Herbal medicine for dementia: a systematic review

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CRD summary
This review concluded that herbal medicines were potentially beneficial for improvement of cognitive function in various age-related dementias, but further large studies were required. The authors' conclusions may be overly optimistic as the included studies were small and disparate and may not be sufficient to draw reliable conclusions about efficacy and safety.

Authors' objectives
To assess the efficacy and safety of herbal medicines for treating dementia.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, BIOBASE and Chinese VIP information were searched from inception to February 2007 for articles in English, Chinese, Japanese and German. Search terms were reported. Reference lists of retrieved articles were searched.

Study selection
Randomised controlled trials (RCTs) and quasi-RCTs that compared herbal medicine with placebo, no intervention or other intervention in ageing patients diagnosed with Alzheimer's disease, vascular dementia or multi-infarct dementia were eligible for inclusion. Trials of ginkgo biloba or its derivatives were excluded as were trials of purified plant compounds. Trials had to include outcomes relevant to memory, cognitive function or symptoms of dementia.

The included studies evaluated single herb preparations (such as Melissa officinalis and Salvia officinalis) and herbal formulations (such as Yi Gan San and Ba Wei Di Huang Wan) with placebo, no treatment or other intervention (such as Duxil, hydergine, piracetam or huperzine). Duration of treatment ranged from eight weeks to six months. Mean age of participants ranged from 63 to 86 years of age. Diagnoses of trial participants included Alzheimer's disease, vascular dementia, multi-infarct dementia and unspecified dementia. Various measures of dementia were reported in the studies including Mini-Mental State Examination (MMSE) and Blessed Dementia Scale.

Pairs of reviewers independently applied inclusion criteria and resolved any differences by discussion with other reviewers.

Assessment of study quality
Pairs of reviewers independently assessed study quality in terms of blinding, randomisation and drop-outs using the Jadad scale to obtain a score out of 5. Studies that scored below 3 on the Jadad scale were excluded. Disagreements were resolved through discussion or arbitration by a third reviewer.

Data extraction
Where possible, baseline and end point data for treatment and control groups were used to calculate the mean change in effect size for each study. The authors stated that the data were extracted using a data extraction form, but did not state how many reviewers performed the task.

Methods of synthesis
Studies were described narratively, grouped as herbal medicines versus no treatment or placebo and herbal medicines versus other interventions. Studies that had suitable outcome data were combined using fixed-effect meta-analysis to obtain pooled weighted mean differences (WMD) and 95% confidence intervals (CIs); again grouped as herbal medicines versus no treatment or placebo and herbal medicines versus other therapies. I² and X² tests were reported. Safety data were discussed narratively.

Results of the review
Thirteen RCTs (n randomised=1,144) were included. All of the included studies were deemed of good quality: four studies scored 5 points; four scored 4 points; and five scored 3 points.

**Herbal medicine versus placebo or no treatment (seven trials):** Seven trials provided data for this comparison, but only two studies (n=188) provided sufficient data that could be used to calculate mean differences. The pooled WMD from these two studies demonstrated that herbal medicines offered a statistically significant benefit compared with placebo or no treatment in terms of MMSE (WMD 2.02, 95% CI: 0.43, 3.61). The $I^2$ for this comparison was 37%, which indicated moderate heterogeneity between studies.

**Herbal medicine versus other intervention (seven trials):** The pooled WMD from five studies (n=567) demonstrated that herbal medicines offered a statistically significant benefit compared with other interventions in terms of MMSE (WMD 0.94, 95% CI: 0.26, 1.62). The $I^2$ for this comparison was 36%, which indicated moderate heterogeneity between studies. However, the pooled WMD from three studies (n=437) could not demonstrate a difference between herbal medicines and other interventions in terms of Blessed Dementia Scale. The $I^2$ for this comparison was 72%, which indicated substantial heterogeneity between studies.

**Safety (10 trials):** There was limited data on safety. Of the 10 studies that reported adverse events, four found no adverse events and six studies showed minor adverse events associated with herbal medicine, which included nausea, vomiting, abdominal pain and dizziness. No pooling was undertaken.

**Authors' conclusions**
Herbal preparations were potentially beneficial for the improvement of cognitive function in various age-related dementias. But due to small sample sizes of included studies, methodological weakness within the studies and a lack of long-term follow-up, more studies were needed to determine the efficacy and safety of herbal medicines for dementia.

**CRD commentary**
The review addressed a clear question and undertook a thorough search for published trials in several languages, including English and Chinese. The potential implications of publication bias (which tend to overestimate treatment effects) were not considered. Study selection and quality assessment were conducted in duplicate, which reduced the potential for error and bias; it was unclear whether data extraction was undertaken in a similarly robust manner. Quality assessment was conducted using the Jadad scale (a validated tool), although the quality threshold of 3 out of 5 may have incorporated potentially weak studies in the review. Meta-analysis was undertaken, which seemed appropriate, but trial heterogeneity was not fully explored despite evidence of moderate heterogeneity. Given the small number and size of most trials included in the review, questionable ascertainment of high study quality and unexplored implications of publication bias and heterogeneity on study results, the authors' conclusion that herbal medicines were potentially beneficial for improvement of cognitive function in various age-related dementias may be overly optimistic. The authors' conclusion that further studies were needed appeared warranted given the evidence presented.

**Implications of the review for practice and research**
**Practice:** The authors did not state implications for practice.

**Research:** The authors stated that more multi-centre studies with larger sample sizes were needed to further investigate the efficacy and safety of herbal medicines in dementia.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.