Evidence Reports of Kampo Treatment (EKAT)

Appendix 2017

漢方治療エビデンスレポート(EKAT) Appendix 2017

18 May 2020

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

ver.1.0 18 May 2020

History of version upgrades

18 May 2020: Kampo Chiryo Ebidensu Repoto Appendix 2017 (Evidence Reports of Kampo Treatment Appendix 2017)

1 Nov. 2018: Kampo Chiryo Ebidensu Repoto 2016 (Evidence Reports of Kampo Treatment 2016)

31 Mar. 2017: Kampo Chiryo Ebidensu Repoto Appendix 2015 (Evidence Reports of Kampo Treatment Appendix 2015)

6 Jun. 2015: Kampo Chiryo Ebidensu Repoto Appendix 2014 (Evidence Reports of Kampo Treatment Appendix 2014)

31 Dec. 2013: Kampo Chiryo Ebidensu Repoto 2013 - 402 no RCT (Evidence Reports of Kampo Treatment 2013: 402 Randomized Controlled Trials)

31 Dec. 2012: Kampo Chiryo Ebidensu Repoto Appendix 2012 (Evidence Reports of Kampo Treatment Appendix 2012)

1 Oct. 2011: Kampo Chiryo Ebidensu Repoto Appendix 2011 (Evidence Reports of Kampo Treatment Appendix 2011)

1 Jun. 2010: Kampo Chiryo Ebidensu Repoto 2010 - 345 no RCT (Evidence Reports of Kampo Treatment 2010: 345 Randomized Controlled Trials)

1 Jun. 2009: Kampo Chiryo Ebidensu Repoto 2009 - 320 no RCT (Evidence Reports of Kampo Treatment 2009: 320 Randomized Controlled Trials)

1 Apr. 2008: Kampo Chiryo Ebidensu Repoto Dai 2-han - RC T wo Shu ni Shite- Chukan Hokoku 2007 ver 1.1 (Evidence Reports of Kampo Treatment 2nd edition - Focusing on RCTs- Interim Report 2007 ver.1.1)

15 Jun. 2007: Kampo Chiryo Ebidensu Repoto Dai 2-han -RC T wo Shu ni Shite- Chukan Hokoku 2007 (Evidence Reports of Kampo Treatment 2nd edition - Focusing on RCTs- Interim Report 2007)

20 Jul. 2005: Kampo Chiryo niokeru Ebidensu Repoto (Evidence Reports of Kampo Treatment) (Nihon Toyo Igaku Zasshi [Kampo Medicine] 2005: 56, EBM supplementary issue)

20 Sept. 2002: Kampo Chiryo niokeru EBM - 2002 nen Chukan Hokoku (EBM in Kampo 2002, Interim Report) (Nihon Toyo Igaku Zasshi [Japanese Journal of Oriental Medicine] 2002: 53 [5], supplementary issue)

version/date	Title	Year of publication of target references	No.of references	No.of structured abstracts (SAs)	No.of excluded references
2020.5.18	Evidence Reports of Kampo Treatment Appendix 2017 (EKAT Appendix 2017)	From EKAT 2016 2016	578 [2]	478 [1), 2)]	188 [2]
2018.11.1	Evidence Reports of Kampo Treatment 2016:467 Randomized Controlled Trials (EKAT 2016)	1986-2015	567	467 [1]	181
2017.3.31	Evidence Reports of Kampo Treatment Appendix 2015 (EKAT Appendix 2015)	From EKAT 2014 2014	545 [2]	447 [1), 3)]	177 [3]
2015.6.6	Evidence Reports of Kampo Treatment Appendix 2014 (EKAT Appendix 2014)	From EKAT 2013 2013 (First half)	513 [3]	418 [1), 4)]	167 [4]
2013.12.31	Evidence Reports of Kampo Treatment 2013:402 Randomized Controlled Trials (EKAT 2013)	1986-2012 (First half)	494 [4]	403 [1),	159
2012.12.31	Evidence Reports of Kampo Treatment Appendix 2012 (EKAT Appendix 2012)	From EKAT 2011 2011 (First half)	457	379 [1), 5)]	150 [5]
2011.10.1	Evidence Reports of Kampo Treatment Appendix 2011 (EKAT Appendix 2011)	From EKAT 2010 2010 (First half)	432	360 [1), 6)]	-
2010.6.1	Evidence Reports of Kampo Treatment 2010:345 Randomized Controlled Trials (EKAT 2010)	1986-2009 (First half)	416	346 [1]	132
2009.6.1	Evidence Reports of Kampo Treatment 2009:320 Randomized Controlled Trials (EKAT 2009)	1986-2008 (First half)	385	321 [1]	111
2008.4.1	Evidence Reports of Kampo Treatment 2nd edition - Focusing on RCTs- Interim Report 2007 ver.1.1	1999-2005	116	98	32
2007.6.15	Evidence Reports of Kampo Treatment 2nd edition - Focusing on RCTs- Interim Report 2007	1999-2005	104	102	42

[1)] Including 1 meta analysis

[2)] Total of all references added or removed in EKAT 2016, EKAT Appendix 2017

[3)] Total of all references added or removed in EKAT 2013, EKAT Appendix 2014 and EKAT Appendix 2015

[4)] Total of all references added or removed in EKAT 2013, EKAT Appendix 2014.

[5)] Total of all references added or removed in EKAT 2010, EKAT Appendix 2011 and EKAT Appendix 2012.

[6)] Total of all references added in EKAT 2010 and EKAT Appendix 2011.

Notes on the current version

The Task Force for Evidence Reports (ER-TF) of the Committee for Evidence-based Medicine (EBM), Japan Society for Oriental Medicine (JSOM), comprehensively gathers data obtained in randomized controlled trials (RCTs) of Kampo formulations in Japan, compiles structured abstracts (SAs), and then publishes them on the website of the Committee for Evidence-based Medicine as Evidence Reports of Kampo Treatment (EKAT). It has been doing this since 2007.

As indicated in the "History of version upgrades" on the previous page, the “Evidence Reports of Kampo Treatment 2016 - 467 RCTs” (EKAT 2016) was published on November 1, 2018. The EKAT 2016 presented the results of 465 RCTs and 2 meta-analyses performed between 1986, when the current quality specifications for Kampo formulations for medical use were established, and 2015. EKAT Appendix 2017 contains SAs (11 RCTs and 1 meta-analysis) of 12 of the RCT reports published within approximately one year after the publication of EKAT 2016. Even though the ER-TF website has not been updated since the publication of the EKAT 2016, the Google search engine available on the website allows users to access all SAs in EKAT 2016 and EKAT Appendix 2017.

