Premenstrual dysphoric disorder and premenstrual syndrome: an overview

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Abstract

Premenstrual dysphoric disorder (PMDD) affects 3-8% of women in the reproductive age group, while premenstrual syndrome (PMS) has a prevalence of 20-30%. PMS and PMDD are associated with significant reduction in quality of life and decreased work productivity. This review examines the current

literature regarding the epidemiology, aetiology, diagnosis, burden of illness and management of PMDD and PMS.

Key words: premenstrual syndrome, premenstrual dysphoric disorder

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Introduction

Premenstrual syndrome (PMS) is defined as recurrent moderate psychological and physical symptoms that occur during late luteal phase of menstrual cycles and resolves during menstruation (1). Premenstrual dysphoric disorder (PMDD) is a severe form of PMS that affects many women of reproductive age across the world. PMDD is characterised by affective, cognitive, behavioural, and somatic symptoms. PMDD and PMS have a negative impact on work attendance, productivity and relationships (2). Table 1 lists the symptoms associated with these two disorders. A better understanding of PMS and PMDD would help early identification and management of this disorder. The objective of this review was to describe the epidemiology, aetiology, symptoms, burden of illness and management of PMS and PMDD.

Table 1. Symptoms associated with premenstrual syndrome and premenstrual dysphoric disorder (3, 4)

Physical	Psychological and behavioural
Abdominal bloating	Anger, irritability
Body aches	Anxiety
Breast tenderness and/or fullness	Overeating
Cramps, abdominal pain	Change in libido
Fatigue	Decreased concentration
Headaches	Depressed mood
Nausea	Feeling out control
Swelling of extremities	Mood swings
Weight gain	Poor sleep
	Withdrawal from usual activities

Method

Electronic databases including Academic Search Premier, EBSCO host, PubMed database and Google Scholar were searched for publications pertaining to PMDD and PMS, using the following key words: Premenstrual dysphoric disorder, premenstrual syndrome, epidemiology, burden of illness, management and treatment. Relevant systematic reviews, consensus statements, evidence-based guidelines and a limited number of eligible case controlled studies were considered.

Epidemiology

PMDD is a severe form of the premenstrual symptom spectrum with a prevalence of 3-8%, while PMS has a prevalence of 20-30% (5). Sveindottir et al in their prospective study of 250 women in Iceland reported that 6% of the women met criteria for PMDD (6). Another prospective study of 1194 women in the United States reported a PMDD prevalence of 4.7% (7). Retrospective studies of severe premenstrual symptoms also reported similar rates of 2-6% (5). A community study of 1091 women in Germany reported that 5.8% of those surveyed met criteria for PMDD (8).

Studies from India have reported similar results. Banerjee et al reported a prevalence of 6.4% among Indian women (9). A higher rate of 10% was reported by Joshi et al in 2010, from Mumbai (10).

Aetiology

PMDD and PMSS are closely linked to the function of hypothalamic pituitary gonadal axis (11). It is hypothesised that PMDD is the result of heightened central nervous system sensitivity to normal cyclical changes in hormone levels, resulting in reduced levels of the neurotransmitter serotonin or 5-hydroxy tryptamine (5-HT) (12). The dorsolateral prefrontal cortex and medial

frontal cortex are particularly sensitive to these hormonal changes. As women with PMDD enter the late luteal phase of their menstrual cycle, the levels of 5-HT are reduced, triggering symptoms associated with 5-HT depletion such as irritability, dysphoria, impulsivity, and carbohydrate craving (11). Another explanation offered for PMDD is the hormonal theory; here it is argued that women with PMS/PMDD develop depressive symptoms in response to either progesterone or oestradiol, and a resolution of these symptoms occur with increase of gonadotropin releasing hormone agonist (GnRH) levels (13). However this theory is disputed, with some studies offering evidence to the contrary (12).

While dysregulation of serotonin appears to be the primary cause of PMDD symptoms, there is evidence that other neurotransmitters may play a significant role. During the late luteal phase of the menstrual cycle, levels of gamma aminobutyric acid (GABA) are low in patients with PMDD and PMS. This may contribute towards the irritability and lability of mood seen during this time (14).

