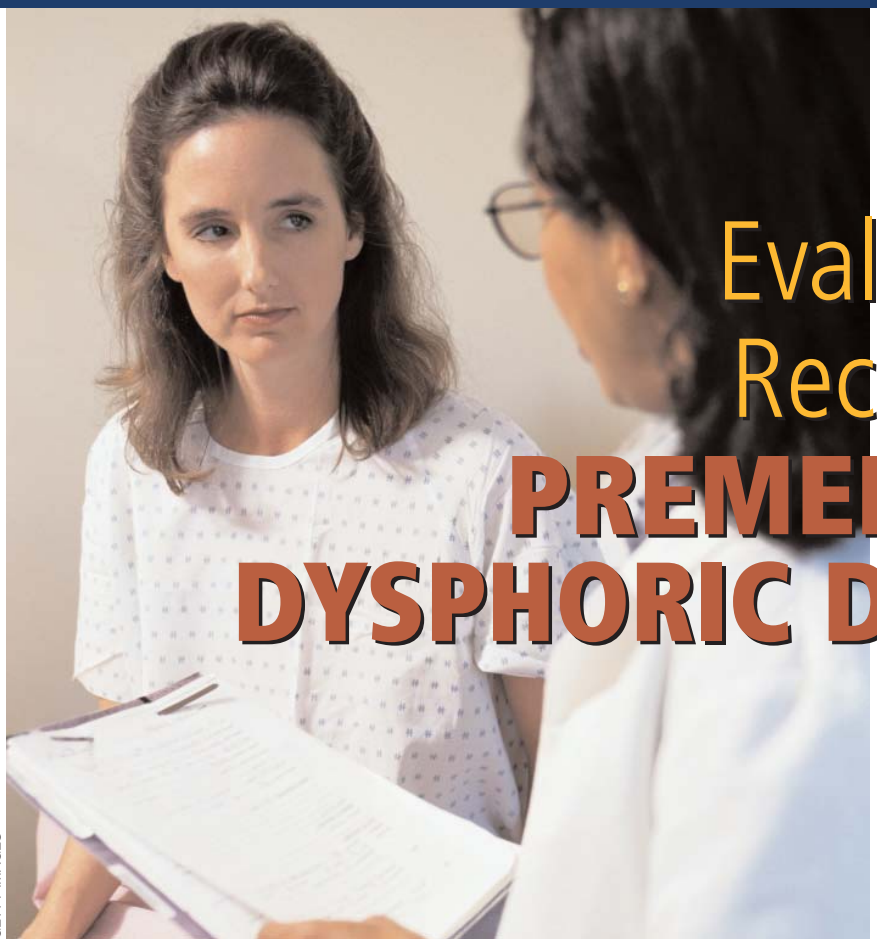

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Evaluation and Recognition of PREMENSTRUAL DYSPHORIC DISORDER

By Peter Kovacs, MD

It is a well-known fact that women experience cyclic emotional and physical symptoms that are present only during the luteal phase of their menstrual cycle — the days before menstruation begins — and that disappear at onset of menstruation. Well over 100 different symptoms have been described in up to 80 percent of women. In three to five percent, these symptoms are so severe that they interfere with normal, everyday activity. Premenstrual syndrome (PMS) is defined as emotional, physical, and behavioral symptoms that are present in the luteal phase and disappear with the onset of menstruation. Premenstrual dysphoric disorder (PMDD), previously known as "luteal-phase dysphoric disorder," is the most severe form and interrupts normal, everyday activity. It is important to differentiate PMDD from other mental and medical conditions with similar symptoms so that effective therapy can be started.

How are PMS and PMDD diagnosed?

