

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

Matsuda Y, Kishi T, Shibayama H, et al. Yokukansan in the treatment of behavioral and psychological symptoms of dementia: a systematic review and meta-analysis of randomized controlled trials. *Human Psychopharmacology* 2013; 28: 80-6. Pubmed ID: 23359469

1. Objectives

To perform a systematic review of the efficacy and tolerability of yokukansan (抑肝散) in the treatment of behavioral and psychological symptoms of dementia (BPSD).

2. Data source

PubMed (-2012), the Cochrane Library (-2012), PsyINFO (-2012).

3. Study selection

Randomized controlled trials (RCTs) comparing yokukansan and conventional medications in patients with BPSD were collected. Reviews, non-RCTs, and experimental studies not conducted in humans were excluded.

4. Data extraction

Necessary information was retrieved from the above databases using the keywords “dementia” and “Yokukansan.” Two persons individually conducted a literature search, and another two confirmed the inclusion and exclusion criteria, respectively. Unpublished data were provided by two researchers. The neuropsychiatric inventory (NPI) score, which is a known measure of BPSD, was used as the primary outcome, and NPI subscores (delusion, hallucination, agitation/aggression, discomfort, anxiety, apathy, irritability/instability, euphoria, disinhibition, and unusual motor behavior) were used as the secondary outcomes. Cognitive function was evaluated by the Mini-Mental State Examination (MMSE), and activities of daily living (ADL) was evaluated by the Barthel index and Disability Assessment for Dementia (DAD). For the meta-analysis, Cochrane Collaboration’s Review Manager (RevMan) ver 5.0 was used.

5. Main results

Forty-six articles were collected, and 42 (6 reviews, 19 non-RCTs, and 17 animal studies) were excluded. Thus, the results of four studies were meta-analyzed. A total of 236 subjects (sample size range: 15 to 106) with a mean age 78.6 years were studied for a mean of 6 weeks. Two of the studies included patients with Alzheimer-type dementia, vascular dementia, and dementia with Lewy bodies, and the other two included only patients with Alzheimer-type dementia. Compared to conventional medications, yokukansan improved the total NPI score ($P=0.0009$, weighted mean difference [WMD] = -7.20 , $I^2=0\%$) and NPI subscores (delusion, hallucination, and agitation/aggression) ($P<0.00001-0.0009$) to a significantly greater extent. Yokukansan also improved ADL ($P=0.04$, standardized mean difference [SMD] = -0.32 , $I^2=0\%$) but not MMSE score. The discontinuation rates were similar between yokukansan and conventional medications.

6. Conclusions

Yokukansan improves the NPI score of BPSD and ADL score with good tolerability.

7. From Kampo medicine perspective

None.

8. Safety assessment in the article

One subject in the yokukansan group developed extrapyramidal symptoms, which were improved by reducing sulpiride (concomitant drug). Two subjects in the yokukansan group developed hypokalemia.

9. Abstractor’s comments

This meta-analysis with RevMan is a good systematic review (SR), the first SR of EKAT, and a welcome effort to promote evidence-based medicine in the field of Kampo. This study of yokukansan as a treatment for BPSD is also a hot, timely topic in clinical practice. Since the comprehensiveness of the search is a key point of SRs, the authors should disclose the search expressions to further improve the quality. They should also use a flowchart to show adopted and rejected trials with inclusion and exclusion criteria. They should provide more detailed information on conventional medications. I hope their research will be further improved.

10. Abstractor and date

Tsuruoka K, 6 June 2015.