

4. Metabolism and Endocrine Diseases**Reference**

Watanabe K, Shimada A, Miyaki K, et al. Long-term effects of goshajinkigan in prevention of diabetic complications: A randomized open-labeled clinical trial. *Evidence-Based Complementary and Alternative Medicine* 2014; 1-8. doi: 10.1155/2014/128726 CENTRAL ID: CN-00993596, Pubmed ID: 24812564

1. Objectives

To evaluate the efficacy and safety of goshajinkigan (牛車腎気丸) for treatment of diabetic complications.

2. Design

Randomized controlled trial (RCT).

3. Setting

Nine hospitals, Japan.

4. Participants

A total of 149 type 2 diabetic patients with HbA1c of $\geq 6.5\%$, aged 40 to 75 years. Exclusion criteria were macroangiopathies including cerebral infarction, myocardial infarction, angina pectoris, leg gangrene, and arteriosclerosis obliterans; nephropathy associated with microalbuminuria or serum creatinine of 1.0 mg/dL; and proliferative or pre-proliferative retinopathy. Other exclusion criteria were related to *sho* (証, pattern) for goshajinkigan and included BMI of 30 kg/m² or more; two or more digestive system symptoms including gastrointestinal weakness, anorexia, nausea, and diarrhea; and three or more symptoms or activities indicative of sensitivity to heat such as a preference for dressing lightly, sweating upwards from the neck, a tendency to drink cold water, flushed face, congestion of the eyeballs, and a high body temperature of 36.7°C or higher.

5. Intervention

Arm 1: TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules administered orally at 2.5 g t.i.d. (n=100).

Arm 2: No treatment (n=49).

6. Main outcome measures

The primary outcome measures were occurrence of nonfatal myocardial infarction or cerebral infarction and frequency of diabetic nephropathy or retinopathy; the progression of diabetic nephropathy as indicated by a new onset of renal failure or an increase in urinary protein; and the progression of diabetic retinopathy as evaluated by fundus photography performed annually by ophthalmologists. Secondary outcome measures were body weight, blood pressure, fasting blood glucose, glycosylated hemoglobin, blood insulin, diabetic neuropathy, etc. Diabetic neuropathy was evaluated on the basis of characteristic symptoms: ankle reflex, lightheadedness, abnormal sweating, occurrence of constipation or diarrhea, etc.

7. Main results

A total of 116 subjects, i.e., 149 subjects minus 33 subjects who stopped visiting the hospital, were included in the analysis (74 subjects in the goshajinkigan arm; 42 subjects in the no treatment arm). The mean observation period was 28 months in Arm 1, and 15 months in Arm 2. No macroangiopathies such as myocardial infarction and cerebral infarction occurred in the two arms. The occurrence of diabetic nephropathy and retinopathy was not significantly different between arms. The deterioration of ankle reflex was significantly more frequent in Arm 2 than in Arm 1 ($P=0.04$). Glycosylated hemoglobin level was significantly lower in Arm 1 than in Arm 2 at 60 months ($P<0.05$). The fasting blood glucose level was significantly decreased from baseline in Arm 1 at 36 months ($P<0.05$).

8. Conclusions

Goshajinkigan inhibits worsening of ankle reflex and improves glycosylated hemoglobin and fasting blood glucose levels.

9. From Kampo medicine perspective

To evaluate patients with *sho* (証, pattern) for goshajinkigan, patients with obesity, gastrointestinal weakness, and sensitivity to heat were excluded from the study.

10. Safety assessment in the article

No dropouts due to adverse reactions to goshajinkigan were noted.

11. Abstractor's comments

This is an interesting clinical study planned to elucidate the long-term effects of goshajinkigan, which is frequently used for treatment of diabetes mellitus. As stated by the authors, however, the desired number of subjects could not be included in the study and the available macroangiopathies occurrence data were inadequate. On the other hand, there were data suggesting that goshajinkigan was effective. Future studies with more subjects are anticipated.

12. Abstractor and date

Goto H, 31 March 2017.