

Trial 2015: Supplements (Wheat Germ)

The effect of wheat germ extract on premenstrual syndrome symptoms

Link: <https://pubmed.ncbi.nlm.nih.gov/25561922/>

Year published: 2015

Trial information: Clinical trial.

Objective: This study aimed to determine the effects of wheat germ extract on the symptoms of premenstrual syndrome.

Blind/double blind? Triple blind.

Randomised? Yes.

Placebo? Placebo group.

Participant information: 84 women, working in hospitals affiliated to Hamadan University of Medical Sciences, with a definitive diagnosis of premenstrual syndrome.

Treatment length: 2 cycles (+2 diagnostic cycles).

Drug and dosage: 400 mg capsules of wheat germ extract were used three times a day, from day 16 until day 5 of the next menstrual cycle; or placebo.

Measuring scales: Subjects completed daily symptom record forms.

Efficacy outcomes: Wheat germ significantly reduced physical symptoms (63.56%), psychological symptoms (66.30%), and the general score (64.99%). Although the severity of symptoms decreased in both groups, this reduction was more significant in the wheat germ extract group ($p < 0.001$). On the other hand, physical symptoms decreased only in the wheat germ extract ($p < 0.001$), and there was no statistically significant difference in the placebo group.

Side-effects assessment: No complications were observed in any of the groups.

Conclusion: It seems that using wheat germ extract reduces general, psychological and physical symptoms.

Trial 2015: Supplements (Curcumin)

Curcumin attenuates severity of premenstrual syndrome symptoms: A randomized, double-blind, placebo-controlled trial

Link: <https://pubmed.ncbi.nlm.nih.gov/26051565/>

Year published: 2015

Pubmed classification: Randomised Controlled Trial.

Further trial information: Clinical trial.

Objective: This study was done to evaluate the effects of curcumin on severity of PMS symptoms.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo group.

Participant information: 70 persons identified as suffering from PMS. The baseline level of PMS symptoms before intervention did not differ between the active and placebo groups.

Treatment length: 3 cycles.

Drug and dosage: Two capsules daily for seven days before menstruation and for three days after menstruation (35); or placebo (35).

Measuring scales: Participants recorded the severity of the symptoms by daily record questionnaire.

Efficacy outcomes: After three consecutive cycles treatment with curcumin, total severity of PMS score had reduced from 102.06 ± 39.64 to 42.47 ± 16.37 (mean change: 59.59; 95% confidence interval [CI]: 46.19-72.99); in the placebo group, the total severity of PMS score changed from 106.06 ± 44.12 to 91.60 ± 43.56 (mean change: 14.45; 95% CI: 2.69 to 26.22). Furthermore, difference between mean changes was significant (mean difference: 45.14; 95% CI: 6.10-14.98).

Conclusion: Our results for the first time showed a potential advantageous effect of curcumin in attenuating severity of PMS symptoms, which were probably mediated by modulation of neurotransmitters and anti-inflammatory effects of curcumin.

Trial 2002: Supplements (Sorbitol placebo)

Unexpected benefit of sorbitol placebo in Mg intervention study of premenstrual symptoms: implications for choice of placebo in RCTs

Link: <https://pubmed.ncbi.nlm.nih.gov/12018972/>

Year published: 2002

Pubmed classification: Clinical trial

Objective: Designed to investigate the dose-response of daily Mg supplementation on premenstrual symptoms.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo controlled - crossover.

Participant information: 85 women.

Treatment length: 2 months active drug or placebo; 1 month non-treatment; 2 months active drug or placebo.

Drug and dosage: Mg (200, 350 or 500 mg/day); or sorbitol placebo (1305mg). Each woman took 2 of the 4 treatments.

Efficacy outcomes: Unexpectedly, sorbitol (1305 mg) reduced anxiety-related and total premenstrual symptoms after 2 months compared with Mg treatments ($P < 0.001$ and $P < 0.001$, respectively). We conclude that low-dose sorbitol reduces premenstrual symptoms beyond that expected of a placebo.

