Attention deficit hyperactivity disorder in children: comparative efficacy of traditional Chinese medicine and methylphenidate

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CRD summary
This review identified trials of traditional Chinese medicine compared with methylphenidate in children with attention deficit and hyperactivity disorder. The authors concluded that traditional Chinese medicine may be equal or superior to methylphenidate, but that more research was needed. Several methodological problems with the review may mean that the authors’ conclusions are not reliable.

Authors' objectives
To summarise existing evidence on the comparative effects of traditional Chinese medicine and methylphenidate for treating children with attention deficit and hyperactivity disorder (ADHD).

Searching
PubMed, The Cochrane library, EMBASE, Chinese Biological Medicine Database and China National Knowledge Infrastructure were searched to June 2008 for published articles in English or Chinese. Search terms were reported. Reference lists of retrieved articles were checked for relevant studies. Selected Chinese journals were searched.

Study selection
Randomised trials of traditional Chinese medicine alone or in combination with methylphenidate versus methylphenidate alone in children aged six to 18 years were eligible for inclusion. Patients had to be diagnosed with ADHD for at least six months and treated with traditional Chinese medicine for at least one month. Studies were excluded if participants had a history of drug abuse or psychiatric disorders, the study used drug therapy in combination with behavioural therapy or if loss to follow-up was more than 20%.

Included trials studied traditional Chinese medicine alone or in combination with methylphenidate versus methylphenidate alone in children with ADHD. Most studies were conducted in children aged six to 14 years. Outcomes recorded included: new criteria of disease diagnosis and treatment at home and abroad; Connor's Hyperactivity Index; and criteria of diagnosis and therapeutic effect of internal diseases and syndromes in traditional Chinese medicine.

The authors did not state how the study selection was performed.

Assessment of study quality
Study quality was assessed using Cochrane Handbook 5th edition to rate method of randomisation, concealment of allocation, blinding and loss to follow-up.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted on number of participants in each intervention group, composition of traditional Chinese medicine and outcomes.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Risk ratio and 95% confidence intervals (CI) were pooled using fixed-effects meta-analysis (where there was no heterogeneity) and a random-effects model (where there was heterogeneity). Heterogeneity was assessed using $I^2$ and
X² statistic. Data was not combined when an I² of 75% or more was detected. Subgroup analysis was undertaken based on outcomes measures used. Publication bias was assessed by visual examination of funnel plots.

**Results of the review**

Thirty four trials (n=3,167) were included in the review. In terms of study quality, seven trials were considered moderately biased and 27 trials were considered highly biased. The main reasons for bias within trials were lack of allocation concealment, no details on randomisation method and no details on blinding. Assessment of funnel plots indicated asymmetry and a high risk of publication bias.

**Short-term effects of traditional Chinese medicine versus methylphenidate (28 trials, n=2,896 participants):**

Overall, traditional Chinese medicine significantly improved outcomes compared to methylphenidate (RR 1.04, 95% CI 1.00 to 1.07, I²=0%).

When outcome measures were formed into subgroups, only criteria of diagnosis and therapeutic effect of internal disease and syndromes showed a benefit of traditional Chinese medicine versus methylphenidate (RR 1.09, 95% CI 1.02 to 1.16, I²=14%).

Only two of the 14 trials that used Connor's Hyperactivity Index (I²>75%, hence narrative synthesis) found an advantage of traditional Chinese medicine over methylphenidate; all other trials found no significant difference.

**Short-term effects of traditional Chinese medicine in combination with methylphenidate versus methylphenidate (seven trials, n=598 participants):**

Overall, traditional Chinese medicine with methylphenidate had significantly improved outcomes compared to methylphenidate alone (RR 1.22, 95% CI 1.12 to 1.32, I²=0%).

When outcome measures were formed into subgroups, all subgroups were statistically significant: new criteria of disease diagnosis and treatment at home and abroad (RR 1.16, 95% CI 1.02 to 1.30, I²=0%; three trials); criteria of diagnosis and therapeutic effect of internal disease and syndromes in traditional Chinese medicine (RR 1.22, 95% CI 1.09 to 1.37, I²=0%; three trials); and outcome measures not clear (RR 1.57, 95% CI 1.14 to 2.18, I² not applicable as based on one trial only).

All three trials that assessed Connor's Hyperactivity Index found a significant advantage of traditional Chinese medicine in combination with methylphenidate compared with methylphenidate alone.

**Long-term effects:**

Five trials of traditional Chinese medicine versus methylphenidate indicated that traditional Chinese medicine was superior to methylphenidate (follow-up ranged from three months to two years).

Two trials of traditional Chinese medicine combined with methylphenidate versus methylphenidate indicated that traditional Chinese medicine in combination with methylphenidate was superior to methylphenidate alone (follow-up ranged from 12 weeks to six months).

**Authors' conclusions**

Traditional Chinese medicine may have a better or equal efficacy to methylphenidate in children with ADHD, but a lack of high-quality trials meant that it was not possible to recommend any particular kind of traditional Chinese medicine preparation for treating children with ADHD.

**CRD commentary**

Inclusion criteria for the review were broadly defined and several relevant sources were searched. The restriction to published literature may have caused unpublished studies to be missed. Funnel plots indicated a high risk of publication bias. It was unclear how many reviewers performed study selection, data extraction and validity assessment, which may have introduced error and bias into the review. Validity assessment was undertaken using Cochrane Handbook criteria,
a standard tool, which indicated low methodological quality of the trials included in the review. Trials were combined using meta-analysis and study heterogeneity was explored. Given the disparate nature of interventions and outcome measures included in the trials and the possibility that some trials were included in the meta-analysis more than once (double counted), the results of meta-analysis may have been misleading. Only limited information about individual studies was provided, which made it more difficult to assess the appropriateness of data synthesis and reliability of results. Overall, the review had several methodological weaknesses and the included trials were of poor quality, so the authors' conclusion that traditional Chinese medicine was equal or superior to methylphenidate may not be reliable.

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

Research: The authors indicated that more high-quality trials of traditional Chinese medicine for treatment of children with ADHD were needed.

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