11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Sasaki D, Uehara A, Hiwatashi N, et al. Clinical efficacy of keishikashakuyakuto for irritable bowel syndrome - a multicenter, randomized, parallel-group clinical trial -*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Medicine*) 1998; 75: 1136-52 (in Japanese). Ichushi Web ID: 1998224171 MOL, MOL-Lib

1. Objectives

To evaluate the efficacy and safety of keishikashakuyakuto (桂枝加芍薬湯) for irritable bowel syndrome.

2. Design

Double-blinded randomized controlled trial (DB-RCT).

3. Setting

Twenty university medical schools (including Tohoku University [Third Department of Internal Medicine, Tohoku University Hospital]; Tokai University [Sixth Department of Internal Medicine, Tokai University Hospital]; Kyushu University [Department of Psychosomatic Medicine, Kyushu University Hospital]), 53 hospitals, and 3 clinics (76 institutions in total), Japan.

4. Participants

Two hundred and eighty-six patients (age, 15–75 years) who were diagnosed with irritable bowel syndrome at one of the participating institutions and gave oral or written consent to participate in the study. Exclusion criteria were as follows: lactose intolerance; complications that might influence the evaluation; serious complications of heart, liver, kidney, or blood; pregnancy (known or possible); lactation; ineligibility as determined by the investigators.

5. Intervention

Arm 1: treatment with Kanebo Keishikashakuyakuto (桂枝加芍薬湯) Extract Fine Granules 2.0 g t.i.d. (n=148).

Arm 2: treatment with placebo (granules containing a small amount of keishikashakuyakuto extract) (n=138).

6. Main outcome measures

Bowel movement abnormalities (abnormal stool properties, number of bowel movements, and feeling of incomplete evacuation), gastrointestinal symptoms (abdominal pain, abdominal bloating, flatulence, borborygmus, anorexia, nausea/vomiting, heartburn, and belching), laboratory findings (hematology, blood biochemistry, and urinalysis), and physical findings (blood pressure, body weight, and presence and degree of edema).

7. Main results

Outcomes were evaluated after 4 weeks, or 8 weeks of treatment if the response at 4 weeks was inadequate. Final global improvement ratings were not significantly different between arms 1 and 2. As for abdominal pain, rates of “moderate” or better improvement tended to be higher in arm 1 than in arm 2 (P=0.051). Stratified analysis of improvement of abdominal pain according to the subtypes of disease revealed that, in the diarrhea subtype, improvement rating tended to be higher (P=0.090) and rate of “moderate” or better improvement was significantly higher (P=0.037) in arm 1. There were no significant differences between arms 1 and 2 in bowel movement abnormalities or gastrointestinal symptoms. In all, 17 and 7 adverse drug reactions occurred in 13 keishikashakuyakuto-treated patients and 6 controls, respectively.

8. Conclusions

Keishikashakuyakuto is an effective and safe agent for treating abdominal pain associated with irritable bowel syndrome, especially in patients with the diarrhea subtype.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Keishikashakuyakuto was “safe” in 110 of 124 patients (88.7%) in the keishikashakuyakuto group, and 98 of 108 (90.7%) in the control group; there was no statistically significant between-group difference in safety.

11. Abstractor’s comments

This is a well-designed clinical study conducted as a multicenter randomized parallel-group trial. Since keishikashakuyakuto is an agent with a relatively early onset of action, it is clinically necessary to monitor the course of action of this agent, including the time of action onset. Also, from a Kampo medicine perspective, discussions on the relationships between the physique or diathesis and the efficacy, would make the study more valuable.

12. Abstractor and date

Arai M, 22 October 2008, 6 January 2010, 1 June 2010, 31 December 2013.