After 2 months of treatment, sorbitol also reduced urinary Mg excretion compared to baseline (no intervention) and Mg treatments ($P = 0.005$). A follow-up study on 17 healthy volunteers confirmed lack of effect on urinary Mg output of a similar sorbitol intervention regime compared with either baseline or cellulose placebo.

Conclusion: It appears that sorbitol may influence Mg homeostasis in women suffering premenstrual symptoms, but not in healthy individuals.

Considerations for future: Implications for placebo choice in RCTs are discussed.

Trial 2000: Supplements (Vitamin B6/Pyridoxine)

A synergistic effect of a daily supplement for 1 month of 200 mg magnesium plus 50 mg vitamin B6 for the relief of anxiety-related premenstrual symptoms: a randomized, double-blind, crossover study

Link: <https://pubmed.ncbi.nlm.nih.gov/10746516/>

Year published: 2000

Pubmed classification: Clinical trial.

Objective: To investigate single and combined effects of daily dietary supplementation with 50 mg of vitamin B6 and 200 mg magnesium (as MgO) for one cycle for the relief of mild premenstrual symptoms.

Blind/double blind? Double-blind.

Randomised? Yes - Latin square design.

Placebo? Placebo controlled - crossover.

Participant information: 44 women, average age of 32 years.

Treatment length: 1 month.

Drug and dosage: Participants were randomly assigned to take consecutively all four of the following treatments daily: (1) 200 mg Mg, (2) 50 mg vitamin B6, (3) 200 mg Mg + 50 mg vitamin B6 and (4) placebo.

Measuring scales: Throughout the study, each volunteer kept a daily record of symptoms using a 5-point ordinal scale in a menstrual diary of 30 symptoms. Symptoms were grouped into six categories: anxiety, craving, depression, hydration, other, and total. Urinary magnesium output for 24 hours was estimated using the Mg/creatinine concentration ratio.

Efficacy outcomes: ANOVA showed no overall difference between individual treatments, but predefined treatment comparisons using factorial contrasts in ANOVA showed a significant effect of 200 mg/day Mg + 50 mg/day vitamin B6 on reducing anxiety-related premenstrual symptoms (nervous tension, mood swings, irritability, or anxiety) ($p = 0.040$). Urinary Mg output was not affected by treatment.

Side-effects assessment: The study indicated that absorption from MgO was poor and daily supplementation for longer than 1 month is necessary for tissue repletion.

Conclusion: A small synergistic effect of a daily dietary supplementation with a combination of Mg + vitamin B6 in the reduction of mild premenstrual anxiety-related symptoms was demonstrated during treatment of 44 women for one menstrual cycle.

Considerations for future: In view of the modest effect found, further studies are needed before making general recommendations for the treatment of premenstrual symptoms.

Trial 2000: Supplements (Magnesium)

A synergistic effect of a daily supplement for 1 month of 200 mg magnesium plus 50 mg vitamin B6 for the relief of anxiety-related premenstrual symptoms: a randomized, double-blind, crossover study

Link: <https://pubmed.ncbi.nlm.nih.gov/10746516/>

Year published: 2000

Pubmed classification: Clinical trial.

Objective: To investigate single and combined effects of daily dietary supplementation with 50 mg of vitamin B6 and 200 mg magnesium (as MgO) for one cycle for the relief of mild premenstrual symptoms.

Blind/double blind? Double-blind.

Randomised? Yes - Latin square design.

Placebo? Placebo controlled - crossover.

Participant information: 44 women, average age of 32 years.

Treatment length: 1 cycle.

Drug and dosage: Participants were randomly assigned to take consecutively all four of the following treatments daily: (1) 200 mg Mg, (2) 50 mg vitamin B6, (3) 200 mg Mg + 50 mg vitamin B6 and (4) placebo.

Measuring scales: Throughout the study, each volunteer kept a daily record of symptoms using a 5-point ordinal scale in a menstrual diary of 30 symptoms. Symptoms were grouped into six categories: anxiety, craving, depression, hydration, other, and total. Urinary magnesium output for 24 hours was estimated using the Mg/creatinine concentration ratio.

