

An Integrative Medicine Approach to Premenstrual Syndrome

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Complementary and alternative medicine (CAM) approaches are widely used by women with premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD). This article provides a comprehensive review of the medical literature on clinical applications of CAM for these conditions. The information was collected via a Medline review dating back to 1966 and subsequent selected review of bibliographies from these articles for non-Medline referenced but relevant clinical studies. For many of the therapies discussed, there is a lack of conclusive evidence either confirming or refuting efficacy. For other therapies, including certain herbal and nutritional approaches, the use of exercise, and the use of mind-body approaches, there is substantial evidence of efficacy. This review will be relevant to the practicing clinician seeking to become aware of and to understand the relevance of the complementary/alternative therapies being used by his/her patients for PMS and PMDD.

Premenstrual syndrome (PMS) is a condition of recurrent physical and psychologic symptoms occurring in a cyclic fashion during the 1- to 2-week period preceding a woman's menstrual period, significant enough to cause disruption in either family, personal, or occupational function.¹ In its most severe form, it affects roughly 2.5% of women of reproductive age²; in a more mild form, it is estimated to affect approximately 40% of women in this age group.³ A variant of PMS that entails more severe psychologic symptoms has recently been described under the diagnosis of premenstrual dysphoric disorder (PMDD).

Many clinicians find that their patients often turn to therapeutic approaches outside of conventional medicine to treat PMS symptoms. This article will review the evidence regarding a number of these strategies for the treatment of PMS.

Review Methodology

Because many of the therapies currently in wide use by patients have been formally studied only minimally to date, it was felt by the authors that a systematic review with rigid exclusion criteria would omit a significant amount of information potentially relevant to the practicing clinician. Thus, this review used an approach designed to cast as wide a net as possible to survey the literature that does exist regarding these therapies. We performed a Medline search dating back to 1966. Articles from this search were included in this review if they were believed by the authors to be of sufficient quality to be relevant to practicing clinicians. Bibliographies of the major studies and reviews were then searched and se-

lected additional articles reviewed that were not Medline referenced. Again here the criteria for inclusion were the judgment of the authors regarding study quality and clinical relevance.

Although this is a nontraditional approach to literature review, and certainly provides less definitive conclusions regarding efficacy than either systematic review or meta-analysis, it is the approach we believe is most suited at this time to close the gap between the knowledge base of practicing physicians and the active complementary/alternative medicine (CAM) practices of their patients. The margin of safety for most of the CAM approaches discussed here is extremely wide; thus, as we move through the current period in which the use of CAM in the community runs far ahead of the clinical evidence basis for that use, it may be possible for a clinician to discuss the use of these therapies with patients and even in some circumstances recommend them, despite a lack of definitive evidence. The wide-net cast in this review is designed to provide clinicians with the information necessary to at least engage their patients in informed discussion of the use of CAM approaches to PMS and PMDD, even as we wait for more definitive evidence to accumulate regarding the efficacy of these approaches or the lack thereof. Wherever possible in this review, the information provided is rated for quality using the A-B-C rating system currently in wide use in clinical reviews. This approach is summarized in Table 1.

In addition to referencing published articles as outlined previously, we have relied also in this review on 2 high-quality internet-based databases: the Cochrane Library and the Natural Medicines Comprehensive Database. The Cochrane Library is a database of clinical trials managed by an international consortium of volunteers at a large number of academic centers, which compiles and rates clinical trials for a huge range of conditions and therapies to facilitate the systematic review of these data for information on efficacy and safety. The Natural Medicines

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Comprehensive Database is a compilation of over 600 monographs on herbal medicines and nutritional supplements. This database is peer reviewed and is produced and updated by the editors of *The Pharmacist's Letter*.

The Integrative Approach

The integrative approach to health care uses the combination of conventional and nonconventional therapies best suited to treat a particular situation. This approach also relies heavily on the intrinsic, internal healing resources of the patient to overcome whatever problem may be confronting them. A major component of the practitioner's role in this model is to assist the patient in becoming aware of and using this intrinsic healing system that has been largely unrecognized and underused by conventional medicine.⁴

Therapeutic strategies that are often used in the integrative approach include conventional pharmaceuticals; psychotherapy; botanical and nutritional supplements; dietary manipulation; acupuncture; homeopathy; mind-body approaches such as visualization, biofeedback, and hypnotherapy; chiropractic manipulation; and massage. One challenge in reviewing the literature on the integrative approach is that many of these therapies—acupuncture, hypnosis, and individualized dietary approaches—rely on highly individualized strategies that are difficult to study within the traditional framework of randomized double-blind placebo-controlled trials.⁵ The need to develop new valid tools for measuring clinical outcomes of these strategies has slowed the process of accumulating evidence regarding efficacy or lack thereof. As is often true in discussions of the integrative approach, a number of the therapies reviewed here—such as cognitive behavioral therapy or aerobic exercise—are not per se unconventional. However, they are included here as essential elements of the integrative approach and elements often overlooked in discussions of this subject.

