5. Psychiatric/Behavioral Disorders

References

Shimada Y, Terasawa K, Yamamoto T, et al. A well-controlled study of choto-san and placebo in the treatment of vascular dementia. *Wakan Iyakugaku Zasshi (Journal of Traditional Medicines)* 1994; 11: 246–55. Ichushi Web ID: 1996055624

Shimada Y, Terasawa K, Yamamoto T, et al. Efficacy of choto-san on vascular dementia: A well, placebo-controlled study. *Wakan Iyakugaku Zasshi* (*Journal of Traditional Medicines*) 1994; 11: 370–1 (in Japanese) Ichushi Web ID: 1996075788

1. Objectives

To evaluate the efficacy of chotosan (釣藤散) in the treatment of vascular dementia.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Multicenter clinical trials involving Toyama Medical and Pharmaceutical University Hospital, Kagoshima University, and three general hospitals, Japan.

4. Participants

Sixty patients (9 males and 51 females; mean age, 78.9 years, including both inpatients and outpatients) who satisfied the DSM-III-R criteria for dementia, were diagnosed with cerebrovascular dementia, had Carlo Loeb modified ischemic scores of ≥ 5 points, were in stable general health, and participated in the study with the consent of one or more family members.

5. Intervention

Arm 1: TSUMURA Chotosan (釣藤散) Extract Granules 2.5 g t.i.d. after meals for 12 weeks (6 males and 26 females).

Arm 2: TSUMURA-manufactured placebo composed of such ingredients as lactose, dextrin, maltose, and cellulose, indistinguishable in appearance (color) and taste from chotosan (釣藤散), as determined before the trial, 2.5 g t.i.d. after meals for 12 weeks (3 males and 25 females).

6. Main outcome measures

Subjective symptoms, neurological manifestations, psychiatric manifestations, severity, and improvement in impaired activities of daily living; dementia status evaluated using the Revised Hasegawa Dementia Scale (HDS-R), every 4 weeks; overall safety and usefulness, evaluated at 12 weeks after the start of treatment.

7. Main results

Of 60 patients, 57 completed treatment (31 with chotosan and 26 with placebo). The following measures were significantly improved in patients receiving chotosan: global improvement rating ($P<0.05$, $P<0.01$, and $P<0.01$ at 4, 8, and 12 weeks, respectively); usefulness ($P<0.01$ at 12 weeks); subjective symptoms ($P<0.05$, $P<0.01$, and $P<0.01$ at 4, 8, and 12 weeks, respectively); psychiatric manifestations ($P<0.05$, $P<0.01$, and $P<0.01$ at 4, 8, and 12 weeks, respectively); and activities of daily living ($P<0.05$, $P<0.05$ at 4 and 12 weeks, respectively). Improvement of neurological manifestations did not significantly differ between arms at 4, 8, and 12 weeks. Subjective symptoms (“dizziness,” “shoulder muscle stiffness,” and “palpitations”) and psychiatric manifestations (“interest in TV programs and books,” “lack of expression,” and “disorientation”) were significantly improved in the chotosan group. Chotosan significantly improved HDS-R from 15.34±3.76 at baseline to 16.65±4.43 at 4 weeks ($P<0.05$), 17.94±4.79 at 8 weeks ($P<0.01$), and 19.39±5.71 at 12 weeks ($P<0.01$), although there was no significant difference between arms.

8. Conclusions

Chotosan is effective for cerebrovascular dementia.

9. From Kampo medicine perspective

Chotosan has traditionally been used to treat headache and dizziness in patients who are past middle age and relatively weak physically. These symptoms are considered to be indicators of cerebral arteriosclerosis and cerebrovascular disorder by modern medicine. The present study succeeded in objectively evaluating the clinical efficacy of chotosan for cerebrovascular dementia.

10. Safety assessment in the article

Treatment was discontinued in 1 patient receiving chotosan (3.1%) who had a history of hepatopathy and whose oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT) levels increased during treatment and returned to normal after treatment discontinuation. Another patient receiving chotosan (3.1%) had a decrease in potassium that was too mild to affect treatment. There was no significant difference in overall safety between arms.

11. Abstractor’s comments

This is a well-designed RCT that generated high-quality evidence. There is much to learn from this study, which included blinding, included a placebo arm, considered dropouts, and analyzed safety and usefulness in an intent-to-treat population. A larger-scale RCT performed later to re-evaluate efficacy (Terasawa K, Shimada Y, Kita T, et al. Choto-san in the treatment of vascular dementia: A double blind, placebo-controlled study. *Phytomedicine* 1997; 4: 15–22.) is also informative.

12. Abstractor and date

Tsuruoka K, 22 September 2008, 31 December 2013.