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

Reference

Okahara K, Ishida Y, Hayashi Y, et al. Effects of yokukansan on behavioral and psychological symptoms of dementia in regular treatment for Alzheimer's disease. *Progress in Neuro Psychopharmacology & Biological Psychiatry* 2010; 34: 532–6. CENTRAL ID: CN- 00752183, Pubmed ID: 20170698

1. Objectives

To investigate the efficacy and safety of yokukansan (抑肝散) as a common treatment for behavioral and psychological symptoms of dementia (BPSD) in patients with Alzheimer's disease (AD).

2. Design

Randomized controlled trial (RCT).

3. Setting

Hospitals and Clinics in Miyazaki and Kagoshima prefecture, 12 institutions, Japan.

4. Participants

Sixty-three outpatients were registered from July 2006 to December 2008 and met the following inclusion criteria: 1) have dementia and a diagnosis of Alzheimer's disease (including mixed-type dementia), 2) show at least one symptom score ≥4 in the Neuropsychiatric Inventory (NPI) subscales, 3) aged ≤85 years, 4) taking donepezil hydrochloride for at least 4 weeks.

5. Intervention

Arm 1: administration of TSUMURA Yokukansan (抑肝散) Extract Granules, 2.5 g t.i.d. for 4 weeks (n=30).

Arm 2: no administration (n=33).

6. Main outcome measures

Evaluations of BPSD using the NPI subscales (delusions, hallucinations, agitation, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability, and aberrant motor activity), cognitive function by the Mini-Mental State Examination (MMSE), activities of daily living (ADL) by the Disability Assessment of Dementia (DAD), burden of caregivers by the Zarit Burden Interview, caregiver's depression by the Self-rating Depression Scale (SDS) at the start and at 4 weeks of the study.

7. Main results

One patient in arm 1 and one patient in arm 2 withdrew, and the efficacy analysis set included 29 patients in arm 1 and 32 patients in arm 2. Inter-group comparison revealed significantly more improvement in arm 1 compared with arm 2 in the total NPI score after 4 weeks of treatment ($P<0.05$). On analysis of individual NPI subscale scores, significant improvement was observed for agitation and irritability in arm 1 compared to arm 2 ($P<0.05$). Intra-group comparison of values at the start and at 4 weeks of treatment identified a significant improvement in the NPI total score in arm 1 ($P<0.05$). Analysis of each NPI subscale scores at baseline and after 4 weeks of treatment demonstrated significant improvement in delusions, agitation, dysphoria, anxiety, apathy, or irritability in arm 1 ($P<0.05$), and in apathy in arm 2 ($P<0.05$). Inter-group and intra-group comparisons found no changes in MMSE, DAD, Zarit Burden Interviews, or SDS.

8. Conclusions

Yokukansan significantly accelerates improvement in BPSD in patients with Alzheimer's disease treated with donepezil.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

None of the patients had any adverse reactions to yokukansan such as decreased serum potassium or edema.

11. Abstractor's comments

This is a clinical trial to determine the efficacy of yokukansan for dementia in patients with Alzheimer's disease treated with donepezil by evaluating its effect on behavioral and psychological symptoms. The result of the clinical trial can be applied immediately to daily practice. Despite improvement in NPI scores, scores reflecting the burden of caregivers were not improved. To assess this effect, further studies with larger sample size and longer study period would be necessary. However, as no drugs effective for peripheral symptoms of dementia are presently available, demonstration of the efficacy of yokukansan is a great achievement.

12. Abstractor and date

Goto H, 27 December 2010, 31 December 2013.