Proposed Etiologies of PMS

Many different etiologies have been proposed for the symptoms of PMS; none have been definitely established as a dominant cause. Possible influences include hormonal imbalance, specifically a low progesterone level during the luteal phase of the cycle; abnormal neurotransmitter response to ovarian signaling; disordered aldosterone function leading to sodium and water retention; abnormal hypothalamic-pituitary-adrenal (HPA) axis function leading to deficient adrenal hormone secretion; nutritional deficiency including magnesium, pyridoxine; carbohydrate intolerance; environmental factors including stress.^{2,6} No single etiology explains every case, and thus many clinicians assume that this disorder is multifactorial in origin. This makes the integrative approach, which allows for a treatment strategy that combines multiple modal-

Table 1. Levels of Evidence

Level A	Large high-quality, randomized, double-blind placebo-controlled trials, meta-analyses
Level B	Lesser quality randomized trials, retrospective studies, systematic reviews
Level C	Expert opinion, case series, uncontrolled studies, consensus statements

ities potentially addressing multiple underlying causes, particularly suited to this condition.

Conventional/Pharmacological Approaches

A wide range of pharmacological approaches have been used to treat the symptoms of PMS, including oral contraceptives and other hormonal supplementation, nonsteroidal anti-inflammatories, bromocriptine, and diuretic agents. Most recently antidepressants, particularly the selective serotonin reuptake inhibitors, have become very popular in women for whom depression or mood instability is a major symptom. Although the use of conventional pharmacotherapeutic agents in the treatment of PMS and PMDD is an important component of the integrative approach, the applications of these agents are reviewed elsewhere,^{7,8} and so will not be discussed in detail in this review.

Nutritional Approaches

The information available on the use of nutritional approaches for PMS is compiled in Table 2.

Dietary Manipulation. Dietary manipulation is often used for PMS symptoms, although no food-based strategy has been properly evaluated to date. Based on findings by Abraham that women with PMS typically consume more dairy products, refined sugar, and high-sodium foods than women without PMS,⁹ many clinicians recommend reducing or eliminating these foods for women with severe symptoms (level C evidence). Limiting caffeine intake is often recommended as well, based on the findings in at least 2 studies associating increased intake of caffeine-containing beverages with increased prevalence and severity of PMS symptoms (level B evidence).^{10,11}

High estrogen levels are believed to be correlated with PMS symptoms in some women. Because diets higher in fat are believed to contribute to higher estrogen levels, and because high-fiber diets are believed to help reduce estrogen levels based on their effect on intestinal flora, another common approach in clinical practice is to recommend a relatively low-fat, high fiber diet (level C evidence).¹² Although the rationale for all of these dietary approaches is appealing, and in fact such a diet is health-promoting for many people for other reasons, none of these dietary manipulation strategies has to date been adequately studied for efficacy in women with PMS.

Magnesium. Because low levels of red cell magnesium have been correlated with women experiencing PMS,¹³ magnesium supplementation has been studied as adjunct-

Table 2. Summary of Evidence on Nutritional Approaches for PMS

<i>Supplement</i>	<i>Typical Dose</i>	<i>Efficacy</i>	<i>Level of Evidence</i>
Magnesium	400–800 mg/d	Likely yes	Level B (small trials)
Vitamin B6	50–100 mg/d	Likely yes	Level B (small trials, systematic review)
Calcium	1,200–1,600 mg/d	Yes	Level A (large trials, systematic review)
Caffeine cessation	N/A	Likely yes	Level B (small trials)
Dietary manipulation	N/A	Possible	Level C (expert opinion)

N/A, not applicable.