The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*), describes the 11 groups of symptoms instrumental in establishing a diagnosis of PMDD: (1) feeling sad, hopeless; (2) feeling tense, anxious; (3) lability of mood; (4) persistent irritability; (5) decreased interest in usual activities, social withdrawal; (6) lack of concentration; (7) fatigue, lethargy; (8) changes in appetite, food cravings; (9) hypersomnia or insomnia; (10) feeling overwhelmed; and (11) breast tenderness, headache, bloating, or other physical symptoms. Five of these 11 symptoms had to have occurred during the second, postovulatory phase of the menstrual cycle and disappeared with the onset of menstruation or by the end of menstruation for most of the previous year. The patient must be symptom-free in the follicular phase, i.e., between menstruation and ovulation. For accuracy, symptoms

need to be evaluated prospectively over at least two months. Several instruments are useful for symptom assessment: Daily Rating Form, Menstrual Distress Questionnaire, Premenstrual Assessment Form, Calendar of Premenstrual Experiences, Prospective Record of the Impact and Severity of Menstrual Symptoms, and various other visual analog scales. Symptoms must be assessed in both the follicular and luteal phases in two consecutive cycles. The mean symptom score has to be at least 30 percent higher in the luteal phase to qualify for the diagnosis of PMDD. Prospective use of screening instruments allows correct diagnosis in the office and helps to characterize patients in research studies.

A diagnosis of PMS requires that only one of the 11 *DSM-IV* symptoms be identified; severity of the symptom does not have to be so great as to interrupt everyday activity. Similar to PMDD, the symptom or symptoms must worsen in the luteal phase.

What other diseases can mimic PMS/PMDD?

It is important to rule out mental and physical diseases with symptoms similar to those of PMDD because they might require more urgent or different treatment. Mood disorders (major depression, dysthymia, anxiety disorders) can present with complaints similar to those with PMDD. However, the adverse mood changes associated with depression are typically present throughout the entire cycle rather than only in the luteal phase. Prospective charting will often fail to detect phasic differences. Such patients usually do not become asymptomatic in their follicular phase. ➔

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The following participant has affiliations with the companies so named:

Peter Kovacs, MD, has no financial information to disclose. **Dr. Kovacs will discuss the unlabeled or investigational use of alprazolam, buspirone, gonadotropin-releasing hormone agonist, clomipramine, danazol, bromocriptine, sertraline, venlafaxine, spironolactone, citalopram, estrogen, and progesterone in the treatment of premenstrual syndrome and premenstrual dysphoric disorder.**

Goals of this activity are:
1. To acquaint the reader with the criteria that must be met for a diagnosis of premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD).
2. To inform the reader about disorders that comprise the differential diagnosis of PMS and PMDD.
3. To familiarize the reader with both pharmacologic and nonpharmacologic approaches to the treatment of PMS and PMDD.

After completing this activity, nurse practitioners and physician assistants should be better able to
1. Identify patients who have PMS or PMDD.
2. Consider and rule out disorders with similar signs and symptoms.
3. Provide patients diagnosed with PMS or PMDD with both pharmacologic and nonpharmacologic treatment choices.

The participating faculty determines the editorial contents of this CME activity, "Evaluation and Recognition of Premenstrual Dysphoric Disorder." Participants' comments do not necessarily reflect the views of their associated institutions or the sponsor.

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This Educational Design II activity is presented by Montefiore Medical Center, Division of Education and Organizational Development which has been approved as a provider of continuing education by the New York State Nurses Association's Council on Continuing Education, which is accredited by the American Nurses' Credentialing Center's Commission on Accreditation as an approver of continuing education in nursing. It has been assigned approval code 4ZDHNB-PRV-022.

All nurse practitioners completing this activity will be granted 1.2 CHs by Montefiore Medical Center, Division of Education and Organizational Development, which is designated as a provider of continuing education by the New York State Nurses Association.

Albert Einstein College of Medicine designates this continuing medical education activity for a maximum of one (1) hour in category 1 credit toward the AMA Physician's Recognition Award. Each course participant should claim only those hours of credit that he/she actually spent in the educational activity.

Albert Einstein College of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education. This CME activity was planned and produced in accordance with the ACCME Essentials.

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Similar to depression, anxiety disorders do not typically follow cyclic changes during the menstrual cycle. Prospective symptom charting will detect the presence of similar symptoms in the luteal and follicular phases.

