, et al. Study of usefulness of Kampo therapy for climacteric disorders*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2002; 19: 111-6 (in Japanese) [Ichushi Web ID: 2002193391]; 2) Takamatsu K. HRT and Kampo medicine*. *Nippon Konenki Igakukai Zasshi* (*The Journal of the Japan Menopause Society*) 2004; 12: 155-7 (in Japanese); 3) Takamatsu K, Makita K, Tanabe K, et al. HRT and Kampo medicine*. *Rinsho Kensa* (*The Journal of Medical Technology*) 2004; 48: 877-84 (in Japanese); and 4) Takamatsu K, Tanabe K. Efficacy of Kampo medicine against climacteric disorders*. *Sanfujinka Chiryo* (*Obstetrical and Gynecological Therapy*) 2004; 89: 408-15 (in Japanese). MOL, MOL-Lib

12. Abstractor and date

Ushiroyama T, 20 January 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

References

Ogita Y, Fujimoto S, Ushiroyama T, et al. Efficacy of formulation TK-061 for various climacteric symptoms – comparison with Teikoku Keishibukuryogan Extract Granules*. *Rinsho Fujinka Sanka* (*Clinical Gynecology and Obstetrics*) 2002; 56: 799-810 (in Japanese). Ichushi Web ID: 2003004448

Ogita Y, Fujimoto S, Ushiroyama T, et al. Keishibukuryogan formulation TK-061 prepared with crude drug – verification of efficacy for various climacteric symptoms*. *Sanka to Fujinka* (*Obstetrics and Gynecology*) 2002; 69: 953-62 (in Japanese). Ichushi Web ID: 2003004359 MOL, MOL-Lib

1. Objectives

To investigate the equivalence between non-extracted keishibukuryogan (桂枝茯苓丸) and keishibukuryogan (桂枝茯苓丸) extract.

2. Design

Randomized controlled trial (RCT).

3. Setting

Twenty facilities (the Department of Obstetrics and Gynecology, Osaka City University School of Medicine, the Department of Obstetrics and Gynecology, Hokkaido University School of Medicine, the Department of Obstetrics and Gynecology, Osaka Medical College School of Medicine, et al.).

4. Participants

One-hundred and ninety-three patients who were diagnosed with climacteric disorders during a 1 year and 5 month period from November 1999 to March 2001, untreated with hormone replacement therapy within 4 weeks before the start of the study, and having body mass index (BMI) ≥20 and body fat <35%. (The per-protocol population included 158 out of these 193 patients).

5. Intervention

Arm 1: oral administration of 6 keishibukuryogan (桂枝茯苓丸) pills containing 5 ingredients (TK-061) t.i.d. (18 tablets/day), n=75.

Arm 2: oral administration of 2.5 g of TEIKOKU Keishibukuryogan (桂枝茯苓丸) Extract Granules (TKK-25) t.i.d. (7.5 g/day), n=83.

6. Main outcome measures

Simple Menopause Index (SMI) improvement rated on a 5-point scale; improvement in blood stasis score; changes in blood hormone concentrations; adverse events.

7. Main results

Response rate to TK-061 and TKK-25 were similar (55.8% *vs* 51.0%, respectively). Blood stasis score was decreased with time after the start of treatment to similarly reduced levels for both arms at week 8. Blood concentrations of estradiole (E2), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) remained unchanged from baseline. The incidences of adverse drug reactions were similar: 22.4% with TK-061 and 23.2% with TKK-25. These adverse drug reactions disappeared naturally or were relieved by symptomatic therapy, suggesting that a causal relationship with treatment cannot be ruled out.

8. Conclusions

TK-061 was equivalent or superior to TKK-255 in increasing the SMI improvement rating, the primary endpoint. Both increased blood stasis score to a similar extent. In addition, neither affected the endocrine system.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse events occurred in 22 patients receiving keishibukuryogan pills (22.4%) and 23 patients receiving keishibukuryogan extract granules (23.2%). No serious adverse events occurred. Adverse drug reactions occurred in 12 patients (12.2%) and 9 patients (9.1%), respectively. The global safety was “satisfactory” in 79 patients (80.6%) and 88 patients (88.9%), respectively.

11. Abstractor’s comments

This paper describes a clinical trial comparing keishibukuryogan pills to its extracted formulation, and demonstrates the efficacy of both for climacteric symptoms. Regrettably, however, *ganzai* (丸剤, pills), which proved more effective than the extract in the per-protocol population, is not on the NHI Drug Price list. For the moment, keishibukuryogan pill is only available as an OTC drug.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Koike K, Ohno S, Takahashi N, et al. Efficacy of the herbal medicine Unkei-to as an adjunctive treatment to hormone replacement therapy for postmenopausal women with depressive symptoms. *Clinical Neuropharmacology* 2004; 27: 157-62. CENTRAL ID: CN-00490860, Pubmed ID: 15319700

1. Objectives

To evaluate the efficacy of unkeito unkeito (温経湯) for climacteric disorders with depressive symptoms.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

One university hospital and one clinic.

4. Participants

Twenty-four women with climacteric disorders with depressive symptoms and unresponsive to hormone replacement therapy (HRT).

5. Intervention

Arm 1: administration of 7.5 g/day of unkeito (温経湯) extract granules for 6 months followed by administration of 7.5 g/day of tokishakuyakusan (当帰芍薬散) extract granules for 6 months, with 1-month washout between interventions.

Arm 2: administration of 7.5 g/day of tokishakuyakusan (当帰芍薬散) extract granules for 6 months followed by administration of 7.5 g/day of unkeitounkeito (温経湯) extract granules for 6 months, with 1-month washout between interventions.

HRT was continued in both arms.

6. Main outcome measures

Zung's Self-Rating Depression Scale (ZSDS), State-Trait Anxiety Inventory (STAI-1, 2).

7. Main results

Administration of unkeito produced significant improvement in ZSDS and STAI-1, 2 at 3 months, which persisted to 6 months. The improvement in ZSDS and STAI-1, 2 was significantly greater after unkeito than tokishakuyakusan at both 3 months and 6 months.

8. Conclusions

Unkeito is effective as an adjuvant therapy for climacteric disorders with depressive symptoms in patients unresponsive to HRT, and has superior efficacy to that of tokishakuyakusan.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions occurred.

11. Abstractor's comments

This study is a randomized cross-over trial of unkeito and tokishakuyakusan. It suggests that the mechanism of efficacy is the promotion of secretion of cytokine-induced neutrophil chemoattractant (CINC).

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Ushiroyama T, Ikeda A, Kakuma K, et al. Comparing the effects of estrogen and an herbal medicine on peripheral blood flow in post-menopausal women with hot flashes: hormone replacement therapy and gui-zhi-fu-ling-wan (keishibukuryogan), a Kampo medicine. *The American Journal of Chinese Medicine* 2005; 33: 259-67. CENTRAL ID: CN-00528621, Pubmed ID: 15974485

1. Objectives

To compare the efficacy of keishibukuryogan（桂枝茯苓丸）and hormone replacement therapy (HRT) for relief of hot flashes and chills.

2. Design

Randomized controlled trial (RCT).

3. Setting

None. (The authors belonged to the Department of Obstetrics and Gynecology, Osaka Medical College.)

4. Participants

Three-hundred and fifty-two postmenopausal patients with hot flashes untreated with HRT in the past 3 months and without past history of chronic diseases, aged 46–58 years. Patients with coronary artery anomaly, thrombotic diseases, cerebral infarction, hypertension, renopathy, and allergic conditions were excluded.

5. Intervention

Arm 1: oral administration of 2.5 g of TSUMURA Keishibukuryogan (桂枝茯苓丸) (TJ-25) t.i.d. (daily dose 7.5 g).
Arm 2: oral administration of 0.625 mg of Premarin and 2.5 mg of Provera s.i.d. (i.e., HRT).

6. Main outcome measures

Peripheral blood flow, measured pre- and post-administration by a laser Doppler velocimeter at 3 sites (jaw, finger tips, and toes).

7. Main results

Both HRT and keishibukuryogan reduced blood flow in the jaw and finger tips. Blood flow in the toes was increased by keishibukuryogan but unchanged by HRT.

8. Conclusions

Keishibukuryogan is effective for chills, especially in the legs, in patients with hot flashes. HRT is ineffective for chills. Although both HRT and keishibukuryogan are effective for hot flashes, the latter is more effective.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is a controlled trial of HRT and keishibukuryogan. It ensures objectivity by measuring hot flashes and chills in terms of blood flow. It would also be interesting to investigate how well these medicines change blood flow in patients without hot flashes.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

References

Matsuo A, Koike K, Hoshina Y, et al. Study of the efficacy of unkeito for depressive and anxiety symptoms during menopause that are refractory to hormone replacement therapy. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2005; 22: 70-4 (in Japanese). Ichushi Web ID: 2005235338

Koike K. A slight advantage of Kampo treatment for gynecological disease 4: Menopausal depressed mood and the herbal medicine Unkei-to. *Sanfujinka Chiryo* (*Obstetrical and Gynecological Therapy*) 2006; 92: 784-6 (in Japanese). MOL, MOL-Lib

1. Objectives

To evaluate the usefulness of Kampo medicine for treatment of depressive patients refractory to hormone replacement therapy (HRT).

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

None (the authors belonged to the Department of Obstetrics and Gynecology, Kanazawa University School of Medicine).

4. Participants

Twenty-four depressive outpatients who visited the menopause clinic and were unresponsive to 6 months of HRT.

5. Intervention

Arm 1: combination of 6-month administration of HRT (1 sheet/2 days administration of estradiol formulation [dose not indicated] and 10-day administration of 5 mg/day of medroxyprogesterone) and 2.5 g of TSUMURA Unkeito（温経湯）, (TJ-106) t.i.d, n=12.

Arm 2: combination of 6-month administration of HRT (1 sheet/2 days administration of estradiol formulation [dose not indicated] and 10-day administration of 5 mg/day of medroxyprogesterone) and 2.5 g of tokishakuyakusan (当帰芍薬散) (TJ-23) t.i.d, n=12.

Patients were crossed over to the other treatment after 6 months with 1-month washout between arms.

6. Main outcome measures

Changes in Self-Rating Depression Scale (SDS) and State Trait Anxiety Inventory (STAI) scores after 6-month treatment with the unkeito or tokishakuyakusan combination.

7. Main results

In arm 1, SDS depression score was significantly decreased ($P<0.01$, testing method not indicated). STAI state and trait anxiety scores were significantly improved ($P<0.01$, testing method not indicated).

8. Conclusions

HRT + unkeito combination therapy is effective for relief of HRT-refractory depression.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This paper is based on the previously published "Koike K, Ohno S, Takahashi N, et al. Efficacy of the herbal medicine Unkei-to as an adjunctive treatment to hormone replacement therapy for postmenopausal women with depressive symptoms. *Clinical Neuropharmacology* 2004; 27: 157-62." This study demonstrated the efficacy of unkeito for depressive and anxiety symptoms refractory to HRT administered as treatment for climacteric disorders. However, something seems wrong with the definition of "depressive and anxiety symptoms refractory to hormone replacement therapy." Kampo medicine as treatment of depressive and anxiety symptoms would be better assessed in comparison with antidepressants and anxiolytics. In addition, the statement in the text that 3-month oral administration produced an effect lasting 6 months raises the concern that a 1-month washout in the cross-over comparison is sufficient. Future research is expected.

12. Abstractor and date

Nakata H, 1 April 2008, 8 April 2009, 8 August 2009.

Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Ushiroyama T, Sakuma K, Nosaka S. Comparison of effects of vitamin E and wen-jing-tang (unkei-to), an herbal medicine, on peripheral blood flow in post-menopausal women with chilly sensation in the lower extremities: a randomized prospective study. The *American Journal of Chinese Medicine* 2006; 34: 969-79. CENTRAL ID: CN-00577271, Pubmed ID: 17163586

1. Objectives

To compare the effects of unkeito (温経湯) and vitamin E on peripheral blood flow.

2. Design

Randomized controlled trial (RCT).

3. Setting

Department of Obstetrics and Gynecology, Osaka University Faculty of Medicine.

4. Participants

One hundred and eighty post-menopausal women (42–61 years old) with chilly sensation in the lower extremities and no treatment by hormone replacement within 3 months.

5. Intervention

Arm 1: administration of unkeito (温経湯) (TSUMURA Unkeito Extract Granules 7.5 g/day) for 8 weeks (60 patients; of these, 58 were included for analysis).
Arm 2: administration of vitamin E (tocopherol nicotinate 600 mg/day) for 8 weeks (60 patients; of these, 55 were included for analysis).
Arm 3: no treatment for 8 weeks (60 patients; of these 48 were included for analysis).

6. Main outcome measures

Items evaluated by questionnaire on a 4-point scale and submandibular, middle finger, and middle toe blood flow measured by Doppler.

7. Main results

Chilly sensation evaluated by questionnaire was significantly improved in arm 1. Doppler blood flow evaluation revealed improved peripheral blood flow in the lower extremities in arm 1 and arm 2. While vitamin E significantly increased middle finger blood flow, unkeito suppressed blood flow (that was originally too high) and increased poor blood flow.

8. Conclusions

Unkeito is superior to vitamin E in improving blood flow and reducing chill.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No special problems noted.

11. Abstractor's comments

This paper compared the ability of unkeito and vitamin E to improve peripheral blood flow. It concluded that unlike vitamin E, unkeito improves chill by increasing poor circulation and improves hot flushes by decreasing excessive blood flow, well characterizing the Kampo medicine.

12. Abstractor and date

Nakata H, 10 January 2009, 8 August 2009.

