Chinese herbal medicine for mild cognitive impairment and age associated memory impairment: a review of randomised controlled trials

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CRD summary
The review concluded that evidence for efficacy of Chinese herbal medicines for mild cognitive impairment and age-associated memory impairment was inconclusive; the best available evidence was for Jia Wei Wu Zi Yan Zong Ke Li and Nao Li Bao Wan. The authors' cautious conclusion appeared appropriate, although its reliability is uncertain due to a lack of reporting of some results.

Authors' objectives
To assess the effectiveness and safety of Chinese herbal medicines for mild cognitive impairment (MCI) and age associated memory impairment (AAMI).

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, Elsevier BIOBASE and Chinese VIP Information databases were searched to February 2007 for studies published in English, Chinese, German and Japanese. Search terms were reported. Handsearches were conducted of the Guangzhou University of Chinese Medicine and journals from the Chinese VIP Information database from inception until 1989 (prior to the electronic database).

Study selection
Randomised controlled trials (RCTs) and quasi-RCTs that compared any form of a single herb or formulation with placebo, no intervention or other therapy and reported outcomes that related to memory, cognitive function, activities of daily living or quality of life were eligible for inclusion. Studies of Ginkgo biloba and plant-derived purified compounds as principal test interventions were excluded. To be included, participants had to have memory and/or other cognitive impairment associated with age and/or other age-related decline in physical or mental functioning consistent with MCI and/or AAM. Studies that included participants with Alzheimer's disease, vascular dementia or other dementia were excluded.

Interventions varied in the included studies and included Jia Wei Wu Zi Yan Zong Ke Li granules, Yi Nao Chong Ji granules, Jian Pi Tian Jing Fang capsules, Yin Zing Ye Jiao Nang capsules, Huan Nao Yi Chong Jiao Nang capsules, Deng Zan Hua Su dry powder for injection, Jin Si Wei Wan pills, Nao Li Bao Wan pills, Jia Jian Da Bu Yin Wan raw herbs in water decoction and Nao Li Bao Wan pills. Concentrations and composition of herbal medicine varied between studies.

Most studies compared Chinese herbal medicines with other interventions; the remaining two studies used a placebo control group. Treatment duration ranged from two to 10 months.

Outcomes were measured using a variety of instruments, including: Adult Memory and Information Processing Battery (AMIPB), Mini-Mental State Examination (MMSE), MMSE-R (revised in China), electrocardiograph (ECG), clinical memory scale (CMS), cognitive effect index (CEI), functional activities questionnaire (FAQ), cognitive capacity screening examination (CCSE), clinical dementia rating scale (CDR), global deterioration scale (GDS), Wechsler memory scale (WMS), Wechsler adult intelligence scale (WAIS), memory quotient (MQ), SF-36 Health Survey, Hachinski Ischemic Scale (HIS) and the Blessed dementia scale (BDS). Triglycerides, total cholesterol, high density lipoprotein (HDL-C), transcranial doppler (TC), superoxide dismutase (DOS), malondialdehyde (MDA) and acetylcholinesterase (AchE) were also measured.

The mean age of included participants ranged from 57 years to 72 years. Most participants in the included studies experienced mild cognitive impairment and others experienced age-related memory decline consistent with age associated memory impairment. All the included studies were conducted in China.

Two reviewers independently selected papers for inclusion.
Assessment of study quality
Validity was assessed using the Jadad criteria (assesses randomisation, double blinding and withdrawals and dropouts with a maximum score of 5). Two reviewers independently assessed validity. Disagreements were resolved by discussion or reference to a third party.

Data extraction
Data were extracted for the relevant outcomes of effectiveness and safety. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Data from outcome measurement instruments that provided continuous data were pooled using a fixed-effect model and used to calculate the weighted mean difference (WMD) and 95% confidence interval (CI). Heterogeneity was assessed using the $I^2$ statistic. Data were also combined in a narrative synthesis with additional data provided in tables.

Results of the review
Ten studies (n=654) were included in the review. Five studies scored three or more points on the Jadad scale. Five studies were double blinded, three studies were single blinded and two were unblinded. Five studies reported quality control data for Chinese herbal medicines in terms of equivalence to the crude herb, but without chromatographic or other standardisation data.

Chinese herbal medicine (Jia Wei Wu Zi Yan Zong Ke Li) versus placebo (two RCTs):
There was a significant improvement in memory quotient and a significantly greater decline in serum Beta amyloid for the Chinese herbal medicine group compared to placebo. However, there was a greater decline in hippocampal volume in the placebo group than in the Chinese herbal medicine group. One RCT reported a significant increase in the Chinese herbal medicine group for Mini-Mental State Examination scores after 12 weeks compared to placebo, although this was followed by a decline, it was reportedly less in the Chinese herbal medicine group than the placebo group.

Chinese herbal medicine (Huan Nao Yi Chong Jiao Nang) versus hydergine (one RCT):
There was a significant improvement in Cognitive Capacity Screening Examination, FAQ and Mini-Mental State Examination scores after 12 weeks for the Chinese herbal medicine group compared to hydergine.

Chinese herbal medicine versus Ginkgo biloba (two RCTs):
Two RCTs reported that Chinese herbal medicines may be equivalent or superior to Ginkgo biloba in improving memory in MCI patients in the short term.

Chinese herbal medicine versus piracetam (six RCTs):
Meta-analyses found no significant differences between Chinese herbal medicine compared to piracetam for Mini-Mental State Examination (WMD 0.37, 95% CI -0.21 to 0.95; three RCTs). There was no evidence of statistical heterogeneity for this analysis. One RCT reported greater improvements on the Chinese Medicine Symptom Score and Mini-Mental State Examination in the Chinese herbal medicine (Nao Li Bao Wan) group compared to piracetam.

Compared with no treatment, all subscales of WMS and memory quotient improved significantly in the high-dose Chinese herbal medicine (Yi Nao Chong Ji) group. Some improvements in WMS subscales and memory quotient were reported for the low-dose Chinese herbal medicine (Yi Nao Chong Ji) group compared to piracetam group in one RCT. One RCT also found more subjects reported improvements or no decline in Mini-Mental State Examination in the Chinese herbal medicine (Da Bu Yin Wan) group compared to the piracetam group.

Authors’ conclusions
While the evidence for efficacy of Chinese herbal medicines for mild cognitive impairment and age associated memory impairment remained inconclusive, the best available evidence was for Jia Wei Wu Zi Yan Zong Ke Li and Nao Li Bao Wan.
CRD commentary
The review question was clear and supported by detailed inclusion and exclusion criteria, although outcomes were not explicitly defined. Several relevant sources were searched and attempts were made to reduce publication and language biases. Appropriate methods were used in the selection of studies, assessment of validity and extraction of data. Validity was assessed using specified criteria and the results of the assessment were reported. Characteristics of the included studies were presented in tables. However, results for individual studies were reported without supporting data or levels of statistical significance and this made it impossible to verify the findings reported in the review. Only three of the 10 included studies were able to be combined in a meta-analysis; the rest were appropriately combined in a narrative synthesis due to differences between studies in interventions and outcomes. Sample sizes were generally small. All the included studies were conducted in China, so the results may not be generalisable to other settings and countries. The authors’ cautious conclusion appeared appropriate, though its reliability is uncertain due to lack of reporting of some results.

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

Research: The authors stated that larger longer-term multi-centre placebo controlled RCTs were required to evaluate the effectiveness and safety of Chinese herbal medicines.

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