Although the PubMed ID and Ichushi Web ID have been recorded in order to facilitate identification of the target reference, the numbers of the references for which the clinical trial registration numbers are known will be recorded in the SAs of this EKAT Appendix 2017. In September 2004, an International Conference of Medical Journal Editors (ICMJE) made trial registration mandatory for the receipt of clinical trial papers. Also in Japan, since April 2009, "Ethical Guidelines for Clinical Research" issued by the Ministry of Health, Labour and Welfare mandated pre-registration of clinical research involving invasive interventions, and subsequently, in the previous Clinical Research Act (Act No. 16 of 2017) required pre-registration of specified clinical research.

The ER-TF carried out a search for RCT reports for the present EKAT in April 2017, to prepare SAs of RCT reports published in most medical journals in 2016. Although publication of EKAT 2017 was planned in 2017, it was actually published in 2020 due to a delay in the publication of EKAT 2016. However, it is expected that the ER-TF
will carry out its search for RCT reports in April of each year and publish the EKAT within the fiscal year going forward.

The next EKAT will be published as an Appendix in the near future.

The Japan Society for Oriental Medicine (JSOM)

Fifth Phase (September 2015 -) Committee for Evidence-based Medicine (EBM)
Task Force for Evidence Reports (ER-TF)

(The affiliations of the EBM Committee members of fiscal year of 2017 may be different from those of the current members.)

Chair and chairperson of Committee for EBM:

Yoshiharu MOTOO Department of Medical Oncology, Kanazawa Medical University

Members (10 persons, order of the Japanese syllabary):

Ichiro ARAI Department of Pharmaceutical Sciences, Nihon Pharmaceutical University Field of herbal pharmacology

Yasuhito KATO, Department of Obstetrics and Gynecology, Asahikawa Medical University

Masamichi KITAGAWA, Academic Information Center, The Jikei University School of Medicine.

Hiroshi KOIKE Department of General Internal Medicine, Tokyo Saiseikai Central Hospital

Toshiaki KOGURE Department of Japanese Oriental Medicine, Gunma Central Hospital

Hirozo GOTO Department of Kampo Medicine, Hokusei Hospital

Hiroki TAKUMA Acupuncture and Physical Therapy Teacher Training School, University of Tsukuba

Hideyuki NAKATA Kampo Internal Medicine/ Health Medical Center Nerima General Hospital

Etsuo HOSHINO General Incorporated Foundation Kukai Memorial Integrated Medicine Foundation Kukai Memorial Integrated Medicine Clinic

Miyuki MINARI Sub Committee to Assess the Efficacy of Kampo Formulations, Committee on Kampo Formulations for Prescription, Japan Kampo Medicines Manufacturers Association

Observer of Committee for EBM, Japan Society for Oriental Medicine (JSOM):

Kiichiro TSUTANI Faculty of Health Sciences, Tokyo Ariake University of Medical and Health Sciences

Trustee in charge of Committee for EBM, Japan Society for Oriental Medicine (JSOM):

Shin-ichi MURAMATSU Division of Oriental Medicine, Center for Community Medicine, Jichi Medical University (trustee in charge of Committee for EBM, JSOM)

Lists of Structured Abstracts
(structured abstract and included references list)

Abbreviations: C, The Cochrane Library (CENTRAL); I, Igaku Chuo Zasshi (Japana Centra Revuo Medicana, Ichushi); N, Hand searching Offered by Nikkankyo (the Japan Kampo Medicines Manufacturers Association)

ICD-10	Research Question	Kampo Formula	References	Study Design	Source	Page No.
C22.0	To evaluate the hepatoprotection effect of inchinkoto (茵チン蒿湯) after hepatectomy with preoperative administration of inchinkoto	inchinkoto (茵チン蒿湯)	Mizutani T, Yokoyama Y, Kokuryo T, et al. Does inchinkoto, a herbal medicine, have hepatoprotective effects in major hepatectomy? a prospective randomized study. *HPB: The Official Journal of The International Hepato Pancreato Biliary Association* 2015; 17: 461-9.	RCT	N	7
C25.9	To evaluate the preventive efficacy of daikenchuto (大建中湯) as treatment for paralytic ileus after pancreatoduodenectomy	daikenchuto (大建中湯)	Okada K, Kawai M, Hirono S, et al. Evaluation of the efficacy of daikenchuto (TJ-100) for the prevention of paralytic ileus after pancreaticoduodenectomy: a multicenter, double-blind, randomized, placebo-controlled trial. *Surgery* 2016; 159: 1333-41.	DB-RCT	C	8
C57.9	To evaluate the efficacy of goshajinkigan (牛車腎気丸) and keishikajutsubuto (桂枝加朮附湯) as treatment for chemotherapy-induced myalgia, arthralgia, and numbness in ovarian cancer	goshajinkigan (牛車腎気丸) keishikajutsubuto (桂枝加朮附湯)	Sato Y, Yamamoto S, Tanoue K, et al. Evaluation of the effects of herbal medicines on the side effects of TC therapy (muscle pain, arthralgia, numbness). A cross-over study between goshajinkigan and keishikajutsubuto. *Sanfujinka Kampo Kenkyu no Ayumi* 2015; 32:68-71 (in Japanese).	RCT-cross over	N	9
J02.9	To evaluate the efficacy of kikyoto (桔梗湯) for treatment of postoperative sore throat	kikyoto (桔梗湯)	Kuwamura A, Komasawa N, Takahashi R, et al. Preoperative oral administration of kikyo-to, a Kampo medicine, alleviates postoperative score throat: a prospective, double-blind, randomized study. *Journal of Alternative and Complementary Medicine* 2016; 22: 294-7.	DB-RCT	C	10
K58.9	To evaluate the effect of daikenchuto (大建中湯) on rectal sensation in patients with irritable bowel syndrome	daikenchuto (大建中湯)	Acosta A, Camilleri M, Linker-Nord S, et al. A pilot study of the effect of daikenchuto on rectal sensation in patients with irritable bowel syndrome. *Journal of Neurogastroenterological Motility* 2016; 22: 69-77.	DB-RCT	N	11