Ante/Post-partum Diseases

Reference

Ushiroyama T, Sakuma K, Nosaka S, et al. Clinical efficacy of kyukikyogaito for imminent abortion with uterine hemorrhage*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2006; 23: 100-3 (in Japanese). Ichushi Web ID: 2006303253

1. Objectives

To evaluate the efficacy of kyukikyogaito（キュウ帰膠艾湯）as a therapeutic drug for imminent abortion in patients with uterine hemorrhage.

2. Design

Randomized controlled trial (RCT).

3. Setting

None. (The authors belonged to the Department of Obstetrics and Gynecology, Osaka Medical College and the Department of Obstetrics and Gynecology, Takatsuki Red Cross Hospital.)

4. Participants

Seventy-two patients who visited the hospital with a complaint of uterine hemorrhage and were given a diagnosis of imminent abortion.

5. Intervention

Arm 1: bed rest and administration of 2.5 g of TSUMURA Kyukikyogaito (キュウ帰膠艾湯) Extract Granules (TJ-77) t.i.d. (n=36).

Arm 2: bed rest and administration of human chronic gonadotropin (hCG) (alternate-day administration of 5,000 U) (n=36).

6. Main outcome measures

EFS (echo free space), number of days to hemostasis.

7. Main results

Statistical analysis was carried out using the chi-square test and Wilcoxon's signed-rank test. Significantly fewer days were required for hemostasis and for EFS disappearance in arm 1 (both $P<0.0001$). EFS on day 7 of treatment was significantly smaller in arm 1 ($P<0.0001$).

8. Conclusions

Kyukikyogaito (TJ-77) shortens the time to hemostasis in patients with imminent abortion and uterine hemorrhage.

9. From Kampo medicine perspective

The explanation of the efficacy of kyukikyogaito for imminent abortion is based on the blood replenishing effect of toki, shakuyaku, and senkyu as well as the hemostatic effect of akyo and gaiyo.

10. Safety assessment in the article

None.

11. Abstractor's comments

This paper shows that EFS disappears significantly earlier in patients with imminent abortion after treatment with a Kampo medicine. Considering that in principle, bed rest is the only treatment for imminent abortion with no effective therapeutic method having been established, the effects of kyukikyogaito are worthy of attention. However, without significant differences in the final outcome of fetal mortality, kyukikyogaito is reasonably considered to have limited efficacy and to contribute to better patient QOL through a reduction in length of hospital stay, etc.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Takushima Y, Inoguchi H, Study on usefulness of kyukichoketsuin for control of puerperium – comparison with methylergometrine maleate (1st report) -*. *Progress in Medicine* 2001; 21: 1535-42 (in Japanese). Ichushi Web ID: 2002032923 MOL, MOL-Lib

1. Objectives

To evaluate the usefulness of kyukichoketsuin（キュウ帰調血飲） for control of puerperium.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

None (authors belong to the Department of Obstetrics and Gynecology, Yamato Municipal General Hospital).

4. Participants

Forty-seven puerperants, who had a vaginal delivery after the 36th week of pregnancy and no abnormal bleeding of more than 1,000 mL, were randomized to receive either kyukichoketsuin or methylergometrine maleate.

5. Intervention

Arm 1: oral administration of 1 sachet (2.0 g) of TAIKODO Kyukichoketsuin (キュウ帰調血飲) Extract Granules (EK-230) t.i.d. (n=23)
Arm 2: oral administration of 1 tablet (0.125 mg) of Metenarin t.i.d. (n=24)

6. Main outcome measures

Uterine volume, length of uterine fundus, lower abdominal pain score, and amount of lactation during 1 to 5 days postpartum. Improvement in outcome measures compared between groups.
Adverse drug reactions: described symptoms.

7. Main results

Statistical analysis used *t*-test, chi-square test, and Wilcoxon's signed-rank test. There was no significant between-group difference in uterine volume or length of uterine fundus. Lower abdominal pain was significantly less frequent in patients receiving kyukichoketsuin on postpartum days 1 ($P<0.0028$), 2 ($P<0.0005$), and 4 ($P<0.0232$). Patients receiving kyukichoketsuin secreted significantly more milk on postpartum days 3 ($P<0.0345$), 4 ($P<0.0368$), and 5 ($P<0.0177$). Regarding safety, pain associated with uterine contraction was so severe in patients receiving Metenarin as to preclude continued treatment in 2 patients, whereas no adverse drug reactions occurred in the kyukichoketsuin group.

8. Conclusions

Kyukichoketsuin could be an alternative medication to methylergometrine maleate.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Treatment was discontinued in two patients receiving methylergometrine maleate because of severe lower abdominal pain (associated with uterine contraction), whereas no adverse drug reactions occurred in the kyukichoketsuin group.

11. Abstractor's comments

The routine use of postpartum methylergometrine maleate has been criticized and is now limited only to cases such as uterine subinvolution. Therefore, this paper highlighting the effect of kyukichoketsuin, which is associated with few adverse drug reactions, is meaningful. However, since this paper does not address the effect of suckling stimulation and breast massage on uterine contraction and lactation promotion, further investigation of the effectiveness of oral kyukichoketsuin is expected.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Ante/Post-partum Diseases

References

Sakuma K, Ushiroyama T, Akise D, et al. Clinical efficacy of kyukichoketsuin for regulation of puerperal psychosomatic functions. *Sanfujinka no Shinpo* (*Advances in Obstetrics and Gynecology*) 2002; 54: 80-6 (text in Japanese with English abstract). Ichushi Web ID: 2002151144 MOL, MOL-Lib

Ushiroyama T, Sakuma K, Souen H, et al. Therapeutic effects of kyuki-choketsu-in in restoring postpartum physical condition. *The American Journal of Chinese Medicine* 2003; 31: 437-44. CENTRAL ID: CN-00457564, Pubmed ID: 12943174

1. Objectives

To evaluate the efficacy and safety of kyukichoketsuin（キュウ帰調血飲）for puerperal psychosomatic disorder.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Osaka Medical College Hospital and associated facilities.

4. Participants

One-hundred and seventy-one women who had a normal delivery.

5. Intervention

Arm 1: daily administration of 6.0 g/day of Kanebo Kyukichoketsuin (キュウ帰調血飲) Extract Fine Granules for up to 1 month from the day of delivery (n=85).
Arm 2: administration of 0.375 mg/day of ergometrine (n=86).

6. Main outcome measures

Length of uterine fundus, blood hemoglobin concentration, body temperature, and amount of lactation measured 1 to 6 days postpartum.
Lochia, lactation, and mental state evaluated by questionnaire.

7. Main results

In arm 1, uterine contraction on postpartum day 5 was significantly greater, blood hemoglobin concentration was significantly higher, and mean amount of lactation was significantly increased from postpartum day 4 onward. The number of patients with subjectively rated depression in arm 1 was approx. half that in arm 2.

8. Conclusions

Kyukichoketsuin is more effective than ergometrine for some patients with puerperal psychosomatic symptomatology.

9. From Kampo medicine perspective

The crude-drug components of kyukichoketsuin associated with oxytocic, lactogenic, or psychotropic activity are mentioned in the discussion.

10. Safety assessment in the article

No adverse drug reactions occurred in either arm.

11. Abstractor's comments

In Japan, randomization by the RCT-envelope method tends not to be maintained. This study suggests the partial efficacy of kyukichoketsuin for some patients with puerperal psychosomatic symptoms. Kyukichoketsuin is also known by a name of kyukihoketsuto and considered to be effective for various postpartum symptoms including *qiketsukyoson* (気血虚損, qi and blood deficiencies), *hiikyojaku* (脾胃虚弱, hypofunctioning of the spleen and stomach), *orofugyo* (悪露不行, lochiometra), *kyoketsukata* (去血過多, hypermenorrhea), *inshokusissetsu* (飲食失節, crapula), and *dokisosho* (怒気相衝, anger) (*Manbyokaishun* [万病回春]: *Recovery from All Ailments*).

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Wada H, Wada K, Motoyama K. Usefulness in postpartum control by kyukichoketsuin. *Sanfujinka no Sekai* (*World of Obstetrics and Gynecology*) 2003; 55: 1057-61. Ichushi Web ID: 2004022822

1. Objectives

To evaluate the clinical usefulness of kyukichoketsuin（キュウ帰調血飲） for "postpartum restoration"

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Single facility (Wada Obstetric and Gynecologic clinic).

4. Participants

Sixty multiparas who visited the above facility between January and the end of December 2001 and had a normal delivery.

5. Intervention

Arm 1: administration of Kanebo Kyukichoketsuin (キュウ帰調血飲) Extract Granules (EK-230) 2.0 g t.i.d. (before meals) from immediately to 2 weeks postpartum in 30 patients.

Arm 2: administration of methylergometrine maleate (MME) 0.125 mg t.i.d. (after meals) from immediately to 5 days postpartum in 30 patients.

6. Main outcome measures

Uterine subinvolution: evaluated based on the length of the uterine fundus at 1 and 4 days postpartum and the amount of lochia at 1 month postpartum.

Amount of lactation: evaluated based on the amount of lactation at 4 days postpartum and the amount of lactation expressed as a percentage of the lactation amount after the previous delivery.

Clinical symptoms: complaint of afterpains evaluated by interview.

Drug compliance: evaluated on a 4-point scale by interview.

7. Main results

There was no between-group difference in the length of uterine fundus (11.4±0.7 cm [kyukichoketsuin] *vs* 11.8±2.8 cm [MME]) at 4 days postpartum and lactation at 4 days postpartum. The lactation index (i.e., amount of lactation in relation to the amount for the previous delivery of 100) was 81.7±15.0 with MME and 136.7±71.0 with kyukichoketsuin, showing a lactation-promoting effect of kyukichoketsuin, although the difference was not significant. There were more complaints of afterpains in the MME group (46.7%) than in the kyukichoketsuin group (23.3%). Drug compliance was significantly higher in patients receiving kyukichoketsuin ($P<0.001$).

8. Conclusions

Compared with MME, kyukichoketsuin ("a medicine for postpartum restoration") is a better restorer of postpartum health and some physiological functions in puerperants.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study follows up a randomized study published in 2002 that verified the efficacy of kyukichoketsuin for "postpartum restoration" as described in *Manbyokaishun* (万病回春, *Recovery from All Ailments*) using objective parameters. The present results showing that kyukichoketsuin has clinical efficacy support the results of the previous study. The psychosomatic condition of postpartum health is referred to as "*qiketsukyoson* (気血虚損, qi and blood deficiencies)" in Kampo medicine, for which kyukichoketsuin is indicated. It is hoped that "*qiketsukyoson*," a Kampo medical pathology, will be scientifically elucidated based on objective clinical parameters as in the present study.

12. Abstractor and date

Ushiroyama T, 1 April 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Narimatsu A, Ito A, Usefulness of kyukichoketsuin during puerperium. *Rinsho Iyaku* (*Journal of Clinical Therapeutics & Medicine*) 2001; 17: 1329-35 (text in Japanese with English abstract). Ichushi Web ID: 2002057351 MOL, MOL-Lib

1. Objectives

To evaluate the clinical usefulness of kyukichoketsuin（キュウ帰調血飲）during puerperium.

2. Design

A randomized controlled trial (RCT).

3. Setting

Department of Obstetrics and Gynecology, Ogori-Daiichi General Hospital.

4. Participants

Eighty women who had normal vaginal delivery at the above facility between July 2000 and March 2001.

5. Intervention

Arm 1: postpartum administration of an oral antibiotic for 5 days + kyukichoketsuin（キュウ帰調血飲）（manufacturer not specified) 2.0 g t.i.d. before meals for 4 weeks, n=40.

Arm 2: postpartum administration of an oral antibiotic and methylergometerine maleate for 5 days, n=40.

6. Main outcome measures

Incidence of poor uterine contraction at 4 weeks postpartum, amount of milk sucked at 2 days postpartum, percentage of participants with ≥15 g/day of lactation, total amount of milk sucked, and incidences of "maternity blues" and depression at 5 days postpartum.

7. Main results

No poor uterine contraction or intrauterine infection occurred in either arm. Those receiving Kampo medicine suffered significantly less afterbirth pains (P<0.05). Kampo medicine suppressed the decrease in newborn weight in all participants, especially in primiparas (P<0.05). Postpartumly, kyukichoketsuin significantly reduced the frequency of hot flushes and twilight state. There was no between-arm difference in the incidence of maternity blues and no incidence of depression in either arm.

8. Conclusions

Kyukichoketsuin safely promotes the physical and mental restoration of puerperants, ultimately contributing to growth of newborns.

9. From Kampo medicine perspective

The increase in lactation is due to the ingredients of kyukichoketsuin (jio [地黄], toki [当帰], kobushi [香附子], chinpi [陳皮], and uyaku [烏薬]), which are also involved in nutritional fortification and physical reconditioning. In addition, kobushi and uyaku have a *qi*-conditioning effect and prevent postpartum depression.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study verified the efficacy of kyukichoketsuin for "restoration of the postpartum psychosomatic condition" as described in *Manbyokaishun* (万病回春, *Recovery from All Ailments*). Although difference in uterine contraction should have been evaluated by measuring the length of the uterine fundus, the study should be praised for evaluating lactation by accurately measuring the amount of sucked milk. Biological evidence of the contribution of mental and physical factors to the restoration of puerperants should be sought. Scientific verification of the efficacy of kyukichoketsuin in various combinations (frequent in *Manbyokaishun*) is desired.

12. Abstractor and date

Ushiroyama T, 12 December 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Ushiroyama T, Sakuma K, Souen H, et al. Xiong-gui-tiao-xue-yin (Kyuki-chouketsu-in), a traditional herbal medicine, stimulates lactation with increase in secretion of prolactin but not oxytocin in the postpartum period. *The American Journal of Chinese Medicine* 2007; 35: 195-202. CENTRAL ID: CN-00609546, Pubmed ID: 17436360

1. Objectives

To evaluate the postpartum lactation-promoting effect and safety of kyukichoketsuin (キュウ帰調血飲).