tive therapy for women with PMS. In a recent review published in the Cochrane Library, 3 small trials were included that compared magnesium and placebo. It was noted that the trials although randomized with adequate methodological quality were small “with poor measurement and reporting outcomes.”¹⁴ One of the larger studies included data on the levels of prostaglandin F₂ alpha. Women taking the magnesium therapy had substantially lower levels of prostaglandin F₂ (PGF₂) alpha in their menstrual blood than those on the placebo ($P < .05$); these lower levels correlated with a decrease in pain by the participants.¹⁴ In this study, 50 women were randomized and given the equivalent dose of 10 mval of magnesium aspartate or placebo for 6 months. Twenty-one out of 25 women in the active treatment group reported improvement of their symptoms, with 4 reporting no therapeutic effects. A possible biological rationale for the effectiveness of magnesium is the inhibition of PGF₂ alpha and the promotion of muscle relaxation and vasodilatation.^{15,16} The overall conclusion in the Cochrane analysis was that magnesium was more effective than placebo for pain associated with PMS (level B evidence).¹⁴ Furthermore, the need for additional medication was less in all the studies included. The limited evidence to date supports the use of magnesium in PMS, but more research is needed.

Vitamin B6. Vitamin B6, a water-soluble B vitamin, is another adjunctive dietary supplement used in treating PMS. The rationale for its use is for its positive effects on neurotransmitters—serotonin, norepinephrine, histamine, dopamine, and taurine.¹⁷ A systematic review on the efficacy of vitamin B-6 on PMS done in 1999 included nine published trials representing 940 patients with PMS, all of which were randomized, placebo control double blinded studies (level B evidence).¹⁸ Two studies included studied B-6 on mastalgia based on the frequency (60%) of women with PMS that report cyclical breast pain.¹⁹ The odds ratio relative to placebo for overall improvement in PMS was 2.32 (95% confidence interval 1.95 to 2.54). The odds ratio for improvement in depressive symptoms from 4 trials included analyzing this aspect of PMS was 1.69 (1.39-2.06). The overall assessment of the review was that women with PMS are likely to benefit from B-6 supplementation at a dose of 50 to 100 mg/d and may even have improvement of depressive symptoms.

However, the conclusions although positive were limited citing that there was “insufficient evidence of high quality to give a confident recommendation for using vitamin B6 in the treatment of premenstrual syndrome.”¹⁹

Pyridoxine, although water soluble, has been given in clinical trials at doses ranging from 50 to 500 mg/d. It has been suggested that daily dosing not exceed 100 mg/d because it has been associated with reports of toxicity.²⁰ Furthermore, detailed animal studies have indicated that nerve damage can occur before manifestation of the gross symptoms such as ataxia and neuropathy.^{21,22}

Calcium. Ovarian hormones influence calcium, magnesium, and Vitamin D metabolism, and estrogen regulates calcium metabolism and intestinal calcium absorption as well as parathyroid function and gene expression.²³ Several clinical trials have suggested that calcium supplementation can improve mood and somatic symptoms in PMS.²⁴

A multicenter random controlled double blind study was done in 1998 with 720 women randomized to receive 1,200 mg of calcium carbonate or placebo for three menstrual cycles (level A evidence). These women were asked to report symptoms on a daily rating scale that had 17 core symptoms and 4 symptom factors (negative affect, water retention, food cravings, and pain).²⁵ By the third cycle of treatment a reduction of 48% ($P < .001$) was found in symptoms in the treatment arm versus 30% in the placebo. Other trials have shown similar modest but significant benefits, and a 1999 review on calcium as a treatment for PMS concluded that 1,200 to 1,600 mg/d of calcium, unless contraindicated, should be considered a sound treatment option for those who experience PMS.²⁶

Recently concerns have been raised regarding potential lead increases in those that take calcium supplements.²⁷ Ross^{27a} published a study reporting on 4 of 7 natural products that had measurable lead content at 1 µg for 800 mg/d of calcium (calcium carbonate). However, the lead content was below the detection limit in two thirds of the 22 products reported overall, and all of the products tested had lead content less than both the 1993 Food and Drug Administration and the 1996 food Chemicals Codex standards.²⁸ In a discussion section following the article, Haney,²⁹ an expert in calcium metabolism, points out that lead found in calcium supplements con-

tributes only a small fraction of the total lead intake. Furthermore, it is stated that most of the lead is not absorbed and that calcium blocks lead absorption from other foods. Therefore, it seems prudent to be mindful of the potential for lead contamination in some calcium carbonate products but useful to continue recommending calcium as a supplement for improving PMS symptoms.

Botanical Medicine

Many women turn to botanical therapies for relief from PMS symptoms; in the United States, over 3 billion dollars are spent on herbs and phytomedicinal products per year.³⁰ A number of the commonly used herbal medicines are discussed later. Information on botanicals is summarized in Table 2.