L20.9	To evaluate the efficacy of unseiin (温清飲) or shimotsuto (四物湯) for the subjective and objective symptoms of atopic dermatitis	unseiin (温清飲) shimotsuto (四物湯)	Kobayashi H, Yanagihara S, Tamiya H, et al. Combined effects of herbal medicines on the subjective and objective symptoms of patients with atopic dermatitis - a comparison study of unseiin or shimotsuto. *The Nishinihon Journal of Dermatology* 2016; 78:171-6 (in Japanese).	RCT-envelope	I	12
N35.9	To evaluate the protective effect of saireito (柴苓湯) on postoperative urethral stricture	saireito (柴苓湯)	Oh-oka H. A study on the usefulness of saireito for the prevention and treatment of urethral stricture. *Japanese Journal of Oriental Medicine* 2016; 67:244-50 (in Japanese).	RCT	I	13
R25.2	To evaluate the efficacy of shakuyakukanzoto (芍薬甘草湯) for muscle spasms in lumbar spinal stenosis	shakuyakukanzoto (芍薬甘草湯)	Takao Y, Takaoka Y, Sugano A, et al. Shakuyaku-kanzo-to (Shao-Yao-Gan-Cao-Tang) as Treatment of Painful Muscle Cramps in Patients with Lumbar Spinal Stenosis and Its Minimum Effective Dose. *Kobe Journal of Medical Sciences* 2015; 61: E132-7.	RCT	C	14
S22.3	Comparison of the efficacy of jidabokuippo (治打撲一方) and non-steroidal anti-inflammatory drugs for fracture of ribs	jidabokuippo (治打撲一方)	Nakae H, Yokoi A, Kodama H, et al. Comparison of the Effects on Rib Fracture between the Traditional Japanese Medicine Jidabokuippo and Nonsteroidal Anti-Inflammatory Drugs: A Randomized Controlled Trial. *Evidence Based-Complementary and Alternative Medicine* 2012: 1-7. doi: 10.1155/2012/837958.	RCT-envelope	N	15
Z01.8	To evaluate the interaction of daijyokito (大承気湯) on the pharmacokinetics of ranitidine	daijyokito (大承気湯)	Endo Y, Ishihara Y, Tsuno S, et al. Pharmacokinetic interaction study of ranitidine and daijokito in healthy volunteers. *Yonago Acta Medica* 2016; 59: 111-7.	RCT-cross over	C	16

[Meta-analysis]

F03	A systematic review of yokukansan (抑肝散) for behavioral psychological symptoms of dementia (BPSD)	yokukansan (抑肝散)	Matsunaga S, Kishi T, Iwata N. Yokukansan in the treatment of behavioral and psychological symptoms of dementia: an updated meta-analysis of randomized controlled trials. *Journal of Alzheimer's Disease* 2016; 54: 635-43.	meta-analysis	N	17

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

Reference

Mizutani T, Yokoyama Y, Kokuryo T, et al. Does inchinkoto, a herbal medicine, have hepatoprotective effects in major hepatectomy? A prospective randomized study. *HPB : The Official Journal of The International Hepato Pancreato Biliary Association* 2015; 17: 461-9. Pubmed ID: 25581163

1. Objectives

To evaluate the hepatoprotective effects of inchinkoto (茵蔯蒿湯) in patients after major hepatectomy.

2. Design

Randomized controlled trial (RCT)

3. Setting

Not mentioned. (The authors belong to university and graduate school surgery departments.)

4. Participants

73 patients undergoing major hepatectomy (resection of 3 or more Couinaud segments) between June 2010 and January 2012. Patients who required choleretic administration for severe icterus; patients who had chemotherapy before surgery; and patients whose remnant liver volume was predicted to fall below 20% before portal vein embolization (PVE) were excluded. The number of participants was determined on the basis of animal experiment results.

5. Intervention

Arm 1: TSUMURA Inchinkoto (茵蔯蒿湯) 7.5g t.i.d from day of participation to day before surgery. Minimum administration period 7 days (n=30).

Arm 2: No TSUMURA Inchinkoto (茵蔯蒿湯) to day before surgery (n=31).

There were no significant differences between arms in age, gender, underlying disease, ICG-F value, or remnant liver volume (based on CT). The operative procedures, surgery time, hemorrhage volume, etc. were the same for the 2 arms. PVE was carried out in at least 50% of participants in the two arms.

6. Main outcome measures

Primary endpoint: Severity of hepatopathy after surgery (serum AST and ALT, postoperative complication, hepatic failure, etc.)

Secondary endpoint: Antioxidant expression in liver

7. Main results

Twelve out of 73 participants were excluded due to peritoneal metastasis, hepatic metastasis, or distant lymph node metastasis. There was no difference between arms 1 and 2 for maximum T-Bil, AST, ALT, or PT-INR after surgery; postoperative complication; or hepatic failure (Clavien-Dindo classification). Induction of antioxidant enzyme gene expression (HO-1 and SOD) was significantly higher in arm 1. Expression of HO-1 RNA was 12 times higher. Expression of Nrf protein was also significantly higher in arm 1, and immunohistochemistry found intranuclear expression was prominent in arm 1. Sub-analysis of patients with ICG-F less than 0.08 (postoperative hepatic failure high-risk group) showed significant reductions in serum AST (days 1 and 3), ALT (days 1, 3, and 5), and LDH in arm 1. Coincidence of grade B or C postoperative hepatic failure was 50% in arm 1 and 75% in arm 2.

8. Conclusions

Preoperative administration of inchinkoto did not have any effect on clinical results after hepatectomy. However, it may induce intrahepatic antioxidant enzyme expression.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

An RCT with a large number of participants, this is excellent research of clinical significance, having analyzed the effects of inchinkoto administration on hepatic function after major hepatectomy. Although no significant difference was found in complications or postoperative hepatic function, monitoring of postoperative antioxidant enzyme expression in the liver using RNA (RT-PCR), protein (Western blot), and immunohistochemistry tests suggested that the expression of antioxidant enzymes was higher in the preoperative inchinkoto administration group. The results show promise for future clinical application, and in fact, sub-analysis of the postoperative hepatic failure high-risk group showed marked improvement in hepatic function tests in the preoperative inchinkoto administration group. The selection of administration method and participating patients may be important in reducing the antioxidant action of inchinkoto into clinical results.