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Osaka Medical College Hospital.

4. Participants

Eighty-two women who had normal spontaneous delivery.

5. Intervention

Arm 1: TAIKODO Kyukichoketsuin (キュウ帰調血飲) Extract Granules (Kanebo) 2.0 g t.i.d. for 6 days, n=41.

Arm 2: methylergometerine maleate 0.375 mg/day in 3 divided doses for 6 days, n=41.

6. Main outcome measures

Amount of lactation, blood prolactin concentration.

7. Main results

The amount of lactation was significantly increased in arm 1 on day 4 to 276.5±21.4 g (compared with 155.3±61.2 g in arm 2; $P<0.042$), on day 5 to 342.6±43.6 g (compared with 245.5±59.4 g in arm 2; $P<0.038$), and on day 6 to 413.7±68.1 g (compared with 293.3±98.5 g in arm 2; $P<0.046$). In addition, blood prolactin concentration was significantly elevated in arm 1 (compared with arm 2) on day 1 ($P<0.037$) and 6 ($P<0.0024$) after delivery.

8. Conclusions

Kyukichoketsuin may increase postpartum lactation.

9. From Kampo medicine perspective

Mentioned in discussion.

10. Safety assessment in the article

No adverse drug reactions occurred.

11. Abstractor's comments

While in Japan the RCT-envelope method of allocation often fails to maintain randomization, this study can suggest that kyukichoketsuin increases postpartum lactation. Kyukichoketsuin, also known as kyukihoketsuto, is considered to be effective for various postpartum symptoms including *qiketsukyoson* (気血虚損, qi and blood deficiencies), *hiikyojaku* (脾胃虚弱, hypofunctioning of spleen and stomach), *orofugyo* (悪露不行, lochiometra), *kyoketsukata* (去血過多, hypermenorrhea), *inshokusissetsu* (飲食失節, crapula), and *dokisosho* (怒気相衝, anger) (*Manbyokaishun* [万病回春], *Recovery from All Ailments*).

12. Abstractor and date

Okabe T, 27 November 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Kawakami S, Nishimura J, Umeki M, et al. Kampo therapy for feeling of lactation deficiency*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2003; 20: 140-3 (in Japanese). Ichushi Web ID: 2004068785

1. Objectives

To determine a Kampo medicine effective for relieving the feeling of lactation deficiency.

2. Design

Randomized controlled trial (RCT).

3. Setting

None (authors belong to the Department of Obstetrics and Gynecology, Fukuda Hospital).

4. Participants

Seventy-two puerperants who complained of feeling of lactation deficiency at 4 to 6 days postpartum between September 2002 and February 2002.

5. Intervention

Arm 1: oral administration of 2.5 g of TSUMURA Kakkonto (葛根湯) Extract Granules t.i.d.
Arm 2: oral administration of 2.5 g of TSUMURA Juzentaihoto (十全大補湯) Extract Granules t.i.d.
Arm 3: oral administration of 2.5 g of Kanebo Kyukichoketsuin (キュウ帰調血飲) Extract Fine Granules t.i.d.
Arm 4: oral administration of 2.5 g of TSUMURA Kakkonto (葛根湯) Extract Granules and 2.5 g of TSUMURA Juzentaihoto (十全大補湯) Extract Granules combined t.i.d.
Arm 5: oral administration of 2.5 g of TSUMURA Kakkonto (葛根湯) Extract Granules and 2.5 g of Kanebo Kyukichoketsuin (キュウ帰調血飲) Extract Fine Granule combined t.i.d.
Arm 6: oral administration of 2.5 g of TSUMURA Kikyoto (桔梗湯) Extract Granules t.i.d.
Arm 7: breast massage.

6. Main outcome measures

Total score from a questionnaire evaluating the amount of breast milk, degree of breast engorgement, milk supplementation, and satisfaction on a 10-point scale.

7. Main results

At 3 weeks after treatment, the score in the juzentaihoto monotherapy group was significantly higher than those in the kyukichoketsuin monotherapy, kakkonto + juzentaihoto combination therapy, and kikyoto monotherapy groups, but not significantly different from that in the breast massage group.

8. Conclusions

Juzentaihoto is effective treatment for feeling of lactation deficiency.

9. From Kampo medicine perspective

Administration according to "*sho* (証, pattern/syndrome)" is recommended.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study is valuable because it demonstrates the differing effects among Kampo prescriptions on lactation after birth and the importance of therapy according to *sho*. However, given that there was no significant effect on lactation deficiency and no difference between juzentaihoto and breast massage, the present data fail to provide evidence for an effect of juzentaihoto as a stimulant of lactation. Further investigations including combined use with breast massage are expected.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Fushiki H, Saeki A, Shiozaki A. Attempt to reduce adverse reactions associated with oral iron preparation for anemia in pregnancy by combination with rikkunshito (TJ-43)*. *Sanfujinka Kampo Kenkyu no Ayumi* (*Recent Progress of Kampo Medicine in Obstetrics and Gynecology*) 2003; 20: 138-9 (in Japanese). Ichushi Web ID: 2004068784

1. Objectives

To determine whether rikkunshito (六君子湯) combined with oral iron can improve hemoglobin level and reduce adverse reactions associated with the administration of iron for anemia in pregnant women.

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital (one obstetrics and gynecology clinic).

4. Participants

One hundred and twenty pregnant women (duration of pregnancy ≥ 5 months) with a hemoglobin (Hb) level of less than 11.0 g/dL, a hematocrit (Ht) of less than 33%, and a mean corpuscular volume (MCV) of less than 85 μm^3.

5. Intervention

Arm 1: treatment with sodium ferrous citrate (50 mg) 1 tablet b.i.d., and rikkunshito (六君子湯) 2.5 g t.i.d. for 14 days in patients with a mean age of 28.2 (20 - 42) years and a mean gestational age of 28.7 (18 - 38) weeks.

Arm 2: treatment with sodium ferrous citrate (50 mg) 1 tablet b.i.d. for 14 days in patients with a mean age of 28.8 (20 - 38) years and a mean gestational age of 28.4 (18 - 37) weeks.

6. Main outcome measures

Post-treatment Hb level.

7. Main results

Increase in Hb from the pre-treatment level was significantly greater after the sodium ferrous citrate plus rikkunshito therapy (arm 1; 0.8 [2.4 to -0.9] g/dL) than after sodium ferrous citrate monotherapy (arm 2; 0.3 [2.1 to -1.2] g/dL) (P=0.002). Also, oral administration of sodium ferrous citrate was better tolerated in arm 1.

8. Conclusions

It was suggested that rikkunshito combined with oral iron for anemia in pregnancy is effective for reducing adverse reactions associated with the administration of iron.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no adverse reactions to rikkunshito treatment.

11. Abstractor's comments

Oral iron preparations are commonly associated with gastrointestinal adverse reactions. Thus, many patients stop the treatment. Great clinical relevance is suggested by the present results, which showed that treatment with iron could be continued in combination with rikkunshito. Although this study was classified as an RCT because of the random assignment, data necessary for the assessment of bias, including the presence or absence of blinding, were inadequate, and further assessment cannot be made. Further studies are expected.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Ante/Post-partum Diseases

Reference

Ushiroyama T, Sakuma K, Ueki M, Efficacy of the Kampo medicine xiong-gui-tiao-xue-yin (kyuki-chouketsu-in), a traditional herbal medicine, in the treatment of maternity blues syndrome in the postpartum period. *The American Journal of Chinese Medicine* 2005; 33: 117-26. CENTRAL ID: CN-00515344, Pubmed ID: 15844839

1. Objectives

To confirm the efficacy of kyukichoketsuin (キュウ帰調血飲) for the "maternity blues."

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Osaka Medical College Hospital and associated facilities.

4. Participants

Two-hundred and sixty-eight puerperants who had a normal single delivery and no pregnancy toxemia, diabetes mellitus, premature rupture of the membrane, etc. They were randomized to either kyukichoketsuin group or control group.

5. Intervention

Arm 1: administration of 2.0 g of Kanebo Kyukichoketsuin (キュウ帰調血飲) t.i.d., n=134.
Arm 2: control group without treatment, n=134.

6. Main outcome measures

Four items (including mood swings, crying over 5 min, and irritation) as judged by questionnaire.
Depressive symptoms as judged on the Edinburgh Postpartum Depression Scale.
Maternity blues as judged on a self-rating maternity blues scale.

7. Main results

Within 3 weeks postpartum, the kyukichoketsuin group had significantly decreased incidences of moderate or severe depressive symptom, crying lasting over 5 minutes, irritation, and maternity blues. During 3 to 6 weeks postpartum, there was no significant difference between arms. The incidence of maternity blues, especially within 3 days postpartum, was decreased in the kyukichoketsuin group.

8. Conclusions

Kyukichoketsuin can be used to stabilize postpartum mood.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions occurred.

11. Abstractor's comments

This study provides objective evidence for efficacy of kyukichoketsuin in the treatment of classic postpartum maternity blues. Maternity blues disappear within 3 weeks postpartum and are followed up without treatment in clinical practice. Thus, in emphasizing importance of postpartum care, this study seems significant. Further study results are expected.

12. Abstractor and date

Nakata H, 1 April 2008, 8 August 2009.

Symptoms and Signs

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Beneficial effect of Chinese tracitional herbal medicine, Mai-Men-Don-Tang (Japanese name: bakumondo-to) on acute pain in patients with acute internalmedical disease: antitussive effect on elderly patients with post infectious persistent coughs, prospective, multicenter, randomized comparative trial between mai-men-dong-tang and forminoben hydrochloride. *Itami to Kampo* (*Pain and Kampo Medicine*) 2003; 12: 13-21 (text in Japanese with English abstract). Ichushi Web ID: 2006247201

1. Objectives

To evaluate the efficacy of bakumondoto (麦門冬湯) for persistent cough after infection in the elderly.

2. Design

Randomized controlled trial (RCT).

3. Setting

Two hospitals and three clinics.

4. Participants

Two-thousand and sixty-nine patients with intense dry cough persisting for 3 weeks or more after common cold syndrome, aged ≥ 65 years.

5. Intervention

Arm 1: administration of TSUMURA Bakumondoto (麦門冬湯) Extract granules 3.0 g t.i.d. between meals (n=1,039).

Arm 2: administration of fominoben hydrochloride 160 mg in three divided doses between meals (n=1,030).

6. Main outcome measures

Antitussive effect
Salivation degree, skin temperature, joint pain
Pain improvement rating
Global improvement rating

7. Main results

The antitussive effect and reduction in sputum expectoration (as measured on a visual analogue scale [VAS]) was superior in arm 1 than arm 2. Improvement in the following items after treatment, compared with baseline, was significant only in arm 1: the amounts of salivation and lacrimation determined by Saxon's test and Schirmer's test; joint pain judged on a VAS; and skin temperature measured with an upper and lower extremity-patch-type skin temperature indicator.

On the global scale, improvement, principally in cough, was better in arm 1 than arm 2. The condition of 89.5% of patients in arm 1 and 46.9% in arm 2 was rated "improved or better," showing the significantly higher efficacy of bakumondoto.

8. Conclusions

Bakumondoto was effective for not only cough but other symptoms in the elderly.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

The "total-disease-related symptoms," a scale for acute pain severity developed by the present authors, is not described but referenced to their previous paper. This, however, should be detailed since the title refers to pain severity. In addition, except for the global improvement rating, the specific numbers of patients are not indicated, except in the graphs, making evaluation of the efficacy for pain impossible.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Symptoms and Signs

References

Yoshida M. Efficacy of goreisan suppository for vomiting in young children*. *Toyoigaku* (*Japanese Journal of Oriental Medicine*) 2000; 28: 36-8 (in Japanese).

Yoshida M, Mizuno T, Mizoguchi F, et al. Efficacy of goreisan suppositories for vomiting in young children (2nd report) – a double-blind study of the hochuekkito suppository–*. *Wakan Iyaku Gakkaishi* (*Journal of Medical and Pharmaceutical Society for WAKAN-YAKU*) 1991; 7: 506-7 (in Japanese). Ichushi Web ID: 1993089053

1. Objectives

To evaluate the efficacy and safety of goreisan (五苓散) for vomiting in young children.

2. Design

Double-blind, randomized controlled trial (DB-RCT).

3. Setting

A single facility (the department of pediatrics of a hospital).

4. Participants

Thirty-five patients who vomited three or more times within 24 hr before visiting the pediatric department and experienced vomiting/nausea during the visit. One of these patients ejected the medicine immediately after insertion and was excluded, resulting in the inclusion of 34 patients (21 males and 13 females, aged 1 – 9 years with a mean of 3.9 years) for analysis.

5. Intervention

Arm 1: administration of a home-prepared suppository containing 1 g of TSUMURA Goreisan (五苓散) Extract Granules (n=16, 10 males and 6 females).

Arm 2: administration of a home-prepared suppository containing 1 g of TSUMURA Hochuekkito (補中益気湯) Extract Granules (n=18, 11 males and 7 females).

6. Main outcome measures

Complete response (disappearance of both vomiting and nausea); partial response (presence of nausea without vomiting); and no response (vomiting of supplied water).

7. Main results

The distribution of baseline characteristics (age, sex, underlying disease, frequency of vomiting, and complication with diarrhea) were similar between arms. Complete response, partial response, and no response were achieved in 12 (75%), 2, and 2 patients receiving goreisan, and in 5 (28%), 2, and 11 patients receiving hochuekkito, respectively. The difference between arm 1 and arm 2 was statistically significant ($P<0.05$).

8. Conclusions

Goreisan suppository reduced vomiting and nausea in young children more effectively than hochuekkito suppository.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions occurred.

