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**Long-term use
of pyridoxine in
doses >200 mg/d
can cause
neuropathy.**

Q / Which complementary therapies can help patients with PMS?

EVIDENCE-BASED ANSWER

A / **CHASTEBERRY TREE AND CALCIUM** have demonstrated efficacy and safety in treating symptoms of premenstrual syndrome (PMS) (strength of recommendation [SOR]: **A**, randomized controlled trials [RCTs]). Pyridoxine and saffron may be effective, but high doses of pyridoxine can cause neuropathy (SOR: **B**, RCT and meta-analysis of lower-quality studies).

Insufficient evidence exists to recommend magnesium. St. John's wort and evening primrose oil aren't effective for managing PMS (SOR: **B**, inconsistent or limited quality patient-oriented evidence). No evidence was found to support black cohosh or vitamin E.

statistically significant differences were noted between the 2 groups. Chasteberry tree was well tolerated; most adverse effects occurred in patients receiving fluoxetine. The most frequent adverse effects with chasteberry tree were nausea in 5 patients and headache in 4.³

Symptoms decrease significantly after 3 calcium treatment cycles

Two RCTs (33 and 466 patients) comparing 1000 and 1200 mg of calcium with placebo found a significant decrease in PMS symptoms after 3 treatment cycles.^{4,5} Calcium improved negative affect, water retention, food cravings, and pain. In the first study, 73% of patients preferred taking calcium, compared with 15% who preferred placebo.

The second study found that, by the third treatment cycle, patients taking calcium had an overall 48% reduction in total symptom scores, compared with a 30% reduction in the control group. The most common adverse effects were headache, rhinitis, and nonspecific pain.

Watch out for neuropathy with high doses of pyridoxine

A meta-analysis of pyridoxine in doses from 50 to 600 mg per day for PMS included 9 RCTs. Relative to placebo, pyridoxine improved PMS symptom scores (odds ratio=2.32, 95%

Evidence summary

A double-blind RCT comparing chasteberry tree with placebo in 170 patients found a decrease in self-reported PMS symptom scores and an increase in response rate (defined as a 50% reduction in symptoms)—52% vs 24%—in the intervention group (number needed to treat [NNT]=3.5). Patients taking chasteberry tree had 1 occurrence of multiple abscesses and 1 of urticaria.¹

A prospective, open-label study of chasteberry tree for PMS symptoms in 43 patients found a 42% decrease in self-assessed PMS symptom scores, with the greatest improvement in pain, behavior changes, negative feelings, and fluid retention. No serious adverse events occurred.²

A third study comparing chasteberry tree with fluoxetine in 19 patients found a decrease in premenstrual symptom scores for both fluoxetine (13 of 19 patients) and chasteberry tree (11 of 19 patients). No

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confidence interval, 1.95-2.54). The overall quality of studies was poor, however, with few subjects, widely varying doses, and different outcome measurements.⁶

Two subsequent RCTs of 40 and 96 patients that weren't included in the meta-analysis failed to demonstrate reduced premenstrual symptoms.^{7,8} Long-term use of pyridoxine in doses >200 mg/d can cause neuropathy.

Saffron shows promise in small study

A recent double-blind RCT evaluated the effect of 2 cycles of treatment with saffron (*Crocus sativus L*), 30 mg twice daily, on PMS symptoms in 50 patients. Nineteen patients in the saffron group showed a response, defined as 50% reduction in symptom severity, compared with 2 patients in the placebo group (NNT=2). The study found no statistically significant difference in frequency of adverse effects.⁹

Evidence for magnesium is sparse

Two RCTs comparing magnesium with placebo had low precision because of small numbers and short treatment duration.^{10,11} The first (N=28) demonstrated reduced total Moos Menstrual Distress Questionnaire scores.¹⁰ The second study reported a decrease in fluid retention symptoms by 2 points on an 80-point

scale ($P<.009$) at 2 months, but no difference in total score.¹¹

A further study, begun as an open trial of magnesium infusion for premenstrual dysphoric disorder (N=6), found a dramatic reduction in mood symptom scores. After converting to a randomized, blinded design (N=10), no difference was found compared with placebo.¹²

St. John's wort, evening primrose oil don't work

One randomized, double-blind controlled trial (N=125) of 600 mg St. John's wort vs placebo over 2 cycles of treatment found no significant changes in symptom score from baseline.¹³ Two double-blind crossover studies of 27 and 38 patients found that evening primrose oil had no effect on PMS symptoms.^{14,15}

Recommendations

The Premenstrual Syndrome Guidelines of the American College of Obstetricians and Gynecologists (ACOG) state that calcium and magnesium have been shown to be effective in small trials and must be validated in larger trials before a strong evidence-based recommendation can be made. ACOG's guidelines also report minimal effectiveness with vitamin B6 and vitamin E.¹⁶

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