12. Abstractor and date

Kogure T, 18 May 2020.

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

Reference

Okada K, Kawai M, Hirono S, et al. Evaluation of the efficacy of daikenchuto (TJ-100) for the prevention of paralytic ileus after pancreaticoduodenectomy: a multicenter, double-blind, randomized, placebo-controlled trial. *Surgery* 2016; 159: 1333-41. CENTRAL ID: CN-01153778, Pubmed ID: 26747224

1. Objectives

To evaluate the preventive effects of daikenchuto (大建中湯) for paralytic ileus after pancreaticoduodenectomy.

2. Design

Double-blind randomized controlled trial (DB-RCT)

3. Setting

Nine hospitals.

4. Participants

224 patients who underwent pancreaticoduodenectomy due to duodenal papillary tumor or pancreatic head tumor.

5. Intervention

Arm 1: TSUMURA Daikenchuto (大建中湯) Extract Granules (15g t.i.d for 17 days) (n=112)
Arm 2: Placebo extract granules (15g t.i.d for 17 days)
Of the 17 days mentioned above, the daikenchuto or placebo were fed via tube retained in the duodenum on the day of surgery and on day 1 after surgery.

6. Main outcome measures

Primary outcome measures: Occurrence of paralytic ileus persisting for at least 72 hours after surgery; time from surgery to onset of paralytic ileus.
Secondary outcome measures: QOL evaluation using GSRS; evaluation of abdominal pain and bloating using VAS.

7. Main results

No significant differences were observed between the 2 groups in any of the primary or secondary outcome measures.

8. Conclusions

Daikenchuto does not reduce the occurrence of paralytic ileus after surgery.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse events of at least grade 3 occurred in the daikenchuto group (11.5%) and the placebo group (7.8%), however, most of them were diarrhea and abnormal laboratory values (no significant difference detected).

11. Abstractor's comments

This is a valuable study using a double-blind RCT to analyze the effectiveness of daikenchuto for the prevention of paralytic ileus in a limited patient group, namely pancreaticoduodenectomy (PD) patients. It can be recognized as a rigorous RCT that took bias risk into very careful consideration. The results of the various sub-group analyses showed that among the 23 participants who underwent pylorus-preserving PD (PPPD), time to first flatus was significantly shorter for those in the daikenchuto group than in the placebo group (P=0.034). However, evaluation is difficult because of the small number of cases. There were no other significant differences, so this result would seem to put the brake on any movement to have daikenchuto approved as a preventive for paralytic ileus in the US and elsewhere at the moment. The authors' discussion seems not to contain adequate mention of why on this occasion daikenchuto showed no effectiveness, when its various mechanisms of action have been reported in basic research to date. While daikenchuto is known in Japan as a Kampo preparation useful for the treatment and prevention of paralytic ileus, the approach of the authors in rigorously evaluating a restricted patient group in this way has major implications for the future direction of clinical research into Kampo treatment in Japan.

12. Abstractor and date

Motoo Y, 18 May 2020.

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

Reference

Sato Y, Yamamoto S, Tagami K, et al. Efficacy of Kampo Medicine on Side Effects (muscular pain, arthralgia and paralysis) in TC therapy – Cross-Over study of goshajinkigan and keishikajutsubuto. Recent Progress of Kampo Medicine in Obstetrics and Gynecology. 2015; 32: 68-71. MOL, MOL-Lib

1. Objectives

To evaluate the efficacy of goshajinkigan (牛車腎気丸) and keishikajutsubuto (桂枝加朮附湯) for chemotherapy-related muscular pain, arthralgia, and paralysis in patients with ovarian cancer

2. Design

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

3. Setting

Study sites not stated (Authors' institution: Gifu Prefectural General Medical Center)

4. Participants

Twelve patients on a monthly TC therapy (paclitaxel and carboplatin) postoperatively for ovarian cancer or uterine body cancer

5. Intervention

Arm 1: Administration of goshajinkigan in the chemotherapy cycle after the onset of muscular pain/arthralgia, followed by administration of keishikajutsubuto in the next cycle (GK group)

Arm 2: Administration of keishikajutsubuto in the chemotherapy cycle after the onset of muscular pain/arthralgia, followed by administration of goshajinkigan in the next cycle (KG group)

6. Main outcome measures

Intensity of paralysis, muscular pain (VAS), and arthralgia (VAS) associated with the TC therapy

7. Main results

Paralysis was lessened in slightly more patients in the GK group than in the KG group.
There were greater muscular pain and arthralgia reductions on the visual analog scale (VAS) in the GK group than in the KG group.

8. Conclusions

Keishikajutsubuto is more effective than goshajinkigan for muscular pain and arthralgia as side effects of the TC therapy.

9. From Kampo medicine perspective

None

10. Safety assessment in the article

None

11. Abstractor's comments

This article reports that keishikajutsubuto is more effective for muscular pain and arthralgia after TC therapy than goshajinkigan commonly used currently. This study with a limited sample size provided insufficient results to establish consensus. Further studies, including evaluation of prophylactic use, with larger samples sizes are warranted. Evaluation of long-term use would also be helpful. It is expected that consideration will be given to the clinical use of keishikajutsubuto for muscular pain and arthralgia after the TC therapy.

12. Abstractor and date

Kato Y, 18 May 2020

10. Respiratory Diseases (including Influenza and Rhinitis)

Reference

Kuwamura A, Komasawa N, Takahashi R, et al. Preoperative oral administration of kikyo-to, a Kampo medicine, alleviates postoperative score throat: a prospective, double-blind, randomized study. *Journal of Alternative and Complementary Medicine* 2016; 22: 294-7. CENTRAL ID: CN-01153279, Pubmed ID: 27028745

1. Objectives

To evaluate the effectiveness of kikyoto (桔梗湯) for postoperative sore throat.

2. Design

Double-blind randomized controlled trial (DB-RCT)

3. Setting

One hospital

4. Participants

Seventy adult female patients, either healthy or with slight underlying disease, who underwent surgery under general anesthetic.

5. Intervention

Arm 1: TSUMURA Kikyoto (桔梗湯) Extract Granules 2.5g taken before sleep on the night before surgery, and in the morning on the day of surgery (n=35).

Arm 2: Non-administration group (n=35)

6. Main outcome measures

Sore throat and nausea, immediately after and at 3 and 24 hours after waking from anesthesia recovery.

