11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

References

Miyoshi A, Masamune O, Fukutomi H, et al. The clinical effect of TSUMURA Daio-Kanzo-To Extract Granules for ethical use (TJ-84) on constipation using double blind design. *Shokakika* (*Gastroenterology*) 1994; 18: 299-312 (in Japanese with English abstract). Ichushi Web ID: 1994189708

Miyoshi A, Masamune O, Fukutomi H, et al. The clinical effect of TSUMURA Daio-Kanzo-to Extract Granules for ethical use (TJ-84) against constipation based on the new standard. *Shokakika* (*Gastroenterology*) 1996; 22: 314-28 (in Japanese with English abstract). Ichushi Web ID: 1996228578

Harasawa S, Miyoshi A. Reevaluation of Kampo medicine in patients with constipation - efficacy of Daio-kanzo-to -. *Shokakigan* (*Japanese Journal of Cancer of the Digestive Organs*) 1996; 6: 271-7 (in Japanese with English abstract). Ichushi Web ID: 1997060417

1. Objectives

A preceding double-blinded controlled trial of daiokanzoto (大黄甘草湯), compared with placebo, in the treatment of constipation found it was effective against constipation, but not useful (no details available). The objective of this study was to reexamine the effects of daiokanzoto on constipation using a newly-defined assessment standard and the same results mentioned above.

2. Design

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

3. Setting

Seven university medical schools (including Tokyo Women's Medical University [Second Department of Internal Medicine, Tokyo Women's Medical University Daini Hospital]; Tokai University School of Medicine [Sixth Department of Internal Medicine]; Kyoto University [First Department of Internal Medicine, Faculty of Medicine]) and 19 hospitals (26 institutions in total), Japan.

4. Participants

One hundred and fifty-six patients who had 3 or fewer bowel movements per week and complaints of constipation; sought therapy; and consented to participate in the study. Exclusion criteria were: age 15 or younger, constipation caused by organic disease; diagnosis of hypertension and severe edema; pregnancy, lactation, or signs of pregnancy, lactose intolerance, serious complications; patients otherwise considered ineligible by the treating physician.

5. Intervention

Arm 1: treatment with usual-dose TSUMURA Daiokanzoto (大黄甘草湯) Extract Granules 2.5 g t.i.d. (containing 1.5 g/day of extract powder) (n=53).

Arm 2: treatment with low-dose TSUMURA Daiokanzoto (大黄甘草湯) Extract Granules 2.5 g t.i.d. (containing 0.5 g/day of extract powder) (n=49).

Arm 3: treatment with placebo (excipient only) 2.5 g t.i.d (n=54).

6. Main outcome measures

Improvement in bowel movement rating, improvement in subjective and objective symptoms (global rating), efficacy, safety, and utility (global rating).

7. Main results

Outcomes were assessed after 2 weeks of treatment, using the new standard that takes "excessive response to test drugs into account. After excluding 10 withdrawals, 146 patients (47 in arm 1, 49 in arm 2, and 50 in arm 3) were included in the analysis. As for final global improvement, "marked improvement" was observed in 43.2%, 31.7%, and 27.7% of patients in arm 1, arm 2, and arm 3, respectively, and "moderate improvement" in 36.8%, 24.4%, and 14.9%, respectively; the differences among three arms ($P<0.05$) and between arms 1 and 3 ($P<0.01$) were significant. Final global improvement rate was high in arm 1. In addition, ratings of efficacy ($P<0.001$) and utility ($P<0.01$) were also high in arm 1.

8. Conclusions

Compared with placebo, Daiokanzoto had significantly higher final global improvement rating, efficacy, and utility (global rating) and was confirmed to be an effective and useful drug for treating constipation. The safety of this drug was apparent over the 2-week period of treatment.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Test drugs were characterized as "having no safety problem" in 91.5% of patients in arm 1, 93.9% in arm 2, and 96.0% in arm 3; as "having a mild safety problem" in 8.5%, 6.1%, and 0%, respectively; and as "having a moderate safety problem" in 0%, 0%, and 4%, respectively. There were no significant among-arm differences. No abnormal changes in laboratory data occurred.

11. Abstractor's comments

Using the new diagnostic standard, Miyoshi et al (1996) reevaluated the data of the preceding paper (Miyoshi et al [1994]). This is a highly valuable paper reporting a well-designed clinical study. Discussion from Kampo medicine perspective of cases with excessive response would make the content more meaningful. Studies that produce high-quality evidence, like this one, need to be developed for other Kampo preparations.

12. Abstractor and date

Arai M, 10 November 2008, 1 June 2010, 31 December 2013.