Systematic review of Chinese herbal medicine for functional constipation

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CRD summary
This review concluded that Chinese herbal medicine interventions or Chinese herbal medicines combined treatments showed benefit in the treatment of functional constipation when compared with cisapride, polyethylene glycol 4000, mosapride, phenolphthalein, itopride and bifidobacteria alone, but not when compared with massage. The reliability of these conclusions is uncertain given the limited quality of included trials and other methodological concerns.

Authors' objectives
To assess the efficacy and safety of Chinese herbal medicine for the treatment of functional constipation.

Searching
The following databases were searched, without language restrictions, from 1994 to May 2009: MEDLINE, DARE, AMED, the Cochrane Library, ACP Journal Club, Health Technology Assessment, NHS EED, BIOSIS Previews, VIP Citation Databases, Traditional Chinese Medical Database System, and China Journal Net. Search terms were reported. Both published and non-published studies were considered.

Study selection
Randomised controlled trials (RCTs) that compared Chinese herbal medicine with a control in patients (of any age) diagnosed with functional constipation (according to the Rome criteria) were eligible for inclusion. Eligible trials could use Chinese herbal medicine in any form and in any dose, or as add-on combination treatments, which could be oral or external preparations. The eligible controls included placebo, no intervention, acupuncture, massage, Western conventional medication, another Chinese herbal medicine, or any other interventions. Patients with secondary constipation due to medication and/or other diseases were excluded.

The primary review outcome was the rate of patients with a mean increase of one or more complete spontaneous bowel movement per week. If this outcome was not available in the trial, the overall effectiveness assessment (defined as 30% or more improvement compared with the baseline in general constipated symptoms and/or objective examination indices) was considered as a primary outcome. Secondary outcomes included changes in symptoms and adverse events.

The included trials evaluated Chinese herbal medicines including LiuWei auxiliary, MaRen auxiliary and RunChangTongBianNongSuo pill. The control arms of the majority of included trials were another Chinese herbal medicine and/or Western conventional medication. None of the included trials used a placebo control, and only one trial used no treatment as a control. The age of included patients ranged from one month to 93 years.

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
The quality of trials was examined using the following criteria: randomisation sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential threats. These were assessed as low risk of bias, high risk of bias or uncertain risk of bias.

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

Data extraction
Event rates were extracted to enable the calculation of relative risks (RRs) with 95% confidence intervals (CIs).

The authors did not state how many reviewers performed the data extraction.
**Methods of synthesis**
The trials were combined in a meta-analysis using a fixed-effect model. The pooled relative risks, with 95% confidence intervals, were calculated. Statistical heterogeneity was assessed using $\chi^2$ and $I^2$ statistics.

**Results of the review**
Thirty-five RCTs were included in meta-analyses (n=3,571 participants). Only two trials clearly reported a random component in the sequence generation process. None of the trials reported withdrawal and/or loss to follow-up rates. There was no blinding for participants, investigators or outcome assessors in any of these trials. Five trials had a high risk of bias relating to selective outcome reporting.

**Chinese herbal medicine versus Western conventional medicine**
Compared with cisapride alone, Chinese herbal medicine alone or with cisapride was associated with a significant decrease in the rate of failure to respond to treatment (RR 0.24, 95% CI 0.17 to 0.34; eight RCTs).

Compared with polyethylene glycol 4000 alone, Chinese herbal medicine alone or with polyethylene glycol 4000 was associated with a significant decrease in the rate of failure to respond to treatment (RR 0.14, 95% CI 0.06 to 0.34; six RCTs).

Compared with mosapride alone, Chinese herbal medicine alone or with mosapride was associated with a significant decrease in the rate of failure to respond to treatment (RR 0.33, 95% CI 0.23 to 0.46; six treatment arms).

Compared with phenolphthalein alone, Chinese herbal medicine in addition to phenolphthalein was associated with a significant decrease in the rate of failure to respond to treatment (RR 0.24, 95% CI 0.13 to 0.46; three RCTs).

Significant heterogeneity was only observed in the above outcome for the comparison of Chinese herbal medicine and/or mosapride versus mosapride alone ($I^2=70\%$).

One RCT reported that a traditional Chinese medicine combined with itopride led to a significant increase in the rate of overall effectiveness compared with itopride alone (p<0.05). One RCT reported that a traditional Chinese medicine combined with bifidobacteria led to a significant increase in the rate of overall effectiveness compared with bifidobacteria alone (p<0.01).

**Chinese herbal medicine versus non-pharmaceutical interventions**
One RCT reported that, compared with massage, Chinese herbal medicine led to a significant decrease in the rate of overall effectiveness (p<0.05).

Few studies reported adverse events of Chinese herbal medicines; these adverse events mainly included abdominal pain and diarrhoea.

Results of comparing a Chinese herbal medicine with another type of Chinese herbal medicine were also reported.

**Authors' conclusions**
Chinese herbal medicine interventions or Chinese herbal medicines combined treatments showed benefit in the treatment of functional constipation when compared with cisapride, polyethylene glycol 4000, mosapride, phenolphthalein, itopride and bifidobacteria alone, but not when compared with massage.

**CRD commentary**
The inclusion criteria of the review were clear. Relevant databases were searched. Efforts were made to find both published and unpublished trials without language restriction, minimising the potential for both publication and language biases. It was unclear whether sufficient attempts have been made to minimise the errors and biases in the review process.

Relevant criteria were used to examine the trial quality. There were no details of the primary trials such as characteristics of included patients. Statistical heterogeneity was assessed, but using a fixed-effect model to pool the results in the presence of significant heterogeneity may have not been appropriate.
Given the limited quality of included trials (as acknowledged by the authors) and the methodological concerns outlined above, the reliability of the authors’ conclusions is uncertain.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors state that further well-designed, double-blind, placebo-controlled RCTs are required to evaluate the efficacy and safety of Chinese herbal medicine for the treatment of functional constipation.

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