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PREMENSTRUAL SYNDROME (PMS) – A REVIEW OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENT APPROACHES

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ABSTRACT

Premenstrual Syndrome (PMS) and its severe form, Premenstrual Dysphoric Disorder (PMDD), are prevalent cyclical disorders affecting the emotional, behavioral, and physical well-being of women of reproductive age. This review aims to present an overview of the current understanding of PMS/PMDD and critically examine both pharmacological and non-pharmacological treatment methods. Based on recent clinical trials and systematic reviews, selective serotonin reuptake inhibitors (SSRIs), hormonal therapies, and emerging drugs like sepranolone and ulipristal acetate demonstrate efficacy in symptom reduction (Bäckström et al., 2021; Comasco et al., 2020; Maranho et al., 2023). Simultaneously, cognitive-behavioral therapy (CBT), mindfulness-based interventions, nutritional supplements, herbal medicine, and even open-label placebos are gaining attention as effective non-pharmacological alternatives (Frey Nascimento et al., 2025; Reilly et al., 2023; Shojiasi et al., 2024; Sultana et al., 2022). Despite promising findings, further high-quality research is needed to tailor personalized and integrative treatment strategies.

KEYWORDS

PMS, PMDD, SSRIs, Sepranolone, Cognitive Behavioral Therapy, Herbal Medicine, Mindfulness, Hormonal Therapy

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Introduction

Premenstrual Syndrome (PMS) is a complex condition characterized by recurring physical, emotional, and behavioral symptoms that emerge during the luteal phase of the menstrual cycle and resolve with menstruation. A more severe manifestation, Premenstrual Dysphoric Disorder (PMDD), significantly impairs social and occupational functioning and is recognized in DSM-5. PMS affects up to 75% of women of reproductive age, with clinically significant symptoms seen in 20–30%, and PMDD affecting approximately 3–8% of women globally (Cunningham et al., 2021; Modzelewski et al., 2024).

These disorders are often underdiagnosed and undertreated due to normalization of symptoms, stigma, and lack of awareness among healthcare professionals. Given their high prevalence and impact, PMS and PMDD represent an important public health concern, necessitating evidence-based, integrative approaches to management.

Diagnostic Criteria and Challenges

PMS is diagnosed based on the cyclic recurrence of physical and/or emotional symptoms that occur during the luteal phase of the menstrual cycle and remit shortly after menstruation begins. Common symptoms include irritability, depression, anxiety, bloating, and breast tenderness. Diagnosis requires the exclusion of other psychiatric or medical disorders.

For the more severe form, PMDD, the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) outlines specific criteria. PMDD diagnosis requires at least five symptoms, including at least one mood-related symptom (e.g., mood swings, irritability, depressed mood, or anxiety), that are present in the final week before the onset of menses, improve within a few days after the onset, and become minimal or absent in the week post-menses. These symptoms must cause clinically significant distress or interference with work, school, usual social activities, or relationships.

Prospective daily symptom ratings over at least two menstrual cycles are recommended to confirm the diagnosis. The Daily Record of Severity of Problems (DRSP) is a commonly used validated tool for symptom tracking and diagnosis (Pearlstein & Steiner, 2023).

Socioeconomic and Cultural Considerations

Socioeconomic status and cultural background significantly influence the experience, reporting, and management of PMS and PMDD. In many societies, menstrual health is stigmatized, leading to underreporting of symptoms and delayed diagnosis. Women from lower socioeconomic backgrounds may face limited access to healthcare services, reducing their likelihood of receiving proper evaluation or treatment (Brown et al., 2024).

Cultural norms also shape how PMS symptoms are interpreted. In some cultures, emotional symptoms may be minimized or attributed to character flaws rather than medical conditions, while in others, somatic symptoms receive more attention. Furthermore, language barriers and lack of awareness among healthcare providers can lead to disparities in care. Addressing these issues through culturally sensitive education and outreach programs is crucial for equitable care.

Pathophysiology of PMS and PMDD

The pathophysiology of PMS and PMDD is multifactorial and not yet fully understood. Unlike other psychiatric disorders, PMS and PMDD are not associated with abnormal hormone levels but with abnormal sensitivity to normal hormonal changes, particularly fluctuations in estrogen and progesterone during the menstrual cycle (Nexha et al., 2024).

One prominent hypothesis involves the neurosteroid allopregnanolone, a metabolite of progesterone, which modulates the gamma-aminobutyric acid type A (GABA-A) receptor. Women with PMDD may have altered sensitivity to allopregnanolone, leading to negative mood symptoms during the luteal phase (Hantsoo & Epperson, 2020).

