Complementary/alternative therapies for premenstrual syndrome: a systematic review of randomized controlled trials

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Authors' objectives
To determine whether the use of complementary or alternative therapies for premenstrual syndrome (PMS) is supported by the evidence from rigorous clinical trials.

Searching
MEDLINE, EMBASE, BIOSIS Previews, CINAHL, PsycINFO and the Cochrane Library (to October, 2000) and CISCOM (to December 1988) were searched. In addition, leading investigators in the field and manufacturers of herbal preparations were contacted. The reference lists of all the retrieved papers were examined for additional publications.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that had been published in a peer-reviewed journal were included.

Specific interventions included in the review
The interventions investigated were: herbal medicine, homeopathy, dietary supplementation, relaxation, massage, reflexology, chiropractic and biofeedback. The herbal medicines included extracts from the chaste tree, ginkgo biloba, and the essential oil of the evening primrose flower. The dietary supplements included calcium, magnesium, vitamin B6, vitamin E, a carbohydrate drink, and a nutritional multi-supplement containing large amounts of magnesium, vitamin B6 and other essential micro-nutrients.

Participants included in the review
Women with symptoms of PMS. While it is reported that 30 to 80% of women experience symptoms consistent with PMS, the authors state that the prevalence of PMS is around 2.5% of women of reproductive age when strict diagnostic criteria are applied. However, in 6 of the 27 studies, the authors reported that the diagnosis of PMS was unchecked.

Outcomes assessed in the review
A range of outcomes were assessed. Some of the trials included in the review used standard questionnaires such as the Menstrual Distress Questionnaire (MDQ) and the Menstrual Symptom Questionnaire (MSQ). The scales assessed a range of constituent symptoms including anger, anxiety, arousal, breast pain, carbohydrate cravings, depression, fluid retention and memory. Performance against these scales was used as an outcome measure.

In addition, some studies used other outcome measures such as visual analogue scales, subjective ratings by the patients and patient diaries.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
A quantitative assessment of methodological quality was not carried out, but the authors commented on the rigour of the individual studies in the tables presented. These comments related to patient recruitment, trial design, and statistical analysis methods. Data pertinent to the validity of the included studies were extracted by the first author and checked by the second author. Any discrepancies were resolved through discussion.

Data extraction

Database of Abstracts of Reviews of Effects (DARE)  
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The data were extracted by the first author and checked by the second author. Any discrepancies were resolved through discussion.

The data extracted included: study identifier (first author and year); study design; the number of patients recruited; the number of patients who contributed data to the analysis; methods of diagnosing PMS; the intervention offered to patients in the active and the control arms of the study; the dose(s) at which the active treatment was administered; the primary outcomes; the reported superiority of the intervention over the controls; the number of adverse events; and comments about the methodological quality of the studies.

**Methods of synthesis**

How were the studies combined?
The studies were stratified according to the type of intervention being investigated. These strata were herbal medicines, homeopathy, dietary supplementation and other interventions. The latter category included biofeedback, chiropractic, massage, reflexology and relaxation.

No attempt to assess publication bias was reported.

How were differences between studies investigated?
The authors grouped the studies according to intervention type. In addition, the studies appeared to differ in terms of their size, the outcomes evaluated, the method of assessment, women included and methodological quality.

**Results of the review**

Twenty-seven RCTs were included in the review, which collectively presented data on 2,724 women.

Forty-one controlled trials were identified from the searches. Of these 14 were excluded for one or more of the following reasons: not randomised (6); published only in conference or dissertation abstract form, and not derived from peer-reviewed publications (5); only one septum investigated and not the syndrome as a whole (4); assessed health volunteers (3); the diagnosis of interest was primary dysmenorrhoea (1). The review, therefore, consisted of 27 studies.

Herbal medicine (7 RCTs).

Two independent investigations of the chaste tree (Vitex agnes castus) failed to find strong evidence to support the herbal preparation. In one of these trials, only one of the 20 symptoms was significantly improved, and this was mirrored by a similar improvement in patients treated with the control intervention. The other trial reported that the chaste tree was at least as effective as vitamin B6, but the trial was also methodologically flawed, partly because of it being underpowered. An assessment of ginkgo (Ginkgo biloba) found that only one of a range of measures related to breast pain was improved. In 4 studies investigating 3 to 6 mg doses of evening primrose oil (Oenothera biennis), no significant association was seen in favour of the oil over control medicines. These studies were, however, of low power.

