
FOR YOUR INFORMATION



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Premenstrual Syndrome (PMS) and Premenstrual Dysphoria (PMD)

Introduction

Premenstrual syndrome (PMS) can be defined as emotional, behavioral, and physical symptoms that occur in the premenstrual cycle with resolution after menses. PMS is a milder form of premenstrual dysphoric disorder (PMDD) and there is now a consensus that PMDD is distinct from other mood disorders. As many as 80% of women experience premenstrual symptoms and the more severe symptoms of PMDD affect 3% to 8% of women of reproductive age. The dysphoria associated with PMDD is cyclical and linked to the late luteal phase of the menstrual cycle. The most common physical complaints are breast tenderness and bloating. Other symptoms include irritability and anger, tension, affect lability, fatigue, headache, difficulty concentrating, avoidance of social activities and carbohydrate craving. The symptoms do not occur during pregnancy and after menopause and PMDD can be prevented by the suppression of gonadal hormones; furthermore, hormone replacement therapy can induce the reappearance of symptoms in menopausal women with a history of PMDD.

Etiology

The fact that symptoms only occur during the menstrual cycle implicates ovarian steroids in the etiology of PMDD. However, serum levels of estradiol or progesterone do not differ in women with PMDD from normal controls. Of interest is the finding of decreased peripheral platelet serotonin uptake and whole blood serotonin levels in women with PMS compared with controls during the late luteal phase. Apart from serotonin's association with mood, appetite, aggression, impulsivity and sexual interest, approximately 60%-70% of women with PMS respond to serotonin enhancing agents (e.g. fluoxetine, sertraline, clomipramine). Consequently, since symptoms of PMS are only evident if menstrual cycling occurs, it would seem likely that a

connection exists between ovarian hormones and serotonin. Although the link between ovarian hormones and serotonin has not yet been established, it has been suggested that estradiol may regulate serotonin receptor numbers and function in such a way as to alter the response to serotonin.

Treatment of PMS and PMDD Antidepressants

Over 30 studies have reported the effectiveness of serotonin-enhancing drugs in the treatment of PMS or PMDD with up to a 70% response rate. Positive studies have been performed with clomipramine and the serotonin reuptake inhibitor antidepressants (i.e. fluoxetine, sertraline, citalopram, fluvoxamine and paroxetine). Antidepressants, which do not or only mildly increase serotonin, such as bupropion and desipramine, have been reported to be no better than placebo in PMS and PMDD.

The onset of action of serotonergic antidepressants is very rapid, sometimes as fast as 1 to 2 days and intermittent treatment of the last two weeks of the menstrual cycle (the luteal phase only) has been found to be more effective than continuous treatment in some studies. These agents are not only effective in alleviating dysphoria and irritability but also somatic symptoms such as breast tenderness and bloating. Doses used in PMDD have been the same as for depression or slightly lower.

Non-Antidepressant Treatment Calcium

Clinical trials using calcium for the treatment of PMS have been conducted because calcium levels markedly decrease at midcycle when estradiol concentrations are increased in women with PMS; parathyroid levels

fluctuate during the cycle as well but remain stable in women without symptoms. Clinical trials using 1000 - 1600 mg/d of calcium (carbonate form) reported that approximately 70% of women with PMS reported an overall 50% improvement in symptoms while taking calcium supplementation. Results of the studies indicated that calcium was effective in reducing all of the emotional and physical symptoms of the PMDD diagnostic criteria except for fatigue and insomnia.

Magnesium

The levels of magnesium in erythrocytes and leucocytes of women with PMS are lower than those of women without PMS; however, no difference in plasma magnesium levels are observed. Three small double-blind studies using 200 to 360 mg per day of magnesium have found some positive effects. One study reported a reduction in fluid retention but no effects on mood symptoms, whereas another study found beneficial effects especially on mood symptoms. In another study, which had enrolled only patients with premenstrual headaches, a reduction in the number of days with headache was reported.

Vitamin B₆

Pooled results from 9 controlled studies with 940 women weakly indicate support for vitamin B₆ (50-100 mg/d) in reducing premenstrual symptoms, particularly depression. There were no reports of neurotoxicity with these doses. The rationale for trying Vitamin B₆ in premenstrual mood problems stems from the fact that it is a cofactor in the synthesis of neurotransmitters.

Ovarian Suppression Treatments

Ovulation suppression therapies include gonadotropin-releasing hormone (GnRH) agonists, danazol, estrogen and progesterone.

Although most of the studies using GnRH agonists and danazol have reported relief of PMS and PMDD symptoms, the low estrogen levels resulting from these agents lead to long-term health problems of cardiac disease and decreased bone density.

GnRH agonists stop ovulation by decreasing the release of follicle-stimulating (FSH) and luteinizing hormone (LH) from the pituitary, which subsequently results in decreased estrogen and progesterone release.

Danazol is a synthetic steroid that also stops ovulation and is associated with similar long-term problems as the

GnRH agonists. Danazol is also associated with weight gain, nausea, acne, facial hair, decreased high-density lipoproteins, and depression.

Replacement estrogen and progesterone and oral contraceptives have not been useful in the treatment of premenstrual symptoms and some studies have reported worsening of the symptoms.

Other

Many other remedies such as evening primrose oil, black cohosh, wild yam root, chaste tree fruit, carbohydrate supplements have been recommended for use in PMS, however, few studies have been performed with each one of these agents individually.

Information on the use of herbal agents, carbohydrate supplements and bright light therapy will be reported in a forthcoming newsletter.

Summary

Between 60 to 70% of women with PMS and PMDD respond to serotonin reuptake inhibitor antidepressants (SSRIs) and clomipramine. These agents can be taken intermittently before menstruation. Of the remaining agents, which are available without a prescription, calcium supplements have the most documented evidence for effectiveness. Less evidence exists for magnesium and vitamin B₆ but they may be useful if the other choices are not acceptable.

Agents which decrease estrogen levels are associated with long-term health problems and are not usually recommended. Oral contraceptives are ineffective and may actually worsen symptoms.

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