Additionally, serotonin dysregulation has been implicated. Reduced serotonin levels or receptor sensitivity may contribute to mood-related symptoms, explaining the efficacy of SSRIs in symptom relief (Jespersen et al., 2024). Abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis and increased inflammatory markers have also been observed in some individuals with severe symptoms (Hantsoo & Riddle, 2021).

Neuroimaging studies have found changes in the amygdala and prefrontal cortex activity in women with PMDD, supporting the notion of altered brain responsiveness to hormonal changes (Aoki et al., 2024). These findings underscore the biological basis of PMS and PMDD while also highlighting the need for personalized approaches to treatment.

Pharmacological Treatment Options

Pharmacological interventions are often necessary for moderate to severe cases of PMS and PMDD. These treatments aim to alleviate mood, physical, and behavioral symptoms.

SSRIs and SNRIs

Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, sertraline, and escitalopram are first-line treatments due to their rapid symptom relief and efficacy. They can be administered continuously or during the luteal phase only. Serotonin-norepinephrine reuptake inhibitors (SNRIs) like venlafaxine may also be effective (Jespersen et al., 2024; Maranho et al., 2023).

Hormonal Therapies

Hormonal treatments aim to suppress ovulation and stabilize hormonal fluctuations. Combined oral contraceptives (COCs), especially those containing drospirenone, have demonstrated efficacy. Gonadotropin-releasing hormone (GnRH) agonists are reserved for refractory cases due to hypoestrogenic side effects (Marais-Thomas et al., 2024).

Emerging Agents

New agents such as sepranolone—a GABA-A modulating steroid antagonist—have shown promise in clinical trials for PMDD (Bäckström et al., 2021). Ulipristal acetate, a selective progesterone receptor modulator, has also demonstrated potential efficacy (Comasco et al., 2020).

Symptom-Specific Medications

Other medications used symptomatically include spironolactone for bloating and fluid retention, NSAIDs for pain, and anxiolytics for severe anxiety. These are generally used as adjuncts to primary therapy (Meth et al., 2025).

Non-Pharmacological and Complementary Therapies

Non-pharmacological approaches play an essential role in the holistic management of PMS and PMDD, especially for individuals seeking alternatives or adjuncts to medication.

Psychological Therapies

Cognitive-behavioral therapy (CBT) is the most well-established psychological intervention for PMS and PMDD. It addresses negative thought patterns and promotes emotional regulation. Mindfulness-based stress reduction (MBSR) and acceptance and commitment therapy (ACT) have also demonstrated benefits in reducing symptom severity (Reilly et al., 2023; Shojiasi et al., 2024; Nurdilan Şener Çetin & Şolt Kırca, 2023).

Lifestyle and Nutritional Interventions

Regular physical activity, balanced nutrition, adequate sleep, and stress management are recommended lifestyle modifications. Nutritional supplements such as calcium (1200 mg/day), magnesium (200–400 mg/day), vitamin B6 (50–100 mg/day), and omega-3 fatty acids may help alleviate symptoms in some individuals (Sultana et al., 2022).

Herbal Medicine

Herbal treatments, including chasteberry (*Vitex agnus-castus*), have shown promise in managing PMS symptoms like breast tenderness and irritability. Kampo medicine (e.g., kamishoyosan) is widely used in Japan and is under investigation in clinical trials (Endo et al., 2024).

Novel Non-Pharmacological Approaches

Recent innovations include the use of open-label placebos, which have shown efficacy even without deception (Frey Nascimento et al., 2025). Digital interventions, such as mobile health apps and internet-delivered CBT, offer scalable and accessible treatment options (Reilly et al., 2023).

Psychosocial Impact of PMS and PMDD

PMS and PMDD significantly affect various aspects of women's lives, including mental health, interpersonal relationships, and work productivity.

Impact on Interpersonal Relationships

Mood instability and irritability can strain romantic, familial, and social relationships. Women often report increased conflict and emotional distance during symptomatic phases, which may contribute to long-term relational stress (Brown et al., 2024).

Workplace and Academic Consequences

Cognitive difficulties, reduced concentration, and emotional distress during the luteal phase can reduce productivity and increase absenteeism. In academic settings, this may impact test performance or attendance (Cunningham et al., 2021).

Stigmatization and Emotional Burden

Social stigma surrounding menstruation and mood disorders may lead to guilt, shame, and reluctance to seek treatment. Women may internalize these attitudes, contributing to self-stigmatization and underreporting of symptoms (Modzelewski et al., 2024).

