Review Article

Pre-menstrual Dysphoric Disorder: A Review

Journal of Psychosexual Health
1(1) 32–36, 2019

DOI: 10.1177/2631831818824439
journals.sagepub.com/home/ssh
SAGE

Dahuja Malvika[1] and Agarwal Supriya[2]

Abstract

Introduction: Premenstrual dysphoric disorder (PMDD) is a distressing disorder amongst women of reproductive age group with significant implication in the productivity and quality of life of women who suffer from it. It is generally neglected as it is mostly undifferentiated from premenstrual symptoms—milder presentation of the same spectrum of problem but of lesser intensity and impairment.

Objective: Here, in this article, we aim to highlight various studies and the research done on PMDD in the context of Indian women.

Method: Reviewing the last 40 years' database including Medline (PUBMED), Cochrane Library, EMBASE, Trip, Psych INFO, CINAHL, the Allied and Complementary Medicine Database (AMED), and the British Nursing Index.

Results: PMDD is a troublesome disorder, often underdiagnosed. A thorough history including menstrual and sexual history, conducting a thorough physical examination, assessing the comorbidities, and finally using a proper and structured treatment protocol for managing the condition are recommended. Sertraline is the most widely studied drug which is found to be effective in PMDD.

Keywords

Premenstrual dysphoric disorder (PMDD), premenstrual syndrome (PMS), menstrual cycle

Introduction

Premenstrual dysphoric disorder (PMDD) is a very distressing disorder among child-bearing females. It is generally neglected and undifferentiated from premenstrual syndrome (PMS).[1,2] It is commonly named as premenstrual tension/premenstrual syndrome/late luteal phase dysphoric disorder/premenstrual tension syndrome (*International Classification of Diseases, Tenth Revision*) or PMDD (*Diagnostic and Statistical Manual of Mental Disorders*, fifth edition).[3,4] In *ICD-11*, it is now out of the appendix.[5] The American College of Obstetricians and Gynecologists also defines PMDD similarly.[6] The prevalence of PMDD is 3% to 9%.[7] Similar numbers have been reported from India across various states.[8-13]

Etiology

Currently, there is no consensus on the cause of PMDD. Biologic, genetic, psychological, environmental and social factors all seem to play a very important role.

Genetic Vulnerabilities

The role of the gene coding for serotonergic 5HT 1A receptor[14-18] and estrogen receptor alpha gene (ESR 1) has been documented.[19]

Various risk factors such as high body mass index, stress and experience of traumatic events play role in the etiology of PMDD.[20-23]

[1] Shaikh-ul-Hind Maulana Mahmood Hasan Medical College, Saharanpur, Uttar Pradesh, India
[2] Netaji Subhash Chandra Bose Subharti Medical College, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India

Corresponding author:
Supriya Agarwal, Department of Psychiatry, Chhatrapati Shivaji Subharti Hospital, Netaji Subhash Chandra Bose Subharti Medical College, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India.
Email: drsupriya.agar@gmail.com

The Role of Sex Steroids and Their Metabolites

Changes in serotonin and γ-aminobutyric acid (GABA) levels with estrogen and progesterone metabolites have interaction with the GABA-A receptor complex in neurobiology of PMDD.[24-30] Studies report that administration of progesterone/allopregnenolone during the follicular phase enhances amygdala reactivity.[31,32]

Other hormones such as thyroid hormone, melatonin, cortisol and relaxin[33-39] also have been implicated in the pathophysiology of PMDD.

Calcium, magnesium, insulin-like growth factor 1 and vitamin D[40-44] have been hypothesized to be responsible for causing various somatic symptoms of PMDD.