Chasteberry (*Vitex agnus-castus*). One botanical used commonly for PMS is the chasteberry tree (*Vitex agnus-castus*). The Latin binomial means “chaste lamb” and refers to the reduction of sexual desire exhibited when one drinks a beverage prepared from the seeds of this plant.³¹ The applicable parts of the chasteberry tree are the fruit. Active constituents in chasteberry are the essential oils, iridoid glycosides, and the flavonoids.³² The mechanism of action relative to PMS is somewhat unclear. However, chasteberry extracts at the lower dose of 120 mg/d have been shown to diminish follicle-stimulating hormone release and increase luteinizing hormone resulting in decreased estrogen, increased progesterone and prolactin levels.^{33,34} However, at higher doses of approximately 480 mg/d prolactin levels seem inhibited.³⁵ Chasteberry extracts also have multiple constituents that seem to have agonistic effects at the dopamine receptors (D2) when used at higher doses.³⁶

Several clinical trials have been done using a proprietary chasteberry extract Agnolyt® (Murdock, Madaus, Schwabe, San Diego, CA), which contains 9 g of a 1:5 tincture for each 100 g of aqueous-alcohol solution. In 1 large trial of 1,571 women with menstrual disturbances related to corpus luteum insufficiency, patients were treated for 135 days with 40 drops of Agnolyt®. The response rate was around 90% with both physicians and patients assessing the clinical outcome as positive.³⁷ Adverse effects were reported at 1.9% (primarily malaise, gastrointestinal complaints, and nausea).

Another study done by Dittmar and Bohnert³⁸ involving 1542 women with PMS was done to monitor the effects of Agnolyt® (40 drops). Thirty-three percent of the patients reported total relief of their symptoms with an additional 57% reporting partial relief. Two percent of patients in this study reported adverse effects (nausea, allergy, diarrhea, weight gain, heartburn, hypermenorrhea, and gastric complaints). Seventeen patients stopped the study because of the side effects, whereas 562 patients continued to take the product after the monitoring period (4 months).³⁸

A third randomized double-blind placebo controlled study in 217 subjects with PMS taking chasteberry (600 mg capsules 3 times a day) for 3 months showed only improvement in alleviating restlessness. There were no other differences noted for other PMS symptoms.³⁹ Finally, Schellenberg⁴⁰ randomized 170 women with PMS to chasteberry extract (20 mg) or placebo for 3 menstrual cycles. The reduction in symptoms was 52% versus 24% (active versus placebo respectively) and considered statistically significant ($P < .001$).⁴⁰

Vitex (Agnolyt® capsule with approximately 3.5 mg of chasteberry extract) was compared with vitamin B6 (100 mg twice a day) in a 3-month randomized controlled study of 127 women with PMS. The chasteberry and vitamin B6 groups both had similar reductions in PMS scores. Seventy-seven percent versus sixty-six percent in the chasteberry and vitamin B6 groups, respectively, showed improvements in PMS symptoms.⁴¹

No long-term randomized trials have been done comparing standard medical treatments (birth control pills or antidepressants) with chasteberry. In general, the data regarding this herb show conflicting results but appears promising (level B evidence). More studies are needed to fully evaluate chasteberry extract's beneficial effects for PMS. However, the German health authorities have approved the use of chasteberry for irregularities of the menstrual cycle, PMS, and mastodynia.³² Because of the potential effects on hormones it is recommended that the use of chasteberry be avoided during pregnancy and during breast-feeding. Theoretically, chasteberry might interfere with medications that are dopamine antagonists as well.³²

Evening Primrose Oil (*Oenothera biennis*). Evening primrose oil has been used for PMS in many patients although it is used primarily for treatment of a variety of inflammatory disorders.⁴² Some researchers have observed that women with PMS have impaired conversion of linoleic acid to gamma linolenic acid.⁴³ These 2 essential acids are important in the formation in one of the anti-inflammatory prostaglandins, PGE1⁴³; for this reason, evening primrose—a good source of both linoleic and gamma-linolenic acid—has been studied as a possible alternative treatment for PMS. Seven clinical trials have been done using evening primrose for PMS; only 5 clearly randomized their subjects. None of these trials found a beneficial effect for PMS; however, it was noted that the sample sizes in all might have been too small to detect a modest benefit (level B evidence).⁴⁴

