REVIEW ARTICLE

Premenstrual Syndrome - A Monthly Menace

MONIKA BANSAL*, MANOJ GOYAL**, SHAILESH YADAV†, VIRENDER SINGH‡

ABSTRACT

Most women feel some discomfort before or during their periods, but if the discomfort is of such a severity that starts interfering with some aspects of life: The diagnosis of premenstrual syndrome or tension (PMS or PMT) should be considered. About 80-95% of females of childbearing age have some premenstrual symptoms. PMS affects upto 30% of women with regular menstrual cycles. Some women (about 3-8% of menstruating women) have a more severe and disabling form of PMS having a psychiatric designation called premenstrual dysphoric disorder (PMDD). The etiology of PMS remains unknown and may be complex and multifactorial, but hormones, neurotransmitters and genetic factors have a role to play. Behavioral symptoms along with physical symptoms should be present to establish a diagnosis. Certain lifestyle changes and dietary modifications along with a number of drug options can improve the quality-of-life of a patient of PMS upto a considerable extent.

Keywords: Premenstrual symptoms, premenstrual dysphoric disorder

Most women feel some discomfort before or during their periods, but if the discomfort is of such a severity that starts interfering with some aspects of life: The diagnosis of premenstrual syndrome or tension should be considered.

Premenstrual syndrome (PMS), also called PMT or premenstrual tension is a collection of physical, psychological and emotional symptoms related to a woman's menstrual cycle that develop during 7-14 days before the onset of menses and subsides when menstruation occurs.[1] About 80-95% of females of childbearing age have some PMS. PMS affects upto 30% of women with regular menstrual cycles. Some women (about 3-8% of menstruating women) have a more severe and disabling form of PMS. This form of PMS has its own psychiatric designation termed as premenstrual dysphoric disorder (PMDD).[2]

ETIOLOGY

The etiology of PMS remains unknown and may be complex and multifactorial. The role of ovarian hormones is unclear, but symptoms often improve when ovulation is suppressed.[3] Changes in hormone levels may influence centrally-acting neurotransmitters such as serotonin, but circulating sex hormone levels are typically normal in women with PMS. Some evidence suggests that the disorder is related to enhanced sensitivity to progesterone in women with underlying serotonin deficiency. Deficiencies in prostaglandins, related to an inability to convert linoleic acid to prostaglandin precursors, may be involved in PMS. Genetic factors also seem to play a role, as the concordance rate is two times higher in monozygotic twins than in dizygotic twins.[4]

CLINICAL PICTURE

Upto 85% of menstruating women report having one or more PMS, and 2-10% report disabling and incapacitating symptoms. More than 150 symptoms have been ascribed to PMS.[5] The most common physical manifestations of PMS are abdominal bloating and an extreme sense of fatigue, both of which occur in 90% of women with this disorder; breast tenderness and headaches are among the other major physical complaints, occurring in >50% of cases. The most common behavioral symptom of PMS is labile mood, occurring in >80% women. Other frequent behavioral complaints include irritability, tension, depressed mood, increased appetite (70%), and forgetfulness and difficulty concentrating (>50%).

DIAGNOSIS

PMS must be distinguished from simple premenstrual symptoms (e.g. bloating, breast tenderness) that do not interfere with daily functioning and are characteristic of normal ovulatory cycles.

*Assistant Professor, Dept. of Physiology
**Associate Professor
†Professor
Dept. of Pharmacology
‡Professor, Dept. of Microbiology
MMIMSR, Mullana, Ambala, Haryana
Address for correspondence
Dr Monika Bansal
Assistant Professor
Dept. of Physiology, MMIMSR, Mullana, Ambala, Haryana
E-mail: dr_manojgoyal@yahoo.co.in

The three key elements of diagnosis are:

- Symptoms consistent with PMS
- Consistent occurrence of symptoms only during the luteal phase of the menstrual cycle
- Negative impact of symptoms on function and lifestyle.[6,7]

Many criteria for identifying women with PMS have been proposed.

The American College of Obstetricians and Gynecologists (ACOG) diagnostic criteria (2000) for PMS are given below.[6]

All of the following must be met:

- At least one of the following physical symptoms present during the five days before menses for three consecutive menstrual cycles: Breast tenderness, swelling of the extremities, headache and abdominal bloating.
- At least one of the following psychological symptoms present during the five days before menses for three consecutive menstrual cycles: Depression, angry outbursts, irritability, anxiety, confusion and social withdrawal.
- Symptoms relieved within four days of menses, not recurring until at least the 13th day of the next cycle.
- Symptoms adversely affect work performance and/or family or social life.
- Symptoms cannot be explained by the use of hormones or other medication, or drugs or alcohol use.
- Symptoms occur reproducibly during two cycles of prospective recording.[8]

The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) also defines and gives diagnostic symptoms of PMDD.[9] When PMS or PMDD is suspected, patients should be instructed to keep a premenstrual daily symptom record for several consecutive months so that cycle-to-cycle variability can be examined.[5]

MANAGEMENT

Treatment goals for PMS are to:

- Ameliorate or eliminate symptoms
- Reduce their impact on activities and interpersonal relationships
- Minimize adverse effects of treatment.