Premenstrual exacerbation of both depression and anxiety has been described. For women who experience such exacerbation, treatments effective in the management of PMDD can also be valuable. While symptoms during premenstrual exacerbation might not respond to treatment, improvements should be achieved in the luteal phase.

Other mental disorders, such as bipolar disorder and psychosis, need to be included in the differential diagnosis. Besides the noncyclic nature of symptoms, other characteristic features of these diseases help to differentiate them from PMDD.

The appetite changes and food cravings of PMDD must be differentiated from other eating disorders (e.g., bulimia nervosa). Substance abuse can also mimic PMDD. Again, the noncyclic nature of the symptoms during evaluation is an important diagnostic clue.

Certain medical conditions can present with symptoms that masquerade as PMDD. Endometriosis, chronic pelvic pain, pelvic congestion syndrome, gastrointestinal diseases (e.g., irritable bowel syndrome), fibromyalgia, and allergic diseases need to be considered. It is important to assess thyroid function, since depression and fatigue are frequently reported in association with hypothyroidism.

Table I.

Guidelines for Evaluating Possible PMS/PMDD

- Take a thorough history and perform a complete physical, including pelvic examination.
- Review previous treatment of mental disorders.
- Review current and past medication use.
- Review any history of substance abuse.
- Order laboratory tests: complete blood counts, blood chemistries, thyroid-stimulating hormone determination.
- Chart symptoms prospectively over two cycles to establish cyclicity of symptoms.
- Consider psychiatric evaluation for patients with noncyclic symptoms.
- If the symptom pattern is cyclic and PMS is diagnosed, explain findings and offer treatment (nonpharmacologic and/or pharmacologic).
- If the pattern is cyclic and PMDD is diagnosed, explain findings and strongly recommend treatment (see *Table 2*).

Is special testing needed?

To rule out conditions that can mimic PMDD, a careful history and thorough physical and pelvic examinations, as well as assessment of basic chemistry and blood values, should be done (*Table 1*). A screening thyroid-stimulating hormone level must be included. Once other medical conditions are excluded, premenstrual symptoms should be charted over two cycles to make the diagnosis of PMDD.

What is the etiology of PMS/PMDD?

The initial belief was that the cyclic occurrence of symptoms was tied to hormonal changes during the menstrual cycle specific to women with PMDD. The follicular phase is dominated by estradiol, while both progesterone and estradiol are elevated following ovulation. No significant differences in serum estradiol, progesterone, or urinary steroid-hormone metabolite levels have ever been detected when asymptomatic women and women with PMDD were compared. On the other hand, normal ovarian function is required to produce symptoms of PMDD, since symptoms disappear during pregnancy and after menopause. Differences in the central nervous system (CNS) metabolism of steroid hormones between women with and without PMDD cannot be ruled out. Such variations in CNS steroid metabolites could lead to different symptoms.

Changes in total and ionized calcium levels have been noted in women with PMDD. Lower calcium levels are believed to play a role in the onset of symptoms, but a clear association has yet to be established.

Currently, the most widely accepted explanation of the pathogenesis of PMDD is based on changes in neurotransmitter levels. Reduced CNS availability of serotonin is thought to play a role in the pathogenesis of de-

pression. Since many of the symptoms of PMDD are similar to those of depression, the role of serotonin in PMDD has also been explored. Blood serotonin levels and platelet serotonin uptake were reduced in women with PMDD. The fact that the most effective known treatment for PMDD is the use of selective serotonin reuptake inhibitors (SSRIs) serves as indirect evidence for the involvement of serotonin. Steroid hormones can influence the turnover of various neurotransmitters, and neurotransmitters in return can influence steroid metabolism. These metabolic changes can trigger PMDD in susceptible women. The neurotransmitter theory was recently discussed in a review by Parry.[1]

The γ-aminobutyric acid, opiate, adrenergic, and endorphin systems have also been evaluated. These other neurotransmitters could be responsible in the 30-40 percent of women with PMDD who do not respond to SSRIs.

