

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 (茵陳蒿湯) 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 (茵陳蒿湯) 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 (茵陳蒿湯) 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.