Initially, all patients with PMS should be offered non-pharmacological therapy. Medication should be offered to patients with persistent symptoms of PMS and those who meet criteria for PMDD.[7]

Nonpharmacologic Therapy:[9-11]

- Education: About the biologic basis and prevalence of PMS.
- Structured sleep schedule with consistent sleep and wake times especially during the luteal phase
- Dietary changes like restriction of sodium and caffeine intake
- Aerobic exercises
- Stress management
- Psychological intervention includes cognitive behavioral relaxation therapy
- Maintaining a daily symptom record
- Complementary approaches like acupuncture, that probably helps due to its effect on serotonergic and opioidergic neurotransmission that modulates various psychosomatic functions.[12]

Dietary Supplementation[6,8,10,13]

Certain dietary supplements that are being evaluated in women with PMS are vitamins A, E, folic acid and B_6, L-tryptophan, calcium, magnesium and evening primrose oil. Various controlled trials have shown the beneficial effect of these supplements. Vitamin E helps by reducing the production of prostaglandins that cause cramps and breast tenderness. Vitamin B_6, calcium and magnesium are cofactors in the synthesis of neurotransmitters such as serotonin and dopamine from tryptophan. Serotonin is deficient in patients with PMS. They help in reduce bloating, breast tenderness and fluid retention.

Evening primrose oil (*Oenothera biennis*) contains polyunsaturated fatty acids, linoleic and gamma-linoleic acids. These are dietary precursors of prostaglandins (PGE_1 and PGE_2) deficiency of which allows an enhanced response to physiological levels of β-endorphins, angiotensin II and ovarian hormones.[9,14] High glycemic index (GI) carbohydrates may increase brain serotonin due to increase in plasma ratio of tryptophan to other large neutral amino acids.[13,15] Some herbs like black cohosh, ginger, raspberry leaf, dandelion and chasteberry and natural progesterone creams derived from wild yams and soybeans are also being used but with an unproven efficacy.

PHARMACOLOGIC THERAPY

If symptoms are not adequately relieved by non-pharmacologic measures the addition of pharmacologic

treatment should be individualized to target the most troublesome symptoms in each patient. Various drug options can be helpful.

Selective serotonin reuptake inhibitors (SSRIs) like fluoxetine and sertraline have been shown to be very efficacious in the treatment of both physical and behavioral symptoms of PMS. Common adverse effects are insomnia, drowsiness, fatigue, nausea, nervousness, headache, tremor and sexual dysfunction. These can be minimized by the use of lowest effective dose, whereas morning dosing can minimize insomnia.[6,9,10,16]

Anxiolytic agents such as alprazolam are not recommended because of their addictive potential, tolerance and significant side effects. Although, some beneficial effects have been demonstrated for other psychotropic agents, including bupropion, tricyclic antidepressants, buspirone and lithium, as well as the β-blockers; (atenolol and propranolol), treatment with these drugs is not recommended because the potential harms outweigh any benefit.[17] Combined serotonin and noradrenaline reuptake inhibitor such as venlafaxine is also being useful in PMS.[9]

Bromocriptine has been shown to relieve breast tenderness and menstrual migraine in women with PMS, but side effects limit its usefulness.[10,18] Spironolactone, an aldosterone antagonist structurally similar to steroid hormones, is the only diuretic that has been shown to effectively relieve PMS symptoms such as breast tenderness and fluid retention. Thiazide diuretics have not been found to be beneficial in the treatment of patients with PMS.[6,10]

Use of nonsteroidal anti-inflammatory drugs (NSAIDs), especially mefenamic acid and naproxen sodium is based on the theory that PMS symptoms are related to prostaglandin excess.[11] Most NSAIDs should be effective, but mefenamic acid and naproxen sodium have been the most studied. Mefenamic acid therapy given during the luteal phase is effective in relieving symptoms, but gastrointestinal toxicity prohibits its use. Naproxen sodium improves physical symptoms and headache in women with PMS. Overall, NSAIDs may alleviate a wide range of symptoms, but they do not appear to improve mastalgia. All NSAIDs must be used with caution in patients with underlying gastrointestinal or renal disorders.[19]