In 1 randomized trial, 27 women with PMS were randomized to 4 cycles of essential fatty acids or placebo with cross over after the fourth cycle. No differences were noted between either group and the conclusion was that the essential fatty acids were ineffective for PMS.⁴⁵

Another small randomized, double-blind placebo controlled trial was done on 38 women with PMS. They re-

ceived evening primrose or placebo for 3 months and were crossed over for another 3 months. An improvement was observed but considered not statistically significant. In addition, no carry-over effect was observed. The conclusion was that "the improvement experienced by these women with moderate PMS was solely a placebo effect."⁴⁶ At this time, it does not appear that evening primrose will improve PMS (level B evidence).⁴⁷ If patients do choose to try this approach, the dose shown to be effective for other prostaglandin-related conditions is 2 to 3 g/d.⁴⁸

Black Cohosh (*Cimicifuga racemosa*). Black cohosh was first used medicinally by Native Americans who introduced it to European colonists.⁴⁹ It was introduced to Germany in the late 19th century and has been used in Germany since the late 1950s as an alternative to manage menopause.⁵⁰ The majority of studies looking at black cohosh have been in the treatment of menopausal symptoms. The mechanism of action remains somewhat unclear. Some clinical evidence suggests black cohosh suppresses luteinizing hormone secretion,⁶¹ whereas another study shows no change in luteinizing hormone and follicle-stimulating hormone.⁶² A number of studies using Remifemin® (Glaxo, Smith, Klein, Research Triangle Park, NC), a proprietary extract of black cohosh, do show a benefit for various menopausal symptoms (hot flashes, profuse sweating, and sleep disturbance and depressive moods).⁶³ Because these symptoms often present as well in women with PMS, many clinicians have recommended the use of black cohosh in this population (level C evidence). Further clinical studies are needed to determine the efficacy of black cohosh in PMS. The recommended dose of black cohosh is 40 to 80 mg of a standardized extract twice daily providing 4 to 8 mg of triterpene glycosides.⁶⁴

Ginkgo (*Ginkgo biloba*). Ginkgo leaf extract comes from the oldest living tree species in the world.⁶⁵ Primarily known as a botanical useful for improving memory, ginkgo has also been evaluated as an extract that can improve PMS. Tamborini and Taurelle⁶⁶ studied the effects of this botanical product in 165 women. Patients were randomized to placebo or a standardized extract (Egb761) for symptoms of PMS (congestion, breast tenderness, and mood) for 2 cycles. The results showed a statistically significant improvement in all symptoms, especially breast tenderness and fluid retention (level B evidence). Ginkgo leaf extracts contain many active constituents including flavonoids and terpenoids. Ginkgo leaf flavonoids have antioxidant and free radical scavenging properties.¹ Ginkgo also inhibits platelet-activating factor⁶⁷ and has anti-inflammatory effects.⁶⁸ Some constituents also can relax vascular smooth muscle.⁶⁹ Further study is needed to determine if there is a significant role for ginkgo in treatment of PMS.

Because ginkgo inhibits platelet-activating factor, medications that affect platelet aggregation could theoretic-

ally increase the risk of bleeding in some people. There is some concern about seizures in some patients; these are anecdotal reports.⁶⁹ As ginkgo interacts at the CYP 450 enzymes in the liver, care should be taken in recommending ginkgo to patients with multiple medications that also effect these enzymes.³² The dose used for PMS in clinical trials was 80 mg twice a day starting on the 16th day of the cycle and on through until the 5th day of menses.⁵⁸

St. John's Wort (*Hypericum perforatum*). The use of serotonin reuptake inhibiting preparations for the mood symptoms of PMS and PMDD is well established.⁶³ With this in mind, St. John's wort is often used as a botanical alternative for treating this aspect of PMS. A number of reviews have suggested that St. John's wort can be useful for mild depression but not severe depression.⁶⁵ In a pilot study done in 2000 at the University of Exeter, 19 women with PMS were treated with 300 mg of hypericin standardized to .3% hypericin. The results showed a reduction of 51% in PMS scores between baseline and the end of the trial with over two thirds showing at least a 50% decrease in symptom severity.⁶⁶ The authors suggested that "there is scope for conducting a randomized, placebo controlled double-blind trial."