7. Main results

A significant reduction in the occurrence of sore throat immediately after anesthesia recovery (p=0.02), and a declining trend in sore throat 3 hours after (p=0.16) were observed in the kikyoto group. A reduction in sore throat intensity was also found immediately after recovery (p=0.02) and 3 hours after (p=0.05) in the kikyoto group. No significant difference in nausea was observed in the 2 groups during monitoring.

8. Conclusions

Sore throat from surgery under anesthesia may be alleviated by administering kikyoto before surgery.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No significant difference between the 2 groups in critical events or nausea, etc. was observed.

11. Abstractor's comments

Alleviating wound pain and sore throat after surgery is a very important matter. This is an interesting clinical study designed to alleviate sore throat after surgery under anesthesia by administering kikyoto before surgery. Given that the participants in this study were female patients, further research into the effects of kikyoto on sore throat in male patients is advisable.

12. Abstractor and date

Kato Y, 18 May 2020.

11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Acosta A, Camilleri M, Linker-Nord S, et al. A pilot study of the effect of daikenchuto on rectal sensation in patients with irritable bowel syndrome. *Journal of Neurogastroenterological Motility* 2016; 22: 69-77. Pubmed ID: 26486374

1. Objectives

To evaluate the effects of daikenchuto (大建中湯) on rectal sensation in patients with irritable bowel syndrome (IBS).

2. Design

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

3. Setting

One hospital.

4. Participants

Forty female IBS patients who fulfilled the Rome III criteria.

5. Intervention

Arm 1: TSUMURA Daikenchuto (大建中湯) Extract Granules (15g t.i.d for 14 days) (n=20)
Arm 2: Placebo granules (15g t.i.d for 14 days) (n=20)

6. Main outcome measures

Primary outcome measures:① Feeling of urgency in reaction to 32mmHg intrarectal expansion pressure (quantified on 100mm VAS); ② pain threshold in reaction to bowel expansion
Secondary outcome measures: ① Physiological measures (rectal sensation threshold, etc.); ② clinical measures (bowel movement frequency, etc.) ③ QOL score

7. Main results

No significant differences were observed between the 2 groups in any of the primary or secondary outcome measures.

8. Conclusions

Daikenchuto does not display any significant effect on rectal sensation in patients with IBS.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

The authors mention in the abstract that they evaluated safety, but there is no mention in the results.

11. Abstractor's comments

This report is valuable for having evaluated the effects of daikenchuto in IBS patients using a method of measuring rectal sensation with an intrarectal balloon. The authors raised various reasons for the daikenchuto not demonstrating a significant effect: while the Kampo preparation they used was TSUMURA Daikenchuto (大建中湯) Extract Granules (TU-100), the participants were Americans, who have a different pharmacokinetics to Japanese people; the number of cases was small; the administration period was short; and the daikenchuto dosage was single-dose. It is certainly possible that these factors affected the results of this study. It is unclear whether there would be any significance in repeating a similar DB-RCT, but increasing the number of cases, extending the administration period, and changing the daikenchuto dosage.

12. Abstractor and date

Motoo Y, 18 May 2020.

12. Skin Diseases

Reference

Kobayashi H, Yanagihara S, Tamiya H, et al. The combined effects of Kampo medicines on subjective/objective symptoms in atopic dermatitis patients—A comparative study of unseiin and shimotsuto—. *The Nishinihon Journal of Dermatology* 2016; 78: 171-6. [In Japanese] Ichushi Web ID: 2016282808

1. Objectives

To evaluate the effectiveness of unseiin (温清飲) and shimotsuto (四物湯) for moderate or more severe atopic dermatitis that does not improve with standard treatment.

2. Design

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

3. Setting

Single-center (Osaka City University Hospital)

4. Participants

Sixteen participants who fulfilled the following conditions between February 2012 and December 2013: 1) diagnosed with atopic dermatitis (AD) according to the Japanese Dermatological Association's diagnostic criteria; 2) currently receiving the standard treatment in the Japanese Dermatological Association's AD treatment guidelines (no change in prescription in the first 2 weeks of the trial) and will continue that treatment during the trial; 3) itch is at least 5 on a visual analog scale (VAS: 0-10).

Patients with infectious disease or severe heart, kidney, or endocrine/metabolic disease, and patients currently taking Kampo or herbal medication were excluded.

5. Intervention

Arm 1: Standard treatment and Kracie Unseiin (温清飲) Extract Fine Granules 6.0g b.i.d. (n=8)
Arm 2: Standard treatment and Kracie Shimotsuto (四物湯) Extract Fine Granules 6.0g b.i.d. (n=8)
As a rule, administration for 4 weeks in both arms. No change of drug or dosage during period of administration.

6. Main outcome measures

Kampo medication compliance; subjective symptoms (itch, dryness, sleep disorder evaluated on a VAS); AD severity (measured with severity scoring of AD [SCORAD]); clinical blood tests (serum thymus and activation-regulated chemokine [TARC]; total serum IgE; peripheral eosinophil count, and LDH); specific skin disease QOL scale (Skindex-16: total and sub-scales [symptoms, emotions, functioning]).

7. Main results

One participant dropped out of arm 1 (after taking another Kampo medication). Trial drug compliance satisfactory in both arms 1 and 2. Significant improvements in 3 subjective symptoms were observed in arm 1, but no significant improvement was observed in arm 2. VAS score variation between the 2 groups before and after administration showed significant reduction only for dryness in arm 1 (P＝0.048). SCORAD decreased significantly only in arm 1 before and after administration (P<0.05), however, there was no significant difference in arm 2. There was no significant change in either group in clinical test values. Skindex-16 showed significant improvement in total, symptoms, and emotions in arm 1, and total, emotions, and functioning in arm 2. Variation before and after administration was lower in arm 1 than arm 2, but there was no significant difference between groups.

8. Conclusions

Unseiin alleviates itch and dryness, and improves QOL in AD, and its effects are superior to shimotsuto.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None.

11. Abstractor's comments

This is a clinically significant paper that evaluated in an RCT the effects of unseiin or shimotsuto for AD that had not improved with standard treatment. The 4-week follow-up found more marked improvements in clinical symptoms with unseiin. However, as the authors remark, there was no placebo group for comparison, which unfortunately meant that the study evaluated the effectiveness of the Kampo preparations by before and after comparison. The authors might have obtained greater significant differences in the effects of unseiin and shimotsu if they had increased the sample size, and they might have gleaned some insights into prescription management. The results of a repeated study with a placebo and larger sample size may be promising.

