

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

Higuchi K, Shimizu Y, Yasumura S, et al. Preventive effect of liver carcinogenesis by juzen-taiho-to in the patients with liver cirrhosis. *Kan-Tan-Sui* 2002; 44: 341-6 (in Japanese) Ichushi Web ID: 2002240679 [MOL](#), [MOL-Lib](#)

1. Objectives

To evaluate the hepatocellular carcinoma-preventive effect of juzentaihoto (十全大補湯) administered for liver cirrhosis.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

A university hospital (Department of Internal Medicine, Toyama Medical and Pharmaceutical University [now Toyama University Hospital]), Japan.

4. Participants

Fifty-two patients with liver cirrhosis due to hepatitis B or C virus. However, patients who had liver cancer within a year after entry into the study and those who received shosaikoto or interferon were excluded.

5. Intervention

Arm 1: juzentaihoto (十全大補湯)-treated (type B, n=8; type C, n=15; type B + type C, n=1).
Arm 2: juzentaihoto (十全大補湯)-untreated (type B, n=5; type C, n=22; type B + type C, n=1).

6. Main outcome measures

Cumulative survival curves were drawn by the Kaplan-Meier method (with difference between curves analyzed by the log-rank test [Mantel-Cox test], Bleslow Gehan-Wilcoxon test, and Peto-Peto-Wilcoxon test). Cumulative hazard curves for hepatocellular carcinoma development were drawn by the Kaplan-Meier method (with difference between curves analyzed by the log-rank test [Mantel-Cox test], Bleslow Gehan-Wilcoxon test, and Peto-Peto-Wilcoxon test). The threshold of liver cancer development was set when liver cancer was first detected on imaging-based clinical diagnosis.

7. Main results

For all liver cirrhosis, the cumulative survival curve showed that vital prognosis was significantly more favorable in arm 1 than arm 2, with chi-square values of 4.066, 6.467, and 5.217 ($P=0.0438$, 0.0190, and 0.0224) by the log-rank test (Mantel-Cox test), Bleslow Gehan-Wilcoxon test, and Peto-Peto-Wilcoxon test, respectively. Analysis of the cumulative survival curve limited to patients with liver cirrhosis type C showed a tendency toward more favorable vital prognosis in arm 1, but no significant between-group difference. For all liver cirrhosis, the cumulative hazard curve for hepatocellular carcinoma development showed significantly lower incidence of hepatocellular carcinoma in arm 1 than in arm 2, with chi-square values of 5.265, 5.578, and 5.921 ($P=0.0218$, 0.0182, and 0.0150) by these tests, respectively. Analysis limited to liver cirrhosis type C revealed significantly lower incidence of hepatocellular carcinoma in arm 1 by the Bleslow Gehan-Wilcoxon test and Peto-Peto-Wilcoxon test (chi-square=4.659, 4.483, respectively; $P=0.0309$, 0.0342, respectively).

8. Conclusions

It is suggested that in liver cirrhosis, administration of juzentaihoto prevents hepatocellular carcinoma development.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned.

11. Abstractor's comments

This study is valuable since hepatocellular carcinoma frequently develops from underlying hepatitis virus infections. This study seems to be similar to the study published in *Methods in Kampo Pharmacology* (2000; 5: 29-33). There were fewer participants in the present study because stricter exclusion criteria were followed: liver cancer development within a year vs half a year in the previous study, and shosaikoto or interferon not permitted. Furthermore, use of diverse statistical tests made the results more meaningful, particularly clinically. Use of a placebo and blinding may have made the results more reliable.

12. Abstractor and date

Tsuruoka K, 15 June 2007, 1 April 2008, 1 June 2010, 31 December 2013.