11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

References

Harasawa S, Miyoshi A, Miwa T, et al. Double-blind multicenter post-marketing clinical trial of TJ-43 TSUMURA Rikkunshi-to for the treatment of dysmotility-like dyspepsia. *Igaku no Ayumi* (*Journal of Clinical and Experimental Medicine*) 1998; 187: 207-29 (in Japanese). Ichushi Web ID: 1999085057

Harasawa S. The role of rikkunshito against NUD (non-ulcer dyspepsia) – especially its efficacy in dysmotility-like NUD*. *Progress in Medicine* 1999; 19: 843-8 (in Japanese). MOL, MOL-Lib

Harasawa S. Evidence from an RCT of rikkunshito (六君子湯) for epigastric complaints*. *Kampo Igaku* (*Science of Kampo Medicine*) 2011; 35: 113-7 (in Japanese).

1. Objectives

To evaluate the efficacy and safety of TJ-43 TSUMURA Rikkunshito (六君子湯) more objectively in patients with dyspepsia caused by dysfunction of the upper gastrointestinal tract.

2. Design

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

3. Setting

A total of 54 institutions obtained approval of Institutional Review Boards, Japan.

4. Participants

Two hundred and ninety-six patients (30–80 years old) with a chief complaint of persistent or intermittent (for more than 4 weeks) dysmotility-like dyspepsia, characterized by anorexia (or poor appetite), gastric distress, and heavy stomach feeling (presumably due to dysfunction of the upper gastrointestinal tract), and indicating some "*kyo-sho* (虚証, deficiency pattern)" conditions such as gastroptosis, physical weakness.

5. Intervention

Arm 1: oral administration of TSUMURA Rikkunshito (六君子湯) Extract Granules (TJ-43) 2.5 g t.i.d. before or between meals for 2 weeks (n=147).

Arm 2: oral administration of low-dose (1:40 dilution) TSUMURA Rikkunshito (六君子湯) Extract Granules 2.5 g t.i.d. before or between meals for 2 weeks (n=149).

6. Main outcome measures

Five symptoms associated with dysmotility-like dyspepsia (anorexia, abdominal distension, stomach discomfort, heavy stomach feeling, and nausea).

Three symptoms associated with ulcer-like dyspepsia (upper abdominal/epigastric pain, heartburn or pyrosis, and eructation).

7. Main results

A total of 235 subjects (TJ-43 group, n=118; low-dose group, n=117) were included for analysis of efficacy. Dysmobility-like dyspepsia symptoms were improved in 59.3% of the TJ-43 group and 40.2% of the low-dose group; overall symptoms including ulcer-like dyspepsia symptoms were also improved in 60.2% of the TJ-43 group and 41.0% of the low-dose group (both P=0.004). These indicate that efficacy is significantly higher in the TJ-43 group. Furthermore, a significantly higher percentage of the TJ-43 group than the low-dose group (58.8% versus 39.3%) deemed the treatment useful (P=0.003).

8. Conclusions

The safety and effectiveness of TJ-43 was validated for the treatment of dysmotility-like dyspepsia in this double-blind study. We therefore conclude that TJ-43 Rikkunshito is clinically useful.

9. From Kampo medicine perspective

In this study, the inclusion criteria were "deficiency pattern" symptoms (i.e., decreased tone of abdominal wall, subjective/objective splashing sound, gastroptosis tendency, and mental/physical weakness) and the exclusion criteria were "*jitsu-sho* (実証, excess pattern)" symptoms (i.e., mental and physical strength, massive and muscular body, and reddish face).

10. Safety assessment in the article

Safety problems were detected in 2 cases in the TJ-43 group (diarrhea, elevated GOT) and 2 in the low-dose group (diarrhea, elevated GOT/GPT). Adverse effects (defined as symptoms undeniably caused by the drug) occurred in 7 of the TJ-43 group and 7 of the low dose group. None were serious.

11. Abstractor's comments

Use of low-dose TJ-43 in the control group and use of Kampo diagnostic considerations when selecting the inclusion and exclusion criteria are appreciated. Improvement in "*kyo-sho*" symptoms are described in Harasawa's report (1999, mentioned above). Another report of Harasawa (2011) is a sub-group analysis (rikkunshito group [n=40] and control group [n=35]) based on the Rome III criteria (2006). Patient backgrounds were similar in both groups, and the study demonstrated significant difference in the actions of rikkunshito. However, interpretations of the study must take heed of the fact that any bias from 'unknown factors', the weakness of the subgroup analysis, is not clearly identified.

12. Abstractor and date

Arai M, 15 June 2007, 1 April 2008, 1 June 2010, 31 December 2012, 31 December 2013.