The use of selective serotonin reuptake inhibitor (SSRI) medications in PMDD has led to another theory regarding the aetiology of this disorder. It has been noted that SSRIs are effective in PMDD, and the response time is usually shorter than for depression, panic disorder, or obsessive-compulsive disorder. Therefore some argue that SSRIs exert their action in PMDD via a different mechanism compared to its action in depression or anxiety. It is hypothesised that SSRIs work in PMDD by indirectly increasing synthesis of allopregnanolone from progesterone. Allopregnanolone, a neurosteroid, has high affinity to GABA receptors and potentially facilitates GABA action at these receptors, leading to rapid relief of PMDD symptoms such as dysphoria and anxiety (13, 15).

Central sensitivity rather than peripheral hormonal abnormality seems to be the cause of the symptoms of PMDD. This has implications for treatment, suggesting that the focus should be on correcting or compensating for the central sensitivity, rather than peripheral modification of menstrual cycle hormones.

Diagnosis

The International Society for Premenstrual Disorders (ISPMD) has introduced a unified diagnosis and classification of PMDD, based on existing diagnostic criteria of International Classification of Diseases (ICD-10), Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), the Royal College of Obstetricians and Gynaecologists (RCOG), the American College of Obstetricians and Gynaecologists (ACOG) and available research evidence (Table 2). The ISPMD has also offered criteria to guide discussions of the next edition of the International Classification of Diseases (ICD-11), and Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V) [16].

The most accurate way to establish diagnosis of PMDD is to document daily symptom ratings over a prospective 2-month time-period (Table 2). Hence PMDD is frequently diagnosed provisionally, and treatment may commence while prospective daily ratings are in progress. Other psychiatric disorders, which may also present with mood symptoms, such as irritability, dysphoria or lability of mood, should be considered and excluded, particularly since treatment for PMDD may exacerbate or precipitate other psychiatric illnesses such as bipolar affective disorder.

The burden of illness

PMDD is a chronic illness and does not completely remit until menopause. PMDD has a significant negative impact on quality of life. Yang et al. reported that the burden of PMDD on health-related quality of life was greater than the burden associated with back pain, and was similar to Type II diabetes, hypertension, rheumatoid arthritis and somewhat similar to depression [18]. Heinemann, Minh, Filonenko, and Uhl-Hochgraber concluded that PMDD is associated with impaired work productivity and absenteeism, thus resulting in a potential reduction of female economic productivity (19). Working women who were classified as having moderate to severe PMS/PMDD, when compared to women with no/mild symptoms, had higher rates of productivity impairment and absenteeism (20).

Treatment

Symptom relief is the goal of treatment of PMS and PMDD (Table 3). Mild premenstrual symptoms may respond to non-pharmacological interventions, such as education on sleep hygiene, exercise, relaxation therapy, and cognitive-behavioural therapy. Dietary modifications, including reduction of salty foods, caffeine, red meat, and alcohol, along with increased consumption of fruits, legumes, whole grains, and water, as well as consumption of smaller and more frequent meals high in carbohydrates, have been reported to improve tension and depressive symptoms (17).

Calcium (not exceeding 1,500 mg/day) and vitamin D may reduce the risk of moderate to severe premenstrual symptoms, while also reducing the risk of osteoporosis (17). Ghanbari et al reported that calcium at a dose of 500 mg twice daily reduced fatigability, changes in appetite and depression in women with PMS (21).

Pharmacological treatment with selective serotonin reuptake inhibitors (SSRIs) has shown good efficacy for moderate to severe PMDD (22). The most evidence is available for fluoxetine and sertraline, with an average response rate of 60% in controlling symptoms (22). Continuous pharmacological treatment (i.e., throughout the month) is best for women with comorbid depressive or anxiety disorders and for women who have difficulty adhering to intermittent therapy regimens. Intermittent treatment with SSRIs is best for patients who have symptoms that are clearly localised to the premenstrual days, and who experience side-effects due to SSRIs (17).

