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Hormonal management of premenstrual syndrome

Sa'adatu Bose Usman* MBChB
Specialist Registrar in Obstetrics and Gynaecology

Radha Indusekhar MRCOG
Locum Consultant in Obstetrics and Gynaecology

Shaughn O'Brien FRCOG
Professor and Consultant in Obstetrics and Gynaecology
Department of Obstetrics and Gynaecology, University Hospital of North Staffordshire, Stoke on Trent ST4 6QG, UK

Premenstrual syndrome (PMS) is a psychological and somatic disorder of unknown aetiology. The symptoms of PMS regularly occur during the luteal phase of the menstrual cycle and resolve by the end of menstruation. The severe and predominantly psychological form of PMS is called 'premenstrual dysphoric disorder'. PMS results from ovulation and appears to be caused by the progesterone produced following ovulation in women who have enhanced progesterone sensitivity. This enhanced sensitivity may be due to neurotransmitter dysfunction. Treatment is aimed at suppressing ovulation or reducing progesterone sensitivity. This chapter will describe the role of hormones and hormonal treatments in PMS.

Key words: premenstrual syndrome; hormonal management; oestrogens; progesterone; progestogens; combined oral contraceptives; drosperinone; gonadotrophin-releasing hormone analogues.

Premenstrual syndrome (PMS) is a range of physical, psychological and behavioural symptoms that are not due to any organic disease, that occur during the luteal phase of the menstrual cycle and disappear at the onset of menstruation.[1] The morbidity of PMS is due to its severity and chronicity in a subset of women and the resulting

* Corresponding author. Tel./Fax: +44 1782 552472.
E-mail address: sau691@yahoo.co.uk (Sa'adatu B. Usman).

impairment in work, family relationships and daily activities.[2] This disorder can manifest with a wide variety of symptoms, including depression, mood lability, abdominal pain, breast tenderness, headache and fatigue.[3] At least one premenstrual symptom occurs in 95% of women of reproductive age. Women with more affective symptoms are classified as having premenstrual dysphoric disorder (PMDD).[3] The main treatment strategies involve ovulation suppression or targeting central nervous system components that are thought to be involved in the aetiology of PMS.

AETIOLOGY

The exact aetiology of PMS remains unknown, although several theories have been proposed implicating several hormones and neurotransmitters. The sex steroids produced by the corpus luteum of the ovary are thought to be symptom provoking, as the cyclicity disappears in anovulatory cycles when a corpus luteum is not formed.[4] Ablation of the ovarian endocrine cycle by oophorectomy or by the administration of gonadotrophin-releasing hormone (GnRH) analogues is associated with the parallel elimination of PMS symptoms.[5] In women whose ovarian cycles have ceased (due to the menopause or bilateral oophorectomy) and who subsequently receive hormone-replacement therapy (HRT), a significant percentage redevelop PMS symptoms during the progestogen phase of therapy.[6]

The neurotransmitters within the brain involved in PMS symptoms are the serotonin and gamma-aminobutyric acid (GABA) systems. It has been proposed that serotonin deficiency in women with PMS enhances sensitivity to progesterone.[7] The efficacy of selective serotonin re-uptake inhibitors (SSRIs) in the treatment of PMS/PMDD supports the influence of serotonin in the aetiology of PMS.

GABA is one of the most important inhibitory neurotransmitters in the human brain; one-third of brain synapses utilize GABA. Clinical studies have reported low levels of GABA in the plasma and cerebrospinal fluid of patients with mood disorders.[8] In patients with PMS, allopregnanolone levels are low in the follicular and luteal phases.[7,9] This appears to be due to impaired synthesis of allopregnanolone by the corpus luteum and other steroidogenic organs.[10] Allopregnanolone has a bimodal action on negative mood symptoms similar to benzodiazepines, barbiturates and alcohol. In high doses, it produces anxioloytic, anti-aggressive, sedative and anti-epileptic effects. In low doses, it causes severe emotional reactions in a subset of individuals (2–3%) and moderate reactions in up to 20% of women.[11,12]

SYMPTOMS

Symptoms of PMS can be somatic, psychological, behavioural or a combination of all three forms. These symptoms are recurrent, occurring during the luteal phase of the menstrual cycle and resolving by the end of menstruation.[13] Women with PMS experience a wide range of symptoms that can be quite varied in terms of severity. Some women experience such severe symptoms that it is emotionally and physically disabling. PMDD is the extreme and mostly psychological form of PMS, and affects 2–6% of women who are menstruating.[14]

Typical psychological symptoms of PMS include anxiety, irritability, depression, mood swings, sleep disorders, loss of self control, fatigue, decreased interest and altered interest in sex.[15] Somatic symptoms are prevalent and they include breast tenderness, weight gain, headaches, change in appetite, general aches and pain, and feeling bloated.[15]