12. Abstractor and date

Kogure T, 18 May 2020.

14. Genitourinary Tract Disorders (including Climacteric Disorders)

Reference

Oh-oka H. Effect of Saireito for Prevention and Improvement of Urethral Stricture after Transurethral Resection of the Prostate. *Kampo Medicine* 2016; 67: 244-50. Ichushi Web ID: 2017003685, J-STAGE

1. Objectives

To evaluate the preventive effect of saireito (柴苓湯) on postoperative urethral stricture.

2. Design

Randomized controlled trial (RCT).

3. Setting

One hospital.

4. Participants

Prostatic hyperplasia patients (142) without overactive bladder, who underwent TUR-P between April 2011 and March 204; received lifestyle guidance at initial consultation, including instruction on fluid intake and sleep hygiene; and were administered an α-blocker as drug therapy. Times since diagnosis ranged from 3.5 to 5.5 (mean 4.3) years, and ages were 68 to 85 (mean 75.5) years.

5. Intervention

Arm 1: Saireito (柴苓湯) administration group (n=70)
Saireito (1g t.i.d before meals for 3 months) from first intake after TUR-P surgery
Arm 2: No administration group (n=72)

6. Main outcome measures

Primary outcome measures examined include preventive effect on urethral stricture after TUR-P surgery; the clinically verified effect of saireito on postoperative urethral stricture; and clinical utility when administering and when not administering saireito in patients who meet and who don't fit the "pattern" indicated for saireito, defined as depressed liver qi transforming into fire, spleen qi deficiency, and water retention.

7. Main results

1) Saireito administration significantly reduced the occurrence of postoperative urethral stricture (P=0.043).
2) Improvement was observed after saireito administration for urethral stricture in 5 out of 8 participants in the no administration group.
3) Comparison of the group without the non-saireito pattern and without medication, with the group with the saireito pattern and with medication showed significantly lower frequency of urethral stricture in the latter (P=0.042).

8. Conclusions

Saireito administration after TUR-P surgery prevents postoperative urethral stricture and its improvement of stricture in clinically ascertained postoperative urethral stricture is acknowledged. It is acknowledged as having most effectiveness for saireito pattern patients.

9. From Kampo medicine perspective

During and after TUR-P, patients are considered to exhibit a half-exterior half-interior pattern; the heat-clearing action of saiko with ogon and the anti-inflammatory action of ogon with bukuryo, also medical insults such as the water dampness caused by perfusate arising from endoscopic surgery, and the urethral ischemia, etc. attributable to resectoscope are considered factors causing postoperative urethral stricture; so saireito, which combines the properties of goreisan, which has a diuretic effect, with shosaikoto, promises effects for postoperative urethral stricture.

10. Safety assessment in the article

The compliance rate across all patients was 88-100% (mean 95%), and there was no dropout due to adverse effect.

11. Abstractor's comments

This is an interesting clinical study designed to clarify the effects of saireito on postoperative urethral stricture. There was 1 clinically verified case of postoperative urethral stricture in the saireito group, and 8 in the no administration group, and the number of confirmed postoperative strictures was significantly smaller in the postoperative saireito administration group, which suggests that saireito administration is a very useful therapy. Hopefully future research will accumulate additional cases and further yield results that take "patterns" into account, and the results from treatment period, etc.

12. Abstractor and date

Kato Y, 18 May 2020.

18. Symptoms and Signs

Reference

Takao Y, Takaoka Y, Sugano A, et al. Shakuyaku-kanzo-to (Shao-Yao-Gan-Cao-Tang) as treatment of painful muscle cramps in patients with lumbar spinal stenosis and its minimum effective dose. *Kobe Journal of Medical Sciences* 2015; 61: 5: E132-7. CENTRAL ID: CN-01140769, Pubmed ID: 27363396

1. Objectives

To evaluate the efficacy and safety of shakuyakukanzoto (芍薬甘草湯) for muscle cramps in patients with lumbar spinal stenosis

2. Design

Randomized controlled trial (RCT)

3. Setting

One university hospital, Japan

4. Participants

Thirty patients with lumbar spinal stenosis

5. Intervention

Arm 1: Oral administration of TSUMURA Shakuyakukanzoto (芍薬甘草湯) Extract Granules 7.5 g (in 3 divided doses)/day for 2 weeks (n=16)

Arm 2: Oral administration of eperisone hydrochloride (dose not specified) for 2 weeks (n=14)

6. Main outcome measures

Frequency of muscle cramps at Week 2 of treatment. Time to maximum therapeutic response.

7. Main results

The frequency of muscle cramps decreased to ≤50% in 14 (87.5%) of the 16 patients in Arm 1, compared with 4 (28.6%) of the 14 patients in Arm 2. Maximum therapeutic response was achieved within 3 days in ≥50% of the patients in Arm 1.

8. Conclusions

The results suggest that shakuyakukanzoto is effective for muscle cramps in lumbar spinal stenosis.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Dizziness was reported in an 80-year-old man with a history of cerebral infarction, and improved after discontinuation of shakuyakukanzoto. No other adverse events were noted.

11. Abstractor's comments

This study evaluated the efficacy and safety of shakuyakukanzoto, compared with eperisone hydrochloride, for muscle cramps in patients with underlying lumbar spinal stenosis. Although the article states that the study consisted of 3 arms (i.e., the above-stated two arms plus Arm 3 [n=28] to determine the minimum effective dose) and was conducted in a total of 58 patients who were randomized to these 3 arms, this randomization to Arm 3 was not further described. Furthermore, regarding the use of a chi-square test for intergroup comparison stated in Figure 2, it is unclear which groups were compared. In addition, it is questionable whether ANOVA used in Figure 3 was an appropriate statistical method. While there have been other reports on the efficacy of shakuyakukanzoto for muscle cramps, this is the first report to specifically evaluate it in patients with lumbar spinal stenosis. Thus, further clinical studies with sufficient sample size and scientifically valid design are warranted.