Neurotransmitters Implicated in PMS/PMDD

Experiments on animals demonstrate that serotonin depletion causes enhanced aggression and sexual activity.[45-47] GABA causes tolerance induction and withdrawal effects in such women.[30] Low levels of glutamate/creatine plus phosphocreatine in luteal phase in the medial prefrontal cortex have also been studied.[32] Decreased levels of endogenous opioids are responsible for increased pain sensitivity.[48,49] In animal studies, an increased startle response is found due to progesterone withdrawal[50-52] and up regulation of the alpha-4 unit of the GABA-A receptor complex.[51]

Somatic Symptom Pathophysiology

Prolactin-lowering agents, such as the dopamine D2 receptor agonist bromocriptine,[53,54] chasteberry[55] administration of danazol in luteal phase, and estrogen receptor antagonists[56,57] all are effective in mastalgia.

Aldosterone, a progesterone metabolite[58] and deoxycorticosterone, an aldosterone agonist[24,58] have a role in treatment of severe abdominal bloating.

Other common somatic complaints such as premenstrual headache, migraine, and epilepsy are comorbid with PMDD and endometriosis.[59]

Classification of PMS

Royal College of Obstetricians and Gynaecologists classifies PMS into four variants[60]:

1. 'Premenstrual exacerbation of an underlying disorder', such as diabetes, depression, epilepsy, asthma, and migraine.
2. 'Non-ovulatory PMDs' occur in the presence of ovarian activity without ovulation.
3. 'Progestogen-induced PMDs' are caused by exogenous progestogens present in hormone replacement therapy and the combined oral contraceptive pill.
4. 'PMDs with absent menstruation' include women who still have a functioning ovarian cycle, but for reasons such as hysterectomy, endometrial ablation or the levonorgestrel-releasing intrauterine system, they do not menstruate.[61]

National Association for Premenstrual Syndrome subdivide PMS into mild, moderate, and severe.[62]

Clinical Features

Symptoms in PMDD include anxiety, depression, irritability, anger, bloating, muscle pain, poor concentration, etc., causing severe distress that is persistent in several cycles, characteristically appearing one week before periods and disappearing within first two days of bleeding.[63] Women with PMDD usually have comorbid physical and psychiatric disorders, and one must always keep these comorbidities as dual diagnosis whenever in doubt.[64-72]

Management

Thorough investigations for comorbidities must always be done. Among psychological tools, the premenstrual symptoms screening tool was developed at McMaster University in 2003 and a new Japanese scale was made in 2009.[73,74] There is a scale currently validated for the Indian population as well.

In psychopharmacological treatment, the British Journal of Obstetricians and Gynecologists protocol emphasizes the use of fluoxetine and sertraline in the treatment of PMDD.[60,75] The hormonal therapies recommended by the British Journal of Obstetricians and Gynecologists include leuprolide depot, leuprolide depot with ovarian hormone supplements, goserelin with estrogen supplementation, danazol, oral contraceptive pills, progesterone-only drugs, estradiol patches, spironolactone, bromocriptine, Ibuprofen, etc.[14,60]

In non-pharmacological treatment, lifestyle changes including regular, frequent, small balanced meals rich in complex carbohydrates and low in salt, fat, and caffeine, regular exercise, smoking cessation, alcohol restriction, regular sleep, and maintaining PMDD charts have been found to be helpful. Nutritional supplements including vitamin B6, up to 100 mg per day, vitamin E, up to 600 IU per day, calcium carbonate, 1200 to 1600 mg per day, magnesium, up to 500 mg per day, tryptophan, up to 6 g per day have been suggested.

Others therapies with some benefit include stress reduction and management, anger management, self-help support group, individual and couples therapy, cognitive behavioral therapy, music therapy, light therapy with 10,000 lux cool white fluorescent light, etc.[14,20,60]