11. Abstractor's comments

Goreisan is generally indicated for thirst, decreased urine output, and gastrointestinal diseases such as watery diarrhea and acute gastroenteritis with nausea, vomiting abdominal pain, headache, or edema. This study demonstrated the efficacy of goreisan suppository (in-home formulation) for reducing acute vomiting in young children. The usefulness has also been demonstrated in a multicenter, double-blind study, as mentioned below. Since the study period was in winter, the target diseases included common-cold-associated dyspepsia, winter diarrhea, vomiting, and common cold. Since it is generally difficult to administer a medicine orally or by drip infusion to young children with vomiting, the suppository is considered to be a clinically useful alternative dosage form. Therefore, it is very meaningful that this study demonstrated usefulness. However, this paper does not describe the methods of randomization and statistical analysis, which should be specified. In addition, another Kampo medicine and not a true placebo was used as the control, therefore it would be useful in the future to conduct a placebo-controlled study. Future development is expected. Notably, the formulation of goreisan extract is only approved for oral use, not for use in suppositories.

Related literature: Yoshida M. Efficacy of goreisan suppository*. *Nihon Syhoni Toyo Igakkaishi* (*The Japan Pediatric Society for Oriental Medicine*) 2003; 19: 13-7. Ichushi Web ID: 2005266312

A multicenter, case-series study with the same design and evaluation methods. The study population consisted of 87 patients (43 males and 44 females, aged 0 – 9 years with a mean of 2.4 years). Complete response was achieved in 72 patients (83%), and partial response in 2 patients. No difference in efficacy for underlying diseases was shown; complete response was achieved in 43 (88%) of 49 patients with winter infantile diarrhea, 22 (76%) of 29 patients with common-cold-associated diarrhea, and 5 (83%) of 5 patients with acute gastroenteritis. No difference in baseline characteristics was shown; there was no statistically significant difference in age, frequency of vomiting, complication with diarrhea, and use of enema between patients with complete or partial response, and patients with no response.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008, 8 April 2009, 8 August 2009.

Symptoms and Signs

Reference

Kumada T, Kumada H, Yoshiba M, et al. Effects of shakuyaku-kanzo-to (Tsumura TJ-68) on muscle cramps accompanying cirrhosis in a placebo-controlled double-blined parallel study. *Rinsho Iyaku* (*Journal of Clinical Therapeutics and Medicine*) 1999; 15: 499-523 (text in Japanese with English abstract). Ichushi Web ID: 1999184114 MOL, MOL-Lib

1. Objectives

To evaluate the efficacy and safety of shakuyakukanzoto (芍薬甘草湯) for relief of muscle cramp.

2. Design

Double-blind, randomized controlled trial (DB-RCT).

3. Setting

A total of 23 nationwide facilities including university hospitals (departments of internal medicine and gastroenterology).

4. Participants

One-hundred and twenty-six patients with 2 or more episodes of muscle cramp weekly during the observation period (4 or more bi-weekly), aged ≥20 years and ≤70 years. These patients were also taking other drugs for a variety of problems including serious hepatic, renal, and cardiac diseases, pregnancy, hepatic failure, complications of hepatocellular carcinoma, electrolyte abnormality, and hypertension. After excluding 12 ineligible patients and 13 with incomplete data, 101 patients were included for statistical evaluation.

5. Intervention

Arm 1: administration of 7.5 g/day of TSUMURA Shakuyakukanzoto (芍薬甘草湯) Extract Granules in 3 divided doses (before meals) for 2 weeks following a 2-week observation period (n=65).

Arm 2: administration of the same dose of placebo granules at the same frequency for 2 weeks following a 2-week observation period (n=61).

6. Main outcome measures

Frequency of episodes of muscle cramp, duration of each episode, severity of pain (at completion of the study compared with baseline values determined during the observation period).

7. Main results

The percentage of patients with frequency of muscle cramp episodes rated "improved" or higher was significantly larger in the shakuyakukanzoto group than in the placebo group (67.3% *vs* 37.5%, respectively). The percentage of patients with improved final global rating, which takes duration of each episode and severity of pain into account, was significantly larger in the shakuyakukanzoto group (69.2% *vs* 28.6%, respectively). The percentage of patients with a utility rating of "useful" or higher was also significantly larger in the shakuyakukanzoto group (63.3% *vs* 34.1%, respectively).

8. Conclusions

Shakuyakukanzoto is a clinically useful Kampo formulation with excellent efficacy and safety for muscle cramp.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse drug reactions occurred in 7 patients (14.3%) receiving shakuyakukanzoto and 2 patients (4.9%) receiving placebo. The main adverse drug reaction was pseudoaldosteronism in the shakuyakukanzoto group and gastrointestinal symptoms in the placebo group. No serious adverse drug reactions occurred.

11. Abstractor's comments

This original article re-evaluates shakuyakukanzoto. The larger total amount of kanzo, contained in shakuyakukanzoto, is associated with higher incidence of pseudoaldosteronism. Since in the present study incidence of adverse drug reactions tended to be higher in the sahkuyakukanzoto group, although there was no significant between-group difference in incidence, reduction in the dose is recommended in the future. This paper is similar to "Kumada T, Kiriyama I, Sone Y, et al. EBM-based Kampo therapy for gastrointestinal diseases 3. Efficacy of shakuyakukanzoto for "muscle cramps in the calves" associated with hepatic cirrhosis*. *Nihon Toyo Igaku Zasshi* (*Kampo Medicine*) 2003; 54: 536-8 (in Japanese)."

12. Abstractor and date

Arai M, 21 February 2007, 31 October 2007, 8 August 2009.

Symptoms and Signs

Reference

Nishizawa Y, Nishizawa Y, Amemori Y, et al. A randomized paralleled group comparison in multicenter cooperation: analgesic effect and safety with gosha-jinki-gan and shakuyaku-kanzo-to in the treatment of painful muscle cramps in patients with cirrhosis. *Itami to Kampo* (*Pain and Kampo Medicine*) 2000; 10: 13-8 (text in Japanese with English abstract). Ichushi Web ID: 2002242334

1. Objectives

To evaluate the efficacy and safety of shakuyakukanzoto (芍薬甘草湯) for muscle cramps in the calves.

2. Design

Randomized controlled trial (RCT).

3. Setting

None.

4. Participants

Seventy-five patients with painful muscle cramps in the calves (PMC) associated with hepatic cirrhosis.

5. Intervention

Arm 1: oral administration of TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules (GJG) 30 mg/kg t.i.d. for 12 consecutive weeks, n=38.

Arm 2: oral administration of 50 mg/kg/day of TSUMURA Shakuyakukanzoto (芍薬甘草湯) Extract Granules (SKT) in 3 divided doses for 12 consecutive weeks, n=37.

6. Main outcome measures

PMC rating (overall QOL, visual analog scale pain [VAS-P], face rating scale), QOL (modified health assessment questionnaire [MHAQ]), overall well-being (quality of well-being score), and psychological well-being (face scale).

7. Main results

GJG was significantly superior to SKT in improving the PMC rating and various QOL measures. The number of days until resolution of PMC was significantly shorter in the GJG group than in the SKT group.

8. Conclusions

Goshajinkigan is effective and safe for PMC associated with hepatic cirrhosis and is superior to shakuyakukanzoto in efficacy.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse drug reaction symptoms and laboratory test abnormalities (increased AST, LDH, and CPK) were noted in 0 patients receiving goshajinkigan and 4 patients receiving shakuyakukanzoto, but these resolved after discontinuation of treatment.

11. Abstractor's comments

This paper suggests that goshajinkigan may be the first-choice drug for PMC associated with hepatic cirrhosis.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Symptoms and Signs

Reference

Odaguchi H, Wakasugi A, Ito H, et al. The efficacy of goshuyuto, a typical Kampo (Japanese herbal medicine) formula, in preventing episodes of headache. *Current Medical Research and Opinion* 2006; 22: 1587-97. CENTRAL ID: CN-00571314, Pubmed ID: 16870083

1. Objectives

To evaluate the efficacy of goshuyuto (呉茱萸湯) for relief of chronic headache and to evaluate the associated adverse drug reactions.

2. Design

Double-blind, randomized controlled trial (DB-RCT).

3. Setting

Three university-associated outpatient headache clinics.

4. Participants

Fifty-three patients with chronic headache that responded to goshuyuto orally administered for 4 weeks.

5. Intervention

Arm 1: oral administration of 7.5 g/day of TSUMURA Goshuyuto (呉茱萸湯) Extract Granules for 12 weeks (n=28).
Arm 2: oral administration of the same dose of placebo granules indistinguishable in appearance, taste, and odor from goshuyuto for 12 weeks (n=25).

6. Main outcome measures

Headache severity, headache frequency, and severity of cold, menstrual cramps, and shoulder stiffness evaluated in all participants.
Surface temperature of fingers and toes, skin blood flow, deep body temperature, brain and femoral oxygen saturation, rigidity of the trapezius muscle, and blood serotonin concentration evaluated in some participants.

7. Main results

After a 12-week treatment, the number of days with headache was significantly decreased from baseline by 2.6 in arm 1 but remained unchanged in arm 2 (decreased by 0.3), showing significantly greater improvement in arm 1 than in arm 2. In addition, the number of doses of an analgesic taken was significantly decreased from baseline by 2.2 in arm 1 but remained unchanged (decreased by 1.4) in arm 2, indicating no between-arm difference. Comparison limited to migraine disclosed the same trend. There were no significant changes in the other parameters in both arms.

8. Conclusions

Goshuyuto decreased the frequency of headache episodes in patients with chronic headache, thereby reducing the number of analgesic doses.

9. From Kampo medicine perspective

This study considers *sho*, since its first stage involved selection of only goshuyuto-responders as "*sho* for goshuyuto," and these were enrolled in a double-blind, randomized controlled trial at the second stage.

10. Safety assessment in the article

No adverse drug reactions occurred except for increases in ALT, AST and γ–GTP in 1 patient receiving goshuyuto. These reactions persisted 3 months after drug discontinuation, suggesting possible development of fatty liver.

11. Abstractor's comments

In this study, goshuyuto was administered to 91 patients with chronic headache at its first stage to select responders (n=53) for a double-blind, randomized controlled trial at its second stage. Thus, it may be a groundbreaking study in that it focused on "*sho*." Besides headache, menstrual cramps and shoulder stiffness also tended to be improved by treatment with goshuyuto, warranting investigation with a larger sample size to clarify "goshuyuto-*sho*." More clinical studies in oriental medicine such as the present study are expected in the future. There is a similar report "Odaguchi H, Hanawa Y. Complementary alternative medicine in headache treatment*. *Igaku no Ayumi* (*Journal of Clinical and Experimental Medicine*) 2005; 215: 1137-40 (in Japanese). [MOL, MOL-Lib]"

12. Abstractor and date

Goto H, 1 April 2008, 8 August 2009.

Symptoms and Signs

Reference

Hasegawa K, Mizutani Y, Kuramoto H, et al. The Effect of L-glutamine and shakuyaku-kanzo-to for paclitaxel-induced myalgia/arthralgia. *Gan to Kagaku Ryoho* (*Japanese Journal of Cancer and Chemotherapy*) 2002; 29: 569-74 (text in Japanese with English abstract). Ichushi Web ID: 2002217069 MOL, MOL-Lib

1. Objectives

To evaluate the efficacy and safety of shakuyakukanzoto (芍薬甘草湯) and L-glutamine for paclitaxel-induced myalgia and arthralgia.

2. Design

Crossover randomized controlled trial (RCT-crossover).

3. Setting

Department of Obstetrics and Gynecology, Okayama University Medical School.

4. Participants

Fifteen patients with ovarian (n=13), cervical (n=1), or vulva (n=1) cancer who: 1) had received chemotherapy including paclitaxel (TXL) in December 1999 through July 2000; 2) had developed myalgia and arthralgia; and 3) were scheduled for 2 or more cycles of chemotherapy. The data from twelve of these patients were analyzed.

5. Intervention

Arm 1: TXL treatment combined with shakuyakukanzoto (芍薬甘草湯) 7.5 g/day, t.i.d. in the second cycle and with L-glutamine 2.0 g/day, t.i.d. in the third cycle, in 7 patients.
Arm 2: TXL treatment combined with L-glutamine 2.0 g/day, t.i.d. in the second cycle and with shakuyakukanzoto (芍薬甘草湯) 7.5 g/day, t.i.d. in the third cycle, in 8 patients.
The first cycle (TXL monotherapy), in which pain occurred, was considered to be a control.
Shakuyakukanzoto (芍薬甘草湯) and L-glutamine were orally administered from 1 week before the TXL treatment until the pain resolved.

6. Main outcome measures

The efficacy was evaluated based on: 1) sum of pain scores; 2) duration of myalgia and arthralgia; 3) duration of grade 2 or greater myalgia and arthralgia; 4) number of analgesics used; and 5) final subjective impressions.

7. Main results

Twelve patients were evaluated in the final analysis. Reductions of the duration of myalgia and arthralgia were significantly different between the control and the L-glutamine-treated patients. Reductions of the duration of grade 2 or greater myalgia and arthralgia in the shakuyakukanzoto- and the L-glutamine-treated patients differed significantly from that of the control patients. No significant differences occurred in any variable between the shakuyakukanzoto- and the L-glutamine-treated patients.

8. Conclusions

Shakuyakukanzoto and L-glutamine had no dramatic effects on paclitaxel-induced myalgia and arthralgia, except for the reduction of the duration of grade 2 or greater pain.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

One L-glutamine-treated patient reported nausea and one shakuyakukanzoto-treated patient could not take the drug for an unspecified reason.