Those taking medications that increase photosensitivity should avoid the use of St. John's wort as this herb can induce photosensitivity if taken in large doses.³² Patients taking protease inhibitors (for HIV), cyclosporine, or other medications that are metabolized by the P450 enzyme system should also avoid use of St. John's wort because it has been shown to reduce serum levels of these medications and so potentially could interfere with their efficacy.³² The dose recommended for mild depression in most clinical trials is 300 mg of a standardized product to hypericin at .3% three times a day.³²

Kava (*Piper methysticum*). Kava, a member of the pepper family used ceremonially to honor special events and esteemed guests in Oceania, has been investigated for its anxiolytic properties in Europe and the United States.⁶⁷ In a recent review, kava has been shown to be effective for mild anxiety.⁶⁸ A number of small trials have been found improvement with the use of this herb in women suffering from menopause-related anxiety and neurovegetative symptoms.⁶⁹⁻⁷¹ No clinical studies have been done in women with PMS. The dose recommended in clinical trials is 100 to 300 mg daily of an extract standardized to 30%.

Recent medical reports have warned of the use of kava and the development of hepatotoxicity. In Germany and Switzerland brands concentrated to a 70% kavalactone concentration have been attributed as a possible cause for hepatotoxicity associated with kava use. Studies are underway at the Food and Drug Administration to determine if hepatotoxicity is causally linked to kava use as the case-by-case evaluation is not entirely convincing of this.⁷²

Currently, those who choose to use kava daily should work with a knowledgeable health care practitioner and monitor their liver function if use is greater than one month. Those patients with liver problems, on multiple medications metabolized in the liver or with heavy alcohol use should not take kava.⁷³ Furthermore, patients should be warned of the potential for sedation with this botanical and should avoid driving or using heavy machinery.⁷⁴

Other Botanicals. Other botanicals used clinically but not well studied are cramp bark (*Vibrium opulus*), dong quai root (*Angelica sinensis*), blue cohosh (*Caulophyllum thalictroides*), wild yam (*Dioscorea villosa*), black haw (*Viburnum prunifolium*), and pulsatilla (*Anemone pulsatilla*) (Table 3).^{75,76}

Mind/Body Approaches

Mind/body therapies (MBTs) are those therapies grounded in the emerging scientific understanding that thoughts and feelings impact physiology and physical health. MBTs for PMS vary widely in their approach and include interventions such as psychotherapy (cognitive-behavioral therapy and group therapy), relaxation techniques/training, bodywork (massage and reflexology), hypnotherapy, biofeedback, guided imagery, and yoga. Although aerobic exercise and light therapy may not be immediately appreciated as MBTs, their impact on mood via physiology will also be considered here.

The general research limitations for integrative medical therapies mentioned above apply here as well: studies of MBTs are either mostly preliminary (randomized controlled trials that are poorly constructed and/or have small patient populations; few studies in each category) or have not been done. The evidence regarding most of the mind/body approaches for PMS is fairly limited. However, because most of these approaches are risk free and because they include strategies traditionally accepted as important components of a healthy lifestyle (exercise, stress reduction, and relaxation), there is still a strong argument for their use in the treatment of PMS.

There is also evidence that some women with PMS do well with therapeutic options that also address psychological issues. A study published in *Sexual and Marital Therapy* evaluated women's self-reports and treatment preferences regarding PMS. Based on subject responses to a questionnaire that explored women's experiences with PMS, their beliefs about its cause, and their beliefs about past and possible future treatment for PMS, a biopsychosocial approach to PMS was advocated.⁷⁷

Relaxation Response. The relaxation response is a technique that consists of quiet sitting, progressive muscle relaxation, and the repetition of a constant stimulus such as the word "one" at each in breath and out breath for 10 to 20 minutes twice daily.⁷⁸ This approach has been found to be useful in the treatment of a wide variety of condi-

tions including hypertension, gastroesophageal reflux disease, insomnia, anxiety, and many other conditions.⁷⁹ A randomized clinical trial of 46 women with PMS found that subjects assigned to the relaxation response group reported significantly greater reduction of mood symptoms compared with controls assigned either charting of symptoms or reading over a 5-month period (level B evidence).⁸⁰

Biofeedback and Guided Imagery. Biofeedback is a strategy in which the patient is taught to control a physiological parameter usually thought of as autonomic or beyond conscious control, such as temperature or blood pressure, using autogenic relaxation training techniques in conjunction with active monitoring of the given parameter. Van Zak⁸¹ has reported a protocol using vaginal temperature biofeedback, in which the patient is taught to control vaginal temperature as a means of regulating PMS symptoms. In this study, the investigators did find a significant rise in temperature from vaginal temperature feedback that correlated with a reduction in PMS symptoms in the treatment group compared with the control group. However, this was not a blinded trial and thus it is difficult to draw conclusions regarding the efficacy of biofeedback beyond that of placebo intervention for this condition.