Conclusion

PMDD is prevalent mental health condition affecting mental and physical well-being of women and yet is underdiagnosed. Careful history and examination regarding PMDD should be a norm in every woman patient presenting to a psychiatrist. Management consists of pharmacological and non-pharmacological intervention with variable prognosis.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Sunita Kumari, Ankur Sachdeva. Patterns and predictors of premenstrual symptoms among females working in a psychiatry hospital. *Scientifica*; 2016:7. http://dx.doi.org/10.1155/2016/6943852. Accessed December 26, 2018.
2. World Health Organization. *International Statistical Classification of Diseases and Related Problems* (ICD-10). 10th revision. Geneva: WHO; 1992.
3. Andrade C. Premenstrual dysphoric disorder: General overview, treatment strategies, and focus on sertraline for symptom-onset dosing. *Indian J Psychiatry*. July-September 2016;58(3):329-331. doi: 10.4103/0019-5545.192014.
4. Freeman EW. Premenstrual syndrome and premenstrual dysphoric disorder: Definitions and diagnosis. *Psychoneuroendocrinology*. 2003;28(Suppl 3):25-37.
5. Browne TK. Is premenstrual dysphoric disorder really a disorder? *J Bioeth Inq*. 2015;12(2):313-330. doi:10.1007/s11673-014-9567-7.
6. Cohen L, Miner C, Brown EW, et al. Premenstrual daily fluoxetine for premenstrual disorder: A placebo controlled, clinical trial using computerized diaries. *Obstet Gynecol*. 2002;10:435-444.
7. Robinson LL, Ismail KM. Clinical epidemiology of premenstrual disorder: Informing optimized patient outcomes. *Int J Womens Health*. 2015;7:811–818.
8. Banerjee N, Roy KK, Takkar D. Premenstrual dysphoric disorder: A study from India. *Int J Fertil Womens Med*. 2000;45:342-344.
9. Raval CM, Panchal BN, Tiwari DS, Vala AU, Bhatt RB. Prevalence of premenstrual syndrome and premenstrual dysphoric disorder among college students of Bhavnagar, Gujarat. *Indian J Psychiatry*. 2016;58:164-170.
10. Mishra A, Banwari G, Yadav P. Premenstrual dysphoric disorder in medical students residing in hostel and its association with lifestyle factors. *Ind Psychiatry J*. 2015;24:150-157.
11. Kamat SV, Nimbalkar AS, Nimbalkar SM. Premenstrual syndrome in adolescents of Anand: Cross-sectional study from India using premenstrual symptoms screening tool for adolescents (PSST-A). *Arch Dis Child*. 2012;97:A136.
12. Parikh MN, Parikh NC, Parikh SK. Premenstrual dysphoric disorder in adolescent girls in Western India. *Gujarat Med J*. 2015;70:65-69.
13. Padhy SK, Sarkar S, Beherre PB, Rathi R, Panigrahi M, Patil PS. Relationship of premenstrual syndrome and premenstrual dysphoric disorder with major depression: Relevance to clinical practice. *Indian J Psychol Med*. 2015;37:159-164.
14. Bhatia SC, Bhatia, SK. Diagnosis and treatment of premenstrual dysphoric disorder. *Am Fam Physician*. October 1, 2002;66(7):1239-1249.
15. Condon JT. The premenstrual syndrome: A twin study. *Br J Psychiatry*. 1993;162:481-486.
16. Kendler K, Karkowski L, Corey L, Neale M. Longitudinal population-based study of retrospectively reported premenstrual symptoms and lifetime major depression. *Am J Psychiatry*. 1998;155:1234-1240.
17. Treloar S, Heath AM, Martin NG. Genetic and environmental influences on premenstrual symptoms in an Australian twin sample. *Psychol Med*. 2002;32:25-38.
18. Dhingra V, Magnay JL, O'Brien PM, Chapman G, Fryer AA, Ismail KM. Serotonin receptor 1A C(−1019)G polymorphism associated with premenstrual dysphoric disorder. *Obstet Gynecol*. 2007;110:788-792.
19. Huo L, Straub RE, Roca C, et al. Risk for premenstrual dysphoric disorder is associated with genetic variation in ESR1, the estrogen receptor alpha gene. *Biol Psychiatry*. 2007;62:925-933.
20. Masho SW, Adera T, South-Paul J. Obesity as a risk factor for premenstrual syndrome. *J Psychosom Obstet Gynaecol*. 2005;26:33-39.
21. Deuster P, Adera T, South-Paul J. Biological, social, and behavioral factors associated with premenstrual syndrome. *Arch Fam Med*. 1999;8:122-128.
22. Girdler SS, Klatzkin R. Neurosteroids in the context of stress: Implications for depressive disorders. *Pharmacol Ther*. 2007;116:125-139.
23. Perkonigg A, Yonkers K, Pfiste H, Lieb R, Wittchen HU. Risk factors for premenstrual dysphoric disorder in a community sample of young women: The role of traumatic events and posttraumatic stress disorder. *J Clin Psychiatry*. 2004;65:1314-1322.
24. MacDonald P, Dombroski R, Casey M. Recurrent secretion of progesterone in large amounts: An endocrine/metabolic disorder unique to young women? *Endocr Rev*. 1991;12:372-401.
25. Birzniece V, Backstrom T, Johansson IM, et al. Neuroactive steroid effects on cognitive functions with a focus on the serotonin and GABA systems. *Brain Res Rev*. 2006;51:212-239.

