18. Symptoms and Signs

Reference

Matsushita S, Ueda S, Ouchi Y, et al. Usefulness of Chotosan (TJ-47) for relieving the accompanying symptoms and sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension*. *Geriatric Medicine* 1995; 33: 1333-41 (in Japanese). Ichushi Web ID: 1996118416

1. Objectives

To evaluate the efficacy and safety of chotosan (釣藤散) for relieving the symptoms and sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension.

2. Design

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

3. Setting

Department of Geriatrics, The University of Tokyo Hospital; Department of Geriatrics, Nippon Medical School Hospital; and five hospitals, Japan.

4. Participants

Twenty-two patients with sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension, and the accompanying symptoms, such as headache, heaviness of head, and dizziness.

5. Intervention

Arm 1: treatment with TSUMURA Chotosan (釣藤散) Extract Granules 2.5 g t.i.d. orally between meals for 12 weeks (n=11).

Arm 2: treatment with dilazep hydrochloride 50 mg t.i.d. orally between meals for 12 weeks (n=11).

6. Main outcome measures

Subjective symptoms (headache, heaviness of head, dizziness, stiff shoulders, palpitation, chest distress, hot flashes, tinnitus, numbness, cold extremities, and fatigue), psychiatric symptoms disorientation, loss of memory, bad mood, depression, anxiety and irritation, deranged speech, and decreased motivation), and blood pressure measured at baseline and 4, 8, and 12 weeks from the start of the study.

7. Main results

Because one patient in arm 2 withdrew due to a staggering walk, 11 patients in arm 1 and 10 in arm 2 were included in the analysis of results. Headache, heaviness of head, dizziness, stiff shoulders, depression, and anxiety and irritation were significantly improved in arm 1 compared to arm 2. Blood pressure in the sitting position was lowered significantly from 156/91 mmHg at baseline to 142/84 mmHg at 12 weeks in arm 1. In contrast, no significant change in blood pressure was observed in arm 2 (149/84 mmHg at baseline to 146/82 mmHg at 12 weeks) and there was no between-arm difference. When the change in blood pressure was subjectively rated on a 4-point scale (1: lowered - 4: elevated), the improvement at 12 weeks was significantly better in arm 1 than in arm 2.

8. Conclusions

Chotosan, compared with dilazep hydrochloride, is more effective for relieving the symptoms and sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension, as well as for lowering blood pressure.

9. From Kampo medicine perspective

To determine which pattern (*kyo-sho* [虚証, deficiency pattern], *chukan-sho* [中間証, intermediate pattern], or *jitsu-sho* [実証, excess pattern]) each participant had, diagnoses were made using the *jitsu-sho* scoring system of the *kyo-jitsu* assessment. All the participants were diagnosed as having *kyo-sho*, making it impossible to determine the efficacy of chotosan for these three different patterns. In addition, no correlation was revealed by stratified analysis of global improvement ratings according to the indication of chotosan, including severity measures of headache, heaviness of head, dizziness, stiff shoulders, palpitation, choking feeling in the chest, hot flashes, tinnitus, disorientation, memory decline. There was no correlation between the degree of blood pressure lowering and the *jitsu-sho* score or the *sho*-related measures.

10. Safety assessment in the article

One patient in arm 1 developed mild elevation of lactose dehydrogenase (LDH) after 12 weeks of treatment. One patient in arm 2 discontinued the treatment due to staggering walk.

11. Abstractor's comments

This is an innovative clinical study that attempted to evaluate the efficacy of chotosan based on a consideration of *sho*, and determined objectively the efficacy of chotosan for relieving the symptoms and sequelae of cerebrovascular disease, chronic cerebrovascular insufficiency, or hypertension. However, each arm included only 11 patients and even fewer patients were included in the analysis of symptom improvement. This may explain why a significant difference was not detected. Furthermore, dilazep hydrochloride, which was used as a control, may cause, although uncommonly, adverse reactions such as headache, dizziness, and palpitation. The selection of this drug as a control would seem to be inappropriate because its adverse reactions are also among the variables used to measure outcome. Yet this is a remarkable clinical study that demonstrated the efficacy of chotosan in spite of the small number of patients.

12. Abstractor and date

Goto H, 18 September 2008, 1 June 2010.