A nonrandomized, noncontrolled trial evaluated the effects of guided imagery on menstrual cycle lengthening and reducing premenstrual distress in 30 healthy college women with regular menstrual cycles over 6 months.⁸² Fifteen subjects completed the entire study and had significant increases in menstrual cycle length during the 3 months of imagery as well as significant declines in total PMS scores (level C evidence).

Cognitive-Behavioral Therapy and Group Therapy. Several small studies have investigated the effectiveness of cognitive therapy in alleviating negative symptoms in women with PMS. Blake et al⁸³ compared a group of women randomized to receive immediate weekly cognitive therapy with a group of controls allocated to a waiting group list that kept a symptom diary over a 12-week period. Results indicated that cognitive-behavioral therapy (CBT) was significantly more effective at remitting psychological and somatic symptoms as well as impairment of functioning compared with controls (level B evidence). Morse et al⁸⁴ found that women utilizing CBT with relaxation instructions had significantly reduced PMS symptoms compared with women randomized to a nonactive control group during two menstrual cycles (level B evidence). In a study by Kirkby,⁸⁵ 37 women with severe premenstrual symptoms were nonrandomly assigned to cognitive-behavioral coping skills treatment, a nonspecific treatment, or a waiting-list group. The author found significant reductions in premenstrual symptoms in the coping skills group compared to control subjects both at posttreatment and at a 9-month follow-up evaluation (level B evidence). Christensen et al⁸⁶ randomized

Table 3. Summary of Evidence on Botanical Medicines for PMS

<i>Botanical</i>	<i>Typical Dose</i>	<i>Efficacy</i>	<i>Level of Evidence</i>
Chasteberry (Vitex)	4-20 mg daily†	Likely yes	Level B (small or lesser-quality trials)
Evening Primrose oil	2-3 g/d	Likely no	Level B (small trials)
Black cohosh	40 mg 2 times a day*	Possible	Level C (expert opinion)
St. John's wort	300 mg 3 times a day*	Possible	Level B (small trials)
Kava	100-300 mg/d*	Possible	Level C (expert opinion)
Ginkgo	80 mg 2 times a day*	Likely yes	Level B (small trials)

*Standardized extract.

†Depending on specific extract used.

women to 2 different cognitive approaches and found that both cognitive-behavioral therapy and information-focused therapy resulted in symptoms reduction (level B evidence). However, lack of a true placebo group makes these results difficult to interpret.

Finally, a highly preliminary study found that PMS-related symptoms such as depression, irritability, and aggression can be alleviated by group therapy (rational-emotive therapy) and relaxation training.⁸⁷

Yoga. A 10-month empirical study of 40 women with menstrual distress was undertaken to investigate the effectiveness of certain yogic practices in relieving negative symptoms.⁸⁸ Women assigned to the study group underwent yoga training (regular practice of specific yoga postures and transcendental meditation); the control group had no training. The authors found significantly lower scores on the subscales of the menstrual distress questionnaire for subjects in the yoga-trained group compared with the control group in both the premenstrual and menstrual periods (level C evidence).

Aerobic Exercise. Exercise as an approach to specific conditions is often overlooked in the practice of conventional medicine. In the case of PMS, a number of studies have examined the role of aerobic exercise and evidence suggests this may be an effective therapy for PMS. One large survey of over 1,800 women found that exercise was used by over half of the women as a self-help measure for alleviating PMS symptoms.⁸⁹ Of those reporting exercise as a self-help measure, over 80% found it helpful. Aganoff et al⁹⁰ also surveyed exercisers and nonexercisers to determine the effects of regular, moderate exercise on mood states and menstrual cycle symptoms. Regular exercisers obtained significantly lower scores on impaired concentration, negative affect, behavior change and pain compared to non-exercisers.

Mood states and physical symptoms of 143 women (35 competitive sportswomen, 2 groups of exercisers [33 high exercisers and 36 low exercisers] and 39 sedentary women) were monitored for 5e days in each of the 3 phases of the menstrual cycle (midcycle, premenstrual, and menstrual) in another study.⁹¹ High exercisers experienced a greater positive affect and the least negative affect; sedentary women experienced the least positive affect (level B evidence). Similarly, Prior et al⁹² evaluated

mood symptoms over a 6-month period in 8 sedentary women who began to exercise and 7 runners who began training for a marathon; 6 women who kept their activity level the same served as a control group. Both groups that increased activity were found to have a reduction in premenstrual mood symptoms compared to the control group (level B evidence). The effects of aerobic and strength training exercise in a three-cycle randomized controlled (but not blinded) study of 23 healthy premenopausal women were investigated.⁹³ The authors found that women participating in both groups had overall improvement in many premenstrual symptoms. However, the aerobic group showed improvement on more symptoms overall, especially premenstrual depression.