The most widely accepted theory behind PMS also involves neurotransmitter abnormality.

Are there effective pharmacologic treatments?

Both pharmacologic and nonpharmacologic therapies have been evaluated as therapy for PMDD (*Tables 2* and *3*).

Several anxiolytics (alprazolam and buspirone were studied most extensively) have been successfully used in the management of PMDD. Their efficacy was documented with both continuous and intermittent administration, i.e., only in the luteal phase (postovulation). The possibility of dependence and tolerance with anxiolytics is the most likely reason for their infrequent use.

Selective serotonin reuptake inhibitors are currently considered first-line therapy for PMS and PMDD. A number of different SSRIs (fluoxetine, sertraline, citalopram, clomipramine) were found to be similarly effective. In one of the earlier trials of fluoxetine, long-term use for the management of PMDD was evaluated in 60 women.[2] Fifty-two percent achieved remission. In a comparison of full-cycle versus half-cycle dosing of sertraline, overall symptom scores were lower in the luteal-phase dosing group, but the difference did not reach significance.[3] This finding could be due to the relatively small sample size. When symptoms were analyzed separately, mood scores were significantly lower in the intermittent dosing group. At the end of the trial, more women with the half-cycle dosing showed improvement (89 percent vs. 46 percent).

Many of the symptoms of PMDD are similar to those of depression.

In another study, Wikander and colleagues evaluated citalopram, a more selective SSRI, in the management of PMDD.[4] Results showed that intermittent dosing was superior to continuous dosing, raising the possibility that continuous dosing leads to tolerance, which may necessitate further dose increases. This would be undesirable, since side effects appear to be dose-dependent. As the onset of action of SSRIs used for the management of PMS occurs within hours to days, luteal phase-only administration is sufficient. With intermittent administration, the total dose of medication can be reduced, leading to fewer side effects and ultimately to better compliance.

Venlafaxine, a serotonin and norepinephrine reuptake inhibitor, was evaluated for the treatment of premenstrual symptoms.[5] Overall, 57 percent of women assigned to venlafaxine experienced relief, while only 31 percent in the placebo group reported improvement. The medication was generally well-tolerated, but insomnia, dizziness, nausea, and decreased libido occurred more often with venlafaxine.

Do SSRIs cause derangements in the menstrual cycle?

To determine whether SSRIs impact the length of the menstrual cycle, Steiner et al assigned women who met the diagnostic criteria for PMDD to receive fluoxetine or placebo in a double-blind fashion.[6] A change in cycle length of more than one standard deviation (four days) was considered significant. Results showed a dose-dependent effect of fluoxetine on menstrual-cycle length. The authors hypothesized that SSRI treatment could affect steroid-hormone metabolism. Alternatively, SSRIs could modify the length of the menstrual cycle by influencing gonadotropin release. Patients taking SSRIs should therefore be advised of possible changes in the length of their menstrual cycle. Otherwise, they might discontinue the drug out of fear of some adverse effect. ➔

What about other side effects?

Decreased sexual functioning and gastrointestinal side effects have been associated with SSRI use. Starting patients on a lower dose and allowing them to titrate the dose to the desired level will keep side effects to a minimum and likely result in increased compliance.

Selective serotonin reuptake inhibitors cross the placenta. They are considered to be pregnancy category C, but data on their safety in pregnancy are limited. While current data on SSRI exposure during pregnancy are reassuring, patients with PMDD who take SSRIs should be advised to use contraception.

Table 2.

Pharmacologic and Nonpharmacologic Treatment Modalities for PMDD

- For mild symptoms
  - — Dietary changes
  - — Exercise
  - — Calcium supplementation
  - — Vitamin B_6 supplementation
  - — Relaxation therapy, cognitive therapy
- For severe symptoms
  - — Selective serotonin reuptake inhibitor (continuous or intermittent)
  - — Ovulation suppression: oral contraceptives, danazol, gonadotropin-releasing hormone agonist
  - — Anxiolytics (rarely used)
- For symptomatic treatment only
  - — Spironolactone
  - — Danazol
  - — Bromocriptine

Can hormones that suppress ovulation ease the symptoms of PMS/PMDD?