Agents used to alter the menstrual cycle, danazol, gonadotropin-releasing hormone (GnRH) agonists, estrogen and progesterone have been studied in the treatment of PMS and PMDD. Although, efficacy has been demonstrated for some of these agents, their use is limited by significant adverse effects and treatment costs. Danazol has been found to be effective in treatment of PMS symptoms. However, long-term therapy is limited by side effects such as masculiniztion (e.g., decreased breast size, deepening of the voice, weight gain) as well as adverse effects on liver function tests and serum lipid profiles.[9,10,20]

GnRH agonists are synthetic analogs of naturally-occurring GnRH and suppress ovulation by inhibiting the release of pituitary gonadotropins. They are leuprolide, goserelin, nafarelin, histrelin. GnRH agonists have been shown to be more effective in treating behavioral and physical symptoms of PMS. Side effects and cost may limit GnRH agonist therapy in patients with severe PMS.[21,22] The hypoestrogenic effects of GnRH agonists can lead to atrophic vaginitis, urinary tract symptoms, and a decrease in skin collagen content. Use of these agents for longer than six months can significantly increase the risk of osteoporosis and cardiovascular disease. Tibolone is an investigational synthetic steroid with weak estrogenic, progestogenic and androgenic activity. Although, this agent has primarily been studied in the treatment of menopause and osteoporosis, it has been shown to provide significant improvement in premenstrual symptoms compared with placebo and a multivitamin.[16]

The administration of estrogen late in the luteal phase (to minimize premenstrual decline in the hormone) relieves premenstrual migraine. For overall symptom management, estrogen must be given continuously to suppress ovarian activity. Because unopposed estrogen can promote endometrial hyperplasia and carcinoma, cyclic progesterone must be added. But progesterone may induce PMS symptoms, thereby limiting the efficacy of estrogen.[23] To avoid this a combination of estrogen and local progesterone (levonorgestrel intrauterine system) is being studied, with systemic levels of progesterone remaining low.[9] Testosterone implants have also been used when decreased libido is a major symptom. Although oral contraceptive pills (OCPs) are widely prescribed for the management of PMS, they have not been shown to be consistently effective. Any benefits are probably due to the estrogenic component; therefore, monophonic pills may be most appropriate. OCPs may improve physical symptoms such as bloating, headaches, abdominal pain and breast tenderness, but they can also exacerbate these symptoms.

A new combined oral contraceptive containing 30 μg of ethinylestradiol and 3 mg of drospirenone (a new progesterone having antimineralocorticoid and antiandrogenic activity) has shown significant reduction in symptoms of PMS apart from being useful as an oral

contraceptive. It is used from Day 1 of the cycle for 21 days, followed by seven-day break.[9]

SURGICAL TREATMENT

Surgical treatment, principally hysterectomy *plus* bilateral oophorectomy followed by hormone replacement therapy with unopposed estrogen may be considered in severely affected patients who fail to respond to other therapies. To confirm whether the procedure is going to be effective or not, a test with GnRH analog should be done before surgery.[24]

CONCLUSION

The symptoms of PMS are distressing and disabling. Moreover, the exact cause of PMS is not known but appears to be due to increased sensitivity to normal ovarian hormones particularly progesterone secondary to serotonin deficiency. A number of nondrug and drug options although with limited efficacy, are available, which if individualized to target the most troublesome symptoms in each patient, the results can be encouraging and the quality-of-life of patients suffering from PMS can be improved upto a significant extent.

