Diet and Sex-Hormone Binding Globulin, Dysmenorrhea, and Premenstrual Symptoms

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Objective: To test the hypothesis that a low-fat, vegetarian diet reduces dysmenorrhea and premenstrual symptoms by its effect on serum sex-hormone binding globulin concentration and estrogen activity.

Methods: In a crossover design, 33 women followed a low-fat, vegetarian diet for two menstrual cycles. For two additional cycles, they followed their customary diet while taking a supplement placebo pill. Dietary intake, serum sex-hormone binding globulin concentration, body weight, pain duration and intensity, and premenstrual symptoms were assessed during each study phase.

Results: Mean (± standard deviation [SD]) serum sex-hormone binding globulin concentration was higher during the diet phase (46.7 ± 23.6 nmol/L) than during the supplement phase (39.3 ± 19.8 nmol/L, P < .001). Mean (± SD) body weight was lower during the diet (66.1 ± 11.3 kg) compared with the supplement phase (67.9 ± 12.1 kg, P < .001). Mean dysmenorrhea duration fell significantly from baseline (3.9 ± 1.7 days) to diet phase (2.7 ± 1.9 days) compared with change from baseline to supplement phase (3.6 ± 1.7 days, P < .01). Pain intensity fell significantly during the diet phase, compared with baseline, for the worst, second-worst, and third-worst days, and mean durations of premenstrual concentration, behavioral change, and water retention symptoms were reduced significantly, compared with the supplement phase.

Conclusion: A low-fat vegetarian diet was associated with increased serum sex-hormone binding globulin concentration and reductions in body weight, dysmenorrhea duration and intensity, and premenstrual symptom duration. The symptom effects might be mediated by dietary influences on estrogen activity. (Obstet Gynecol 2000;95:245–50. © 2000 by The American College of Obstetricians and Gynecologists.)

Up to 10% of women in their teens and early twenties suffer from severe, mostly primary, dysmenorrhea. Its cause is believed to be related to uterine muscle contraction and ischemia induced by prostaglandins (PGs) (particularly PGE₂ and PGF₂α) produced in endometrial tissue under the influence of estrogens and progesterone. Cyclic hormonal changes also affect premenstrual symptoms, which affect an estimated 20–40% of women, with 2.5–5% reporting adverse effects on work or social adjustment.

Dietary factors alter serum sex-hormone concentrations and activity. Plant-based and vegetarian diets increase serum concentration of sex-hormone binding globulin, which binds and inactivates estrogens. In addition, independent of the effect of diet, serum sex-hormone binding globulin concentration is inversely associated with body weight, which is typically lower in vegetarians. Low-fat and vegetarian diets also reduce serum estrogen concentrations in premenopausal and postmenopausal women.

Anecdotal reports indicate that a low-fat, vegetarian diet might reduce menstrual pain in some individuals. The present study tested the hypothesis that a low-fat, vegetarian diet reduces dysmenorrhea and premenstrual symptoms in women with moderate to severe menstrual pain, by its effect on serum sex-hormone binding globulin and estrogen activity.

Materials and Methods

The study was approved by the institutional review board and the Department of Obstetrics and Gynecology of the Georgetown University. Volunteers were recruited through newspaper advertisements and notices mailed to gynecologists in the Washington, DC, area. All participants gave written informed consent before enrollment. Participants were to be at least 18 years of age, with menstrual periods accompanied consistently by moderate to severe abdominal pain causing significant distress or impairment in social or occupational functioning, with pain-free intervals of at

From the Physicians Committee for Responsible Medicine, Washington, DC, and the Department of Obstetrics and Gynecology, Georgetown University School of Medicine, Washington, DC.
least 2 weeks between periods. Premenstrual symptoms were not a criterion for participation. No monetary compensation was provided.

