11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Kainuma M, Furusyo N, Murata M, et al. The effectiveness of traditional Japanese medicine (Kampo), in combination with pegylated interferon α plus ribavirin for patients with chronic hepatitis C: A pilot study. *Journal of Traditional Medicines* 2013; 30: 132-9. Ichushi Web ID: 2014095582 J-STAGE

1. Objectives

To evaluate whether use of Kampo medicines (Shimbuto [真武湯] and Ninjinto [人参湯]) in combination with pegylated interferon α plus ribavirin promotes therapeutic responses in patients with chronic hepatitis C.

2. Design

Randomized controlled trial (RCT).

3. Setting

General clinical department of a university hospital and 5 related hospitals.

4. Participants

Fifty-one patients (20 males and 31 females) diagnosed with chronic hepatitis C. All patients were hepatitis C virus (HCV) antibody-positive and HCV-RNA-positive for more than 6 months. The exclusion criteria were: (1) history of upper gastrointestinal (UGI) bleeding, ascites, hepatocellular carcinoma, hepatic failure, and cirrhosis with a risk of esophageal varices, (2) hemoglobin <11.5 g/dL, leukocyte count $<3 \times 10^3$/L, platelet count $<50 \times 10^9$/L; (3) hepatitis B surface antigen positive or human immunodeficiency virus (HIV) positive; (4) excessive alcohol use (>60 g/day), drug addiction; (5) severe mental disorder; (6) treatment with an antiviral drug and steroid therapy for 12 months before enrollment.

5. Intervention

Arm 1: Patient group treated with Kampo medicines (Group A) (n=26). Oral administration of pegylated interferon α 1.5μg/kg/week plus ribavirin 600–1000 mg/day (600mg for 60kg of body weight or below, 800mg for 60–80kg of body weight, 1000 mg for 80 kg of body weight or over) concurrently with Kampo medicines (mixed formulation of Shimbuto [真武湯] extract and Ninjinto [人参湯] extract, each 5g t.i.d. before each meal).

Arm 2: Control group (Group B)(n=25). Oral administration of pegylated interferon α 1.5μg/kg/week plus ribavirin 600–1000mg/day (600mg for 60kg of body weight or below, 800mg for 60–80kg of body weight, 1000 mg for 80kg of body weight or over) alone.

6. Main outcome measures

Early virological response (EVR), Sustained virological response (SVR).

7. Main results

EVR rate and SVR rate were significantly higher in Group A than in Group B (EVR, 22/26 patients [84.6%] vs 14/25 patients [56.0%], *P*=0.034; SVR, 20/26 patients [76.9%] vs 12/25 patients [48.0%], *P*=0.033). The minimum dose (80% or higher of pegylated interferon α and 60% or higher of ribavirin) was given to 22/26 patients (84.6%) in Group A and 18/25 patients (72.0%) in Group B. SVR rate showed no differences between arms. The dropout rate was significantly different between Group B (5/25 patients [20.0%]) and Group A (0/26 patients; *P*=0.0023).

8. Conclusions

Administration of a mixed formulation of Shimbuto and Ninjinto to patients with chronic hepatitis C who received concurrent administration of pegylated interferon α plus ribavirin decreases the dropout rate and promotes treatment efficacy.

9. From Kampo medicine perspective

The reason for the efficacy of Shimbuto and Ninjinto in patients with chronic hepatitis C has not been identified.

10. Safety assessment in the article

No adverse events were observed in the Kampo-administered group. Five patients dropped out in the control group. Adverse events, vomiting (week 4), interstitial pneumonia (week 10), hyperthyroidism (week 22), and hepatocellular carcinoma (week 19) were observed in 1 patient each. The remaining patient stopped treatment, as no clinical efficacy was observed at week 44.

11. Abstractor's comments

This RCT demonstrated the efficacy of concurrent use of Kampo medicines (mixed formulation of Shimbuto and Ninjinto) with pegylated interferon α plus ribavirin in patients with chronic hepatitis C. The study showed that the treatment decreased the onset rate of adverse events and increased the rate of early virological response and concluded that Kampo medicines were effective. In the original abstract, the line "Kampo medicines were given to Group B" was considered a misprint. This trial was carefully designed including the intent-to-treat (ITT) analysis; however blinding was not mentioned. If the trial had used measures such as blinding to reduce bias, it would have increased confidence in the results. We anticipate further developments.

12. Abstractor and date

Tsuruoka H, 31 March 2017.