9. Cardiovascular Diseases

Reference

Otomo E, Togi H, Kogure K, et al. Clinical usefulness of TSUMURA Orengedokuto for the treatment of cerebrovascular disease: a well-controlled study comparing TSUMURA Orengedokuto versus Ca hopantenate, using sealed envelopes for allocation*. *Geriatric Medicine* 1991; 29: 121–51 (in Japanese). Ichushi Web ID: 1991224400

1. Objectives

To evaluate the efficacy and safety of orengedokuto (黄連解毒湯) for relieving psychiatric symptoms in patients with late effects of cerebrovascular disease.

2. Design

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

3. Setting

Thirty university hospitals (including departments of neurology of Iwate Medical University, Tohoku University School of Medicine, and Gunma University Faculty of Medicine) and 20 general hospitals, Japan.

4. Participants

One hundred and forty-eight post-stroke patients with psychiatric symptoms due to cerebral infarction, cerebral hemorrhage, or stoke with unknown origin.

5. Intervention

Arm 1: TSUMURA Orengedokuto (黄連解毒湯) Extract Granules 2.5 g t.i.d. orally after meals for 12 weeks (n=81).

Arm 2: calcium hopantenate 500 mg t.i.d. orally after meals for 12 weeks (n=67).
The treatment was discontinued at the time of disappearance of symptoms.

6. Main outcome measures

Psychiatric symptoms (apathy; problematic behaviors; emotional, intellectual, and mental disturbances), subjective symptoms (heaviness of head, headache, hot flush, etc.), neurological symptoms (aphasia, dysarthria, motor paralysis, etc.), and impairment in activities of daily living (sitting up, standing, walking, etc.) were evaluated at baseline and after 4, 8, and 12 weeks of treatment. Hasegawa's dementia scale and laboratory tests were performed at baseline and after 12 weeks of treatment.

7. Main results

Five patients in arm 1 (1 with concomitant cancer, 3 lost to follow-up after the initial treatment, and 1 who acted contrary to envelope method) were excluded from the study. The safety analysis included 76/67 patients (arm 1/arm 2) and efficacy analysis included 74/67. The percentages of patients who achieved moderate-or-greater and mild-or-greater overall improvement in psychiatric symptoms were significantly higher in arm 1 than in arm 2 at 8 and 12 weeks. There were no between-arm differences in each of the global improvement scores for subjective symptoms, neurological symptoms, and impairment in activities of daily living. The percentages of patients who achieved moderate-or-greater improvement in abulia at 4 weeks and moderate-or-greater and mild-or-greater improvements at 8 and 12 weeks were significantly higher in Arm 1 than in arm 2. Among other items of spontaneity, reduced expression of desires, decreased interest in others, decreased interest in performing activities of daily living, decreased interest in housekeeping, leisure activities, hobbies, etc., and inability to communicate with others were significantly improved at 12 weeks compare with at baseline in both arms to a similar extent.

8. Conclusions

Orengedokuto is effective for relieving psychiatric symptoms in patients with cerebrovascular disease and its efficacy is comparable to that of cerebral metabolic activator.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Three patients in arm 1 (3.9%) discontinued treatment, respectively, because of nausea and abdominal distention, chest discomfort, and headache. In arm 2, one patient (1.5%) discontinued treatment due to fever and disturbances in consciousness. Changes in laboratory data were within normal range in both arms.

11. Abstractor's comments

This clinical study revealed the effects of orengedokuto on psychiatric symptoms in patients with late effects of cerebrovascular disease in a controlled trial using sealed envelopes for allocation. As noted by the authors, the evaluation of the efficacy of orengedokuto may have been influenced by the following two factors: i) the designation of calcium hopantenate as a powerful drug around the same time as this study was performed, which biased selection of cases; and ii) lower efficacy of calcium hopantenate in the present trial than in other clinical trials. Despite the limitations on evaluation, this clinical study was excellent and demonstrated comparable efficacy of orengedokuto and a cerebral metabolic activator.

12. Abstractor and date

Goto H, 12 September 2008.