26. Smith S, Gong Q, Hsu F, Markowitz R, French-Mullen J, Li X. GABA A receptor alpha-4 subunit suppression prevents withdrawal properties of an endogenous steroid. *Nature*. 1998;392:926-930.
27. Smith S, Ruderman Y, Frye C, Homanics G, Yuan M. Steroid withdrawal in the mouse results in anxiogenic effects of 3alpha, 5beta-THP: A possible model of premenstrual dysphoric disorder. *Psychopharmacology (Berl)*. 2006;186:323-333.
28. Sundstrom Poromaa I, Smith S, Gulinello M. GABA receptors, progesterone and premenstrual dysphoric disorder. *Arch Womens Ment Health*. 2003;6:23-41.
29. Griffiths J, Lovick T. Withdrawal from progesterone increases expression of alpha4, beta1, and delta GABA(A) receptor subunits in neurons in the periaqueductal gray matter in female Wistar rats. *J Comp Neurol*. 2005;486:89-97.
30. Backstrom T, Andersson A, Andree L, et al. Pathogenesis in menstrual cycle-linked CNS disorders. *Ann N Y Acad Sci*. 2003;1007:42-53.
31. van Wingen G, van Broekhoven F, Verkes R, et al. Progesterone selectively increases amygdala reactivity in women. *Mol Psychiatry.* 2008;13:325-333.
32. Cunningham J, Yonkers KA, O'Brien S, Eriksson E. Update on research and treatment of premenstrual dysphoric disorder. *Harv Rev Psychiatry*. 2009;17(2):120-137. doi: 10.1080/10673220902891836.
33. Schmidt P, Grover G, Roy-Byrne P, Rubinow D. Thyroid function in women with premenstrual syndrome. *J Clin Endocrinol Metab*. 1993;76:671-674.
34. Girdler S, Pedersen C, Light K. Thyroid axis function during the menstral cycle in women with premenstrual syndrome. *Psychoneuroendocrinology*. 1995;20:395-403.
35. Portella AT, Haaga DA, Rohan KJ. The association between seasonal and premenstrual symptoms is continuous and is not fully accounted for by depressive symptoms. *J Nerv Ment Dis*. 2006;194:833-837.
36. Dalgleish T, Rosen K, Marks M. Rhythm and blues: The theory and treatment of seasonal affective disorder. *Br J Clin Psychol*. 1996;35:163-182.
37. Frank R. The hormonal causes of premenstrual tension. *Arch Neurol Psychiatry*. 1931;26:1053-1057.
38. Parry BL, Newton RP. Chronobiological basis of female-specific mood disorders. *Neuropsychopharmacology*. 2001;25(Suppl 5): 102–108.
39. Pehrsson M, Westberg L, Landén M, Ekman A. Stable serum levels of relaxing throughout the menstrual cycle: A preliminary comparison of women with premenstrual dysphoria and controls. *Arch Womens Ment Health.* 2007;10:147-153.