Because of the cyclic appearance of PMDD symptoms, steroid hormones were thought to play an etiologic role. Several studies evaluated the effect of ovulation suppression and hormonal manipulation on the severity of symptoms. Oral contraceptives (OCs) were among the earliest hormonal methods used in the management of PMS/PMDD. A report from the early '80s assessed the effect of OCs on five different symptoms, based on a cross-sectional analysis.[7] Women of reproductive age were asked about OC use and the presence and severity of irritability, sadness, anxiety, breast tenderness, and swelling throughout the menstrual cycles. Age-matched users and nonusers were compared. This study showed that anxiety, irritability, and breast tenderness were less frequent among OC users in the 25-year-old age group. Breast tenderness was also less common with OCs in 32-year-old women, but there were no significant differences in symptom severity in any other age group.

Using a double-blind protocol, Backstrom et al compared the effects of monophasic and triphasic OCs on PMS in women who took a monophasic pill containing 30 µg ethinyl estradiol and either 150 µg desogestrel or 150 µg levonorgestrel or a triphasic pill containing levonorgestrel.[8] Overall mood and physical symptoms decreased during the first three treatment cycles. By the fourth cycle, however, no significant differences from the screening baseline symptoms were observed. The OC containing desogestrel was more effective in decreasing swelling, tension, and irritability and resulted in better relaxation than the pill combined with levonorgestrel. Monophasic pills were superior in reducing tension and irritability, but triphasic pills reduced breast tenderness more effectively. The lack of effect in the fourth treatment cycle suggests a significant placebo effect that disappeared over time. Absence of a placebo group, however, makes it impossible to evaluate the magnitude of the placebo effect.

Drospirenone, a new progestin, was evaluated in combination with estradiol in a randomized, prospective, double-blind, placebo-controlled trial of women with PMDD.[9] Beneficial, though not significant, changes were observed in all symptoms. Acne, food cravings, and appetite improved significantly with the OC containing drospirenone.

Other studies have shown mixed results. Potential beneficial effects with OCs are challenged by frequent complaints of bloating and breast tenderness. An increase in adverse mood changes has been reported with the use of OCs. If OCs are given to help with the symptoms of PMS, close monitoring is necessary, since worsening of symptoms is possible. Current evidence suggests only a limited role for OCs in the management of PMS/PMDD.

Does noncontraceptive hormone therapy relieve PMS/PMDD?

Estradiol and progesterone preparations, used as single-agent therapy, have also been evaluated. Vanselow et

al studied oral and vaginal progesterone preparations in the treatment of PMS and found no difference when compared with placebo.[10] Another study of vaginal progesterone administered only in the luteal phase showed greater improvement in premenstrual symptoms with progesterone than with placebo.[11] In another placebo-controlled, randomized study, vaginal progesterone was superior to placebo in reducing irritability, tension, anxiety, and mood swings.[12] On the other hand, no symptom improvement was found with vaginal progesterone in a similarly designed study.[13] In a double-blind, randomized, placebo-controlled trial, alprazolam was superior to oral micronized progesterone in reducing premenstrual symptoms; progesterone was no more effective than placebo.[14] Overall, most of these studies failed to show that progesterone was beneficial in the management of PMS. Differences could have been the result of the route of administration or the dose used. Thus, progesterone does not play a significant role in the pharmacologic management of PMS/PMDD.

Can cycle interruption at other levels relieve symptoms of PMS/PMDD?

To maintain the proper ovarian cycle, there has to be an intact, functioning hypothalamic-pituitary axis. The pulsatile release of hypothalamic gonadotropin-releasing hormone (GnRH) stimulates the pituitary release of gonadotropins, follicle-stimulating hormone, and luteinizing hormone. These, in turn, stimulate the ovarian granulosa and theca cells and increase estradiol and progesterone production. Pharmacologic manipulation of the hypothalamic-pituitary axis leads to improvement in several gynecologic diseases (endometriosis, fibroids, precocious puberty, etc.). Gonadotropin-releasing hormone agonists (GnRHa) are peptides that bind to the pituitary GnRH receptors and result in down-regulation of the receptor, thereby rendering the pituitary resistant to further stimulation. After an initial stimulatory effect, GnRHa is associated with profound suppression of pituitary gonadotropin release and low circulating ovarian steroid-hormone levels.