Homeopathy (1 RCT).

One study that investigated homeopathy had such strict inclusion criteria that only 10 of the 205 patients who were screened actually participated in the study.

Dietary supplements (13 RCTs). Calcium supplements were studied in 2 RCTs, both led by the same investigator. Despite methodological flaws, the studies both reported that patients offered supplements had improvements in a range of symptoms, compared with patients in the control arm. In investigations of magnesium supplements, 2 separate small studies found improvements with magnesium, compared with control therapy, but for different symptoms. The investigators of one of these studies repeated their study to find no advantage of magnesium alone, but an improvement for magnesium when taken in combination with vitamin B6.

Two small studies, each by the same investigators, assessed vitamin E. One, a dose response study, found 300 IU/day to be optimal when compared with 150 and 600 IU/day. The subsequent study, using a dose of 400 IU/day, failed to find any association at the 5% level of significance.
In investigations of a nutritional multi-supplement containing large amounts of magnesium, vitamin B6 and the essential micro-nutrients, researchers used doses of 4 to 12 tablets/day. One study found that 6 tablets/day was significantly better than placebo in terms of the overall response to the MSQ scale, anxiety levels and cravings. Another study that compared 8 tablets with 4 tablets found, on subjective ratings, that significantly more women reported improvements on the higher dose. An additional study investigated 6 and 12 tablets and found both to be superior to placebo, but the reviewers raised ethical concerns owing to the 12-tablet dose exceeding the safe daily intake for two of its components.

A study of another supplement consisting of magnesium, vitamin B6 and yeast, found significant improvements in 5 out of 7 septum clusters at 6 months, measured in terms of the MDQ scale.

Positive effects on appetite, memory and mood were found in study of a drink containing simple and complex carbohydrates, compared with one of two control drinks containing a protein-carbohydrate mixture or simple carbohydrates alone. However, only 24 of the 99 participants in this study were analysed owing to protocol breeches. Other interventions.

A small trial of progressive muscle relaxation, compared with reading or charting symptoms, found significant improvements in the physical symptoms of PMS. In those women with more severe PMS, the overall score on the two rating scales and the emotional septum cluster were also improved. Another trial compared massage therapy with progressive relaxation. Although improvements over baseline were reported, no comparisons between the groups were reported.

Sham-controlled reflexology was found to be effective in terms of the overall somatic and psychological symptoms reported in diary format by the patient. In this study, therapist blinding was not possible.

The initial results of a sham-controlled chiropractice crossover trial appeared to show a benefit of chiropractice. However, reanalysis showed the first intervention led to significant improvements over baseline, irrespective of the order in which the sham therapy and chiropractic were administered, whereas there was little further improvement associated with the second intervention.

Two related studies of biofeedback were reported by the same investigators. A significant reduction was seen in the overall condition of the patients, including significant results in relation to physiological and affective symptoms.

Authors' conclusions
On the basis of the current evidence, no complementary or alternative therapy may be recommended as a treatment for PMS.

CRD commentary
The research question was clearly stated in terms of the participants, interventions and comparators. The outcomes of interest were not cited a priori.

The authors appear to have searched a wide range of sources for relevant publications. The electronic searches appeared comprehensive but the report would have benefited from examples of the search terms.

While the authors report their decision not to address the validity of the studies quantitatively, it is unclear why patient recruitment, trial design and the statistical analysis methods were selected for comment. The decision not to pool the data appears justified in view of the differences between the interventions, outcomes and methods used in the various studies.

The overall conclusions follow from the data presented, and the implications that were identified seem appropriate.

Implications of the review for practice and research
Practice: The authors state that several therapies for PMS symptoms, such as dietary changes and relaxation, may not have been proven to be effective for PMS, but can be recommended for general good health since they have few, if any, side-effects.
Research: The authors state that all potential complementary or alternative therapies for PMS symptoms require testing in adequately designed RCTs, especially since these therapies are widely used by women with PMS and by those with more general symptoms of PMS.

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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.