Light Therapy. It has been postulated that shifts in reproductive hormones throughout a woman's life may adversely affect neurotransmitter, neuroendocrine, and circadian systems.⁹⁴ It has also been hypothesized that the negative mood symptoms experienced in PMDD may be due to a maladaptive response to light in the symptomatic luteal phase or to a disturbance in the circadian clock itself.⁹⁵ As a result of these considerations, light therapy has been investigated as a possible therapeutic intervention in PMS.

A 6-menstrual cycle randomized, double-blind, counterbalanced, crossover study of dim (500 lx red fluorescent light = placebo) versus bright light therapy (10,000 lx cool-white fluorescent light = treatment) in 14 women with late luteal phase dysphoric disorder (LLPDD) was undertaken by Lam et al.⁹⁶ The women completed 2 menstrual cycles of prospective baseline monitoring of premenstrual symptoms, followed by 2 cycles of each treatment; subjects were randomized to receive 30 minutes of evening light therapy using a light box at their homes. Results showed that the active bright white light condition significantly reduced depression and premenstrual tension scores during the symptomatic luteal phase compared with baseline, whereas the placebo dim red light condition did not.

Another 3-month crossover study evaluated the effects of bright (more than 2500 lux) white morning, bright white evening, and placebo dim (less than 10 lux) red evening light administered daily for 1 week during the premenstrual phase of the menstrual cycle in 19 patients with LLPDD and 11 healthy comparison subjects. The au-

thors reported that depressive ratings were significantly reduced from baseline levels by all light treatments in the patients with LLPDD (level B evidence).⁹⁷

Manipulative Medicine Approaches

This category of therapies includes those focusing on the impact of musculoskeletal structure on function and physiology and typically includes osteopathic manipulation, chiropractic, and the spectrum of massage and bodywork approaches. In the case of PMS, some limited data exist regarding the use of massage and chiropractic for symptom control.

Massage. Twenty-four women with premenstrual dysphoric disorder were randomly assigned to receive either massage therapy or relaxation therapy.⁹⁸ The authors reported decreases in anxiety, depressed mood, and pain in subjects receiving massage (immediately following first and last massage) compared with the control group.

Reflexology is the application of manual pressure to designated reflex points on the ears, hands, and feet that are believed to somatotopically correspond to specific areas of the body.

Oleson et al⁹⁹ evaluated the effectiveness of reflexology therapy in alleviating symptoms in 35 women with PMS. Women receiving true reflexology demonstrated a significantly greater decrease in PMS symptoms compared with women receiving sham reflexology (level B evidence).

Chiropractic. A randomized, placebo-controlled crossover trial of chiropractic for treatment of PMS was done in 1999.¹⁰⁰ This study used a spring-loaded adjustment instrument as the placebo, included 25 subjects, and measured outcome using a standardized PMS questionnaire and daily symptom monitoring. Interestingly, although this study found an improvement over baseline in all groups in terms of symptom control, and a significant difference in scores between treatment and placebo in the group that had the active treatment first, there was no difference between treatment and placebo in the group that had the placebo treatment first. More study is obviously required to distinguish between the role of placebo adjustment and specific adjustment in the use of chiropractic for PMS.

Homeopathy. A small but well-done study of individualized homeopathic prescription for PMS showed an improvement of at least 30% in symptoms in 90% of those receiving active treatment compared to 37.5% of those receiving placebo (level B evidence).¹⁰¹ Additional larger studies are needed to determine if there is a significant role for homeopathy in treatment of this condition.

Conclusion

The integrative approach seeks to combine the best of conventional medicine with the range of treatment options available through other, unconventional therapeutic modalities. In the case of PMS, particularly given its

multifactorial etiology and its tendency to present in different ways in different women, this approach is well suited and will provide benefit for many patients. Although much of the clinical research is preliminary and/or inadequately controlled to this point, many of these therapies have an extremely wide margin of safety and so may have a role in treatment even as we wait for more substantial data to accumulate regarding efficacy.

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