Efficacy outcomes: ANOVA showed no overall difference between individual treatments, but predefined treatment comparisons using factorial contrasts in ANOVA showed a significant effect of 200 mg/day Mg + 50 mg/day vitamin B6 on reducing anxiety-related premenstrual symptoms (nervous tension, mood swings, irritability, or anxiety) ($p = 0.040$). Urinary Mg output was not affected by treatment.

Side-effects assessment: The study indicated that absorption from MgO was poor and daily supplementation for longer than 1 month is necessary for tissue repletion.

Conclusion: A small synergistic effect of a daily dietary supplementation with a combination of Mg + vitamin B6 in the reduction of mild premenstrual anxiety-related symptoms was demonstrated during treatment of 44 women for one menstrual cycle.

Considerations for future: In view of the modest effect found, further studies are needed before making general recommendations for the treatment of premenstrual symptoms.

Trial 1998 Supplements (Calcium)

Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. Premenstrual Syndrome Study Group

Link: <https://pubmed.ncbi.nlm.nih.gov/9731851/>

Year published: 1998

Pubmed classification: Clinical trial.

Objective: To evaluate the effect of calcium carbonate on the luteal and menstrual phases of the menstrual cycle in premenstrual syndrome.

Blind/double blind ? Double-blind.

Randomised ? Yes.

Placebo ? Placebo group.

Participant information: 720 healthy, premenopausal women in the United States between the ages of 18 and 45 years were screened for moderate-to-severe, cyclically recurring premenstrual symptoms; 497 were enrolled; and 466 were valid for analysis. There was no difference in age, weight, height, use of oral contraceptives, or menstrual cycle length between treatment groups.

Treatment length: 3 cycles (+2 screening cycles).

Drug and dosage: 1200 mg of elemental calcium per day in the form of calcium carbonate; or placebo.

Measuring scales: Symptoms were prospectively documented over 2 menstrual cycles with a daily rating scale that had 17 core symptoms and 4 symptom factors (negative affect, water retention, food cravings, and pain). The primary outcome measure was the 17-parameter symptom complex score. Routine chemistry, complete blood cell count, and urinalysis were obtained on all participants. Daily documentation of symptoms, adverse effects, and compliance with medications were monitored.

Efficacy outcomes: During the luteal phase of the treatment cycle, a significantly lower mean symptom complex score was observed in the calcium-treated group for both the second ($P = .007$) and third ($P < .001$) treatment cycles. By the third treatment cycle calcium effectively resulted in an overall 48% reduction in total symptom scores from baseline compared with a 30% reduction in placebo.

All 4 symptom factors were significantly reduced by the third treatment cycle. There were no differences between groups in the mean screening symptom complex score of the luteal ($P = .659$), menstrual ($P = .818$), or intermenstrual phase ($P = .726$) of the menstrual cycle.

Conclusion: Calcium supplementation is a simple and effective treatment in premenstrual syndrome, resulting in a major reduction in overall luteal phase symptoms.

Trial 1991: Supplements (Nutritional)

Effect of a nutritional supplement on premenstrual symptomatology in women with premenstrual syndrome: a double-blind longitudinal study

Link: <https://pubmed.ncbi.nlm.nih.gov/1955626/>

Year published: 1991

Pubmed classification: Clinical trial.

Further trial information: Longitudinal study.

Objective: To assess the effectiveness of a vitamin/mineral supplement in controlling symptoms of premenstrual syndrome (PMS).

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo group.

Participant information: 44 women with PMS. Subjects were carefully screened and excluded if underlying physical or psychopathological conditions were noted.

Treatment length: 3 cycles (+1 month baseline measurement).

Drug and dosage: 6 or 12 tablets of vitamin/mineral supplement per day; or placebo.

Measuring scales: Follicular and luteal testing with a menstrual symptom questionnaire, subdividing PMS into four subgroups, was completed for 1 month prior to treatment.

