

5. Psychiatric/Behavioral Disorders**Reference**

Fujita H, Yoshida M, Yomoda S. Effects of Yokukansankachimpihange on cognitive ability, an open randomized controlled trial. *Psychiatry* 2013; 23: 130-8 (in Japanese with English abstract).

1. Objectives

To evaluate the efficacy and safety of yokukansankachimpihange (抑肝散加陳皮半夏) on cognitive function.

2. Design

Quasi-randomized controlled trial (quasi-RCT).

3. Setting

Residents or users and staff of 3 institutions in Toyama Prefecture, Japan.

4. Participants

Forty-one adult males and females aged 55 years or older with moderate strength, slightly weak gastrointestinal system, easy fatigability, aggressiveness, irritability, insomnia, and mild psychiatric symptoms

5. Intervention

Arm 1: Kracie Yokukansankachimpihange (抑肝散加陳皮半夏) Extract Granules 7.5 g/day (3.75 g b.i.d) for 4 weeks (n=20)

Arm 2: no administration of yokukansankachimpihange (n=21)

6. Main outcome measures

Prior to and 4 weeks after the study, the Mini-Mental State Examination (MMSE), Japanese version of the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-J cog.), and assessments of behavioral and psychological symptoms of dementia (BPSD) and activities of daily living (neuropsychiatric inventory [NPI] and disability assessment for dementia [DAD]) were performed. In addition, changes in oxyhemoglobin concentration (ΔO_2Hb) were measured using an infrared oxygen monitor to determine cerebral blood flow during execution of the following tasks: standard clinical assessment for attention, tapping span, memory updating test, digit span, and compound digit cancellation test.

7. Main results

Three subjects in arm 1 dropped out of the study. There was no significant between-group difference in MMSE score, NPI score, or DAD score. The amount of change in ADAS-J cog. was -2.9 ± 3.5 in arm 1 and 0.22 ± 2.6 in arm 2, indicating a significant improvement in arm 1 compared to arm 2 ($P < 0.01$). The ΔO_2Hb value in the left hemisphere during task execution was significantly higher in arm 1 than in arm 2 ($P < 0.05$). Of the tasks executed during measurement of cerebral blood flow, the standard clinical assessment for attention showed a significantly larger difference in total number of answers between the baseline and 4 weeks after the study in arm 1 than in arm 2 ($P < 0.05$).

8. Conclusions

Yokukansankachimpihange improves ADAS-J cog. for core symptoms and oxygen metabolism in the brain during task execution.

9. From Kampo medicine perspective

The inclusion criteria for the study are the *sho* (証, pattern) for yokukansankachimpihange.

10. Safety assessment in the article

Treatment was discontinued in 2 subjects receiving yokukansankachimpihange due to increased blood pressure and vomiting. Changes in blood components were within the normal range in both groups.

11. Abstractor's comments

This landmark clinical study has clarified the effects of yokukansankachimpihange on cognitive function, based on clinical symptoms (including core symptoms, BPSD and activities of daily living), and changes in cerebral blood flow in the frontal lobe. On the other hand, the authors state only that residents and staff of institutions were included in the study without providing detailed information on them; that is, effects in dementia patients and those in normal persons are mixed in study results. The authors also state that subjects were stratified and randomized by sex, age, and MMSE score, although the number of the subjects was small and other measurements may be biased. In fact, there was no between-group difference in mean baseline ADAS-J cog. score, but the yokukansankachimpihange group included many subjects with high ADAS-J cog. scores. For this reason, the amount of change in score may have been larger in the yokukansankachimpihange group. Moreover, as described in the Discussion section, the amount of change in oxyhemoglobin concentration (ΔO_2Hb), which was measured to determine brain metabolism during task execution, was less in the control group than in the yokukansankachimpihange group after 4 weeks, thereby contributing to the significant difference between the two groups. However, these laborious investigations and evaluations of cerebral blood flow will play an important role in determining the effects of Kampo medicines on cognitive function. It is hoped that clinical studies in dementia patients will be continued.

12. Abstractor and date

Goto H, 6 June 2015