

## 11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

### 21. Others

#### References

Kaido T, Shinoda M, Inomata Y, et al. Effect of herbal medicine daikenchuto on oral and enteral caloric intake after liver transplantation: A multicenter, randomized controlled trial. *Nutrition* 2018 54: 68-75. Pubmed ID: 29747091

#### 1. Objectives

To evaluate the efficacy and safety of daikenchuto (大建中湯) to enhance oral and enteral caloric intake after liver transplantation

#### 2. Design

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

#### 3. Setting

Fourteen institutions including university hospitals, Japan

#### 4. Participants

A total of 112 patients with end-stage liver disease.

Inclusion criteria: Patients aged  $\geq 20$  years who met the indication criteria for liver transplantation at each study center.

Exclusion criteria: Uncontrollable acute infection other than in the liver, uncontrollable malignant disease other than hepatocellular carcinoma, severe postoperative adhesions, use of psychotropic, gastrointestinal prokinetic, or other Kampo medicines, current pregnancy or lactation.

#### 5. Intervention

Arm 1: administration of TSUMURA Daikenchuto (大建中湯) Extract Granules 15.0 g/day (5 g three times daily orally immediately before meals or enterally via tube every 8 hours) (n=57)

Arm 2: administration of placebo 15.0 g/day (5 g three times daily orally immediately before meals or enterally via tube every 8 hours) (n=55)

In both Arms 1 and 2, the treatment was given from postoperative day (POD) 1 to POD 14.

#### 6. Main outcome measures

Primary endpoints: total oral/enteral caloric intake at POD 7, abdominal distension, abdominal pain (numeric rating scale [NRS]).

Secondary endpoints: 1) chronological changes in total oral or enteral caloric intake, 2) chronological changes in abdominal distension and abdominal pain, 3) elapsed time from extubation to first postoperative defecation, 4) quality of life (QOL) assessment using the Gastrointestinal Symptom Rating Scale (GSRS) score, 5) liver regeneration rate between POD 14 and POD 21, 6) incidence of sepsis, 7) incidence of acute cellular rejection, 8) rate of discharge from the hospital within 2 months after liver transplantation, 9) portal vein flow volume and velocity.

#### 7. Main results

Since 2 patients in Arm 1 and 6 patients in Arm 2 dropped out of the study, the analysis was conducted in 55 patients in Arm 1 and 49 patients in Arm 2. Arm 1 and Arm 2 did not significantly differ in total caloric intake ( $972.6 \pm 595.3$  kcal in Arm 1 and  $966.0 \pm 615.7$  kcal in Arm 2;  $P=0.957$ ), abdominal distension ( $3.5 \pm 2.9$ ,  $3.2 \pm 2.8$ ;  $P=0.609$ ), and abdominal pain ( $3.4 \pm 2.5$ ,  $3.0 \pm 2.3$ ;  $P=0.530$ ). As for chronological changes, the total caloric intake at PODs 3, 5, 7, 10, and 14 did not significantly differ between the two arms. However, between POD 3 and POD 10, the rate of increase in the caloric intake was significantly higher in Arm 1 ( $P=0.023$ ). No significant intergroup differences were shown in the chronological changes in abdominal distension or abdominal pain, elapsed time from extubation to first postoperative defecation, QOL, liver regeneration rate, incidence of sepsis, incidence of acute cellular rejection, discharge rate within 2 months after liver transplantation. On the other hand, the portal vein flow volume was significantly higher in Arm 1 than in Arm 2 at POD 10 and POD 14 ( $P=0.047$ ,  $P=0.025$ ). The portal vein flow velocity at POD 14 was significantly higher in Arm 1 than in Arm 2 ( $P=0.014$ ). In a subgroup analysis conducted on 70 patients (i.e., 37 in Arm 1 and 33 in Arm 2) in whom oral or enteral nutrition was started within 3 days postoperatively, the total caloric intake between POD 3 and POD 7 was significantly higher in Arm 1 than in Arm 2 ( $P=0.014$ ). The portal vein flow volume was significantly higher in Arm 1 between POD 0 and POD 14 ( $P=0.010$ ), and the portal vein flow velocity and volume were significantly higher in Arm 1 at POD 14 ( $P=0.032$  and  $P=0.030$ , respectively).

#### 8. Conclusion

Administration of daikenchuto after liver transplantation may enhance total oral and enteral caloric intake in the early postoperative period, in which involvement of increased portal vein flow volume and velocity is suggested.

#### 9. From Kampo medicine perspective

None

#### 10. Safety assessment in the article

There was no significant difference in the frequency of grade  $\geq 3$  major complications between the daikenchuto group and the placebo group.

#### 11. Abstractor's comments

This is a highly objective article describing an analysis from a DB-RCT (14 study centers) on the effect of daikenchuto in enhancing oral/enteral caloric intake in patients who underwent liver transplantation. As the authors described, unfortunately no significant intergroup difference was shown in total caloric intake as a primary endpoint. However, a subgroup analysis among the patients with early resumption of oral/enteral caloric intake showed significantly higher caloric intake in the daikenchuto group. Follow-up of this finding is awaited.

#### 12. Abstractor and date

Kogure T, 1 June 2020.