11. Abstractor's comments

Shakuyakukanzoto is effective for pains associated with smooth and skeletal muscle spasm. In contrast, arthralgia (a paclitaxel-induced adverse reaction) is not included as an indication for treatment with shakuyakukanzoto. However, excellent responses were reported in the present study. The efficacy of this drug for this indication might be confirmed in the future by increasing the number of patients, as well as by identifying candidate patients for this treatment from an analysis of responders and non-responders.

12. Abstractor and date

Okabe T, 15 June 2007, 1 April 2008, 8 August 2009.

Symptoms and Signs

Reference

Satoh N, Sakai S, Kogure T, et al. A randomized double-blind placebo-controlled clinical trial of Hochuekkito, a traditional herbal medicine, in the treatment of elderly patients with weakness, N of one and responder restricted design. *Phytomedicine* 2005; 12: 549-54. CENTRAL ID: CN-00524047, Pubmed ID: 16121514

1. Objectives

To evaluate the efficacy of hochuekkito (補中益気湯) for the elderly with weakness.

2. Design

Randomized controlled trial (RCT). N-of-1 randomized controlled trial restricted to hochuekkito-responders.

3. Setting

Five hospitals associated with Toyama Medical and Pharmaceutical University (now Toyama University).

4. Participants

Fifteen elderly patients (3 males and 12 females; age [mean ± SD], 78.4±7.8 years) with weakness satisfying the following 4 inclusion criteria: (1) complaint of discomfort and anorexia due to chronic debilitating disease; (2) no history of infection or vascular disorder within 1 month before the start of the trial; (3) no malignant diseases; and (4) aged ≥60 years and <90 years.

5. Intervention

Responders during the 2-week run-in period were randomly assigned to the following 3 arms:

Arm 1: administration of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules (2.5 g t.i.d.) before meals for 6 weeks followed by administration of the same dose of placebo at the same frequency for 6 weeks, with a 2-week washout between both administration periods.

Arm 2: administration of placebo (2.5 g t.i.d.) before meals for 6 weeks followed by administration of the same dose of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules at the same frequency for 6 weeks, with a 2-week washout between both administration periods.

Arm 3: administration of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules (2.5 g t.i.d.) before meals for 6 weeks followed by administration of the same dose of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules at the same frequency for 6 weeks, with a 2-week washout between both administration periods.

Responders had to meet criterion (1) and one of the three other criteria (2) to (4): (1) good drug compliance; (2) subjective overall evaluation improved; (3) clinical symptoms improved; or (4) symptoms other than chief complaint improved.

6. Main outcome measures

36-item short-form health survey (SF36), profile of mood states (POMS), natural killer (NK) activity, interleukin (IL)-2-producing activity of peripheral lymphocytes, lymphocyte-proliferating activity, and lymphocyte cell-surface antigens.

7. Main results

PCS (physical component summary) of SF36 was significantly improved in the hochuekkito group (P<0.05). There were significant among-arm differences in 4 (anger-hostility, fatigue, tension-anxiety, confusion) of 6 subscales of the POMS (P<0.01, P<0.05, P<0.01, P<0.05, respectively). Lymphocyte cell-surface antigens, CD3-positive cells, and CD3/CD4 double-positive cells were significantly increased in the hochuekkito group (P<0.05).

8. Conclusions

Hochuekkito improved the QOL of elderly patients with weakness and activated their immune systems.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions occurred.

11. Abstractor's comments

This is a valuable N-of-1 RCT. Unlike the well-known parallel controlled design, this RCT has a self-controlled design, in which each patient receives both the candidate drug and placebo for before-after comparison. As RCT is considered difficult to perform in the Kampo field, this study opened new possibilities for clinical studies of Kampo medicines.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Symptoms and Signs

Reference

Kishida Y, Miki H, Nishii T, et al. Therapeutic effects of Saireito (TJ-114), a traditional Japanese herbal medicine, on postoperative edema and inflammation after total hip arthroplasty. *Phytomedicine* 2007; 14: 581-6. CENTRAL ID: CN-00609214, Pubmed ID: 17292595

1. Objectives

To investigate the efficacy and safety of saireito (柴苓湯) on postoperative edema and inflammation after total hip arthroplasty (THA).

2. Design

Randomized controlled trial (RCT).

3. Setting

Two departments (Department of Kampo Medicine and Department of Orthopaedic Surgery) of Osaka University, and one hospital.

4. Participants

Female patients who underwent THA because of unilateral osteoarthritis, n=17.

5. Intervention

Arm 1: Tsumura Saireito（柴苓湯）Extract Granules 9.0 g/day for 2 days before surgery and for 2 weeks after surgery, n=8.
Arm 2: no administration, n=9.

6. Main outcome measures

The circumference of the lower limb at three locations (the lower leg, ankle, and forefoot), Merle d'Aubigne hip score for clinical evaluation including pain, and serum C-reactive protein (CRP) level.

7. Main results

At three weeks after surgery, the circumference of the lower leg was less in arm 1 than in arm 2. The serum CRP level became negative by 2 weeks after surgery in 6 of 8 patients in arm 1 and in 0 of 9 patients in arm 2 (P<0.001).

8. Conclusions

Administration of saireito was suggested to reduce postoperative lower leg edema and inflammation after THA.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No side effects were reported in arm 1 and documented in arm 2.

11. Abstractor's comments

This study suggests the efficacy of saireito for postoperative lower leg edema after THA. In this trial, all patients had a pneumatic foot compression device and wore compression stockings concurrently to prevent postoperative lower leg swelling. This study also indicated that saireito is effective in decreasing postoperative inflammation. All patients received an intravenous infusion of prophylactic antibiotics for 4 days, subsequently oral antibiotics for 4 days, and nonsteroidal anti-inflammatory drugs (NSAIDs) for 1 week after surgery. However, CRP level remained positive in all subjects in arm 2, two weeks after surgery. In general, a few days' treatment with antibiotics should lead to a negative CRP level by two weeks after surgery. Further clinical studies with more patients and fewer concomitant therapies for knee replacement arthroplasty and bipolar hip arthroplasty are awaited and anticipated.

12. Abstractor and date

Okabe T, 11 December 2008, 8 August 2009.

Symptoms and Signs

References

Hioki C, Yoshimoto K, Yoshida T. Efficacy of Bofu-tsusho-san, an oriental herbal medicine, in obese Japanese women with impaired glucose tolerance. *Clinical and Experimental Pharmacology and Physiology*, 2004; 31: 614-9. CENTRAL ID: CN-00505762, Pubmed ID: 15479169

Hioki C, Yoshimoto K, Yoshida T. Efficacy of Bofu-tsusho-san in obese Japanese women with IGT. *Rinsho Kampo Yakuri Kenkyukai Kaishi*, 2004; 100th Memorial Issue: 19-22. Ichushi Web ID: 2006163538

1. Objectives

To evaluate the efficacy and safety of bofutsushosan (防風通聖散) in obese Japanese women with impaired glucose tolerance.

2. Design

A double-blind randomized controlled trial (DB-RCT).

3. Setting

An university hospital (Kyoto Prefectural University of Medicine).

4. Participants

Eighty-one obese women (mean body mass index, 36.5 kg/m^2) with impaired glucose tolerance were included. Patients with kidney, heart and/or liver disease, any metabolic or endocrine disease, psychiatric disorders, or cancer were excluded.

5. Intervention

Arm 1: treatment with TSUMURA Bofutsushosan (防風通聖散) Extract Granules for 24 weeks + low-calorie diet (1,200 kcal) + exercise therapy (300 kcal) (44 patients; of these, 41 were included for analysis).

Arm 2: treatment with placebo for 24 weeks + low-calorie diet (1,200 kcal) + exercise therapy (300 kcal) (41 patients; of these, 40 were included for analysis).

6. Main outcome measures

Body weight, the proportion of body fat (% weight), visceral and subcutaneous fat accumulation, systolic and diastolic blood pressure, heart rate, biochemical data (triglyceride, total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, uric acid, glycosylated hemoglobin (HbA1c), and fasting glucose), and waist and hip circumference were measured before treatment, and after 12 and 24 weeks of treatment. Values for 2-h oral glucose tolerance test (OGTT) glucose, glucose area under the curve (AUC) 120, fasting insulin, insulin AUC120, and homeostasis model assessment of insulin resistance (HOMA-IR) were measured or calculated after 24 weeks.

7. Main results

Waist circumference decreased in both arms after 12- and 24-week treatment compared with before treatment. The decrease was significantly greater after 24 weeks in Arm 1 compared with Arm 2. There were significant differences in more measures after 24 weeks than after 12 weeks in both arms. In Arm 2, body weight, body fat (%), and subcutaneous fat decreased only after 24 weeks; systolic and diastolic blood pressure, triglyceride, and total cholesterol reduced after 12 and 24 weeks. In Arm 1, body weight, body fat (%), visceral and subcutaneous fat, systolic and diastolic blood pressure, biochemical data (LDL cholesterol, HDL cholesterol, uric acid, and insulin [fasting and AUC120]), 2-h OGTT glucose, and HOMA-IR improved after 24 weeks. The decrease in body weight in Arm 1 was associated with decreased visceral and subcutaneous fat but not with a decrease in adjusted resting metabolic rate, whereas the weight loss in Arm 2 was not associated with decreased visceral fat.

8. Conclusions

Bofutsushosan is useful in the treatment of obese patients with impaired glucose tolerance.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There was no effect on cardiovascular or central nervous system in the two arms. Although no subject had steatorrhea, 3 subjects in the bofutsushosan arm discontinued treatment and withdrew from the study because of diarrhea. One subject in the placebo arm dropped out of the study owing to noncompliance.

11. Abstractor's comments

This DB-RCT (examining the efficacy and safety of bofutsushosan in obese Japanese women with impaired glucose tolerance) provides a high quality of evidence. Although body weight tended to decrease between 12 and 24 weeks of treatment in the placebo arm, it can still be concluded that the anti-obesity effect of bofutsushosan combined with diet and exercise therapies is more likely to persist potently. Further studies should be conducted to evaluate the effect of bofutsushosan monotherapy without diet and exercise therapies. Investigations with Kampo diagnostic considerations are also needed.

References with a similar content: 1) Hioki C. The first randomized trial of Bofutsushosan in obese patients with IGT. *Pharma Medica* 2007; 25: 43-8 (in Japanese) [Ichushi web ID: 2008035994] [MOL, MOL-Lib], 2) Hioki C, Arai M. Bofutsushosan use for obesity with IGT: search for scientific basis and development of effective therapy with Kampo medicine. *Journal of Traditional Medicine* 2007; 24: 115-27. *Journal of Traditional Medicine* 2007; 24: 115-27. J-STAGE

12. Abstractor and date

Namiki T, 15 Septmber 2007, 1 April 2008, 8 August 2009.

Others

Reference

Saruwatari J, Hisaeda S, Higa Y, et al. The *in-vivo* effect of bakumondoto (TJ-29), a traditional Japanese medicine used for treatment of chronic airway disease, on cytochrome p450 1A2, xanthine oxidase, and N-acetyltransferase 2 activity in man. *Journal of Pharmacy and Pharmacology* 2004; 56: 1171-7. CENTRAL ID: CN-00490887, Pubmed ID: 15324486

1. Objectives

To evaluate the effect of bakumondoto (麦門冬湯) on cytochrome p450 1A2, xanthine oxidase, and N-acetyltransferase 2 activities.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

Single facility (university).

4. Participants

Twenty-six healthy university students.

5. Intervention

Arm 1: administration of bakumondoto (麦門冬湯) 3.0 g t.i.d. for 1 week followed by administration of the same dose of placebo at the same frequency for 1 week, with 2-week washout between both administration periods.

Arm 2: administration of placebo 3.0 g t.i.d. for 1 week followed by administration of the same dose of bakumondoto (麦門冬湯) at the same frequency for 1 week, with 2-week washout between both administration periods.

6. Main outcome measures

Urinary cytochrome p450 1A2, xanthine oxidase, and *N*-acetyltransferase 2 activities (determined by a caffeine test).

7. Main results

There were no significant differences in urinary cytochrome p450 1A2, xanthine oxidase, and N-acetyltransferase 2 activities on days 1 and 7 from baseline in either arm.

8. Conclusions

Caffeine test is a safe and noninvasive screening test for herb-drug interaction measuring the ratio of urinary caffeine metabolites (cytochrome p450 1A2, xanthine oxidase, *N*-acetyltransferase 2). Bakumondoto did not affect cytochrome p450 1A2 (a hepatic enzyme metabolizing theophylline), xanthine oxidase, or *N*-acetyltransferase 2 activity, suggesting the unlikeliness of interaction.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse drug reactions occurred in the subjects receiving bakumondoto.

11. Abstractor's comments

This study offers no data on direct clinical efficacy.

12. Abstractor and date

Fujisawa M, 15 June 2007, 1 April 2008, 8 August 2009.

Others

Reference

Ohnishi N, Yonekawa Y, Fumihara T, et al. Studies on interactions between traditional herbal and Western medicines, II. Lack of pharmacokinetic interaction between Shoseiryu-to and carbamazepine in healthy volunteers. *TDM Kenkyu* (*Japanese Journal of Therapeutic Drug Monitoring*) 1999; 16: 399-404. Ichushi Web ID: 2000070928 MOL, MOL-Lib

1. Objectives

To evaluate the effect of shoseiryuto (小青竜湯) on blood carbamazepine concentration.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

None (authors belong to the Department of Hospital Pharmacy, Kyoto Pharmaceutical University).

4. Participants

Four healthy adult males.

5. Intervention

Arm 1: administration of 9.0 g/day of TSUMURA Shoseiryuto (小青竜湯) Extract Granules in 3 divided doses before meals for 7 days and 200 mg of carbamazepine in the morning of day 4 (n=4).
Arm 2: administration of 200 mg of carbamazepine (n=4).

