5. Psychiatric/Behavioral Disorders

References

Miyaoka T, Furuya M, Horiguchi J, et al. Efficacy and safety of yokukansan in treatment-resistant schizophrenia: a randomized, double-blind, placebo-controlled trial (a Positive and Negative Syndrome Scale, five-factor analysis). *Psychopharmacology* 2015; 232: 155-64.

Miyaoka T, Furuya M, Horiguchi J, et al. Efficacy and safety of yokukansan in treatment-resistant schizophrenia: a randomized, multicenter, double-blind, placebo-controlled trial. 2015 *Evidence-Based Complementary and Alternative Medicine* 2015; 1-11.

1. Objectives

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

2. Design

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

3. Setting

34 psychiatric hospitals (The authors belong to the Department of psychiatry, University Hospital), Japan.

4. Participants

One hundred and twenty hospitalized patients aged between 20 and 59, who were diagnosed with treatment-resistant schizophrenia (DSM-IV-TR), diagnosed at least 3 years previously, had taken at least 2 types of antipsychotic (equivalent to at least 600mg/day chlorpromazine) for 4 weeks but scored at least 4 on 2 or more subscales for positive psychiatric symptoms on the Positive and Negative Syndrome Scale (PANSS) or a total score greater than 60, a Clinical Global Impression (CGI) score more than 4, and were suitable for the clozapine USA multicenter trial. Patients 6-months pregnant or less, patients in an unstable condition, and patients who have abused alcohol or drugs were excluded.

5. Intervention

Arm 1: TSUMURA Yokukansan (抑肝散) Extract Granules 7.5g/day (2.5g t.i.d.) for 4 weeks (n=56).
Arm 2: Placebo 2.5g t.i.d. for 4 weeks (n=64).

6. Main outcome measures

The clinical effects used were 5 PANSS scores (excitement/hostility, depression/anxiety, cognition, positive, negative), CGI-S and Global Assessment of Functioning (GAF). Overall adverse effects and motor disorder were assessed, and motor disorder was assessed with the Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS). Effects and tolerability were assessed by the principle researcher. The primary results were measured by changes in the 5 PANSS scores, and then by measuring changes in CGI-S.

7. Main results

For *Psychopharmacology*, mITT was used for statistical analysis, 3 participants dropped out of arm 2, leaving 56 participants in arm 1 and 61 in arm 2 for analysis. Excitement/hostility subscale PANSS scores improved significantly in arm 1 compared to arm 2 (P=0.018). For *Evidence-Based Complementary and Alternative Medicine*, PPS was used for statistical analysis, 48 participants in arm 1 were analyzed and 50 in arm 2. This analysis resulted in significant differences between arm 1 and arm 2 for lack of spontaneity and flow of conversation, tension, and poor impulse control (P<0.018, P<0.045, P<0.037).

8. Conclusion

Yokukansan for treatment-resistant schizophrenia improves PANSS excitement and hostility, etc. subscores.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

No adverse effect from administration of yokukansan was observed.

11. Abstractor's comments

This is a very interesting clinical study that sheds light on the efficacy of yokukansan for treatment-resistant schizophrenia using the Positive and Negative Syndrome Scale. Two papers were written using the differing mITT and PPS analytical methods, which is why the numbers of dropouts differed and the results were described differently. However, the authors have therefore identified a new indication for yokukansan and further evaluations of its effectiveness for similar pathological conditions are anticipated.

12. Abstractor and date

Goto H, 27 January 2017.