Evidence Reports of Kampo Treatment

Task Force for Evidence Reports, the Japan Society for Oriental Medicine

Note) The quality of this RCT has not been validated by the EBM committee of the Japan Society for Oriental Medicine.

2. Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anticancer 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, UMIN ID: UMIN000007975 Maeda H, Okada KI, Fujii T, et al. Transition of serum cytokines following pancreaticoduodenectomy: A subsidiary study of JAPAN-PD. Oncol Lett 2018; 16: 6847-53. CENTRAL ID: CN-01651625, Pubmed ID: 30333892, UMIN ID: UMIN000007975 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 (15 g 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, assessment of 27 serum cytokine levels on day 1 after surgery (POD1) and day 3 after surgery (POD3), etc. 7. Main results No significant differences were observed between the 2 groups in any of the primary or secondary outcome measures. Among the POD3/POD1 ratios evaluated for 27 serum cytokines, the POD3/POD1 ratios for IL-4, IL-9, IL-10, PFGF-BB, and TNF- α were significantly higher (*P*<0.05). 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 the prevention of paralytic ileus in a limited patient group, namely for pancreaticoduodenectomy (PD) patients. It is recognized as a rigorous RCT that took risk of bias into very careful consideration. Although the study included a limited number of patients who underwent pylorus-preserving PD (PPPD) (n=23), the results of sub-group analyses showed that time to first flatus was significantly shorter for those in the daikenchuto group than those in the placebo group (P=0.034). In the additional article, the ratio of POD3/POD1 for some of the cytokines was significantly higher in the daikenchuto group than in the placebo group but its significance is unclear. As to why the efficacy of daikenchuto, which has been reported in basic and clinical studies, was not demonstrated in the present study, the authors consider that complex factors are involved in the postoperative course of PD. 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, namely PD patients, has major implications for the future direction of clinical research into Kampo treatment in Japan. 12. Abstractor and date Motoo Y, 18 May 2020, 14 Feb 2021.