6. Main outcome measures

Concentrations of carbamazepine and its metabolite carbamazepine-10,11-epoxide in blood sampled before, and 1.5, 4, 8, 24, 48, and 72 hr after administration of carbamazepine.

7. Main results

Combination with shoseiryuto did not affect the following parameters of carbamazepine and its metabolite carbamazepine-10,11-epoxide in blood: the maximum blood concentration; time to reach the maximum blood concentration; slope of the elimination phase; elimination half-life; area under the plasma concentration-time curve; and mean residence time.

8. Conclusions

Oral administration of shoseiryuto does not affect blood carbamazepine concentration.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This study objectively demonstrated that combination of shoseiryuto does not affect blood carbamazepine concentration, which is susceptible to the effects of various drugs. This study does not evaluate the efficacy of the Kampo medicine, but is considered meaningful, given that Western and Kampo medicines are commonly combined in clinical practice. There is a similar report "Yonekawa Y, Ohnishi N, Kitano N, et al. Drug interaction with Kampo medicines (2): kinetic characteristics of carbamazepine combined with shoseiryuto in healthy volunteers. *TDM Kenkyu* (*Japanese Journal of Therapeutic Drug Monitoring*) 1999; 16: 191-2.[MOL, MOL-Lib]"

12. Abstractor and date

Goto H, 15 June 2007, 1 April 2008, 8 August 2009.

Others

Reference

Isobe H, Yamamoto K, Cyong JC. Effects of hachimi-jio-gan (ba-wei-di-huang-wan) on blood flow in the human central retinal artery. *The American Journal of Chinese Medicine* 2003; 31: 425-35. CENTRAL ID: CN-00457563, Pubmed ID: 12943173

1. Objectives

To evaluate the effect of hachimijiogan (八味地黄丸) on human central retinal artery.

2. Design

Randomized cross-over controlled trial (RCT-cross over).

3. Setting

Single facility (the University of Tokyo).

4. Participants

Twelve healthy volunteers (6 males and 6 females; mean age, 26.0 years).

5. Intervention

Arm 1: single-dose administration of 27 g of hachimijiogan (八味地黄丸) (n=12).
Arm 2: single-dose administration of 27 g of placebo (lactose) (n=12).

6. Main outcome measures

Systolic blood flow velocity, diastolic blood flow velocity, mean blood flow velocity, and vascular resistance of the central retinal artery, measured by ultrasonic diagnosis device before administration and every 15 min after administration for 60 min.

7. Main results

In arm 2, there were no changes from baseline in systolic blood flow velocity, diastolic blood flow velocity, mean blood flow velocity or vascular resistance of the central retinal artery. In arm 1, although vascular resistance did not change, there were increases in systolic velocity at 15 and 45 min, diastolic velocity at 45 min, and mean velocity at 30, 45, and 60 min. Group comparison revealed significantly higher systolic blood flow velocity at all postdose time points until 60 min, higher diastolic blood flow velocity at 45 min, and significantly higher mean blood flow velocity in the time period from 30 to 60 min in arm 1.

8. Conclusions

This study provided evidence that hachimijiogan increases the blood flow velocity of the central retinal artery.

9. From Kampo medicine perspective

When compared with hachimijiogan-non-responders (with unsuitable *sho*, n=9), hachimijiogan-responders (with suitable *sho*, n=3) had higher systolic, diastolic, and mean flow rates in the time period from 15 to 60 min (statistical analysis not performed due to the small sample size).

10. Safety assessment in the article

None.

11. Abstractor's comments

It was reported some time ago that hachimijiogan acts on the central nervous system to improve hypobulia in the elderly, and to improve eye symptoms. The present report showed an increase in blood flow rate of the central retinal artery, providing evidence for efficacy in improving visual acuity. Moreover, it was shown that intracerebral blood flow may also increase, suggesting effects on the central nervous system. Also, this report provides a valuable discussion from a Kampo medicine perspective of increased blood flow velocity in responders. However, a larger sample size will be necessary in the future. Another problem is that the systemic blood pressure was not indicated, making it impossible to determine whether the increase in blood flow velocity is attributable to a systemic or local reaction. Furthermore, since this RCT did not evaluate clinical efficacy and used single-dose administration, it is hoped that clinical research examining the persistent effects of long-term oral administration will be conducted.

12. Abstractor and date

Namiki T, 15 June 2007, 1 April 2008, 8 August 2009.

Others

Reference

Hamazaki K, Sawazaki S, Itomura M, et al. No effect of a traditional Chinese medicine, Hochu-ekki-to, on antibody titer after influenza vaccination in man: a randomized, placebo-controlled, double-blind trial. *Phytomedicine* 2007; 14: 11-4. CENTRAL ID: CN-00576087, Pubmed ID: 16644196

1. Objectives

To assess the efficacy and safety of hochuekkito (補中益気湯) on antibody production after influenza vaccination.

2. Design

Double-blind, randomized, controlled trial (DB-RCT).

3. Setting

No description of the setting is available; the authors belong to the Division of Clinical Application, Institute of Natural Medicine, University of Toyama.

4. Participants

Of the 49 healthy males aged between 20 and 60 years who volunteered to enter this trial of hochuekkito, 36 were enrolled. None of the 36 had been taking any herbal medicine, hormone therapy, or anti-inflammatory drugs.

5. Intervention

Arm 1: administration of Kanebo Hochuekkito (補中益気湯) Extract Fine Granules 3.75 g b.i.d. before breakfast and supper for 14 days until the day prior to influenza vaccination, n=18.

Arm 2: administration of placebo (consisted mainly of cane sugar) 3.75 g b.i.d. before breakfast and supper for 14 days until the day prior to influenza vaccination, n=18.

6. Main outcome measures

Blood samples were taken at weeks 0, 1, 2, 4, and 12. Hemagglutination inhibition (HI) was used to measure influenza antibody titer, and a chromium (Cr)-release assay was used to measure natural killer (NK) activity.

7. Main results

Three subjects in arm 2 (because of common cold and diarrhea) and one subject in arm 1 (for a personal reason) dropped out of the study. There were no significant between-arm differences in postvaccination titer and NK activity.

8. Conclusions

Oral administration of hochuekkito for 14 days before influenza vaccination did not affect postvaccination antibody production.

9. From Kampo medicine perspective

Subjects not intending to use hochuekkito, as well as subjects with easy fatigability, a high susceptibility to colds, slow recovery from colds, a high susceptibility to other infections like herpes and wound infection, poor appetite, loose bowels, and somnolence especially after meals, were excluded from the study.

10. Safety assessment in the article

No adverse effects were observed.

11. Abstractor's comments

This is a high-quality, well-designed, and double-blind clinical trial to assess the effect of hochuekkito on antibody production after influenza vaccination. A similar report (Yamaguchi H et al., Assessment of the effect of hochuekkito extract on antibody response to influenza vaccination. *Kampo to Saishin-chiryo* [*Kampo & the Newest Therapy*] 2006; 15: 235-7 [in Japanese]) concluded similarly that oral administration of hochuekkito for 1 week after the vaccination has no effect on antibody production. On the other hand, as mentioned in the discussion of this paper, Takagi et al. reported that hochuekkito increased antibody production in old mice (Takagi et al. Antibody response of Kampo-hozai after infuluenza B immunization in old mice. *The Japanese Society for Vaccinology* 2002; 6: 72 [abstract in Japanese]). Considering that all the clinical trials were conducted with healthy subjects, further investigation in the elderly with decreased ability to produce antibodies is awaited. The design of this clinical trial, based on the result from basic studies, should be emulated by researchers who conduct clinical trials of Kampo medicines.

12. Abstractor and date

Goto H, 21 November 2008, 8 August 2009.

Others

Reference

Terashima Y, Hamazaki K, Itomura M, et al. Effect of a traditional Chinese medicine, maobushisaishinto, on the antibody titer after influenza vaccination: A randomized, placebo-controlled, double-blind trial. *Journal of Traditional Medicines* 2007; 24: 59-66. Ichushi Web ID: 2007258196 J-STAGE

1. Objectives

To evaluate the effect of maobushisaishinto (麻黄附子細辛湯) on antibody titer after influenza vaccination.

2. Design

Double-blind randomized controlled trial (DB-RCT).

3. Setting

Two university hospitals.

4. Participants

One hundred and six healthy subjects aged 20–71 years.

Intervention

Maobushisaishinto (麻黄附子細辛湯) and placebo capsules were donated by Kotaro Pharmaceutical Co., Ltd.

5. The following drugs were orally administered from day –14 to –1 of influenza vaccination (A/H1N1, A/H3N2, B). All subjects were vaccinated in late November, before the influenza season.
Arm 1: Kotaro Maobushisaishinto (麻黄附子細辛湯) Extract Capsules (6 capsules/day), n=23.
Arm 2: placebo capsules, n=24.

6. Main outcome measures

Serum hemagglutination inhibition titers were measured at weeks 0, 1, 2, 4, and 12.

7. Main results

After excluding 57 subjects with antibody titers of more than 1:80 and 2 subjects diagnosed with influenza during the study period (one in each arm), 23 and 24 subjects were enrolled for analysis. There was no significant between-arm difference in antibody titer against A/New Caledonia/20/99(H1N1), A/New York/55/2004(H3N2), and B/Shanghai/361/2002. However, anti-H3N2 virus antibody titer was significantly higher in arm 2 than in arm 1 at week 4. Subgroup comparisons (smokers *vs* non-smokers and older subjects [≥40 years old] *vs* younger subjects [<40 years old]) found no significant between-arm differences in antibody titers.

8. Conclusions

No adjuvant effect of maobushisaishinto on antibody titer after influenza vaccination was observed.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Previous studies have shown the adjuvant effect of maobushisaishinto on influenza vaccination in animals and in elderly subjects. This paper aims to verify this effect.

12. Abstractor and date

Fujisawa M, 15 January 2009, 8 August 2009.

Others

Reference

Sato Y, Katagiri F, Itoh H, et al. Bushi-richu-to raises calcitonin gene-related peptide, substance P, somatostatin, and vasoactive intestinal polypeptide levels in human plasma. *Journal of Health Science* 2007; 53: 615-21. Ichushi Web ID: 2008127570 J-STAGE

1. Objectives

To elucidate the mechanism of bushirichuto (附子理中湯) activity in raising gut-regulated peptide levels.

2. Design

Randomized crossover controlled trial (RCT-cross over).

3. Setting

Department of Clinical Pharmacy, Oita University Hospital.

4. Participants

Five healthy male volunteers recruited at the facility mentioned above, n=5.

5. Intervention

Arm 1: Kanebo Bushirichuto (附子理中湯) Extract Fine Granules (EK-410) 4.5 g was orally administered with 100 mL of water for 4 weeks.
Arm 2: placebo was orally administered with 100 mL of water for 4 weeks.
Each subject was administered these drugs with an interval of four weeks.

6. Main outcome measures

Blood samples were obtained before administration, and at 20, 40, 60, 90, 120, 180, and 240 min after administration of the test substances, and plasma levels of calcitonin gene-related peptide (CGRP), substance P, vasoactive intestinal polypeptide (VIP), somatostatin, and motilin-like immunoreactive substance (IS) were measured by enzyme immunoassay (EIA).

7. Main results

One dose of bushirichuto significantly increased CGRP, somatostatin, and VIP levels (which peaked at 40–60 min) and significantly increased substance P level (which peaked at 180 min). CGRP level increased 5.7-fold at 40 min (85.2±58.7 pg/mL in arm 1 *vs*. 14.9±1.9 pg/mL in arm 2) (P<0.01), somatostatin level increased 2.1-fold at 60 min (20.2±6.1 pg/mL in arm 1 *vs*. 9.8±2.1 pg/mL in arm 2) (P<0.01), VIP level increased 2-fold at 60 min (16.9±7.0 pg/mL in arm 1 *vs*. 8.3±1.4 pg/mL in arm 2) (P<0.01), and substance P increased 2-fold at 180 min (68.5±18.7 pg/mL in arm 1 *vs.* 34.3±17.9 pg/mL in arm 2) (P<0.01). On the other hand, plasma motilin-like IS level was unaffected during observation for 240 min after administration.

8. Conclusions

Administration of bushirichuto may reduce sensitivity to cold, gastrointestinal discomfort, and gastrointestinal dysfunction *via* increasing plasma levels of CGRP, somatostatin, VIP, and substance P.

9. From Kampo medicine perspective

The authors suggest that the taste and smell of bushirichuto may affect the kinetics of gut-regulated peptides.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Although this investigation had only a small number of subjects, the results helped us to reveal the mechanism of bushirichuto activity. As bushirichuto is an "*onchu-sankan*" (温中散寒) medicine which contains herbs (Aconiti tuber [附子] and Zingiberis siccatum rhizome [乾姜]) with strong anti-coldness ("*sankan*") activity, it is used for patients with "*hie*" (or a feeling of coldness in the body). However, the authors did not reveal whether the male volunteers had *kan-sho* (寒証, cold pattern). Most subjects treated with bushirichuto in clinical practice are frail women. From that point of view, to minimize the discrepancy between bushirichuto use in actual clinical practice and experimental study, clinical studies of "*sho*" in women with and without symptoms, and having the same study design as this trial, are awaited.

12. Abstractor and date

Ushiroyama T, 19 December 2008, 8 August 2009.

Others

Reference

Takahashi H, Nakao R, Hirasaka K, et al. Effects of single administration of Rokumi-gan (TJ-87) on serum amino acid concentration of 6 healthy Japanese male volunteers. *Journal of Medical Investigation* 2007; 54: 91-8. Ichushi Web ID: 2007295608 J-STAGE

1. Objectives

To examine effects of rokumigan (六味丸) on serum amino acid concentrations.