12. Abstractor and date

Motoo Y, 18 May 2020

19. Post-anesthesia and Postoperative Pain

Reference

Nakae H, Yokoi A, Kodama H, et al. Comparison of the effects on rib fracture between the traditional Japanese medicine jidabokuippo and nonsteroidal anti-inflammatory drugs: a randomized controlled trial. *Evidence Based-Complementary and Alternative Medicine*. 2012; 837958. Pubmed ID: 22888367

1. Objectives

To evaluate the effectiveness and safety of jidabokuippo (治打撲一方) on rib fracture.

2. Design

Randomized controlled trial (RCT).

3. Setting

Three centers (Akita University Hospital and 2 others).

4. Participants

Rib fractures were diagnosed by X-ray and CT images. Patients who could not ingest, who had multiple injuries, or who were examined 4 days or more after the injury occurred were excluded. Young patients under 15 years and pregnant women were also excluded. (n=170)

5. Intervention

Arm 1: TSUMURA Jidabokuippo (治打撲一方) (Dosage and daily frequency not mentioned.) (n=85)

Arm 2: NSAIDs (Loxoprofen, diclofenac sodium, lornoxicam, etodolac, meloxicam, celecoxib, naproxen) (Dosage and daily frequency not mentioned.) (n=85)

In both groups, administration continued until the visual analog scale (VAS) score for pain due to rib fracture were less than 50% of the pre-administration score.

6. Main outcome measures

The study compared the period until the visual analog scale (VAS) score for pain due to rib fracture were less than 50% of the pre-administration score. At the same time, it compared the medical costs required in the 2 groups.

7. Main results

In arm 1, 3 of the patients switched to NSAIDs because their symptoms did not improve, and 1 patient could take jidabokuippo because of its taste, so a total of 4 patients were excluded. In arm 2, 2 of the patients switched to jidabokuippo because their symptoms did not improve, 1 patient could not continue administration due to dyspepsia, and 1 patient discontinued administration before the VAS score fell below 50%, so a total of 4 patients were excluded. In each group 81 participants were analyzed. The median treatment periods were 7 days in arm 1 (7-77 days), and 14 days (5-77 days) in arm 2, meaning a significantly shorter period in arm 1 than arm 2 (P=0.0003). The median medical costs were 509.3 yen (339.5-5,601.8 yen) in arm 1 and 1,581.3 yen (468.3-10,256.4 yen) in arm 2, meaning a significantly lower amount in arm 1 than arm 2 ($P < 0.0001$).

8.Conclusions

Jidabokuippo is more effective in improving pain from rib fracture compared to NSAIDs, and the medical costs required are less.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Dyspepsia or other adverse effects were not observed in the jidabokuippo group, they were observed in 5 out of 85 patients in the NSAIDs group, however, there was no significant difference between the groups (P=0.0588).

11. Abstractor's comments

This clinical trial compared jidabokuippo to NSAIDs for their analgesic effect for pain from rib fracture, making it a valuable clinical trial examining the effects of a Kampo medication in the acute phase. However, the paper does not mention the drug dosages. Furthermore, while it was useful from a medical economy perspective, the medical costs of NSAIDs might be lower than jidabokuippo depending of the choice of NSAID. However, even after taking these points into consideration, jidabokuippo had few adverse effects, it did not require the combined use of gastric mucosal protective agents, etc., and appeared to effectively relieve pain from rib fracture. This clinical trial elucidated the effectiveness of Kampo medications in the field of orthopedics, suggesting further similar research into acute-phase pathologies and prescriptions is desirable.

12. Abstractor and date

Goto H, 18 May 2020.

21. Others

Reference

Endo Y, Ishihara Y, Tsuno S, Matsuda A, et al. Pharmacokinetic Interaction Study of Ranitidine and Daijokito in Healthy Volunteers. *Yonago Acta Medica* 2016; 59: 111-7. CENTRAL ID: CN-01178387, PubMed ID: 27493481

1. Objectives

To verify the effect of daijokito (大承気湯) on the pharmacokinetics of ranitidine.

2. Design

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

3. Setting

Not mentioned. (The author belongs to a university drug therapy department.)

4. Participants

Seven healthy males.

5. Intervention

Arm 1: Ranitidine (300mg) taken after fasting, then after at least 5 days, ranitidine (300mg) and TSUMURA Daijokito (大承気湯) Extract Granules (2.5g) taken after fasting (n=4).

Arm 2: Ranitidine (300mg) and TSUMURA Daijokito (大承気湯) Extract Granules (2.5g) taken after fasting, then after at least 5 days, ranitidine (300mg) taken after fasting (n=3).

6. Main outcome measures

Changes in ranitidine blood concentration over time, up to 12 hours after administration.

7. Main results

The area under the plasma concentration-time curve (AUC) and the maximum plasma concentration (C_{max}) up to 12 hours after ranitidine administration were significantly lower when daijokito was taken compared to when daijokito was not taken.

8. Conclusions

Daijokito lowers ranitidine blood concentration.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No clinically significant adverse reaction was observed in blood tests, vital signs, or physical findings.

11. Abstractor's comments

There have been few findings on the interactions of Kampo and Western medications and there is little awareness in clinical practice of the effects of Kampo medications on Western medications, and vice versa. Against that background, the results indicated by this research are important. While the reduction in plasma drug concentration is not directly connected to the reduction in clinical effect, practitioners must be aware of the possibility that when a Kampo medication is administered the blood concentration of an important therapeutic drug might not reach the clinically required concentration and thereby might have no effect. Similar studies of frequently used Kampo preparations other than daijokito are desirable. In current clinical practice, very large numbers of patients are being administered multiple drugs, not only Kampo medications, whose blood concentrations are difficult to infer: this is a problem. The results of this research point to the constant need in clinical practice to curb the numbers and types of Kampo and Western medications used to the minimum required, and to vigilantly assess whether the anticipated effects are being achieved or not.

12. Abstractor and date

Koike C, 18 May 2020.

Meta-analysis

Reference

Matsunaga S, Kishi T, Iwata N. Yokukansan in the treatment of behavioral and psychological symptoms of dementia: an updated meta-analysis of randomized controlled trials. *Journal of Alzheimer's Disease* 2016; 54: 635-43. PubMed: 27497482

1. Objectives

To evaluate by meta-analysis the effectiveness and safety of yokukansan (抑肝散) for behavior and psychological symptoms of dementia (BPSD).

2. Data sources

PubMed, the Cochrane Library database, PsycINFO, and clinical trial registries (ClinicalTrials.gov, ISRCTN, the WHO portal), all data sourced before April 20, 2016.

