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

References

Teranishi M, Kurita M, Nisiho S, et al. Efficacy and tolerability of risperidone, yokukansan, and fluvoxamine for the treatment of behavioral and psychological symptoms of dementia: A blinded, randomized trial. *Journal of Clinical Psychopharmacology* 2014; 33: 600-7.

Kurita M, Efficacy and tolerability of yakukansan for behavioral and psychological symptoms of dementia (BPSD) – A 3-way comparative trial of risperidone and fluvoxamine. *Brain 21* 2015; 18: 249-52.

1. Objectives

To evaluate the efficacy and safety of yokukansan (抑肝散) for behavioral and psychological symptoms of dementia (BPSD).

2. Design

Randomized controlled trial (RCT).

3. Setting

One psychiatric hospital, Japan.

4. Participants

Eighty-two patients who met the diagnostic criteria of dementia according to the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) with total score on the Mini-Mental State Examination (MMSE) of <19 and at least one symptom score of >4 in the Neuropsychiatric Inventory-Nursing Home Version (NPI-NH). Patients meeting any of the following criteria were excluded from the study: participation in any other drug study within 4 weeks of the study; hypersensitivity to risperidone, yokukansan, or fluvoxamine; evidence of chronic and/or severe disease that could interfere with the study.

5. Intervention

Arm 1: Yokukansan (抑肝散) (manufacturer unknown) 2.5 to 7.5 g/day for 8 weeks (n=27).
Arm 2: Risperidone 0.5 to 2.0 g/day for 8 weeks (n=27).
Arm 3: Fluvoxamine 25 to 200 mg/day for 8 weeks (n=28).
The study was initiated after a 1-week washout of drugs used for treatment of BPSD. The dose of each drug was adjusted at the discretion of the investigator and based on his/her analysis of NPI-NH subscales.

6. Main outcome measures

At baseline and Weeks 2, 4, 6, and 8, an assessment was made of neuropsychiatric symptoms using the NPI-NH, cognitive function using the MMSE, and daily life function using the Functional Independence Measure (FIM). To evaluate drug tolerability, blood and other tests and the Drug-induced Extra-pyramidal Symptoms Scale (DIEPSS) were performed.

7. Main results

Of the 82 subjects, 76 were included in the analysis. NPI-NH scores were significantly improved from baseline to Week 8 in all arms ($P=0.034$ in Arm 1; $P=0.022$ in Arm 2; $P<0.001$ in Arm 3), but with no significant difference among the three arms. MMSE and FIM scores did not change significantly in the three arms.

8. Conclusion

Yokukansan is as effective as risperidone and fluvoxamine for BPSD but safer to use than risperidone.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

DIEPSS scores were similar between the yokukansan and fluvoxamine arms, but significantly higher in the risperidone arm than in the yokukansan and fluvoxamine arms. One subject in the risperidone arm died suddenly during the study.

11. Abstractor's comments

BPSDs are important symptoms to treat, but there are no good drugs for BPSD treatment at this time. This clinically meaningful study evaluated the efficacy and safety of risperidone and yokukansan, which are frequently used in clinical settings, and fluvoxamine used by the authors. However, as acknowledged by the authors, no placebo was used in this study; the investigator's assessment might have been affected by this omission. In addition, since hospitalized patients were included in this study, care by staff members might have improved NPI-NH scores in all arms. However, the intent of this study was to improve the state of current treatment. It is anticipated that similar future studies will be conducted to establish the guidelines for treatment of BPSD with Kampo medicines.

12. Abstractor and date

Goto H, 31 March 2017.