## 6. Nervous System Diseases (including Alzheimer's Disease)

**References**

**Monji A, Takita M, Samejima T, et al. Effect of yokukansan on the behavioral and psychological symptoms of dementia in elderly patients with Alzheimer's disease. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 2009; 33: 308-11. 33: 308-11. Pubmed ID: 19138715**

Monji A, Kanba S. Effectiveness of yokukansan (抑肝散) on BPSD in Alzheimer's disease — Results of a long-term antipsychotic combination trial at a department of neuropsychiatry in Kyushu*. *No 21* (*Brain 21*) 2009; 12: 446-51 (in Japanese). Ichushi Web ID: 2010037668, MOL, MOL-Lib

**1. Objectives**

To evaluate the efficacy and safety of yokukansan (抑肝散) in the treatment of behavioral and psychological symptoms of dementia (BPSD) in elderly patients with Alzheimer's disease

**2. Design**

Randomized controlled trial (RCT)

**3. Setting**

Kyushu University and its affiliated hospitals (number of institutions, not specified), Japan

**4. Participants**

Fifteen patients (2 males and 13 females, mean age 80.2±4.0 years) who were diagnosed with dementia and Alzheimer's disease based on the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV and National Institute of Neurological and Communicative Disorders and Stroke / the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria, respectively, and had a Mini-Mental State Examination (MMSE) score of 6 to 23 and a Neuropsychiatric Inventory (NPI) score of 6 or higher after 2 weeks of pre-study treatment with sulpiride 50 mg/day

**5. Intervention**

**Arm 1:** Continuation of oral sulpiride 50 mg/day plus treatment with oral yokukansan (抑肝散; manufacturer, not specified) 2.5 g (containing 1.5 g of extracts) t.i.d. for 12 weeks (n=10)

**Arm 2:** Continuation of oral sulpiride 50 mg/day alone (n=5).

During the evaluations performed every 4 weeks, the dose of sulpiride was increased when any NPI subscore was 8 or higher and decreased when all NPI subscores were below 4.

**6. Main outcome measures**

BPSD and cognitive functions were evaluated using the NPI and MMSE, respectively. The Barthel Index was used for the evaluation of activities of daily living. Patients were evaluated at baseline, 4, 8, and 12 weeks.

**7. Main results**

One patient in arm 2 was excluded due to severe edema. NPI was significantly improved at 8 and 12 weeks compared with the baseline in arm 1 ($P<0.001$), whereas no change was observed in arm 2. The dose of sulpiride at 12 weeks was less, but not significantly less, in arm 1 than in arm 2. There were no changes in MMSE and Barthel Index from the baseline in both arms.

**8. Conclusions**

Yokukansan improves BPSD in elderly patients with Alzheimer's disease and can reduce the dose of antipsychotics.

**9. From Kampo medicine perspective**

None

**10. Safety assessment in the article**

Hypokalemia was reported in 2 patients in arm 1. In addition, extrapyramidal symptoms developed and the dose of sulpiride was decreased from 150 mg/day to 100 mg/day in one patient in arm 1.

**11. Abstractor's comments**

This is a valuable clinical study that evaluated the efficacy of yokukansan in elderly patients with Alzheimer's disease over 12 weeks from various aspects, including behavioral and psychological symptoms, cognitive functions, and activities of daily living. Because patients in both arms were prescribed sulpiride at baseline and yokukansan was evaluated in an add-on design, there is a possibility that the efficacy of yokukansan alone was not adequately evaluated. The differences in NPI and MMSE score from those in arm 2 were not significant owing to the small number of patients. However, the trend in these scores over time suggests that significant improvements over baseline might be found if more patients were included. Even in a small population, it is suggested that yokukansan may improve NPI and reduce the dose of antipsychotics. In the future, the efficacy of yokukansan in the field of psychiatry could be more convincingly demonstrated by increasing the number of patients and selecting the appropriate control agent.

**12. Abstractor and date**

Goto H, 1 June 2010, 1 February 2011, 31 December 2013