3. Research selection

Randomized controlled trials (RCTs) comparing yokukansan with usual treatment or placebo for BPSD in dementia patients were collected.

4. Data sampling

Searches were conducted using keywords such as the following: "dementia" OR "Alzheimer's" OR "Alzheimer" OR "Lewy" AND "Yokukansan" OR "Yigansan". Two of the authors checked the various inclusion and exclusion criteria, and independently analyzed the results using Review Manager (RevMan) ver 5.3.

5. Main outcome measures

The primary outcome measure for effectiveness was overall Neuropsychiatric Inventory (NPI) score; the primary outcome measure for safety was discontinuation of treatment for any reason; and the secondary outcome measure was NPI subscale (delusions, hallucinations, agitation/aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability/emotional instability, aberrant motor activity, nighttime behavior changes, eating changes).

6. Main results

Five RCTs (control groups: 4 RCTs with a no-yokukansan-administration group, and 1 RCT with a placebo group) were included in the meta-analysis. Overall NPI scores for a total of 381 BPSD patients were significantly lower in yokukansan groups compared to control groups (P=0.003). Yokukansan was useful for the BPSD sub-scores delusions, hallucinations, and agitation/aggression. However, yokukansan did not demonstrate effectiveness for Alzheimer's disease on either the overall BPSD score or the subscales. Of the cognitive functions, yokukansan improved activities of daily life (ADL), but did not improve mini-mental state examination (MMSE) scores.

7. Conclusions

Yokukansan is an effective and safe therapeutic drug for BPSD, excluding Alzheimer's disease.

8. From Kampo medicine perspective

None.

9. Safety assessment in the article

There was no significant difference between yokukansan groups and control groups for frequency of adverse effects, discontinuation due to adverse effects, or discontinuation of therapy for any reason.

10. Abstractor's comments

This meta-analysis of the effectiveness and safety of yokukansan, frequently used in clinical settings, is an important report. However, the authors have done the same meta-analysis of the groups in 4 RCTs (Hum Psychopharmacol 2013; 28: 80-6), this time adding the placebo group, which wasn't in the previous meta-analysis. The results are the same: yokukansan was verified to be effective for BPSD, excluding Alzheimer's disease. As the authors also mention, there were a number of problems: they analyzed a small number of RCTs, there were few patients registered to participate in the RCTs, and in particular, the blinding bias risk was high, the periods of yokukansan administration were short (from 4 - 12 weeks), and the concomitant use of antidementia and antipsychotic agents may have affected the results. The authors mention that research outside Japan is desirable, but achieving that goal is not simple. A question for future research is why the effectiveness of yokukansan differs by dementia type.

11. Abstractor and date

Motoo Y, 18 May 2020.

List of Excluded References (Appendix 2017)

Abbreviations: C, The Cochrane Library (CENTRAL); I, Igaku Chuo Zasshi (Japana Centra Revuo Medicana, Ichushi); N, Hand searching Offered by Nikkankyo (the Japan Kampo Medicines Manufacturers Association)

Reasons for exclusion were classified as follows:

1) Clinical studies that were not RCTs or meta-analyses.
2) Studies using medicines that were not approved as Kampo preparations in Japan (Kampo tozai [decoctions], Chinese preparations, and others).
3) Studies using Kampo preparations manufactured before 1985 (their quality being different from that currently available).
4) Studies citing existing RCT papers.
5) Studies with unclear content.
6) Others (reasons are described in the list).

ICD-10	Research Question	Kampo Formula	References	Reason for exclusion	Source
A09	To evaluate the efficacy of goreisan (五苓散) for treatment of acute vomiting and diarrhea in pediatric patients with acute gastroenteritis	goreisan (五苓散)	AHMED S, Uchida R. Children's water metabolism and goreisan: Effects of goreisan extract on acute vomiting and diarrhea mainly in the digestive system in Bangladeshi pediatric patients with acute gastroenteritis: a randomized, double-blind, placebo-controlled study; *Accessible Chinese Medicines for Pediatric Diseases*. 2016; 14:38-43.	5)	N
F03	Efficacy of ninjinyoeito (人参養栄湯) for cognitive and depressive disorders in patients with Alzheimer's disease	ninjinyoeito (人参養栄湯)	Kudoh C, Arita R, Honda M, et al. Effect of ninjin'yoeito, a Kampo (traditional Japanese) medicine, on cognitive impairment and depression in patients with Alzheimer's disease: 2 years of observation. *Psychogeriatrics* 2016; 16: 85-92.	1)	C
G30.1	Efficacy of N Chinpi (N 陳皮) for cognitive impairment	N Chinpi (N 陳皮)	Seki T. Clinical effects of the N Chinpi on the cognitive impairment of patients with Alzheimer's disease. *Journal of Pharmacological Sciences* 2015; 145; 234-6.	2)	I
G30.1	A correlation between monoamines changed by yokusankan (抑肝散) and pharmacological treatment in BPSD	yokukansan (抑肝散)	Takeyoshi K, Kurita M, Nishino S, et al. Yokukansan improves behavioral and psychological symptoms of dementia by suppressing dopaminergic function. *Neuropsychiatric Disease and Treatment* 2016; 12: 641-9.	1)	C
M30.3	Efficacy of ohrengedokuto (黄連解毒湯) for Kawasaki disease	ohrengedokuto (黄連解毒湯)	Hirota A, Senaga R, Kawashima S. The effects of ohrengedokuto extract on Kawasaki disease by a double-blind study. *Journal of Traditional Medicines* 1985; 2:230-1.	3)	I

ICD-10	Research uestion	Kampo Formula	References	Reason for exclusion	Source
M30.3	Efficacy of ohrengedokuto (黄連解毒湯) for Kawasaki disease	ohrengedokuto (黄連解毒湯)	Hirota A, Senaga R, Kawashima S. A double blind study of the effects of ohrengedokuto extract on Kawasaki disease. *Pediatric Clinical* 1985; 38:2329-35.	3)	I
L20.9	Efficacy of shosaikoto (小柴胡湯) in dermatologic conditions	shosaikoto (小柴胡湯)	Nakajima H, Tani T. Chinese medicine therapy for inflammatory dermatosis (2nd report): A clinical trial and a double-blind trial of shosaikoto in the dermatological field. *The Japanese Journal of Clinical and Experimental Medicine.* 1983; 60:2621-7.	3)	I