Table 2. DSM-5 criteria for premenstrual dysphoric disorder (17)

625.4 (N94.3)

A. In the majority of menstrual cycles, at least five symptoms must be present in the final week before the onset of menses, must start to *improve* within a few days after the onset of menses, and become *minimal* or absent in the week post-menses.

B. One (or more) of the following symptoms must be present:

1. Marked affective lability (e.g., mood swings; feeling suddenly sad or tearful, or increased sensitivity to rejection).
2. Marked irritability or anger or increased interpersonal conflicts.
3. Marked depressed mood, feelings of hopelessness, or self-deprecating thoughts.
4. Marked anxiety, tension, and/or feelings of being keyed up or on edge.

C. One (or more) of the following symptoms must additionally be present, to reach a total of *five* symptoms when combined with symptoms from Criterion B above.

1. Decreased interest in usual activities (e.g., work, school, friends, hobbies).
2. Subjective difficulty in concentration.
3. Lethargy, easy fatigability, or marked lack of energy.
4. Marked change in appetite; overeating; or specific food cravings.
5. Hypersomnia or insomnia.
6. A sense of being overwhelmed or out of control.
7. Physical symptoms such as breast tenderness or swelling, joint or muscle pain, a sensation of "bloating," or weight gain.

Note: The symptoms in Criteria A-C must have been met for most menstrual cycles that occurred in the preceding year.

D. The symptoms are associated with clinically significant distress or interference with work, school, usual social activities, or relationships with others (e.g., avoidance of social activities; decreased productivity and efficiency at work, school, or home).

E. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as major depressive disorder, panic disorder, persistent depressive disorder (dysthymia), or a personality disorder (although it may co-occur with any of these disorders).

F. Criterion A should be confirmed by prospective daily ratings during at least two symptomatic cycles. (Note: The diagnosis may be made provisionally prior to this confirmation.)

G. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or another medical condition (e.g., hyperthyroidism).

Table 3. Intervention/treatments for PMDD (5)

Available interventions /treatments	Evidence available
SSRIs (luteal phase and continuous cycle dosing) (First-line pharmacotherapy)	Good
Combined oral contraceptives (First-line pharmacotherapy for women desiring contraception)	Good
Combination of SSRI and cognitive behavioral therapy (Increased effectiveness in combination)	Good
Dietary supplements E.g., Calcium, magnesium, vitamin B6, tryptophan and vitamin E	Limited, further study recommended
Diet modifications E.g., Reducing salt, caffeine, chocolate, alcohol and fat, increasing complex carbohydrates, raising levels of tryptophan	Limited, recommended for milder symptoms
Lifestyle modifications E.g., regular aerobic exercise, avoidance of stress during luteal phase and good sleep hygiene	Limited, recommended for overall health

Contraceptive pill types containing ethinyl oestradiol and drospirenone may represent another effective treatment for PMDD (2). Not all evidence supports the use of contraceptives, but they could be considered as first-line pharmaceutical interventions for women with PMDD who also require contraception (23).

Cognitive behaviour therapy (CBT) is also a proven strategy for management of PMDD. Combination of CBT along with SSRIs has been proven more efficacious than SSRIs alone (2).

Although medical and psychological treatment provides excellent symptomatic relief to many women, a small proportion of women may experience poor therapeutic response or adverse effects. In such cases oophorectomy (with concomitant hysterectomy) followed by low-dose oestrogen therapy has been shown to be an effective alternative (24).

Evidence suggests that up to 8% women meet diagnostic criteria for PMDD in their lifetime. The key factor in diagnosis is the demonstration of a pattern of PMDD symptoms that recurs during the late luteal phase of the menstrual cycle and remits soon after menses, which occurs over at least 2 menstrual cycles, and which are associated with significant dysfunction. Other psychiatric disorders that may mimic PMDD need to be considered

as differential diagnosis. Current theories suggest that severe PMS and PMDD are due to CNS sensitivity to hormonal cycling rather than due to abnormality of hormone levels.

SSRIs and oral contraceptives are the current mainstay of the treatment of PMDD. Measures such as lifestyle modification, dietary supplements and dietary modification maybe helpful in mild PMS, but have limited proven efficacy in severe PMDD.

Declaration of interest

None declared

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