Exclusionary criteria included menstrual cycles that were irregular or consistently shorter than 25 days or longer than 35 days; physical illness affecting eating behavior or causing pain; any history of a hormone-related illness, such as diabetes or thyroid disease; history of mental illness or alcohol or drug abuse; use in the previous 6 months of oral contraceptives or other drugs known to affect hormonal function; or a structural abnormality that could account for pain. The study was conducted in two successive replications with 24 and 27 participants, respectively. After medical history and physical examination, volunteers were assigned randomly, using a computer-generated random number list, to two groups that received the same treatments (a diet intervention phase and a placebo supplement phase), but in opposite order in a crossover design.

During the baseline period of one full menstrual cycle, participants were asked to make no diet changes. On day 2 of the next menstrual cycle (counting the first day of menstruation as day 1), one group was asked to begin an intervention diet for two full menstrual cycles, after which they were asked to resume their customary diets and take a daily supplement pill for two full menstrual cycles. The remaining participants had the conditions in the reverse order.

The intervention diet consisted of grains, vegetables, legumes, and fruits, with no quantitative restrictions. Animal products, added oils, fried foods, avocados, olives, nuts, nut butters, and seeds were proscribed. The diet was generally adequate in all nutrients except for vitamin B-12, for which supplementation was recommended for any participants who chose to follow the intervention diet after the study’s conclusion. The diet provided approximately 10% of calories from fat.

The supplement consisted of 2 μg of vitamin B-12. Participants were told that the supplement they received could consist of a vitamin or a placebo, and that if it were a vitamin, its identity and dose would not be revealed until the end of the study.

Participants attended weekly 1-hour meetings of their assigned groups for the duration of the study. Meetings included nutrition lectures, cooking demonstrations, informal discussions, and emotional support. Spouses or partners were invited to specially scheduled cooking demonstrations and lectures. Samples of groceries, such as brown rice, canned beans, and instant soups, were provided occasionally during the intervention diet phase.

During the baseline cycle and the second cycle of each intervention phase, the following data were collected: On day 6, blood samples for sex-hormone binding globulin and serum lipids were collected after an overnight fast. Serum was separated and frozen so laboratory determinations for all participants in each replication could be run in the same batch at the end of the study.

Serum sex-hormone binding globulin was measured by DSL-6300 radioimmunoassay (Diagnostic Systems Laboratories, Inc., Webster, TX.) Methods and results for serum lipids are reported elsewhere. An exploratory assessment of serum estrogen concentrations, including estradiol (E2) (total, free, and albumin-bound), estrone (E1), and E1 sulfate, was made using radioimmunoassay techniques in a subsample of 17 participants. No clear pattern emerged in those determinations, and the assays were discontinued.

Between days 6 and 14, each participant completed a 3-day dietary record, including 2 weekdays and 1 weekend day. Records were analyzed using Nutritionist V for Windows 95 (First DataBank Inc., Hearst Corporation, San Bruno, CA). At the same time, participants also completed a food-supplement questionnaire that addressed acceptability of the diet and any beneficial or adverse effects experienced.

Between days 14 and 21, body weight in street clothes but without shoes was measured to the nearest 0.2 kg. Premenstrual symptoms, including pain, altered concentration, behavioral change, autonomic reactions, water retention, negative affect, arousal, sleep disturbances, and food cravings, were assessed daily from day 14 through the end of menstrual flow using the Menstrual Symptom Diary, a modification of Moos’ Menstrual Distress Questionnaire.

Menstrual pain was assessed on the same schedule as the Menstrual Symptom Diary, using a short form of the Brief Pain Inventory developed by the Pain Research Group of the World Health Organization Collaborating Centre for Symptom Evaluation in Cancer Care. It records pain at its worst during the preceding 24 hours using a scale from 0 (no pain) to 10 (pain as bad as you can imagine). Throughout the study, participants were asked to use pain medications only when pain was experienced, rather than prophylactically.

At the conclusion of the supplement phase, each participant was asked to describe on a four-point scale the extent to which the supplement reduced menstrual pain. Participants also were asked to guess if the supplement they had received was a placebo or an active compound. Participants who believed it to be an active compound were asked if it seemed to reduce pain or to cause side effects.