REFERENCES

1. Johnson SR. Premenstrual syndrome, premenstrual dysphoric disorder, and beyond: a clinical primer for practitioners. Obstet Gynecol 2004;104(4):845-59.
2. Deuster PA, Adera T, South-Paul J. Biological, social, and behavioral factors associated with premenstrual syndrome. Arch Fam Med 1999;8(2):122-8.
3. Daugherty JE. Treatment strategies for premenstrual syndrome. Am Fam Physician 1998;58(1):183-92, 197-8.
4. Kendler KS, Karkowski LM, Corey LA, Neale MC. Longitudinal population-based twin study of retrospectively reported premenstrual symptoms and lifetime major depression. Am J Psychiatry 1998;155(9):1234-40.
5. American College of Obstetricians and Gynecologists. Current information and opinions on subjects related to women's health (Pamphlet) Washington, DC. American Congress of Obstetricians and Gynecologists. March 2010.
6. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 15, April 2000. Premenstrual syndrome. Obstet Gynecol 2000;95:1-9.
7. Steiner M, Born L. Diagnosis and treatment of premenstrual dysphoric disorder: an update. Int Clin Psychopharmacol 2000;15 Suppl 3:S5-17.
8. Wyatt KM, Dimmock PW, Jones PW, Shaughn O'Brien PM. Efficacy of vitamin B-6 in the treatment of premenstrual syndrome: systematic review. BMJ 1999;318(7195):1375-81.
9. Govind A, O'Brien PM. Dysmenorrhea and premenstrual syndrome. Gynecology for postgraduates and practitioners. 2nd edition, Sengupta BS, Chattopadhyay SK, Varma TR, Sengupta PS (Eds.), Elsevier: New Delhi 2007:96-108.
10. Wyatt K, Dimmock PW, O'Brien PM. Premenstrual syndrome. In: Clinical Evidence. 4th issue. Barton S (Ed.), BMJ Publishing Group: London 2000:1121-33.
11. Moline ML, Zendell SM. Evaluating and managing premenstrual syndrome. Medscape Womens Health 2000;5:1-16.
12. Habek D, Habek JC, Barbir A. Using acupuncture to treat premenstrual syndrome. Arch Gynecol Obstet 2002;267(1):23-6.
13. Rapkin A. A review of treatment of premenstrual syndrome and premenstrual dysphoric disorder. Psychoneuroendocrinology 2003;28 Suppl 3:39-53.
14. Bayles B, Usatine R. Evening primrose oil. Am Fam Physician 2009;80(12):1405-8.
15. Murakami K, Sasaki S, Takahashi Y, Uenishi K, Watanabe T, Kohri T, et al. Dietary glycemic index is associated with decreased premenstrual symptoms in young Japanese women. Nutrition 2008;24(6):554-61.
16. Drug Facts and Comparisons. St.Louis: MO Facts and Comparisons, 2002.
17. Freeman EW, Rickels K, Sondheimer SJ, Polansky M. A double-blind trial of oral progesterone, alprazolam, and placebo in treatment of severe premenstrual syndrome. JAMA 1995;274(1):51-7.
18. Herzog AG. Continuous bromocriptine therapy in menstrual migraine. Neurology 1997;48(1):101-2.
19. Burke A, Smyth E, FitzGerald GA. Analgesic-antipyretic agents; pharmacotherapy of gout. In: Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 11th edition, Brunton LL, Lazo JS, Parker KL (Eds.), The McGraw Hill Companies: USA 2006:671-715.
20. Freeman EW, Sondheimer SJ, Rickels K. Gonadotropin-releasing hormone agonist in the treatment of premenstrual symptoms with and without ongoing dysphoria: a controlled study. Psychopharmacol Bull 1997;33(2):303-9.
21. Sundström I, Nyberg S, Bixo M, Hammarbäck S, Bäckström T. Treatment of premenstrual syndrome with gonadotropin-releasing hormone agonist in a low dose regimen. Acta Obstet Gynecol Scand 1999;78(10):891-9.
22. Leather AT, Studd JW, Watson NR, Holland EF. The treatment of severe premenstrual syndrome with goserelin with and without 'add-back' estrogen therapy: a placebo-controlled study. Gynecol Endocrinol 1999;13(1):48-55.
23. Kessel B. Premenstrual syndrome. Advances in diagnosis and treatment. Obstet Gynecol Clin North Am 2000;27(3):625-39.
24. Kumar P, Malhotra N. Premenstrual syndrome and other menstrual phenomena. In: Jeffcoate's Principles of Gynaecology. 7th edition, Jaypee Brothers Medical Publishers (P) Ltd.: New Delhi 2008:627-36.

DISTURBED

BY

SIDE EFFECTS

OF HIGH
ELEMENTAL IRON ?

NAUSEA

CONSTIPATION

G.I DISTURBANCE

IRON OVERLOAD

℞ **DEXORANGE®**

(Ferric Ammonium Citrate + Cyanocobalamin + Folic Acid) **Syrup**

(with Zinc advantage) **Capsule**

The Most Tolerated Iron Supplement

For further information, please write to:
FRANCO - INDIAN
PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road,Mumbai 400 011.
website : http://www.francoindian.com
e-mail : francoip@bom7.vsnl.net.in

Fatigue… involves both body & mind

Geriforte®

(SYRUP, TABLET)

Rejuvenates both BODY & MIND

- **Restores physical health**
  - Revives physical capacity
  - Exhibits significant antioxidant activity
  - Possesses revitalizing effect
- **Restores mental health**
  - Helps combat mental fatigue
  - Relieves stress
  - Possesses nootropic activity

Indications

- As a daily health tonic
  – general weakness, fatigue, etc.
- Prolonged illness
  – typhoid, tuberculosis, malaria, etc.
- Postoperative convalescence
- Occupational stress
- Age-related debility

Dosage

Syrup: Initially, 2 teaspoonfuls twice daily, followed by 1 teaspoonful twice daily.

Tablet: Initially, 2 tablets twice daily, followed by 1 tablet twice daily.

℞ **Geriforte** – Rejuvenates both BODY & MIND

The Himalaya Drug Company

www.himalayahealthcare.com