

18. Symptoms and Signs

References

Kumada T, Kumada H, Yoshiba M, et al. Effects of Shakuyaku-kanzo-to (Tsumura TJ-68) on muscle cramps accompanying cirrhosis in a placebo-controlled double-blinded parallel study. *Rinsho Iyaku (Journal of Clinical Therapeutics and Medicine)* 1999; 15: 499-523 (in Japanese with English abstract). Ichushi Web ID: 1999184114 [MOL](#), [MOL-Lib](#)

Kumada T, Kiriyaama I, Sone Y, et al. EBM-based Kampo therapy for gastrointestinal diseases 3. Efficacy of shakuyakukanzoto for “muscle cramps in the calves” associated with hepatic cirrhosis*. *Nihon Toyo Igaku Zasshi (Kampo Medicine)* 2003; 54: 536-8 (in Japanese) [CiNii](#)

1. Objectives

To evaluate the efficacy and safety of shakuyakukanzoto (芍薬甘草湯) for relief of muscle cramp.

2. Design

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

3. Setting

A total of 23 nationwide facilities including university hospitals (departments of internal medicine and gastroenterology), Japan.

4. Participants

One-hundred and twenty-six patients with 2 or more episodes of muscle cramp weekly during the observation period (4 or more bi-weekly), aged ≥ 20 years and ≤ 70 years. These patients were also taking other drugs for a variety of problems including serious hepatic, renal, and cardiac diseases, pregnancy, hepatic failure, complications of hepatocellular carcinoma, electrolyte abnormality, and hypertension. After excluding 12 ineligible patients and 13 with incomplete data, 101 patients were included for statistical evaluation.

5. Intervention

Arm 1: administration of 7.5 g/day of TSUMURA Shakuyakukanzoto (芍薬甘草湯) Extract Granules in 3 divided doses (before meals) for 2 weeks following a 2-week observation period (n=65).

Arm 2: administration of the same dose of placebo granules at the same frequency for 2 weeks following a 2-week observation period (n=61).

6. Main outcome measures

Frequency of episodes of muscle cramp, duration of each episode, severity of pain (at completion of the study compared with baseline values determined during the observation period).

7. Main results

The percentage of patients with frequency of muscle cramp episodes rated “improved” or higher was significantly larger in the shakuyakukanzoto group than in the placebo group (67.3% vs 37.5%, respectively). The percentage of patients with improved final global rating, which takes duration of each episode and severity of pain into account, was significantly larger in the shakuyakukanzoto group (69.2% vs 28.6%, respectively). The percentage of patients with a utility rating of “useful” or higher was also significantly larger in the shakuyakukanzoto group (63.3% vs 34.1%, respectively).

8. Conclusions

Shakuyakukanzoto is a clinically useful Kampo formulation with excellent efficacy and safety for muscle cramp.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse drug reactions occurred in 7 patients (14.3%) receiving shakuyakukanzoto and 2 patients (4.9%) receiving placebo. The main adverse drug reaction was pseudoaldosteronism in the shakuyakukanzoto group and gastrointestinal symptoms in the placebo group. No serious adverse drug reactions occurred.

11. Abstractor’s comments

This original article re-evaluates shakuyakukanzoto. The larger total amount of kanzo, contained in shakuyakukanzoto, is associated with higher incidence of pseudoaldosteronism. Since in the present study incidence of adverse drug reactions tended to be higher in the shakuyakukanzoto group, although there was no significant between-group difference in incidence, reduction in the dose is recommended in the future.

12. Abstractor and date

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