Efficacy outcomes: All subjects had significant differences in severity of symptoms between the follicular and luteal phase of the control cycle. Comparing pre- vs posttreatment luteal phase scores, significant placebo effects were noted for two PMS subgroups. Significant treatment effects were noted in 3 subgroups for the 6-tablet group, and in all 4 subgroups for the 12-tablet group.

Conclusion: These results suggest that this nutritional supplement may play a role in the management of women with PMS.

Trial 1991: Supplements (Magnesium)

Oral magnesium successfully relieves premenstrual mood changes

Link: <https://pubmed.ncbi.nlm.nih.gov/2067759/>

Year published: 1991

Pubmed classification: Clinical trial

Objective: To evaluate the effects of an oral Mg preparation on premenstrual symptoms.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo controlled.

Participant information: 32 women (24-39 years old) with PMS, confirmed by the Moos Menstrual Distress Questionnaire.

Treatment length: 2 months active drug or placebo; 2 months active drug or placebo (+2 months baseline recording).

Drug and dosage: Magnesium pyrrolidone carboxylic acid (360 mg Mg) was administered three times a day, from the 15th day of the menstrual cycle to the onset of menstrual flow; or placebo.

Measuring scales: The Menstrual Distress Questionnaire. Blood samples for Mg measurement were also drawn premenstrually, during the baseline period, and in the second and fourth months of treatment.

Efficacy outcomes: The Menstrual Distress Questionnaire score of the cluster "pain" was significantly reduced during the second month in both groups, whereas Mg treatment significantly affected both the total Menstrual Distress Questionnaire score and the cluster "negative effect."

In the second month, the women assigned to treatment showed a significant increase in Mg in lymphocytes and polymorphonuclear cells, whereas no changes were observed in plasma and erythrocytes.

Conclusion: These data indicate that Mg supplementation could represent an effective treatment of premenstrual symptoms related to mood changes.

Trial 1989: Supplements (Calcium)

Calcium supplementation in premenstrual syndrome: a randomized crossover trial

Link: <https://pubmed.ncbi.nlm.nih.gov/2656936/>

Year published: 1989

Pubmed classification: Clinical trial.

Objective: To determine the efficacy of calcium supplementation in women with premenstrual syndrome (PMS).

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo controlled - crossover.

Participant information: 78 women were initially screened. Trial selection was based on a history of recurrent PMS symptoms and on the results of a prospective assessment of daily symptom scores. Only women with symptom scores during the late luteal phase that were at least 50% greater than those during the intermenstrual phase were selected. 33 women completed the trial.

Treatment length: 3 months active drug or placebo; 3 months active drug or placebo.

Drug and dosage: 1,000 mg of calcium carbonate daily; or placebo.

Measuring scales: Efficacy was assessed prospectively by changes in daily symptom scores over a six-month period and retrospectively by an overall global assessment.

Methodology further information: A preliminary evaluation included physical examination, routine laboratory tests, dietary assessment, and psychiatric evaluation.

Efficacy outcomes: Multivariate repeated measures analysis of variance on symptom ratings derived from daily PMS symptom scores demonstrated a reduction in symptoms on calcium treatment during both the luteal ($p = 0.011$) and the menstrual phases ($p = 0.032$) of the reproductive cycle. Calcium supplementation had no effect during the intermenstrual phase.

Retrospective assessment of overall symptoms confirmed this reduction: 73% of the women reported fewer symptoms during the treatment phase on calcium, 15% preferred placebo, and 12% had no clear preference.

Three premenstrual factors (negative affect [$p = 0.045$]; water retention [$p = 0.003$]; pain [$p = 0.036$]) and one menstrual factor (pain [$p = 0.02$]) were significantly alleviated by calcium.

Conclusion: Calcium supplementation is a simple and effective treatment for premenstrual syndrome

Considerations for future: Further studies will be needed to determine its precise role in PMS

Trial 1989: Supplements (Vitamins)

Pyridoxine (vitamin B6) and the premenstrual syndrome: a randomized crossover trial

Link: <https://pubmed.ncbi.nlm.nih.gov/2558186/>

Year published: 1989

Pubmed classification: Clinical trial.