40. Thys-Jacobs S, McMahon D, Bilezikian JP. Cyclical changes in calcium metabolism across the menstrual cycle in women with premenstrual dysphoric disorder. *J Clin Endocrinol Metab*. 2007;92:2952-2959.
41. Rosenstein D, Elin R, Hosseini J, Grover G, Rubinow D. Magnesium measures across the menstrual cycle in premenstrual syndrome. *Biol Psychiatry*. 1994;35:557-561.
42. Ho H, Olsson M, Westberg L, Melke J, Eriksson E. The serotonin reuptake inhibitor fluoxetine reduces sex steroid-related aggression in female rats: An animal model of premenstrual irritability? *Neuropsychopharmacology*. 2001;24:502-510.
43. 43. Schneider T, Popik P. Attenuation of estrous cycle-dependent marble burying in female rats by acute treatment with progesterone and antidepressants. *Psychoneuroendocrinology*. 2007;32:651-659.
44. Eriksson E, Andersch B, Ho H, Landen M, Sundblad C. Diagnosis and treatment of premenstrual dysphoria. *J Clin Psychiatry*. 2002;63(Suppl 7):16-23.
45. Griffin L, Mellon S. Selective serotonin reuptake inhibitors directly alter activity of neurosteroidogenic enzymes. *Proc Natl Acad Sci U S A*. 1999;96:13512-13517.
46. Halbreich U, Endicott J. Possible involvement of endorphin withdrawal or imbalance in specific premenstrual syndromes and postpartum depression. *Med Hypotheses*. 1981;7:1045–1058.
47. Reid R, Yen S. Premenstrual syndrome. *Am J Obstet Gynecol*. 1981;139:85-104.
48. Kask K, Gulinello M, Backstrom T, Geyer MA, Sundstrom-Poromaa I. Patients with premenstrual dysphoric disorder have increased startle response across both cycle phases and lower levels of prepulse inhibition during the late luteal phase of the menstrual cycle. *Neuropsychopharmacology*. 2008;33:2283-2290.
49. Epperson CN, Pittman B, Czarkowski KA, Stiklus S, Krystal JH, Grillon C. Luteal-phase accentuation of acoustic startle response in women with premenstrual dysphoric disorder. *Neuropsychopharmacology*. 2007;32:2190-2198.
50. Ylostalo P, Kauppila A, Puolakka J, Ronnberg L, Janne O. Bromocriptine and norethisterone in the treatment of premenstrual syndrome. *Obstet Gynecol*. 1982;59:292-298.
51. Wuttke W, Jarry H, Christoffel V, Spengler B, Seidlova-Wuttke D. Chaste tree (Vitex agnus-castus): Pharmacology and clinical indications. *Phytomedicine*. 2003;10:348-357.
52. O'Brien P, Abukhalil I. Randomized controlled trial of the management of premenstrual syndrome and premenstrual mastalgia using luteal phase-only danazol. *Am J Obstet Gynecol*. 1999;180:18-23.
53. Oksa S, Luukkaala T, Maenpaa J. Toremifene for premenstrual mastalia: A randomised, placebo-controlled crossover study. *BJOG*. 2006;113:713-718.