A number of trials have looked at the effects of various GnRHa in the treatment of PMS. In a crossover study, intranasal buserelin was evaluated in 31 women with PMS.[15] Buserelin was found to be superior in the management of headaches, depressed mood, irritability, and swelling. Breast tenderness and overall energy levels were similarly affected by buserelin and placebo.

The GnRHa goserelin was studied in 32 women with PMS.[16] Potential candidates were prospectively evaluated with daily symptom scoring over two months. Eligible women were randomly assigned to monthly subcutaneous goserelin 3.6 mg or placebo. Such physical symptoms as breast tenderness and swelling improved significantly with goserelin, but mood symptoms, irritability, and depression were not significantly affected.

In a study of 25 women with PMS, depot leuprolide was superior to placebo in reducing irritability, neurologic symptoms, fatigue, and breast tenderness.[17] Leuprolide was less effective in women with more severe symptoms and ineffective in those with the most severe symptoms.

Are there risks associated with GnRHa therapy?

Since GnRHa use leads to low steroid-hormone levels, most patients who use GnRHa complain of vasomotor symptoms. It has not been determined whether hot flashes affect the symptoms associated with PMS. A recent study, however, found that menopausal women who had significant hot flashes also had worse mood and physical symptoms.[18]

Low estradiol levels will ultimately have an adverse effect on the skeletal system. Prolonged GnRHa use results in reduced bone mineral density (BMD). This is especially troubling if adequate BMD is not achieved during the early reproductive years, when peak bone mass is accumulated. Low BMD can lead to significant morbidity and mortality later, due to fractures associated with osteoporosis. Therefore, it is recommended that steroid hormones be added back if GnRHa is used for longer than six months.

In most studies, progesterone did not relieve PMS symptoms.

Does "add-back" therapy affect GnRHa treatment?

Adding back estrogen and progesterone during GnRHa treatment has been shown to effectively prevent ➔

bone loss and vasomotor symptoms. The effect of add-back therapy on PMS-related symptoms was evaluated by Schmidt et al.[19] Participants whose symptoms improved while on leuprolide had transdermal estradiol and vaginal progesterone added to their regimen. In the first part of the study, GnRHa treatment resulted in significant symptom improvement when compared with baseline and placebo. During the months of steroid add-back, sadness was significantly worse than during leuprolide treatment only. Other symptoms (anxiety, bloating, irritability, impaired function) were all worse with add-back therapy than with GnRHa treatment alone.

This was not the case, however, in a study by Mortola et al. They found that after two months of GnRHa alone, GnRHa plus conjugated equine estrogen and medroxyprogesterone add-back was comparable with use of GnRHa alone and superior to hormone replacement alone.[20]

Different estrogen and progesterone preparations may have different effects. If symptoms recur during the months of add-back, lower doses of estrogen and progesterone can be tried, and BMD should be followed.

Can other agents be added back effectively?

Use of a synthetic compound instead of natural hormone add-back was evaluated by DiCarlo in a study of 30 women given leuprolide. Instead of adding back estrogen and progesterone, these women were given tibolone, a synthetic compound that can have estrogenic, androgenic, or progestogenic effects depending on the tissue.[21] Used in Europe, GnRHa therapy plus tibolone effectively reduced hot flashes and increased BMD without stimulating the endometrium or breast tissue. However, combination of GnRHa and tibolone also decreased HDL cholesterol and might have a negative effect on cardiovascular disease. After two months, add-back with tibolone did not adversely affect symptom improvement seen with leuprolide alone. These results indicate that tibolone could be useful for add-back therapy. Unfortunately, it is not yet available in the United States.

Table 3.