Objective: To study the effects of pyridoxine (vitamin B6) on symptoms characteristic of premenstrual syndrome.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo-controlled - crossover.

Participant information: 63 women aged 18-49 years in UK entered the trial. They were identified by means of a general practice based survey of menstrual patterns in the community (UK). All of the women had noticed moderate to severe premenstrual symptoms during the previous year. 32 women completed the full 7 months of study.

Treatment length: 3 months active drug or placebo; 3 months active drug or placebo (+1 month pre-trial menstrual diary).

Drug and dosage: 50mg vitamin B daily; or placebo.

Measuring scales: The women kept a daily menstrual diary which graded the severity of nine individual symptoms from zero to three.

Efficacy outcomes: In the women who completed the study, a significant beneficial effect (P less than 0.05) of pyridoxine was observed on emotional type symptoms (depression, irritability and tiredness). No significant effect was observed on premenstrual symptoms of any other type.

Trial 1989: Supplements (Vitamins)

Pyridoxine (vitamin B6) and the premenstrual syndrome: a randomized crossover trial: PIP

Link: <https://pubmed.ncbi.nlm.nih.gov/2558186/>

Year published: 1989

Pubmed classification: Clinical trial.

Further trial information: Part of a community based postal survey of menstrual patterns.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo-controlled - crossover.

Participant information: 68 women in England started the trial. 37 women completed 6 months, and 32 completed the full 7 months.

Treatment length: 3 months active drug or placebo; 3 months active drug or placebo (+1 month study cycle).

Drug and dosage: 50 mg/day of pyridoxine; or placebo.

Measuring scales

Each woman jotted down daily the severity of symptoms (e.g., depression, headache, etc.)

Efficacy outcomes: The results of the study show pyridoxine to significantly affect emotional type symptoms (depression, irritability, and tiredness [p.05]), but not somatic (headache, breast discomfort, swollen abdomen, swollen hands or feet) or menstrual (stomach cramps, backache, other) symptoms.

Women who took oral contraceptives (OCs) had nonsignificant higher adjusted premenstrual symptom scores, particularly for emotional type symptoms, during both pyridoxine and placebo months, than did those who did not take OCs.

This study was complicated by a placebo effect. It revealed a significant decrease in the level of all symptom scores from the 1st month to the 4th month by a mean of 57% (p=.001) when the women took the placebo initially. Emotional type symptoms decreased by 69% (p.05), somatic type by 52% (p.05), and menstrual type nonsignificantly by 15%. On the other hand, when women took the placebo after taking pyridoxine for a month, the combined level of all symptom scores only increased 37% on average (nonsignificant).

Conclusion: Based on the results of this study, pyridoxine appears to alleviate premenstrual depression.

Considerations for future: Further research is needed to confirm the results of this and other similar studies.

Trial 1987: Supplements (Vitamins)

The effects of vitamin B6 supplementation on premenstrual symptoms

Link: <https://pubmed.ncbi.nlm.nih.gov/3299182/>

Year published: 1987

Pubmed classification: Clinical trial.

Objective: To assess the effects of vitamin B6 supplementation on premenstrual symptoms.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo group.

Participant information: 55 women who reported moderate to severe premenstrual mood changes.

Treatment length: 2 months (+1 month baseline).

Drug and dosage: 150 mg of vitamin B6 daily; or placebo.

Measuring scales: Symptoms were monitored prospectively through daily home record-keeping.

Efficacy outcomes: Analysis of covariance suggested that even though vitamin B6 may improve premenstrual symptoms related to autonomic reactions (eg, dizziness and vomiting) and behavioral changes (eg, poor performance and decreased social activities), a significant amount of physical and affective symptomatology remained during the premenstrual phase.

