## 5. Psychiatric/Behavioral Disorders

**Reference**

Mizukami K, Asada T, Kinoshita T, et al. A randomized cross-over study of a traditional Japanese medicine (kampo), yokukansan, in the treatment of the behavioural and psychological symptoms of dementia. *The International Journal of Neuropsychopharmacology* 2009; 12: 191-9. CENTRAL ID: CN-00704589, Pubmed ID: 19079814

**1. Objectives**

To evaluate the efficacy and safety of yokukansan (抑肝散) in the treatment of behavioural and psychological symptoms of dementia.

**2. Design**

Randomized controlled trial (cross-over) (RCT cross-over).

**3. Setting**

Twenty medical institutions (the first author belongs to the faculty of the Department of Clinical Neuroscience, Doctoral Program in Clinical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba), Japan.

**4. Participants**

One hundred and six patients aged 55–85 years and diagnosed with Alzheimer's disease, including mixed-type dementia or dementia with Lewy bodies. There were 59 outpatients (20 males and 39 females, mean age 78.7±5.4 years) and 47 inpatients (19 males and 28 females, mean age 78.5±6.7 years).

**5. Intervention**

Arm 1: TSUMURA Yokukansan (抑肝散) Extract Granules 2.5 g t.i.d. orally for 4 weeks, followed by observation with no treatment for 4 weeks (n=54).

Arm 2: No treatment with observation for 4 weeks, followed by TSUMURA Yokukansan (抑肝散) Extract Granules 2.5 g t.i.d. orally for 4 weeks (n=52).

**6. Main outcome measures**

Behavioural and psychological symptoms of dementia (BPSD) and cognitive functions were evaluated using the Neuropsychiatric Inventory (NPI) and Mini-Mental State Examination (MMSE), respectively. Activities of daily living were evaluated using the Instrumental Activities of Daily Living (IADL) in outpatients and the Barthel Index in inpatients. Patients were evaluated at baseline, 4 weeks, and 8 weeks.

**7. Main results**

In both arms, total scores on the NPI significantly improved after 4 weeks of yokukansan treatment ($P$<0.01), but not during the no-treatment period. Among the NPI subscales, delusion, hallucination, agitation/aggression, and irritability/lability ($P$<0.01 for each) improved in arm 1 and agitation/aggression ($P$<0.01), depression, anxiety, and irritability/lability ($P$<0.05 for each) improved in arm 2 after the yokukansan treatment.

**8. Conclusions**

Oral administration of yokukansan improves behavioural and psychological symptoms associated with dementia.

**9. From Kampo medicine perspective**

None.

**10. Safety assessment in the article**

Adverse drug reactions were reported in 6 patients. Gastrointestinal symptoms including vomiting, diarrhea, nausea, and epigastric pain developed in 3 patients. When yokukansan treatment was discontinued, these symptoms promptly resolved. Hypokalemia was reported in 2 patients, one of whom experienced oversedation. When yokukansan treatment was discontinued, serum potassium levels returned to normal in both patients. Another patient developed lower leg edema. No serious adverse reactions, such as extrapyramidal symptoms and hallucination, were observed.

**11. Abstractor's comments**

This is a very meaningful clinical study that demonstrated the efficacy of yokukansan for improving BPSD in a multicentre setting. In both arms, symptoms improved during yokukansan treatment compared with the no-treatment period. The results would be more valuable if the data had been analyzed rigorously as a cross-over design. In the future, larger-scale multicentre placebo-controlled studies and clinical studies of longer-term treatment with yokukansan are needed to further demonstrate the efficacy of this agent.

**12. Abstractor and date**

Goto H, 1 June 2010.