Chinese herbal medicine for dysfunctional uterine bleeding: a meta-analysis

Tu X, Huang G, Tan S

CRD summary
This review concluded that, due to the poor methodology of the included trials and the lack of placebo-controlled studies, it was not possible to determine the efficacy of Chinese herbal medicines for the treatment of dysfunctional uterine bleeding. Despite a number of concerns about the review methods, the authors' cautious conclusions appropriately reflect the limitations of the evidence.

Authors' objectives
To determine the efficacy and safety of Chinese herbal medicine for the treatment of dysfunctional uterine bleeding.

Searching
The following databases were searched, in English and Chinese, from inception to 2006: PubMed, Chinese Biomedical Disk (CBM disk), Chinese Journals full text, Dissertations of China (DOC) full text, and China Scientific and Technological Journals (CSTJ). Search terms were reported. Also, 32 relevant Chinese journals were handsearched. Studies in any language were eligible for inclusion.

Study selection
Randomised controlled trials (RCTs) and quasi-RCTs comparing Chinese herbal medicine for dysfunctional uterine bleeding with no intervention, placebo, general non-specific surgery, or conventional western medicine, were eligible for inclusion in the review. Trials comparing Chinese herbal medicine plus conventional western medicine versus conventional Western medicine were also included. The following types of trials were excluded: trials of animal derived products (trials of processed products from minerals and animal excretions were permitted to be used as adjunctive treatment); trials comparing different Chinese herbal medicines; trials that did not report diagnostic criteria; and trials including women with bleeding due to pregnancy, use of an intrauterine contraceptive device or a systemic disease or disorder. Eligible patients had to have a confirmed diagnosis of dysfunctional uterine bleeding which ruled out organic causes. Eligible outcome measures were: total effect rate; normalisation rate of menstruation; haemostasis rate; menstrual blood loss; recurrence rate; and adverse events.

Reported Chinese herbal medicine interventions included oral Tiaojing hao, Bazhen Tang, Bushen Tiaojing Fang, and Fufang ShuDi. Conventional western medicines included one of more of the following: intramuscular progesterone, oral diethylstilbestrol, medroxyprogesterone acetate, oral norethindrone, and conjugated oestrogens. Half of the trials compared Chinese herbal medicines with conventional western medicines; the remainder of the trials compared combinations of Chinese herbal medicines plus conventional western medicines with conventional western medicines alone. Treatments were usually administered for three menstrual cycles. Included participants ranged in age from 11 to 50 years, with symptoms ranging in duration from 20 days to 120 months, where reported.

The authors did not state how papers were selected for review or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed using the Jadad scale for randomisation, blinding and loss to follow-up. Allocation concealment was also assessed using the Cochrane Collaboration criteria. Each trial was awarded a Jadad score between 0 and a maximum of 5 points; allocation concealment was graded from A (highest) to D (lowest). Trials with scores below 3 points were considered to be low quality.

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

Data extraction
Two reviewers independently extracted the study data and discrepancies were resolved through discussion. Trial authors were contacted for further clarification and data if necessary. The authors reported that odds ratios with 95%
confidence intervals were calculated for dichotomous outcomes. Means with standard deviations were extracted for continuous outcomes.

**Methods of synthesis**
Trials were grouped according to whether they compared Chinese herbal medicine with conventional western medicine or Chinese herbal medicine plus conventional western medicine with conventional western medicine alone. The authors reported that data were combined using a fixed-effect model to calculate pooled odds ratios (for dichotomous outcomes) or weighted mean differences for continuous outcomes, with 95% confidence intervals. Statistical homogeneity was assessed using the $\chi^2$ test. A funnel plot analysis to detect publication bias could not be performed due to the small number of included trials.

**Results of the review**
Four randomised controlled trials (RCTs) were included in the review (n=525 participants). Three trials were reported to be of low quality (<3 Jadad points) and the remaining trial scored 3 points. All of the trials were awarded a grade D (lowest) for allocation concealment. Sample size ranged from 35 to 316. Only one trial reported the duration of follow-up used (six months).

**Chinese herbal medicine versus conventional western medicine** (two RCTs): One RCT reported a significant difference in the normalisation rate of menstruation in favour of Chinese herbal medicine (odds ratio 2.35, 95% confidence interval (CI): 1.25 to 4.41). The second RCT, which was a high quality trial, reported no statistically significant difference. The pooled odds ratio for both trials was 1.83 (95% CI: 1.09 to 3.09; p=0.02). No statistically significant differences were observed between the groups for total effect rate (two RCTs) or haemostasis rate (two RCTs). Recurrence rate was reported in one trial and was marginally significant in favour of Chinese herbal medicine (odds ratio 0.1, 95% CI: 0.02 to 0.44; p=0.003).

**Chinese herbal medicine plus conventional western medicine versus conventional western medicine alone** (two RCTs): Both trials were low quality. They both reported statistically significant differences in favour of Chinese herbal medicine plus conventional western medicine for total effect rate (pooled odds ratio 12.74, 95% CI: 2.72 to 59.72; p=0.001) and normalisation of menstruation (pooled odds ratio 7.43, 95% CI: 3.16 to 17.44; p<0.0001).

No serious adverse events were reported.

**Authors’ conclusions**
Due to the poor methodology of the included trials and the lack of placebo-controlled studies, it was not possible to determine the efficacy of Chinese herbal medicines for the treatment of dysfunctional uterine bleeding.

**CRD commentary**
This review assesses a clearly defined review question. A number of data sources were searched, but given the topic area and the limited searches for unpublished data, there may be a risk of publication bias. An assessment of publication bias was planned, but not carried out due to the small number of included trials. Searching was carried out in English and Chinese, although studies published in any language were eligible for inclusion. Whether this increased the risk of language bias is unclear. There may also be a risk of reviewer error and bias, as it is unclear how studies were assessed for inclusion, but two reviewers extracted the study data, suggesting a lower risk of bias. Trial quality was assessed using a validated tool, but the overall quality of the trials was found to be low, so the reliability of the data is questionable. Trials were pooled according to broadly defined comparisons, despite the fact that there appeared to be significant differences in the specific types of interventions and comparators included. Few details regarding the baseline characteristics of the patients were reported, so it was difficult to assess if the trial populations were clinically similar. The authors stated that statistical homogeneity was examined and P values were reported, but some values were missing from the tables. Effect sizes were also only reported as odds ratios, despite some outcomes appearing to be continuous and not dichotomous, which contradicted the authors’ stated methods. However, despite a number of concerns about the review methods, the authors’ cautious conclusions appropriately reflect the limitations of the evidence.

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

Research: The authors stated that further well-designed, randomised, double-blind, placebo-controlled trials of Chinese herbal medicines, using large sample sizes, are required.

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