54. Kornstein SG, Harvey AT, Rush AJ, et al. Self-reported premenstrual exacerbation of depressive symptoms in patients seeking treatment for major depression. *Psychol Med*. 2005;35: 683-692.
55. O'Brien P, Craven D, Selby C, et al. Treatment of premenstrual syndrome by spironolactone. *Br J Obstet Gynaecol*. 1979;86:142-147.
56. Tietjen GE, Bushnell CD, Herial NA, Utley C, White L, Hafeez F. Endometriosis is associated with prevalence of comorbid conditions in migraine. *Headache*. 2007;47:1069-1078.
57. Hantsoo L, Epperson CN. Premenstrual dysphoric disorder: Epidemiology and treatment. *Curr Psychiatry Rep*. 2015;17:87.
58. Halbreich U, Backstrom T, Eriksson E, et al. Clinical diagnostic criteria for premenstrual syndrome and guidelines for their quantification for research studies. *Gynecol Endocrinol*. 2007;23:123-130.
59. Hardoy MC, Serra M, Carta MG, Contu P, Pisu MG, Biggio G. Increased neuroactive steroid concentrations in women with bipolar disorder or major depressive disorder. *J Clin Psychopharmacol*. 2006;26:379-384.
60. Green LJ, O'Brien PMS, Panay N, Craig M on behalf of the Royal College of Obstetricians and Gynaecologists. Management of premenstrual syndrome. *BJOG*. 2017;124: e73-e105.
61. O'Brien PM, B€ackstrom T, Brown C, et al. Towards a consensus on diagnostic criteria, measurement and trial design of the premenstrual disorders: The ISPMD Montreal consensus. *Arch Womens Ment Health*. 2011;14:13-21.
62. National Association for Premenstrual Syndrome. *Advice for Sufferers and Health Professionals*. Kent, TN: National Association for Premenstrual Syndrome; 2008.
63. Wittchen HU, Becker E, Lieb R, Krause P. Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. *Psychol Med*. 2002;32:119-132.
64. Yonkers K, Steiner M. Depression in women. London: Dunitz; 1999.
65. Pearlstein TB, Frank E, Rivera-Tovar A, Thoft JS, Jacobs E, Mieczkowski TA. Prevalence of Axis I and Axis II disorders in women with late luteal phase dysphoric disorder. *J Affect Disord*. 1990;20:129-134.
66. Halbreich U, Endicott J. Relationship of dysphoric premenstrual changes to depressive disorders. *Acta Psychiatr Scand*. 1985;71:331-338.
67. Stone AB, Pearlstein TB, Brown WA. Fluoxetine in the treatment of late luteal phase dysphoric disorder. *J Clin Psychiatry*. 1991;52:290-293.
68. Steiner M, Peer M, Soares CN. Comorbidity and premenstrual syndrome: Recognition and treatment approaches. *Gynaecol Forum*. 2006;11:13-16.
69. Steiner M, Born L. Psychiatric aspects of the menstrual cycle. In: Kornstein SG, Clayton AH, eds. *Women's Mental Health: A Comprehensive Textbook*. New York: Guilford Press; 2002: 48-69.
70. Hartlage SA, Brandenburg DL, Kravitz HM. Premenstrual exacerbation of depressive disorders in a community-based sample in the United States. *Psychosom Med*. 2004;66(5):698-706.
71. Ducasse D, Jaussent I, Olie E, Guillaume S, Castroman L, Courtet P. Personality traits of suicidality are associated with premenstrual syndrome and premenstrual dysphoric disorder in a suicidal women sample. *PLOS ONE*. 2016;11(2):e0148653. doi: 10.1371/journal.pone.0148653.
72. Endicott J, Halbreich U, Schacht S, Nee J. Premenstrual changes and affective disorders. *Psychosom Med*. 1981;43:519-529.
73. Miyaoka Y, Akimoto Y, Ueda K, Kamo T. The reliability and validity of the newly developed PMDD scale. *J Jpn Soc Psychosom Obstet Gynecol*. 2009;14(2):194-201. doi: https://doi.org/10.18977/jspog.14.2_194.
74. Steiner M, Macdougall M, Brown E. The premenstrual symptoms screening tool (PSST) for clinicians. *Arch Womens Ment Health*. 2003;6(3):203-209.
75. Marjoribanks J, Brown J, O'Brien PM, Wyatt K. Selective serotonin reuptake inhibitors for premenstrual syndrome. *Cochrane Database Syst Rev*. 2013;(6):CD001396.