Sample size was based on the primary outcome of pain duration and was estimated to provide 80% power in a repeated measures analysis of variance with α =
Table 1. Baseline Demographic and Clinical Characteristics

<table>
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<th>Completers (n = 33)</th>
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<td>Living children (median)</td>
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Results

Fifty-one volunteers met the criteria for participation. Their demographic characteristics are listed in Table 1.

Twelve volunteers failed to complete the study due to menopause (1), pregnancy (1), repeatedly missing group meetings (2), noncompliance with the intervention diet (2), extended overseas travel (1), death in the family (1), major financial problems (1), spouse objections to the diet (1), scheduling difficulties (1), and unknown reasons (1). In addition, six participants were excluded from the data analysis for failure to return all data forms. There were no significant demographic differences between completers and noncompleters.

Nutrient intake is presented in Table 2. The reductions in energy, protein, fat, and cholesterol intake and the increase in fiber intake from baseline to the intervention diet phase were significantly greater than the corresponding changes from baseline to the supplement phase.

Mean body weight was 2.7 kg lower during the intervention diet phase than at baseline, a significant difference compared with the change from baseline to supplement phase (Table 3). Mean BMI fell from baseline to intervention diet phase. An order effect was
evident, such that weight lost by those having the intervention diet phase first was not regained fully during the subsequent supplement phase.

Mean serum sex-hormone binding globulin concentration was 19% higher during diet phase, compared with supplement phase (Table 3). The change from baseline to diet phase was significantly greater than from baseline to supplement phase. There were no significant associations between serum sex-hormone binding globulin concentration and body weight or intake of any single nutrient.

Menstrual flow duration did not differ significantly by treatment condition. However, pain duration (defined as number of days during which participants reported scores of 1 or greater on the Brief Pain Inventory for pain at its worst during the preceding 24 hours, from 3 days before the onset of menses to 5 days after) dropped significantly more from baseline to diet phase compared with the change from baseline to supplement phase (Table 3).

Pain intensity, defined as the Brief Pain Inventory value for pain at its worst during the preceding 24 hours on each of the 3 days of maximal severity during each study phase, shifted toward lower values during the diet phase. Median values for the 3 days of maximal severity were 7, 5, and 3 at baseline; 6, 4, and 2 during the supplement phase; and 6, 3, and 0 during the intervention phase. Using Wilcoxon matched-pairs, signed-rank test, we found that differences between intervention phase and diet phase values. Differences between diet and supplement phases were significant for the second-worst day (P = .05). There were no significant associations between serum sex-hormone binding globulin concentration and pain duration or intensity.

When asked the extent to which the supplement had reduced their pain, 28 participants reported that it had minimal or no effect, whereas five described its effect as moderate. When asked to guess, 25 participants believed the supplement to be a placebo. Eight believed it to be an active compound, of whom six thought it reduced their pain, whereas two believed it caused side effects.

The mean duration of premenstrual symptoms, defined as the number of days during which any symptom was rated as present during the 5 days preceding the onset of menses, regardless of symptom intensity, was significantly reduced during the diet phase for three symptom clusters (comparing the change from baseline to diet phase with the change from baseline to the supplement phase). For water retention, mean symptom durations in the baseline, supplement, and intervention phases were 2.9, 2.5, and 1.3 days, respectively (P < .01). For behavioral change symptoms, mean durations were 1.7, 1.7, and 1.1 days, respectively (P < .05), and for concentration symptoms, mean durations were 1.9, 1.5, and 0.7 days, respectively (P < .01).

On the food-supplement questionnaire, 23 participants noted weight loss during the intervention diet phase, compared with three during the supplement phase (McNemar Q = 18.18, P < .001), and 17 reported improved energy during diet phase, compared with five during supplement phase (McNemar Q = 10.28, P < .001). Related to those perceived benefits, several participants who had the vegetarian phase first in sequence refused to return fully to their customary diets during the supplement phase, despite the fact that the crossover design required it.