Developmental and Adolescent Considerations

Adolescents with severe PMS or PMDD may experience confusion about their identity and emotional regulation, which can complicate normal psychosocial development. Early intervention and education are essential for reducing long-term psychosocial consequences (Pearlstein & Steiner, 2023).

Historical Perspectives on PMS Management

Historical references to menstrual-related mood disturbances date back to ancient Greece and Rome, where female behavioral changes were often attributed to imbalances in bodily humors or hysteria. In the 19th and early 20th centuries, PMS-like symptoms were often pathologized under vague labels such as “female madness.”

Modern recognition of PMS began in the 1930s, but it wasn't until the 1980s that standardized diagnostic criteria emerged. The incorporation of PMDD into DSM-IV and later DSM-5 represented a milestone in legitimizing premenstrual mood disorders (Hantsoo & Riddle, 2021). Treatments have evolved from rest cures and hysterectomies to targeted SSRIs, hormonal interventions, and behavioral therapies.

Understanding this historical context underscores both the progress made and the continuing need to dismantle gendered stigmas in reproductive psychiatry.

Future Perspectives and Research Directions

The future of PMS and PMDD management lies in personalized, interdisciplinary, and patient-centered approaches.

Biomarker Identification

Research into genetic, hormonal, and neurobiological markers may enable earlier and more accurate diagnosis, paving the way for precision medicine (Nexha et al., 2024).

Innovative Therapeutics

Emerging treatments, including neurosteroid modulators, digital therapeutics, and even psychedelics like psilocybin in microdoses, are under investigation for mood regulation in cyclical disorders (Hantsoo & Riddle, 2021).

Technological Integration

Mobile health (mHealth) applications, symptom tracking tools, and telemedicine platforms are expanding access to care and enhancing patient engagement (Reilly et al., 2023).

Health Policy and Education

There is a growing need for public health campaigns to reduce menstrual stigma, increase awareness among healthcare providers, and promote early diagnosis and intervention strategies (Brown et al., 2024).

Conclusions

PMS and PMDD are multifaceted disorders requiring nuanced and individualized care strategies. A growing body of evidence supports the efficacy of both pharmacological and non-pharmacological interventions, and recent innovations—including neuroactive steroids, mindfulness-based therapies, and digital tools—present new opportunities for symptom management. A summary of treatment approaches and their characteristics is provided in Table 1.

Table 1. Overview of Selected Treatment Modalities for PMS/PMDD

Treatment Approach	Examples	Mechanism	Notes
SSRIs	Fluoxetine, Sertraline	Serotonin reuptake inhibition	Fast symptom relief, luteal or continuous dosing
Hormonal Therapy	COCs (e.g. with drospirenone)	Ovulation suppression	Risk of side effects
Sepranolone	GABA-A modulation	Targets neurosteroid sensitivity	Under investigation
CBT	Cognitive restructuring	Improves emotional regulation	Well-supported in trials
Mindfulness	MBSR, ACT	Stress and symptom management	Increasing evidence
Supplements	Calcium (1200 mg), Mg (200–400 mg), Vit B6 (50–100 mg)	Nutritional support	May help somatic and mood symptoms
Herbal Medicine	Vitex agnus-castus, Kampo	Hormonal modulation, unknown	Variable quality of evidence
Open-label Placebo	Inert pills	Psychosocial mechanisms	Surprisingly effective
Digital Tools	mHealth apps, iCBT	Accessibility and education	Promising for reach and scale

However, persistent barriers such as diagnostic ambiguity, social stigma, and limited access to care continue to hinder optimal outcomes. Future research should focus on biomarker identification, personalization of therapies, and system-level reforms to enhance menstrual mental health equity. Interdisciplinary collaboration and patient-centered care remain essential to addressing this complex but treatable spectrum of conditions.

Disclosure

Author's contributions:

Conceptualization: Aleksandra Białas, Kamil Kerknawi, Weronika Lusarczyk, Paulina Mikulec, Natalia Sapeda; Methodology: Karolina Gorczyca; Software: Emilia Loch, Aleksandra Młocek; Check: Zuzanna Romanowska, Adrianna Truszyńska-Zawisza; Formal analysis: Zuzanna Romanowska; Investigation: Paulina Mikulec, Natalia Sapeda; Resources: Adrianna Truszyńska-Zawisza; Data Curation: Kamil Kerknawi, Aleksandra Białas, Karolina Gorczyca; Writing - rough preparation: Emilia Loch, Weronika Lusarczyk; Writing - review and editing: Aleksandra Młocek; Visualization: Zuzanna Romanowska; Supervision: Weronika Lusarczyk; Project administration: Aleksandra Białas; Receiving funding, not applicable.

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