2. Design

Randomized crossover controlled trial (RCT-cross over).

3. Setting

Department of Internal Medicine, the Komatsushima Hospital.

4. Participants

Six healthy men (mean age 35.5 years), n=6.

5. Intervention

Arm 1: lactose 5 g administered once at 9:00, n=6.
Arm 2: Asahi amino GET 5 tablets (contains a similar amount of amino acids as 10 g of Tsumura Rokumigan (六味丸) Extract Granules) administered once at 9:00, n=6.
Arm 3: Tsumura Rokumigan (六味丸) Extract Granules (TJ-87) 10 g administered once at 9:00, n=6.
There was a washout period of 3 months between treatments.

6. Main outcome measures

Serum amino acid concentrations before and at 1, 2, 4, and 6 h after the intervention.

7. Main results

In arm 1, concentrations of Ala, Gly, and Ile were significantly decreased from pretreatment levels at 6 h, and Arg, Glu, His, Leu, Lys, Phe, Ser, and Val levels were unchanged. In arm 2, concentrations of Ala, Glu, Gly, Ile, Leu, and Ser were significantly decreased at 6 h, but Arg, His, Lys, Phe, and Val levels remained unchanged. In arm 3, the levels of Ala at 2 h and Gly and Ser at 1 h were significantly increased, but Arg, Glu, His, Ile, Leu, Lys, Phe, and Val levels remained unchanged. In all three arms, serum levels of Asn, Cys, Gln, Met, Pro, Thr, Trp, and Tyr were not determined, and Asp were undetectable.

8. Conclusions

Serum amino acid concentrations are higher after administration of rokumigan than after administration of a supplement containing a similar amount of amino acids.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

This interesting well-designed cross-over clinical trial investigates the entry of amino acids from rokumigan into the blood. Changes in the concentration of amino acids after rokumigan administration were compared with those after administration of lactose or an amino acid mixture containing almost the same amount of amino acids. Amino acid levels (e.g., the pretreatment Ala level) were widely dispersed in all three arms, suggesting possible measurement errors in serum level for some amino acids. To adjust for dispersion in the data, relative changes in amino acid concentrations were calculated and are shown in Fig. 1. However, symbols a, b, and c are not defined. Also, the amino acid mixture administered in arm 2 contains several ingredients besides amino acids such as beer yeast, and their influence on absorption should be considered. Importantly, this study found that administration of rokumigan increased amino acid levels in blood and suppressed the gradual decrease observed in other arms. This observation may have important pharmacologic implications. Further studies on several Kampo medicines are anticipated.

12. Abstractor and date

Goto H, 27 November 2008, 8 August 2009.

Others

Reference

Saida Y, Takase M, Okumura C, et al. Efficacy of combined use of shakuyakukanzoto in pretreatment for large bowel endoscopy – prospective randomized trial*. *Nihon Daicho Kensa Gakkai Zasshi* (*Journal of the Japan Society of Colon Examination*) 2003; 20: 34-7 (in Japanese). Ichushi Web ID: 2005123565

1. Objectives

To evaluate the efficacy of shakuyakukanzoto (芍薬甘草湯) combined with polyethylene glycol solution (PEG) in pretreatment for large bowel endoscopy.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

None (authors belong to the Department of Colon and Rectal Surgery, Tohokamagaya Hospital).

4. Participants

Seventy patients who were scheduled to undergo large bowel endoscopy between November 2000 and March 2001 and gave informed consent to participate in this trial.

5. Intervention

Arm 1: oral administration of shakuyakukanzoto (芍薬甘草湯) (2.5 g t.i.d.) starting from lunchtime on the day before endoscopy (n=37).
Arm 2: non-treatment (n=33).
Endoscopy was performed by an experienced specialist.

6. Main outcome measures

Frequency of defecation on the day of endoscopy, time until defecation, presence or absence and severity of abdominal pain associated with pretreatment, presence or absence and severity of nausea, pretreatment condition (residue), and time required to reach cecum.

7. Main results

Frequency of defecation and time until defecation were 6.9±2.5 times and 234±36 min, respectively, in arm 1 and 7.6±3.4 times and 171±30 min, respectively, in arm 2, showing reduced frequency and extended time until defecation in arm 1, although there were no significant differences between arms. The incidence and score of abdominal pain were 11% and 0.6±0.4, respectively, in arm 1 and 12% and 0.5±0.4, respectively, in arm 2, showing no difference between arms. Nausea was more prevalent in arm 1 with the incidence of 33%, compared with 12% in arm 2, although there was no difference in nausea score between arms. Pretreatment score and time required to reach cecum were 0.9±0.8 and 7.9±5.4 min, respectively, in arm 1 and 0.7±0.8 and 7.9±5.5 min, respectively, in arm 2, showing no difference between arms.

8. Conclusions

Shakuyakukanzoto combined with PEG tends to slightly suppress the cleansing of the bowel needed prior to large bowel endoscopy and may induce nausea, suggesting its ineffectiveness in such pretreatments.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

To achieve adequate intestinal lavage in preparation for large intestine endoscopy, a large amount of PEG has to be swallowed. In terms of efficacy and patient satisfaction, however, currently available pretreatments are not always useful. Focusing on this issue, the present study is meaningful. To further enhance the quality of this clinical research, however, the control should be a placebo that has no effect on bowel motility rather than no treatment. With no other useful concomitant drugs available, it is hoped that new drugs and useful approaches will be investigated.

12. Abstractor and date

Arai M, 23 February 2007, 30 October 2007, 8 August 2009.

Others

Reference

Ai M. Assessment of the antipasmodic effect of peppermint oil and shakuyaku-kanzon-to (TJ-68); a Chinese herbal medicine on the clonic wall. *Medical Tribune Online* (*Digestive Disease Week: DDW*) 2005: 10-1 (in Japanese).

1. Objectives

To evaluate the efficacy of directly sprayed shakuyakukanzoto (芍薬甘草湯) on large bowel spasm.

2. Design

Randomized controlled trial (RCT).

3. Setting

Single facility (university).

4. Participants

One-hundred and thirty-one patients scheduled to undergo large bowel endoscopy for polyp surveillance, etc.

5. Intervention

Arm 1: shakuyakukanzoto (芍薬甘草湯) group (0.5 g of TSUMURA Shakuyakukanzoto (芍薬甘草湯) Extra Granules dissolved in physiological saline to make 50 mL [concentration: 10 g/L]).
Arm 2: peppermint oil group (0.4 mL of peppermint oil and 0.05 g of sorbitan fatty acid ester dissolved in water to make 50 mL [concentration: 8 mL/L]).
Arm 3: Physiological saline group.
In all arms, conventional fluoroscopy (CF) was performed in the left lateral position, and the contraction ring in the gastric antrum was sprayed, kept 1 cm from the tip of the endoscope inserted 20–25 cm from the anus.

6. Main outcome measures

Contraction ring lumen area (presented as the number of pixels on videotaped digital images of contraction-relaxation motions of the contraction ring during the 3-min period beginning before and ending after each drug was sprayed), and area under the expanded area-time curve.

7. Main results

Lumen area was significantly larger in the shakuyakukanzoto group and peppermint oil group than in the physiological saline group. The area under the expanded area-time curve was also significantly larger in both treatment groups than in the physiological saline group. There was no difference in outcome measures between the shakuyakukanzoto group and peppermint oil group.

8. Conclusions

Shakuyakukanzoto and peppermint oil have comparable large intestinal wall-relaxing activity.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

Direct spray of large intestinal wall with shakuyakukanzoto may be applicable as an antispastic in the CF test.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Others

Reference

Sugihara N. Effectiveness of shakuyaku-kanzo-to as a pretreatment for upper digestive tract endoscopic examination*. *Kampo Shinryo* 1999; 18: 17-9 (in Japanese).

1. Objectives

To evaluate the efficacy of pretreatment with shakuyakukanzoto (芍薬甘草湯) for upper gastrointestinal tract endoscopy.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Single facility (clinic).

4. Participants

Fifty-eight subjects who underwent endoscopy.

5. Intervention

Arm 1: shakuyakukanzoto (芍薬甘草湯) group (oral administration of 80 mg of dimethicone syrup followed by 5.0 g of shakuyakukanzoto (芍薬甘草湯) extract granules) (n=11).

Arm 2: anticholinergic drug group (oral administration of 80 mg of dimethicone syrup followed by subcutaneous injection of 40 mg of scopolamine butylbromide) (n=28).

6. Main outcome measures

Symptoms during endoscopy (pain evaluated subjectively on a visual analogue scale), peristalsis (Niwa's classification).

7. Main results

Among those under 70 years, the anticholinergic drug was significantly superior to shakuyakukanzoto in suppression of peristalsis, but was more frequently associated with experience of pain/discomfort.

8. Conclusions

Shakuyakukanzoto provides as much pain relief as the anticholinergic drug.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

Of 58 subjects, only 39 were actually assigned to either group (arm 1, n=11; arm 2, n=28). This sample size seems to be slightly too small to evaluate efficacy.

12. Abstractor and date

Kogure T, 15 June 2007, 1 April 2008, 8 August 2009.

Others

Reference

Saida Y, Sumiyama Y, Nagao J, et al. Dai-kenchu-to, a herbal medicine, improves precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage: results of a prospective randomized controlled trial. *Digestive Endoscopy* 2005; 17: 50-3. Ichushi Web ID: 2006000780

1. Objectives

To evaluate the efficacy of daikenchuto (大建中湯) combined with polyethylene glycol solution (PG solution) in pretreatment for large bowel endoscopy.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

None (authors belong to the 3rd Department of Surgery, Toho University School of Medicine).

4. Participants

Two-hundred and eighty-five patients who underwent total large bowel endoscopy between January and December 2001, gave informed consent to participate in this trial, and remained after excluding those under 18 years old, pregnant women, and other ineligible patients.

5. Intervention

Arm 1: combination of PG solution and TSUMURA Daikenchuto (大建中湯) Extract Granules (oral administration of 2.5 g each at 12:00 and 21: 00 on the day before and 7:00 on the day of large bowel endoscopy) (n=144).

Arm 2: PG solution alone (n=141).

Endoscopy was performed by an experienced specialist.

6. Main outcome measures

Frequency of defecation on the day of endoscopy, time until defecation, presence or absence of abdominal pain, abdominal score, presence or absence of nausea, nausea score, pretreatment score, and time required to reach the ileocecal area.

7. Main results

The PG solution/daikenchuto combination group and PG solution group defecated 7.9±3.1 times and 7.7±3.6 times, respectively, and required 3.3±1.6 hr and 3.0±1.5 hr until defecation, respectively. The incidence of abdominal pain (score) was 17% (0.17±0.38) and 15% (0.15±0.35), respectively, and the incidence of nausea (score) was 24% (0.28±0.55) and 21% (0.21±0.43), respectively. Thus, there were no significant between-group differences in these parameters. Pretreatment score was significantly improved in the PG solution/daikenchuto combination group (0.28±0.52 *vs* 0.81±0.77 in the PG solution group; $P<0.01$). The time required to reach the ileocecal area was also significantly reduced in the PG solution/daikenchuto combination group (6.4±3.6 min *vs* 7.3±4.0 min in the PG solution group; $P=0.04$).

8. Conclusions

PG solution/daikenchuto pretreatment for large bowel endoscopy is a more patient-friendly effective method for facilitating insertion (compared with pretreatment with PG solution alone) and does not increase the level of uncomfortable symptoms such as abdominal pain, nausea, and frequent defecation.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This randomized controlled trial demonstrated that daikenchuto combined with PG solution is superior to PG alone in the preparation of the large intestine for endoscopy. This study has a large sample size and is well designed, but fails to explain pretreatment score and abdominal pain score. It has been presented in a previous report "Saida Y. The 15th Surgery and Kampo Medicine Study Meeting 1. Efficacy of combined use of daikenchuto in pretreatment for large bowel endoscopy - 6 prospective studies -*. *Progress in Medicine* 2005; 25: 3058-9 (in Japanese)."

12. Abstractor and date

Arai M, 10 March 2007, 30 October 2007, 8 August 2009.

Others

Reference

Ai M, Yamaguchi T, Odaka T, et al. Objective assessment of the antispasmodic effect of shakuyaku-kanzo-to (TJ-68), a Chinese herbal medicine, on the colonic wall by direct spraying during colonoscopy. *World Journal of Gastroenterology* 2006; 12: 760-4. CENTRAL ID: CN-00563124, Pubmed ID: 16521190

1. Objectives

To evaluate the efficacy and safety of direct spraying of shakuyakukanzoto (芍薬甘草湯) on the colonic mucosa for suppression of bowel movement during colonoscopy.

2. Design

A randomized controlled trial (RCT).

3. Setting

Not specifically mentioned (the authors belong to one university hospital).

4. Participants

One-hundred and ten patients with suspected intestinal hemorrhage, acute abdomen due to acute enteritis, inflammatory bowel disease, or a history of abdominal surgery, and treated with an oral drug affecting bowel movement, who visited our hospital between July 2002 and March 2004.

5. Intervention

Arm 1: spray of 0.5 g/50 mL of a solution of TSUMURA Shakuyakukanzo (芍薬甘草湯) Extract Granules in physiological saline maintained at 36℃ over the area of spasms in the intestine, 10 mm apart (n=51).

Arm 2: spray of physiological saline maintained at 36℃ in the same manner as arm 1.

Colon preparation involved oral administration of Magcorol (59 g/250 mL) on the day before colonoscopy and 2 L of Niflec on the day of colonoscopy. No sedatives were used during colonoscopy (n=50).

Five patients in arm 1 and 4 patients in arm 2 were excluded from the study population because of poor or incomplete bowel preparation.

