5. Psychiatric/Behavioral Disorders

Reference

Miyaoka T, Furuya M, Yasuda H, et al. Yi-gan san as adjunctive therapy for treatment-resistant schizophrenia: An open-label study. *Clinical Pharmacology* 2009; 32: 6–9.

1. Objectives

To evaluate the efficacy and safety of yokukansan (抑肝散) for treatment-resistant schizophrenia.

2. Design

Randomized controlled trial (RCT).

3. Setting

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4. Participants

Patients diagnosed with schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) who met treatment-resistance criteria as follows:

a) no satisfactory response to antipsychotic drugs from at least 2 different classes, in a dose equivalent to at least 1000 mg/d of chlorpromazine for at least 6 weeks during the course of illness;

b) no period of good functioning within the preceding 2 years;

c) positive and negative syndrome scale (PANSS) scores in the 70th percentile or higher, based on normative data for patients with chronic schizophrenia.

5. Intervention

The study was brief (4 weeks) and had an open-label design.

Arm 1: administration of Yokukansan (抑肝散) 6.7 ±2.5 g (range, 2.5–7.5 g)/day (n=34).

Arm 2: no administration of Yokukansan (抑肝散) (n=25).

All patients were taking conventional and/or atypical antipsychotic medications, including olanzapine, risperidone, quetiapine, aripiprazole, perospirone, haloperidol, levomepromazine, and zotepine.

6. Main outcome measures

PANSS and drug-induced extrapyramidal symptom scale (DIEPSS) were assessed at baseline, and after 2 and 4 weeks of treatment.

7. Main results

In Arm 1, treatment with Yokukansan significantly reduced the PANSS positive symptoms subscale score of 27.7±6.1 at baseline by 68.2% at 2 weeks (means score 18.9±5.0) (P<0.001) and 43.0% at 4 weeks (mean score, 11.9±3.7) (P<0.001), the PANSS negative symptom subscale score of 30.4±5.8 at baseline by 73.7% at 2 weeks (mean score, 22.4±4.3) (P<0.001) and 59.9% at 4 weeks (mean score, 18.2±2.2) (P<0.001), and the PANSS general psychopathology subscale score of 65.1±5.4 at baseline by 70.5% (mean score, 45.9±9.0) (P<0.001) at 2 weeks and 60.8% (means score, 39.6±6.9) (P<0.001) at 4 weeks. In the control group, each PANSS subscale remained unchanged. There was no significant difference in the DIEPSS scores in both groups.

8. Conclusions

In this pilot study, statistically significant improvement in clinical assessment scale was observed after yokukansan treatment, suggesting that yokukansan has efficacy for treatment-resistant schizophrenia.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

DIEPSS corresponds to the safety assessment, and no serious adverse effects of yokukansan were reported. A few mild and transient adverse events included 2 cases of nausea and 1 case of tiredness.

11. Abstractor's comments

This RCT was designed to evaluate the efficacy of yokukansan for schizophrenia, as it has been shown to be effective in treating psychiatric disorders such as dementia. The idea is great and the result is clinically significant. As the authors discuss, the absence of blinding may have introduced bias into the outcome assessment. The total number of the participants of the two arms is 59. However, the Figure 1 legend states that 54 completed a 4-week trial, making unclear the number of subjects who dropped out. Because of the small sample size, the number of subjects used as denominator for analyses is a concern. More precise design for the main trial is anticipated.

12. Abstractor and date

Tsuruoka K, 2 January 2011.