Cardiovascular disease

Reference

Ito K, Yamamoto H, Saibara T, et al. The usefulness of Kanebo Hachimijiogan in patients with hypertension or cerebrovascular disease (excluding acute phase symptoms) and their concomitant symptoms: a multicenter, double-blind, crossover study. *Shindan to Chiryo* (*Diagnosis and Treatment*) 1988; 76: 1096-114 (in Japanese). Ichushi Web ID: 1989037772

1. Objectives

To evaluate the efficacy and safety of hachimijiogan (八味地黄丸) in patients with hypertension or cerebrovascular disease and their concomitant symptoms.

2. Design

Double-blind, randomized, controlled trial (crossover design) (DB-RCT-cross over).

3. Setting

A total of 13 hospitals (Kochi Medical School Hospital and 12 community hospitals).

4. Participants

Patients with hypertension or cerebrovascular disease (excluding acute phase symptoms) (n=105) were recruited. After excluding 2 patients whose data could not be analyzed, 103 were included and treated with either hachimijiogan (n=53) or placebo (n=50). Data were collected on patients with hypertension (n=60), cerebral infarction (n=23), intracranial hemorrhage (n=1), cerebral atherosclerosis (n=18), and cerebral stroke sequelae (n=1).

5. Intervention

Arm 1: Kanebo Hachimijiogan (八味地黄丸) Extract Fine Granules (EK-7) 2 g t.i.d. before meals for 4 weeks and then switched to placebo for 4 weeks.

Arm 2: Placebo granules 2 g t.i.d. before meals for 4 weeks and then switched to Kanebo Hachimijiogan (八味地黄丸) Extract Fine Granules (EK-7) for 4 weeks.

6. Main outcome measures

Improvement in each subjective symptom (mental and neurological) was evaluated before and after 2, 4, 6, and 8 weeks of administration; general improvement, overall safety, and usefulness were evaluated after 4, and 8 weeks of administration.

7. Main results

General improvement and usefulness were significantly greater in arm 1 than in arm 2 in the latter half of treatment (i.e., 4 to 8 weeks); treatment was more than slightly useful in significantly more patients in the hachimijiogan arm (arm 1; 70%) than in the placebo arm (arm 2; 51%) (P<0.05). Improvement in neurological symptoms and subjectively evaluated improvement were significantly greater in arm 1 in the latter half of treatment (P<0.05). As for individual symptoms, tinnitus in the first half of treatment and cold and itchy feeling in the limbs and leg pain in the latter half of treatment showed greater improvement in arm 1. In arm 2, nausea improved in the latter half of treatment, which is seemingly due to a reversal of gastrointestinal problems by hachimijiogan. Analysis after stratification by background factors found hachimijiogan was significantly superior in men than in women, in out-patients than in in-patients, and in patients receiving concomitant drugs than in patients not receiving these drugs.

8. Conclusions

Hachimijiogan is effective in treating subjective symptoms (tinnitus, cold and itchy feeling in the limbs, leg pain, low back pain, and residual urine). It is more useful in men than in women.

9. From Kampo medicine perspective

Patients were classified into several groups from a Kampo medicine perspective and evaluated. Hachimijiogan was significantly more effective in patients with obesity, cold feeling in the limbs, and/or without hot flashes.

10. Safety assessment in the article

There was no significant difference in overall safety between arms. Adverse reactions were observed in 5 patients in arm 1 (gastrointestinal problems [n=3], constipation [n=1], and headache [n=1]) and 5 patients in arm 2 (abdominal distention [n=1], stomach pressure sensation [n=1], drug rash [n=1], epigastric pain [n=1], worsening of dizziness/headache [n=1]).

11. Abstractor's comments

As noted in the section of "From Kampo medicine perspective", hachimijiogan is more useful in men and likely to lead to gastrointestinal problems, which is mostly consistent with the "*sho* (証, pattern/syndrome)" of hachimijiogan. Validity of the "*sho*" in treatment with hachimijiogan was demonstrated in this study.

12. Abstractor and date

Namiki T, 29 December 2008, 6 January 2010, 1 June 2010.