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## Premenstrual syndrome

### Khaled M.K. Ismail\*, Shaughn O'Brien

Academic Unit of Obstetrics and Gynaecology, Keele University School of Medicine, University Hospital of North Staffordshire, Newcastle Road, Stoke on Trent ST4 6QG, UK

#### **KEYWORDS**

Premenstrual syndrome; Premenstrual dysphoria; PMS; Serotonin; Ovulation; Selective serotonin re-uptake inhibitors **Summary** Until relatively recently there has been a reluctance to accept premenstrual syndrome as a serious condition. Premenstrual *symptoms* occur in 95% of all women of reproductive age. Premenstrual syndrome (PMS) occurs in about 5% of those women. PMS patients appear more susceptible to their normal ovarian hormone cycle. The increased sensitivity may be due to neurotransmitter dysfunction (possibly serotonin). However, the definitive aetiology is not known. PMS results from ovulation and appears to be caused directly by the progesterone produced following ovulation in women who have enhanced sensitivity to this progesterone. Treatment can thus be achieved by suppression of ovulation or reducing progesterone sensitivity; the latter seems achievable by the administration of selective serotonin re-uptake inhibitors. Ovulation can be suppressed by a variety of methods, and oestrogen is frequently employed with success. Here, the authors describe an evidence-based approach to the management of PMS. © 2004 Elsevier Ltd. All rights reserved.

#### Introduction

Premenstrual symptoms occur in 95% of all women of reproductive age. Premenstrual syndrome (PMS) occurs in about 5% of those women. The terminology of premenstrual disorders has become complex. PMS is most often used in the UK; PMT (premenstrual tension) is the lay term; premenstrual dysphoric disorder (PMDD) is the extreme, predominantly psychological, end of the PMS spectrum, estimated to occur in 3–9% of women. PMDD requires the specific diagnostic criteria outlined in the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV) (Table 1). It should be noted that these are research rather than clinical diagnostic criteria and the term has not been accepted in European or UK gynaecological practice.

#### Definition

PMS is the term most often used, and its criteria are outlined in the *Tenth Revision of the International Classification of Disease (ICD-10)*. A woman has PMS if she complains of recurrent psychological or somatic symptoms (or both), recurring specifically during the luteal phase of the cycle and resolving by the end of menstruation. This separates PMS

<sup>\*</sup>Corresponding author. Tel.: +44 1782 552409.

E-mail address: khaled.ismail@uhns.nhs.uk (K.M.K. Ismail).

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Table 1 DSM-IV diagnostic criteria for PMDD(1994).

A. In most menstrual cycles, five (or more) of the following symptoms are present, with at least one of the symptoms being either (1), (2), (3), or (4):

- 1. Markedly depressed mood, feelings of hopelessness, or self-depreciatory thoughts
- 2. Marked anxiety, tension, feeling of being 'keyed up' or 'on edge'
- 3. Marked affective lability (e.g. feeling suddenly sad or tearful or with increased sensitivity to rejection)
- 4. Persistent and marked anger or irritability or increased interpersonal conflicts
- 5. Subjective sense of difficulty in concentrating
- 6. Decreased interest in usual activities (e.g. work, school, friends, hobbies)
- 7. Lethargy, easy fatiguability, or marked lack of energy
- 8. Marked change in appetite, overeating, or specific food cravings
- 9. Hypersomnia or insomnia
- 10. A sense of being overwhelmed or out of control

11. Other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of 'bloating', weight gain

B. Interference with work, school, or social relationships

C. Symptoms of PMDD must be present for most of the time during the last week of the luteal phase (premenses) and absent during the week after menses

D. The disturbance can not be merely an exacerbation of the symptoms of another disorder

E. Confirmation by prospective daily ratings for two consecutive menstrual cycles

from background psychiatric disorders. An enormous range of symptoms has been described and their character is less important than their timing and severity. Many symptoms have been described: irritability, aggression, depression, tension, feeling out of control, bloatedness and mastalgia are wellknown 'classical' symptoms.

The symptoms of PMS must be sufficiently severe to disrupt women's normal functioning, quality of life and interpersonal relationships. This distinguishes PMS from the physiological premenstrual symptoms that occur during the normal menstrual cycle.

#### Aetiology

The aetiology and pathophysiology of PMS remain unknown. The syndrome is seen in women of reproductive age and is not present before puberty, during pregnancy, or after the menopause. Elimination of the ovarian endocrine cycle by oophorectomy or by administration of analogues of GnRH is associated with the parallel suppression of PMS symptoms. The hypothesis that ovarian steroids, particularly progesterone, have a role in the pathophysiology of the syndrome is intuitively obvious.

Over the past 20 years, research studies into PMS have generated data which could support theories of progesterone deficiency, oestrogen/progesterone imbalance or progesterone excess. However, serum ovarian steroid concentrations have repeatedly been found to be normal in the women studied. Therefore, factors other than differences in the levels of individual hormones must be important. The interactions of fluctuating levels of ovarian steroids or their metabolites with neurotransmitter systems or receptor imbalances in the brain may be relevant in PMS pathogenesis. Several neurotransmitters are clearly influenced by ovarian steroids. These include serotonin, acetylcholine, noradrenaline and dopamine. Oestrogen acts cumulatively as an agonist on serotonergic function by increasing the number of serotonin receptors, serotonin (5-HT) postsynaptic responsiveness, neurotransmitter transport and uptake. It also increases serotonin synthesis and boosts the levels of the metabolite 5-Hydroxyindole acetic acid (5-HIAA). The precise inter-relationship between progesterone and serotonin is not yet clear. It is also likely to be more complex because of the potential interaction between the metabolite of progesterone, allopregnanolone, and GABA-ergic receptors.

#### Diagnosis

An enormous range of symptoms has been described. The character of the symptoms is less important than their timing and severity. For the diagnosis of PMS, the symptoms must:

- occur in the luteal phase of the cycle;
- resolve by the end of menstruation;

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