Doses of Medications/Vitamins Used for PMDD Treatment*

- Calcium 1200 mg
- Vitamin B_6 <100 mg
- Danazol 200-400 mg
- Oral contraceptive pills <50 µg ethinyl estradiol
- Leuprolide 3.75 mg subcutaneously every month
- Sertraline (SSRI) 25-100 mg
- Fluoxetine (SSRI) 10-20 mg
- Citalopram (SSRI) 5-20 mg
- Alprazolam (anxiolytic) 0.25 mg t.i.d.

SSRI = selective serotonin reuptake inhibitor

* Doses must be adjusted based on response. It is recommended to start with lower dose and allow the patient to titrate the dose as needed.

Tibolone has also been assessed as a single agent: In a double-blind, crossover study of tibolone used alone, 18 women were randomly assigned to receive 2.5 mg tibolone or placebo.[22] After three months, patients were crossed over to the other treatment group. Symptoms improved in the second and third treatment cycles with tibolone. In the third month, symptoms were significantly improved compared with baseline findings.

Is danazol effective?

Danazol is a synthetic androgen that suppresses ovarian function, but it did not relieve physical and psychological symptoms, compared with placebo.[23] Breast tenderness, however, was significantly reduced. While danazol has also been shown to be effective in managing cyclic mastalgia in other studies, it can increase hirsutism and acne and adversely affect the lipoprotein profile. In addition, menstrual cycles become irregular. These adverse effects compromise compliance. Pregnancy must be avoided by women who are using danazol, so adequate contraception is important.

Do nonpharmacologic treatments work?

Calcium supplementation has been looked at in several studies, since reduced calcium levels in women with PMS were thought to play a pathogenetic role. In one study, calcium administration in the luteal phase significantly lowered symptom scores.[24] Overall, 50 percent of women improved with calcium, while 30 percent of those receiving placebo reported less severe symptoms. Other studies have also found reduced negative affect and improvement in water retention and pain with added calcium.

A recent meta-analysis summarized the results of trials evaluating the

risks and benefits of using vitamin B_6 in the management of PMS.[25] The analysis revealed a small improvement in premenstrual symptoms; the beneficial effect was not dose-dependent. This is an important finding since ingestion of higher doses of vitamin B_6 is associated with toxic side effects (peripheral neuropathy).

Other dietary changes that had an effect on either individual symptoms or overall improvement include magnesium supplementation, reduced caffeine intake, and increased consumption of complex carbohydrates.

A few smaller studies evaluated relaxation therapy, exercise, and cognitive therapy in PMS management. Results were controversial, and any benefits were usually modest, suggesting a placebo effect. Relaxation and exercise improve general well-being, so they should be encouraged. If effective treatment for PMS is urgently needed, pharmacologic and nonpharmacologic therapies should be combined.

Are there effective ways to treat individual symptoms?

As discussed earlier, danazol has been shown to improve luteal-phase mastalgia. Significant reductions in premenstrual tension have been found with spironolactone and medroxyprogesterone when compared with placebo.[26] Vellacott et al demonstrated that 100 mg spironolactone, administered in the luteal phase only, was superior to placebo in reducing premenstrual bloating.[27] A number of studies, including one by Ylostalo and colleagues, found bromocriptine to be effective in the treatment of premenstrual breast tenderness.[28] However, a prospective evaluation of bromocriptine for PMS demonstrated similar symptom reduction as with placebo.[29] In yet another study, Andersen et al found that bromocriptine reduced premenstrual mastalgia when administered in the luteal phase only; compared with placebo, bromocriptine had no superior effects on other symptoms.[30] ●

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CME/Instructional Learning Questions on "Evaluation and Recognition of Premenstrual Dysphoric Disorder"

On the answer sheet on the next page, please circle the one answer to each question that is true. Completed answer sheets should be placed in a stamped envelope and returned to the address shown on the form. This examination was reviewed by Staci E. Pollack, MD, Assistant Professor, Department of Obstetrics, Gynecology, and Women's Health, Albert Einstein College of Medicine, Bronx, New York, and Clemencia S. Wong, RNC, MEd, and Mary McLoughlin, RN, MSN, CEN, who are Clinical Inservice Instructors for Medicine, Division of Education and Organizational Development, Montefiore Medical Center, Bronx, New York. Credit available through August 31, 2004.

