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

Reference

Shimada M, Morine Y, Nagano H, et al. Effect of TU-100, a traditional Japanese medicine, administered after hepatic resection in patients with liver cancer: a multi-center, phase III trial (JFMC40-1001). *International Journal of Clinical Oncology* 2015; 20: 95-104.

1. Objectives

To evaluate the safety and effectiveness of daikenchuto (大建中湯) for gastrointestinal motility after surgery for liver cancer.

2. Design

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

3. Setting

Twenty-six centers, including University Hospitals, Japan.

4. Participants

Patients (231) with primary or metastatic liver cancer who met the following conditions: 1) resection by laparotomy or laparoscopy, 2) ECOG Performance Status of 0-2, 3) drugs can be taken orally, 4) age of 20 years or more, 5) no chemotherapy or radiotherapy in the 4 weeks before surgery, 6) function in heart, lungs, liver and kidneys retained, 7) can tolerate hepatic resection, 8) serum CRP <2.0 mg/dL.

5. Intervention

Arm 1: TSUMURA Daikenchuto (大建中湯) Extract Granules 15.0g/day (5g t.i.d.) (n=119).
Arm 2: Placebo 15.0g/day (5g t.i.d.) (n=112).
Administration in each group was from 3 days before surgery to the 10^{th} day after surgery, excluding the day of surgery.

6. Main outcome measures

FBM-T (period from decannulation to first bowel movement). Serum CRP and serum ammonia levels. Presence/absence of post-operative ileus or complications. Period of hospital stay after surgery.

7. Main results

In arm 1, 4 participants were excluded due to worsening condition, and 7 were excluded as they could not take the Daikenchuto: 108 patients were evaluated. In arm 2, 11 were excluded due to worsening condition: 101 patients were evaluated. There were no significant differences in clinical features between arms 1 and 2. With FBM-T of 88.2h (95% CI 74.0-94.1) in arm 1, and 93.1h (95% CI 83.3-99.4) in arm 2, it was significantly shorter in arm 1 (P=0.0467). There was no significant difference in CRP ($AUC_{-3\text{-}10\ day}$) or ammonia ($AUC_{-3\text{-}10day}$). 4 patients in arm 1 (3.7%) and 2 in arm 2 (2.0%) had post-operative ileus, and 13 patients in arm 1 (12.0%) and 19 in arm 2 (18.8%) had postoperative complications, but there was no significant difference. There was no significant difference in period of hospital stay after surgery. Analysis of the subgroup of patients with liver damage B found CRP ($AUC_{-3\text{-}10day}$) was 29.9±18.5 in arm 1 and 62.0±56.7 in arm 2, showing a trend toward lower levels in arm 1 (P=0.0587).

8. Conclusion

Taking daikenchuto accelerated improvement of gastrointestinal motility impairment after liver resection and tended to decrease inflammation responses in patients with liver damage B.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Arm 1: Hyperbilirubinemia (1 patient), paralytic ileus (1), diarrhea (1), upper gastrointestinal bleeding (1).
Arm 2: Abdominal pain (3 patients), nausea (1), vomiting (1), intra-abdominal hemorrhage (1). There was no significant difference between the 2 groups.

11. Abstractor's comments

This research paper studied the effects of daikenchuto for gastrointestinal motility impairment after liver resection through a multicenter randomized placebo controlled trial and has a high evidence level. It is praiseworthy for having elucidated once more the effectiveness of this preparation for gastrointestinal motility impairment, which has been suggested in the classic texts, with the period to first bowel movement in the 10 days of observation after surgery having been significantly shortened. It also suggested that by having decreased CRP levels in patients with liver damage B, it improves blood flow and also has an anti-inflammatory effect. Yet, there were no significant differences in secondary endpoints such as postoperative complications or postoperative ileus, etc., so further study (with extension of observation period, etc.) of its clinical significance is required.

12. Abstractor and date

Kogure T, 31 December 2016.