5. Psychiatric/Behavioral Disorders

Reference

Matsunaga S, Kishi T, Iwata N. Yokukansan in the treatment of behavioral and psychological symptoms of dementia: an updated meta-analysis of randomized controlled trials. *Journal of Alzheimer's Disease* 2016; 54: 635-43. PubMed: 27497482

1. Objectives

To evaluate by meta-analysis the effectiveness and safety of yokukansan (抑肝散) for behavior and psychological symptoms of dementia (BPSD).

2. Data sources

PubMed, the Cochrane Library database, PsycINFO, and clinical trial registries (ClinicalTrials.gov, ISRCTN, the WHO portal), all data sourced before April 20, 2016.

3. Research selection

Randomized controlled trials (RCTs) comparing yokukansan with usual treatment or placebo for BPSD in dementia patients were collected.

4. Data sampling

Searches were conducted using keywords such as the following: "dementia" OR "Alzheimer's" OR "Alzheimer" OR "Lewy" AND "Yokukansan" OR "Yigansan". Two of the authors checked the various inclusion and exclusion criteria, and independently analyzed the results using Review Manager (RevMan) ver 5.3.

5. Main outcome measures

The primary outcome measure for effectiveness was overall Neuropsychiatric Inventory (NPI) score; the primary outcome measure for safety was discontinuation of treatment for any reason; and the secondary outcome measure was NPI subscale (delusions, hallucinations, agitation/aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability/emotional instability, aberrant motor activity, nighttime behavior changes, eating changes).

6. Main results

Five RCTs (control groups: 4 RCTs with a no-yokukansan-administration group, and 1 RCT with a placebo group) were included in the meta-analysis. Overall NPI scores for a total of 381 BPSD patients were significantly lower in yokukansan groups compared to control groups (P=0.003). Yokukansan was useful for the BPSD sub-scores delusions, hallucinations, and agitation/aggression. However, yokukansan did not demonstrate effectiveness for Alzheimer's disease on either the overall BPSD score or the subscales. Of the cognitive functions, yokukansan improved activities of daily life (ADL), but did not improve mini-mental state examination (MMSE) scores.

7. Conclusions

Yokukansan is an effective and safe therapeutic drug for BPSD, excluding Alzheimer's disease.

8. From Kampo medicine perspective

None.

9. Safety assessment in the article

There was no significant difference between yokukansan groups and control groups for frequency of adverse effects, discontinuation due to adverse effects, or discontinuation of therapy for any reason.

10. Abstractor's comments

This meta-analysis of the effectiveness and safety of yokukansan, frequently used in clinical settings, is an important report. However, the authors have done the same meta-analysis of the groups in 4 RCTs (Hum Psychopharmacol 2013; 28: 80-6), this time adding the placebo group, which wasn't in the previous meta-analysis. The results are the same: yokukansan was verified to be effective for BPSD, excluding Alzheimer's disease. As the authors also mention, there were a number of problems: they analyzed a small number of RCTs, there were few patients registered to participate in the RCTs, and in particular, the blinding bias risk was high, the periods of yokukansan administration were short (from 4 - 12 weeks), and the concomitant use of antidementia and antipsychotic agents may have affected the results. The authors mention that research outside Japan is desirable, but achieving that goal is not simple. A question for future research is why the effectiveness of yokukansan differs by dementia type.

11. Abstractor and date

Motoo Y, 18 May 2020.