1. What percentage of reproductive-age women suffer from PMDD?
- A. 3-5 percent
- B. 25 percent
- C. 50 percent
- D. 80 percent

2. To diagnose PMDD:
- A. Symptoms have to occur for most of the preceding year
- B. Five of 11 *DSM-IV* criteria have to be met
- C. Symptoms need to be identified prospectively
- D. all of the above

3. Major depression cannot be differentiated from PMDD.
- A. True
- B. False

4. The symptoms of PMDD typically occur:
- A. during the follicular phase
- B. during the luteal phase
- C. throughout the cycle
- D. only during menstruation

5. The precise etiology of PMDD is:
- A. chronic anovulation
- B. low progesterone levels in the luteal phase
- C. high neurotransmitter levels
- D. not known

6. Effective pharmacologic treatment for PMDD includes:
- A. selective serotonin reuptake inhibitors (SSRIs)
- B. gonadotropin-releasing hormone agonist (GnRHa)
- C. anxiolytics
- D. all of the above

7. The most common first-line treatment for PMDD is:
- A. SSRIs
- B. GnRHa
- C. oral contraceptives
- D. calcium

8. Side effects of GnRHa are:
- A. amenorrhea
- B. hot flashes
- C. vaginal dryness
- D. lowered bone mineral density
- E. all of the above

9. A common side effect of SSRIs is:
- A. bone loss
- B. tremor
- C. sexual dysfunction
- D. polyuria

10. Nonpharmacologic methods that improve certain symptoms of PMS are:
- A. calcium
- B. vitamin B_6
- C. relaxation
- D. dietary changes
- E. all of the above

ANSWER SHEET: **Circle correct answers to questions in the CME activity on "Evaluation and Recognition of Premenstrual Dysphoric Disorder."**

1.	A	B	C	D	4.	A	B	C	D	7.	A	B	C	D	10.	A	B	C	D	E
2.	A	B	C	D	5.	A	B	C	D	8.	A	B	C	D	E					
3.	A	B			6.	A	B	C	D	9.	A	B	C	D						

To obtain credit, you must have 70 percent or more of the answers correct. Please fill out the answer sheet and mail, along with payment, as noted:

• PAs — Send a check in the amount of $10 made out to Montefiore Medical Center CME and the completed answer sheet to: Albert Einstein College of Medicine, Center for Continuing Medical Education, 3301 Bainbridge Avenue, Bronx, NY 10467.

• NPs — Send a check in the amount of $10 made out to Montefiore Medical Center and the completed answer sheet to: Montefiore Medical Center, Division of Education and Organizational Development, 3331 Steuben Avenue, Bronx, NY 10467.

Name _____ Degree _____ Address _____

City _____ State _____ Zip _____

State(s) where you want credit _____ Specialty _____

I hereby state I have completed this course independently in _____ hour(s).

_____
Signature Date

INSTRUCTIONS: Please complete the following statements by circling the one number that describes your rating.

The rating scale ranges from 1 to 4, where 1 = poor, 2 = fair, 3 = good, and 4 = excellent.

	Poor	Fair	Good	Excellent
1. To what extent did the objectives relate to the overall purpose of this activity?	1	2	3	4
2. To what extent have you achieved each objective of this activity?				
(a) To identify patients who have premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD)	1	2	3	4
(b) To rule out disorders with symptoms similar to those of PMS/PMDD	1	2	3	4
(c) To provide patients diagnosed with PMS/PMDD with both pharmacologic and nonpharmacologic treatment choices	1	2	3	4
3. To what extent were the teaching/learning resources effective?	1	2	3	4
4. How long did it take you to complete this activity? _____				

COMMENTS: _____

_____

_____

_____

_____

(Return by mail)