A systematic review of herbal medicinal products for the treatment of menopausal symptoms

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CRD summary
This review assessed whether herbal medicinal products improved symptoms of the menopause. The authors concluded that there is no convincing evidence that any product is effective, although black cohosh may be of use and red clover may help severe symptoms. The review was generally well conducted, although the reporting was variable, and the conclusions are likely to be reliable.

Authors' objectives
To evaluate the benefit of herbal medicinal products for the treatment of menopausal symptoms.

Searching
MEDLINE, EMBASE, Phytodok and the Cochrane Library were searched from inception to December 2002; the search terms were given. No language restrictions were applied. In addition, the reference lists of retrieved studies and personal files were searched. The manufacturers of herbal products were contacted for published and unpublished studies.

Study selection
Study designs of evaluations included in the review
The inclusion criterion was randomised controlled trials.

Specific interventions included in the review
The inclusion criteria were herbal medicinal products. Soy was excluded from the review. The treatments included in the review were black cohosh, red clover, kava, dong quai, evening primrose oil, ginseng, and combination products.

Participants included in the review
Women undergoing the menopause or experiencing menopausal symptoms were included in the review. Women experiencing artificially induced menopause were excluded from the study. Women who had undergone hysterectomies and women who were being treated for breast cancer were included in the review, as were those for whom the treatment histories were not given.

Outcomes assessed in the review
The inclusion criteria were measures relating to the physical or psychological impact of the menopause, including compendium scores, questionnaires or participants' symptom diaries. Excluded from the review were non-clinical end points such as blood hormonal level data and vaginal cytology. Several assessment scales were included in the review, of which the most frequently used were the Kupperman Index and the Hamilton Anxiety Scale (HAMA).

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

Assessment of study quality
Validity was assessed using the Jadad scale. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

Data extraction
One reviewer extracted the data.

**Methods of synthesis**

How were the studies combined?
A detailed, narrative synthesis of the studies was undertaken and evidence tables were presented.

How were differences between studies investigated?
The studies were grouped by the herbal medicine used.

**Results of the review**

Eighteen studies were included in the review. The number of patients in one study was not stated; the remaining 17 studies involved 1,295 patients.

Four trials examined the effectiveness of black cohosh given as the brand Remifemin. Two studies compared Remifemin, conjugated estrogen and diazepam over 12 weeks. The data for one study (n=60) were not reported, although it was stated that the Remifemin group experienced greatest improvement on a number of outcome measures. The second study (n=80) found significant reductions from baseline in the Kupperman Index and the HAMA Scale (P<0.001 in both cases) in the Remifemin group. A study involving women with hysterectomies and one intact ovary (n=60) compared Remifemin, estriol, conjugated estrogens and estrogen-progesterone therapy. All groups showed significant improvement (P=0.01) on the Kupperman Index with no difference between the groups. Finally, a study of breast cancer patients (n=85), of whom 69% were being treated with tamoxifen, compared Remifemin and placebo over 60 days. Hot-flash diaries showed improvements in both groups, with no differences between the groups.

Four trials examined the effectiveness of red clover given as the brand Promensil. A crossover study (n=51) administered Promensil or placebo for 12 weeks, with a 1-month washout, followed by 14 weeks of the alternate treatment. There were no significant differences between the groups on any of the outcome measures. A trial (n=37) compared two different doses of Promensil with placebo over 12 weeks. There were no significant differences between the groups on either of the outcome measures. A third study (n=30) administered single blind placebo tablets for 4 weeks, followed by randomisation to placebo or Promensil for 12 weeks. A significantly larger decrease in hot flush frequency occurred in the treatment group (P<0.01) during the randomised stage. The final study (n=30) compared Promensil and placebo over 16 weeks. Significant reductions in frequency and severity of hot flushes were seen in the treatment group compared with placebo (P<0.001).

Three trials examined the effectiveness of kava. One study (n=40) compared kava extract with placebo over 12 weeks. For all the measures used (Kupperman Index, Anxiety-State Index and symptom diary), the kava group showed significant improvements on all measures (P<0.001) while the placebo group showed no changes. The drop-out rates prevented analysis at subsequent intervals. A second study (n=40) compared Kava WS 1490 with placebo over 8 weeks. A number of health-related quality of life measures were used, including the Kupperman Index, HAMA and the Depression Status Index. Significant improvements were seen in the first two indices in the kava group at 1, 4 and 8 weeks, and in the Depression Status Index at 4 and 8 weeks. A final study (n=40) compared kava in combination with hormone replacement therapy (HRT) with HRT and placebo over 6 months. Both groups showed improvement on the HAMA compared with baseline, but improvement was greatest in the group given kava (P<0.05). The groups were not compared directly.

One trial (n=71) examined the effectiveness of dong quai compared with placebo over 24 weeks. The outcome measures used were the Kupperman Index and a daily flush diary. There were no differences between the groups, although both groups showed improvements on both measures.

One trial (n=56) examined the effectiveness of evening primrose oil compared with placebo over 24 weeks. There was no benefit of treatment on any outcome measure, but there was a significant reduction from baseline in the maximum number of night-time flushes (P<0.05).

One trial (n=384) examined the effectiveness of ginseng compared with placebo over 16 weeks. Of several quality of life questionnaires employed, only the Psychological General Well-being Index showed a significant benefit for ginseng
(P<0.01), as did its depression, well-being and health subscales (P<0.05).

Four trials examined the effectiveness of herbal combinations. One (n=179) looked at black cohosh and St. John's Wort (Remifemin Plus) compared with placebo for 6 weeks. There was a greater reduction in the Kupperman Index in the treatment group, but this was not clinically significant. A small study (n=13) compared a combination of burdock, licorice root, motherwort, dong quai and Mexican wild yam with placebo over 12 weeks. The outcomes were patient symptom records of occurrence and severity. More women in the treatment group experienced reductions in these measures, but statistical tests were not reported. A defined Chinese herbal formula with 12 active constituents was also compared with placebo (n=55). There were no significant differences between the groups in either frequency of vasomotor events or Menopause Specific Quality of Life Score. Finally, a crossover study (n=50) compared a BioGest cream containing four active ingredients with placebo over 3 months. A symptom diary showed no differences between the groups.

Authors' conclusions
There was no convincing evidence for the efficacy of any herbal medicinal product in the treatment of menopausal symptoms. The authors also stated that the evidence for black cohosh is promising, and that red clover may benefit women with more severe menopausal symptoms.

CRD commentary
The review question and the inclusion criteria were reasonably clear. The search was adequate, while attempts to locate unpublished studies and the lack of language restrictions make the occurrence of publication and language bias less likely. The authors did not use methods to reduce bias and error, such as the involvement of two reviewers, when extracting the data and did not report the use of such methods when selecting the studies for inclusion and assessing their quality. The decision to adopt a narrative synthesis was appropriate in view of the clinical heterogeneity of the included studies, and both a synthesis and evidence tables were detailed. The authors' conclusions accurately reflect the evidence included in the review.

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

Research: The authors stated that further work on the efficacy and safety of herbal medicinal products is warranted.

Bibliographic details

PubMedID
14501609

DOI
10.1097/01.GME.0000058147.24036.B0

Indexing Status
Subject indexing assigned by NLM

MeSH
Angelica sinensis; Cimicifuga; Female; Humans; Kava; Menopause /drug effects; Oenothera biennis; Panax; Phytotherapy; Plant Preparations /therapeutic use; Trifolium

AccessionNumber
12003001980
Date bibliographic record published
31/03/2005

Date abstract record published
31/03/2005

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.