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

Reference

Yoshikawa K, Shimada M, Wakabayashi G, et al. Effect of daikenchuto, a traditional Japanese herbal medicine, after total gastrectomy for gastric cancer: a multicenter, randomized, double-blind, placebo-controlled, phase II trial. *Journal of American College of Surgeons* 2015; 221: 571-8.

1. Objectives

To verify the effects of daikenchuto (大建中湯) for intestinal tract motility after total gastrectomy for gastric cancer patients.

2. Design

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

3. Setting

Multiple centers (40 centers), Japan.

4. Participants

Two hundred and seven gastric cancer patients with total gastrectomy (aged 20-85).

5. Intervention

Arm 1: TSUMURA Daikenchuto (大建中湯) Extract Granules 15.0g/day (5g t.i.d. before meals) taken orally (or by tube) from day 1 to 12 after surgery (n=102).
Arm 2: Placebo (TSUMURA & Co.) taken orally (or by tube) for the same period as above (n=105).

6. Main outcome measures

Primary endpoints: time until first flatus and bowel movement after completion of surgery (intratracheal tube removal), and frequency of bowel movements per day after surgery.
Secondary endpoints: QOL evaluated from Gastrointestinal Symptom Rating Scale (GSRS) and Functional Assessment of Cancer Therapy-Gastric (FACT-Ga), serum CRP level, presence or absence of severe disorder in intestinal tract motility after surgery, presence or absence of postoperative ileus.

7. Main results

There were 6 dropouts in arm 1 and 6 in arm 2: 96 patients were analyzed in arm 1 and 99 in arm 2. There was no significant difference in the primary endpoints with the median time until first flatus after tube removal being 68.9 hours in the daikenchuto (DKT) group and 68.3 hours in the placebo group (P=0.95). Similarly, median time until first bowel movement was 94.7 hours in the DKT group and 113.9 hours in the placebo group, showing a shorter tendency in the DKT group (P=0.051). There was no difference between groups for the secondary endpoints QOL and CRP. However, the frequency of intestinal motility disorder was significantly lower in the DKT group on day 12 after surgery (P=0.02). Postoperative ileus was observed in 3 participants in the DKT group and 2 in the placebo group, but there was no difference. Subgroup analysis showed that time until first bowel movement was significantly shorter in the group with lymph node dissection below D2, and the group who took 125g or more of DKT in total (P=0.02 and P=0.01, respectively).

8. Conclusion

Administration of daikenchuto immediately after total gastrectomy promotes early recovery of intestinal motility.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse events of at least grade 3 were observed in six participants in the DKT group (2 cases of diarrhea, etc.) and 3 in the placebo group (1 case of diarrhea, etc.), but there was no significant difference between groups.

11. Abstractor's comments

Daikenchuto (DKT) is commonly used in clinical practice, and is known for its preventive effect for postoperative ileus, this is the first such large scale multicenter trial and has attracted attention for being a double-blind trial using a placebo. The results show that administering DKT from day 1 significantly reduced the frequency of intestinal tract motility disorder on day 12. However, there was no significant difference in the primary endpoints, only a trend toward shorter times until first bowel movement in the DKT group. Yet, the P value of 0.051 was close to a significant difference. Although subgroup analysis showed that time until first bowel movement was significantly shorter in the group that took larger doses of DKT and the group with less surgical invasion among the DKT group. However, it should be clearly noted in the abstract that these significant differences were seen only in subgroup analysis. Nevertheless, this is a valuable paper that verified the efficacy and safety of DKT in a high-quality RCT.

12. Abstractor and date

Motoo Y, 4 January 2017