**Discussion**

In women with moderate to severe dysmenorrhea, a low-fat, vegetarian diet was associated with a significant increase in mean serum sex-hormone binding globulin concentration and reductions in mean body weight and BMI as well as significant reductions in menstrual pain duration, pain intensity, and duration of premenstrual symptoms related to concentration, behavioral change, and water retention.

There are several ways that diet might affect PG synthesis. Diet influences sex hormone concentration and activity. Populations on plant-based or vegetarian diets typically have increased serum sex-hormone binding globulin concentrations. Such diets also often reduce body weight, which is correlated inversely with serum sex-hormone binding globulin concentrations.

Low-fat diets also reduce serum estrogen concentrations in premenopausal and postmenopausal women. Estrogen conjugates are excreted in bile and are subject to enterohepatic circulation, which can be interrupted by dietary fiber, encouraging fecal estrogen elimination. Elevated serum sex-hormone binding globulin or reduced serum estrogen concentrations might reduce estrogenic stimulation of the endometrium, limiting proliferation of tissues that produce PGs.

In the current study, mean serum sex-hormone binding globulin concentration during the diet phase was 19% higher than that during the supplement phase. Sex-hormone binding globulin concentration was not associated with intake of nutrients or body weight, nor was it associated with pain duration or intensity during any phase. We found no significant changes in serum estrogen concentrations in a subsample of participants. Pulsatile release of estrogens might have prevented us
from detecting changes in estrogen concentrations. Also, we measured serum hormones earlier than in previous studies, after only about 5 weeks on the diet.

Vegetables and legumes, particularly soy products, are rich in phytoestrogens, which compete with other estrogens for receptor binding, potentially affecting the pituitary-ovarian axis. The addition of 60 g of soy protein to the diets of premenopausal nonvegetarian women was associated with a lengthening of the follicular phase by a mean of 2.5 days and lower midcycle peaks of luteinizing hormone and FSH.

Limited evidence suggests that ovulatory disturbances might be less frequent among vegetarians. In a 6-month study, 15% of cycles among 22 nonvegetarians were anovulatory, compared with fewer than 5% of those of 23 vegetarians. The distribution of ovulatory, anovulatory, and short-luteal-phase cycles differed significantly between groups ($\chi^2 = 9.64, P < .01$).

Vegetables, fruits, and legumes are typically low in total fat, but their content of omega-3 fatty acids, relative to other fats, is often high. Omega-3 fatty acids are precursors of 3-series PGs, which have anti-inflammatory actions. In contrast, diets rich in animal fats and cooking oils are proportionately richer in omega-6 fatty acids, which promote the formation of PGE2 and PGF2α. In a group of Danish women, a higher intake of omega-3 fatty acids or a higher ratio of omega-3/omega-6 fatty acids was associated with reduced menstrual pain.

Duration of premenstrual symptoms related to concentration, behavioral change, and water retention was significantly reduced during the diet phase. In a previous study of 30 healthy women, a reduction in dietary fat from 40% to 20% of energy was associated with reduced premenopausal water retention symptoms.

Interpretation of our data is limited by several factors. A placebo pill is clearly not as engaging as a diet change. We did not believe that an alternative diet, such as a gluten-free diet, could be presented credibly as a potential treatment for menstrual symptoms. Our participants appeared to believe that an active substance was being tested during the supplement phase, at least on some participants, and eight believed they received an active compound.

Some individuals with dysmenorrhea might have endometriosis or other conditions that are not detectable on routine examination. We excluded volunteers who had been diagnosed with such conditions, but we did not conduct laparoscopic examinations or biopsies. Our control over analgesics was limited to our request that they be used only during pain, rather than prophylactically. We believed that prostration of analgesics was not ethically permissible with an experimental treatment and placebo. For future studies it would help to provide a standardized medication and dose that would facilitate comparisons of medication use across different study phases. In future research, it would be useful to measure changes in the quantity of endometrial flow and its prostaglandin concentration in the context of a low-fat, vegetarian diet and to explore effects of that regimen on biochemical indices in other hormone-related conditions, such as endometriosis, leiomyomas, or hormone-related cancers.

**References**


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