6. Main outcome measures

Lumen area (pixels) × time (min), determined before and after spraying over the area of spasms.

7. Main results

Before spraying, there was no significant difference between arms. After spraying, the area × time value was significantly larger in arm 1.

8. Conclusions

Direct spray of shakuyakukanzoto is effective for suppression of bowel movement during colonoscopy.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no complications throughout the study period.

11. Abstractor's comments

This is an excellent study because it quantifies bowel movement by monitoring digital images over time, enabling objective evaluation.

12. Abstractor and date

Kogure T, 27 January 2009, 8 August 2009.

Others

Reference

Mizukami T, Maruyama K, Yamauchi H, et al. Assessment of antispasmodic effect of herbal medicine, shyakuyakukanzoto (TJ-68) on colonoscopy – Using colonoscopy insertion technique "collapsing method" –. *Kampo to Saishin-chiryo* (*Kampo & the Newest Therapy*) 2006; 15: 69-76 (in Japanese). Ichushi Web ID: 2006142071

1. Objectives

To evaluate the efficacy of shakuyakukanzoto (芍薬甘草湯) solution in preparation for colonoscopy used with the water method of distension.

2. Design

A quasi-randomized controlled trial (quasi-RCT).

3. Setting

Not mentioned (the authors belong to one specialty hospital).

4. Participants

Forty-two males undergoing colonoscopy who gave consent to participate in the study.

5. Intervention

Arm 1: intrarectal injection of a solution of TSUMURA Shakuyakukanzoto (芍薬甘草湯) Extract Granules (1.25 g/100 mL) instead of water used in preparation for colonoscopy used with the water method, simultaneously performed with colonoscope insertion (n=21).

Arm 2: intramuscular injection of butylscopolammonium bromide (Buscopan) (20 mg/mL/A), simultaneously performed with colonoscope insertion (n=21).

One patient in each arm was considered unresponsive because of failure to achieve spasmolysis during the test and was excluded.

6. Main outcome measures

Duration of spasmolysis determined by measuring the time between the first and second appearance of colonic ring contractions.
Pulse rate measured before and 10 min after endoscope insertion.
Pain evaluated on a 5-point scale.

7. Main results

There was no significant difference in duration of spasmolysis or pain scale score between arms. Percent increase in pulse rate from before to 10 min after insertion was significantly larger in arm 2. Spasmolytic effect persisted until completion of the test in 68.8% of subjects in arm 1 and 25.0% of subjects in arm 2, showing a significant between-arm difference.

8. Conclusions

Shakuyakukanzoto solution in preparation for colonoscopy, used with the water method, prolongs spasmolysis.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This excellent paper suggests the potential of a Kampo medicine as a bowel pretreatment for colonoscopy. Evaluation of spasmolysis by colonoscopy is limited to the visual field. Combined use of fluoroscopy may enable observation to be extended to the whole intestine. Studies on the effects of distension methods other than the water method during colonoscopy are expected.

12. Abstractor and date

Kogure T, 26 January 2009, 8 August 2009.

Others

Reference

Saida Y, Nagao J, Nakamura Y, et al. Dai-kenchu-to and mosapride in combination with precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage: results of a prospective randomized controlled trial. *Nihon Daicho Kensa Gakkai Zasshi* (*Journal of the Japan Society of Colon Examination*) 2005; 22: 145-8 (in Japanese). Ichushi Web ID: 2007146750

1. Objectives

To determine the bowel cleansing effect of precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage solution (PG solution) combined with daikenchuto (大建中湯) and mosapride.

2. Design

Randomized controlled trial (RCT).

3. Setting

None (the authors belong to the Third Department of Surgery, Toho University School of Medicine and/or Tohokamagaya Hospital).

4. Participants

Two hundred and twenty-two patients (155 males and 67 females) who underwent colonoscopy between April 2004 and October 2004 and gave informed consent, including consent to disclose relevant information.

5. Intervention

Arm 1: treatment with 2 L of polyethylene glycol (PG) solution plus daikenchuto (大建中湯) (7.5 g; manufacturer, not specified) (n=116).

Arm 2: treatment with 2 L of PG solution plus daikenchuto (大建中湯) (7.5 g; manufacturer, not specified) and mosapride (15 mg; 3 tablets) (n=106).

PG solution was administered orally for about 2 hours, at least 6 hours prior to the colonoscopy. Daikenchuto (大建中湯) and mosapride were administered in three divided doses, starting at noon one day before colonoscopy.

6. Main outcome measures

Number of bowel movements, duration time of defecation, presence and severity of abdominal pain and nausea, ease/difficulty of taking the combined medication, adequacy of bowel preparation, and cecal intubation time.

7. Main results

The mean number of bowel movements was significantly higher in arm 2 (7.8) than in arm 1 (7.0). Defecation time tended to be slightly longer in arm 2 (3 h 18 min) than in arm 1 (2 h 59 min). No between-arm differences in abdominal pain (13% of patients in arm 1 and 17% in arm 2) and nausea (24% and 25%, respectively) were observed. The percentage of patients who reported that taking the combined medication was “difficult” or “slightly difficult” was significantly higher in arm 2 (38%) than in arm 1 (28%). No between-arm differences in mean bowel preparation scores (0.9 in both arms) and median cecal intubation times at colonoscopy (6 minutes in both arms) were observed.

8. Conclusions

The addition of mosapride offers no benefit to precolonoscopy bowel preparation with PG solution plus daikenchuto alone.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor’s comments

This paper follows up a previous paper that discussed the efficacy of precolonoscopy bowel preparation with PG solution plus daikenchuto: Saida Y, Sumiyama Y, Nagao J, et al. Dai-kenchu-to, an herbal medicine, improves precolonoscopy bowel preparation with polyethylene glycol electrolyte lavage: results of a prospective randomized controlled trial. *Digestive Endoscopy* 2005; 17: 50-3. The present trial had a large sample size and was well-designed. There are yet some drawbacks, including the following: 1) possible dependence of some results on skills of the colonoscopist is not mentioned; and 2) the method used for scoring bowel preparation quality was not described. Further studies, like this one, are anticipated.

12. Abstractor and date

Arai M, 19 January 2009, 8 August 2009.

Others

Reference

Arai J, Nakajima S, Fujinuma S, et al. A Comparative study of bowel preparation for barium enema using divided administrations of powdered magnesium citrate with mosapride or DAIKEN CHUTOU. *Nihon Daicho Kensa Gakkai Zasshi* (*Journal of the Japan Society of Colon Examination*) 2002; 19: 170-3 (in Japanese). Ichushi Web ID: 2003041591

1. Objectives

To determine the effectiveness of daikenchuto (大建中湯) in bowel preparation for barium enema X-ray study.

2. Design

Randomized crossover controlled trial (RCT).

3. Setting

Ohashi Hospital, Toho University School of Medicine.

4. Participants

Forty-five patients who underwent barium enema X-ray study on an outpatient basis between March and August 2001.

5. Intervention

Arm 1: conventional bowel preparation plus oral administration of daikenchuto (大建中湯) (manufacturer, not specified) 5 g t.i.d. on the day before the X-ray examination (n=24).

Arm 2: conventional bowel preparation plus oral administration of mosapride citrate 10 mg t.i.d. on the day before the X-ray examination (n=21).

6. Main outcome measures

The number and amount of fecal residues and the adherence of barium.

7. Main results

No significant between-arm differences were observed in the number and amount of fecal residues or in the adherence of barium.

8. Conclusions

Daikenchuto is suggested to be as effective as mosapride citrate in bowel preparation for barium enema X-ray study.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This paper compares the effectiveness of daikenchuto with that of mosapride citrate in bowel preparation for barium enema X-ray study. Prokinetic agents combined with conventional bowel preparation for barium enema X-ray decreases the number and amount of fecal residues and improves the adherence of barium. The authors of the present paper concluded that daikenchuto is as effective as a prokinetic agent. The effectiveness of daikenchuto in preparation for lower gastrointestinal endoscopy has been suggested in a previous report and the usefulness of shakuyakukanzoto has already been demonstrated. The use of Kampo medicines in this field is expected to increase in the future.

12. Abstractor and date

Oikawa T, 31 December 2008, 8 August 2009.

Others

Reference

Ueda T, Yamashita K, Nakamori Y, et al. Study of the MRSA carriage-preventing effect of hochuekkito (TJ-41): 1st report*. *Progress in Medicine* 1999; 19: 1000-3 (in Japanese). MOL, MOL-Lib

1. Objectives

To evaluate the effects of hochuekkito (補中益気湯) on prevention of MRSA carriage, prevention of *Pseudomonas aeruginosa* carriage, prevention of infection development, neutrophil count, and C-reactive protein (CRP) value.

2. Design

Randomized controlled trial (RCT).

3. Setting

Single facility (Osaka University Hospital ER).

4. Participants

Twenty patients with trauma (aged 16 years or older) who were hospitalized in the above facility for at least 1 week.

5. Intervention

Arm 1: hochuekkito group (補中益気湯) (n=8 [2/10 enrolled were excluded]; male: female = 3:1; mean age, 46.8 years; injury severity score [ISS], 26.1).
Arm 2: non-treatment group (n=12; male: female = 3:1; mean age, 31.2 years; ISS, 24.0).

6. Main outcome measures

Incidences of MRSA and *Pseudomonas aeruginosa* colonization and infection, CRP level, and neutrophil count.
Bacteriological examination of nasopharyngeal swabs, sputum, midstream urine, feces, and wound scraping was performed on the 1st, 3rd and, 7th day of hospitalization.

7. Main results

There was no significant between-arm difference in neutrophil count and CRP level. Meningitis occurred in 0 of 2 treated patients and 4 of 5 untreated patients. There was no difference in the incidence of pneumonia. MRSA was detected in 1 of 8 treated patients and 4 of 12 untreated patients, although the difference was not significant. *Pseudomonas aeruginosa* was detected in 1 of 8 treated patients.

8. Conclusions

Hochuekkito tended to prevent MRSA carriage and infections in trauma patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This is a valuable RCT performed in an emergency setting. As admitted by the authors in the text, the timing of hochuekkito administration varied. Specification of the method, duration of hochuekkito administration, and presence or absence of blinding, would increase the reliability of this assessment. More results from their study, now underway with a new protocol, are expected.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 8 August 2009.

Structured Abstract

(1 abstract describing a meta-analysis)

Ante/Post-partum Diseases

Reference

Koinuma M, Narikawa H, Kamei M, et al. Meta-analysis on the usefulness in postpartum control by Kyukichoketsuin with Methylergometrine Maleate as control. *Nihon Toyo Igaku Zasshi* (*Kampo Medicine)* 2006; 57: 45-55 (text in English with Japanese abstract). Ichushi Web ID: 2006097925 CiNii

1. Objectives

To evaluate the efficacy of kyukichoketsuin (キュウ帰調血飲) (KCL) in puerperal care in comparison with methylergometrine maleate (MME) by conducting a meta-analysis.

2. Data source

Articles in *Igaku Chuo Zasshi* (*Japana Centra Revuno Medicina*) (1983 – 2004) and Medline (1966 – 2004) were searched and collected using key words such as kyukichoketsuin, etc.

3. Selection of study

Inclusion criteria: 1) RCT; 2) original article; 3) study population consisting of puerperal primipara and pluripara who had normal delivery; 4) use of KCL as an intervention drug and MME as control; and 5) indices of therapeutic effect including length of uterine fundus, amount of lactation, and severity of afterbirth pains.

4. Data extraction

Data extraction was performed independently of data integration by a different researcher. Extracted data were baseline characteristics of subjects, sample size, method of randomization, method of blinding, method of administering the investigational and control drugs, dosage, number of daily doses, number of days of administration, concomitant drugs, and study endpoints. If study end points data were shown just graphically without numerical values, points on the graph with calipers were measured and converted graphical values to numerical values. The quality of selected RCTs was evaluated using the Chalmers' scoring system.

5. Main results

Of 44 RCTs gathered, 5 satisfied the selection criteria. One of these 5 overlapped and was excluded, leaving 4 RCTs for analysis. These RCTs were equivalent in quality. Analysis of three RCTs evaluating breast pain revealed that KCL significantly attenuated afterbirth pains compared with MME (combined odds ratio: 0.32 [95%CI, 0.17 – 0.60]). On day 5 after delivery, there was statistically significant difference in the length of the uterine fundus between groups treated with KLC and MME in 1 trial, but no difference based on the combined data from all 4 trials. On day 4 after delivery, neither data from individual trials nor the combined data showed significant differences in the length of the uterine fundus, suggesting comparable effect of KCL and MME on involution of the uterus. Combined data form 2 contradictory articles compared the amount of lactation on day 4 after delivery, one showed no difference and another showed that both KCL and MME increased the amount of lactation, demonstrated significantly less lactation with KCL (combined odds ratio: -8.20 [95%CI, -16.17 to -0.23]). Combined data on day 5 after delivery revealed that KCL increased the amount of lactation, although not significantly, showing the efficacies of KCL and MME for inducing lactation were similar.

6. Conclusions

Compared to MME, KCL is more effective in attenuating afterbirth pains. Analysis of safety is necessary.

7. From Kampo medicine perspective

None.

8. Safety assessment in the article

None.

9. Abstractor's comments

The authors deserve praise for conducting a meta-analysis of RCTs restricted to Kampo medicine. As the point of meta-analysis is to gather data from all related studies, it would be better to provide the details of the gathering process; for example, whether the search was exhaustive and included a hand-search of textbooks, reference books, and specialists' opinions. Considering current movement towards evidence based medicine (EBM) in Kampo field, the authors' meta-analysis is epoch-making. It is expected that this study will stimulate further meta-analyses and systematic reviews of Kampo medicine studies.

10. Abstractor and date

Tsuruoka K, 19 February 2009, 8 August 2009.