Considerations for future: In light of recently reported, potentially toxic effects of low doses of vitamin B6, our results call for caution in using this therapy for premenstrual symptoms

Trial 1987 Supplements (Nutritional)

Clinical and biochemical effects of nutritional supplementation on the premenstrual syndrome

Link: <https://pubmed.ncbi.nlm.nih.gov/3302251/>

Year published: 1987

Pubmed classification: Clinical trial.

Objective: The effect of a nutritional supplement at high and low dosage on premenstrual symptoms was assessed

Blind/double blind? Double-blind.

Randomised? Unknown.

Placebo? Placebo controlled.

Treatment length: Unknown.

Drug and dosage: A multivitamin/multimineral supplement, at high and low dosage.

Efficacy outcomes: There was laboratory evidence of significant deficiencies in vitamin B6 and magnesium, as well as other deficiencies. The multivitamin/multimineral supplement was shown to correct some of these deficiencies and, at the appropriate dosage, to improve the symptoms of premenstrual tension.

Trial 1985: Supplements (Vitamins) **Controlled trial of pyridoxine in the premenstrual syndrome**

Link: <https://pubmed.ncbi.nlm.nih.gov/3891456/>

Year published: 1985

Pubmed classification: Clinical trial

Blind/double blind? Blind.

Randomised? Yes.

Placebo? Placebo group.

Participant information: 617 patients diagnosed by their general practitioner as having premenstrual syndrome (UK); 434 patients were analyzed.

Treatment length: 3 cycles.

Efficacy outcomes: An improvement was found in 7 of the 9 symptoms assessed for both treatments, but the differences between treatments did not reach conventional significance levels. However, improvement, as measured by global assessment, after three cycles was significantly greater in the patients treated with pyridoxine (p less than 0.02)

Trial 1985 Supplements (Vitamins) **No effect of vitamin B-6 against premenstrual tension. A controlled clinical study**

Link: <https://pubmed.ncbi.nlm.nih.gov/3914180/>

Year published: 1985

Pubmed classification: Clinical trial.

Further trial information: Controlled clinical study.

Blind/double blind? Double-blind.

Randomised? Yes.

Placebo? Placebo controlled - crossover.

Participant information: 34 women who suffered from premenstrual tension.

Treatment length: Unknown.

Drug and dosage: Vitamin B-6 100 mg given daily; or placebo (crossover).

Efficacy outcomes : Vitamin B-6 was no better than placebo. There was a substantial period effect, as the women evidenced a considerable preference for the second drug they received, irrespective of whether this was vitamin B-6 or placebo.

Blood magnesium was measured; no significant difference was found between the 34 women with premenstrual tension and 10 healthy women without such complaints.

Conclusion: Vitamin B-6 caused a small but statistically significant rise in blood magnesium level. In the individual patients, no correlation was found between changes in blood magnesium and premenstrual symptoms.

Trial 1983: Supplements (Multivitamins)

Effect of a nutritional supplement, Optivite, on symptoms of premenstrual tension

Link: <https://pubmed.ncbi.nlm.nih.gov/6685186/>

Year published: 1983

Blind/double blind? Unknown.

Randomised? Unknown.

Placebo? Unknown.

Participant information: 31 patients.

Treatment length: 1 to 6 menstrual cycles.

Drug and dosage: Daily dose of 3-12 tablets, Optivite.

Measuring scales: Menstrual symptom questionnaire (MSQ) to assess the presence and severity of premenstrual tension (PMT) for the week after the period (F) and the week before it (L).

Efficacy outcomes: The total MSQ scores decreased significantly in all patients after Optivite administration at a daily dose of 3-12 tablets for one to six menstrual cycles. The mean +/- S.E. total MSQ scores were F = 8.1 +/- 1.8 and L = 31.5 +/- 2.1 for control cycles and F = 2.3 +/- 0.72 and L = 10.3 +/- 1.4 for treated cycles. The best responses were observed in patients taking 6-12 tablets/day for three or more cycles.

Considerations for future: If these results can be confirmed by well-controlled studies, this simple and safe nutritional approach can be recommended in the initial management of PMT.