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

References

Furukawa, K, Tomita N, Une K, et al. Randomized double-blind placebo-controlled multicenter trial of Yokukansan for neuropsychiatric symptoms in Alzheimer's disease. *Geriatrics and Gerontology International* 2017; 17: 211-8. CENTRAL ID: CN-01337019, Pubmed ID: 26711658

1. Objectives

To evaluate the efficacy and safety of yokukansan（抑肝散）for behavioral and psychological symptoms of dementia (BPSD) in Alzheimer’s disease

2. Design

Double-blind, randomized, controlled trial (DB-RCT)

3. Setting

Twenty-two sites (clinics, hospitals, and nursing homes), Japan

4. Participants

A total of 145 patients with probable Alzheimer’s disease, diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, third edition, revised (DSM-III-R) and the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) criteria. Main inclusion criteria were age 55–84 years, total score of greater than 4 on the Neuropsychiatric Inventory Brief Questionnaire (NPI-Q), the sum of the NPI-Q subcategory scores for “agitation/aggression” and “irritability/lability” greater than 2, and the Mini-Mental State Examination (MMSE) score within the range of 10–26. Patients were excluded if they had cerebral infarction possibly affecting cognitive function, or they had depression, bipolar disorder, malignant tumor, or other life-threatening disease within the previous 2 years. Patients were also excluded if they had received typical or atypical neuroleptics, tricyclic or tetracyclic antidepressants, or Kampo medicines other than yokukansan.

5. Intervention

Arm 1: TSUMURA Yokukansan（抑肝散）Extract Granules 7.5 g/day (2.5 g t.i.d.) administered orally for 12 weeks (n=75)

Arm 2: Matching placebo (3 times daily) administered orally for 12 weeks (n=70)

The first 4 weeks of the treatment were double-blinded for comparison of the effects, and the following 8 weeks were non-double-blinded for safety assessment.

6. Main outcome measures

The primary outcome measure was the 4-week change in the NPI-Q total score. The secondary outcome measures were 12-week changes in NPI-Q total score, NPI-Q subcategory scores, MMSE total score, rescue drug dose, and safety.

7. Main results

The 4-week change in NPI-Q total score, which was the primary outcome measure, and the changes in NPI-Q subcategory scores did not differ significantly between the two arms. The NPI-Q total score significantly decreased from baseline at Week 4 in both arms (P <0.001 for both). Among the secondary outcome measures, the 12-week changes in NPI-Q total score and MMSE total score did not differ between the arms. However, a subgroup analysis showed that the agitation/aggression score significantly decreased after 4 weeks of treatment in Arm 1 compared with Arm 2 among patients with baseline MMSE <20 and patients aged ≤74 years (P =0.007 and P =0.049, respectively). Also, among patients with hallucinations at baseline, NPI-Q total score significantly decreased in Arm 1 compared with Arm 2 (P =0.019).

8. Conclusion

Yokukansan improves symptoms including agitation/aggression and hallucinations with low frequencies of adverse reactions.

9. From Kampo medicine perspective

None

10. Safety assessment in the article

Hypokalemia was observed in 4 of the 72 patients in the yokukansan group. However, there were no significant differences between the two arms.

11. Abstractor’s comments

This is a valuable clinical study that evaluated the efficacy and safety of yokukansan for BPSD in Alzheimer’s disease, conducted as a multicenter, double-blind, randomized, controlled trial. Although primary and secondary outcome measures did not demonstrate efficacy of yokukansan, the subgroup analysis revealed some significant findings. Further clinical studies based on these findings are awaited, to further clarify the disease conditions for which yokukansan is indicated.

12. Abstractor and date

Goto H, 1 June 2020.