Premenstrual syndrome

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Abstract

Premenstrual syndrome (PMS) is a condition characterized by a combination of psychological and physical symptoms that begin during the luteal phase of the menstrual cycle, cease by the end of menstruation, with a symptom-free period till ovulation. A thorough history, along with other assessment tools, both in primary care and secondary care, is key in identifying and classifying the severity of the symptoms, which can range from mild to very severe. Symptoms can really affect a woman's quality of life and with up to 8% of women debilitated by severe PMS, it is vital that they are appropriately identified using investigations available and managed accordingly. Treatment can range from complementary therapies to hormonal and non-hormonal medication, to even surgery, and is introduced in a step-wise manner, often involving a multidisciplinary team. This review outlines the theories of the pathophysiology surrounding the condition, the classification of the disease, key investigations and management options advised in guidelines and research.

Keywords menstrual cycle; premenstrual disorders; premenstrual dysphoric disorder; premenstrual syndrome; quality of life

Introduction

Premenstrual syndrome (PMS) is a combination of psychological and physical symptoms that begin during the luteal phase of the menstrual cycle (up to 14 days prior to menses). It is also characterized by symptoms which usually cease by the end of menstruation, with a symptom-free period till ovulation. To differentiate between physiological menstrual symptoms and PMS, the clinician needs to take a thorough history. It is the timing of the symptoms in association to the patient's menstrual cycle (as described), together with the degree of impact on quality of life, that determines the diagnosis of PMS.

With 3%–8% of women affected by severe PMS and as many as 40% presenting with symptoms of PMS, it is crucial that health professionals understand the disease and manage it appropriately. Currently there are two theories postulated for the aetiology of PMS. Both involve the ovarian hormone cycle. The theories are:

1. Some women are particularly sensitive to progesterone and progestogens, as serum estrogen or progesterone are the same in those with or without PMS.
2. The second theory is that estrogen and progesterone reduce serotonin levels, a chemical neurotransmitter known to regulate mood. This theory is proven by selective serotonin reuptake inhibitors (SSRIs) reducing PMS symptoms by increasing serotonin levels. Low serotonin levels are also associated with depression and anxiety.

The concept that PMS is caused by the ovarian cycle is supported by the fact that PMS is absent prior to puberty, during pregnancy, after the menopause, and during treatment with gonadotrophin-releasing hormone (GnRH) analogues.

Classification

The International Society of Premenstrual Disorders (ISMDs) divides PMS into 'core' and 'variant' using precise criteria. Core (or typical) premenstrual disorders (PMDs) are the most common type of PMS. Like all PMDs, symptoms should impair daily functioning or affect work or school performance, or interpersonal relationships. The symptoms of core PMDs are nonspecific (predominantly physical, emotional or mixed) and recur with spontaneous ovulatory cycles.

PMDs that do not fit into the criteria of 'core' are called 'variant,' of which there are four subtypes:

1. Premenstrual exacerbation of an underlying disorder can occur in patients with diabetes, depression, epilepsy, asthma and migraine. They will experience symptoms associated with their disorder throughout the whole menstrual cycle but they are worse in the luteal phase.
2. Non-ovulatory PMDs occur during ovarian activity without ovulation. It is seen in women who are having medication to suppress menstruation, but the ovarian follicular activity continues and can cause symptoms.
3. Progestogen-induced PMDs are caused by exogenous progestogens in hormone replacement therapy (HRT) and the combined oral contraceptive (COC) pill. In women sensitive to progestogens, these treatments can recommence symptoms.
4. PMDs with absent menstruation occur in women who still have an ovarian cycle, but no longer menstruate due to having a hysterectomy, endometrial ablation or the levonorgestrel-releasing intrauterine system (LNG-IUS).

Premenstrual dysphoric disorder (PMDD) is another condition described by the American Psychiatric Association, that also occurs in the luteal phase but requires fulfilment of very strict criteria of severe symptoms that interfere with daily activities. The Diagnostic and Statistical Manual of Mental Disorders (DSM-V) is commonly used to identify this disorder, and needs 5 out of 11 symptoms identified, one of which must be mood. However, these restrictive criteria can exclude women with a narrow range of severe symptoms, who actually should receive treatment.

When considering PMS as a diagnosis, a diary of symptoms and times should be kept by the patient for at least the length of two menstrual cycles. This should identify symptoms occurring during the luteal phase, ceasing when menstruation begins, followed by a symptom-free week until ovulation. Underlying physical or psychological disorders should also be ruled out as a cause for the exacerbation of symptoms. Figure 1 shows the classification, to assist clinicians in placing a patient in the right category of PMD.

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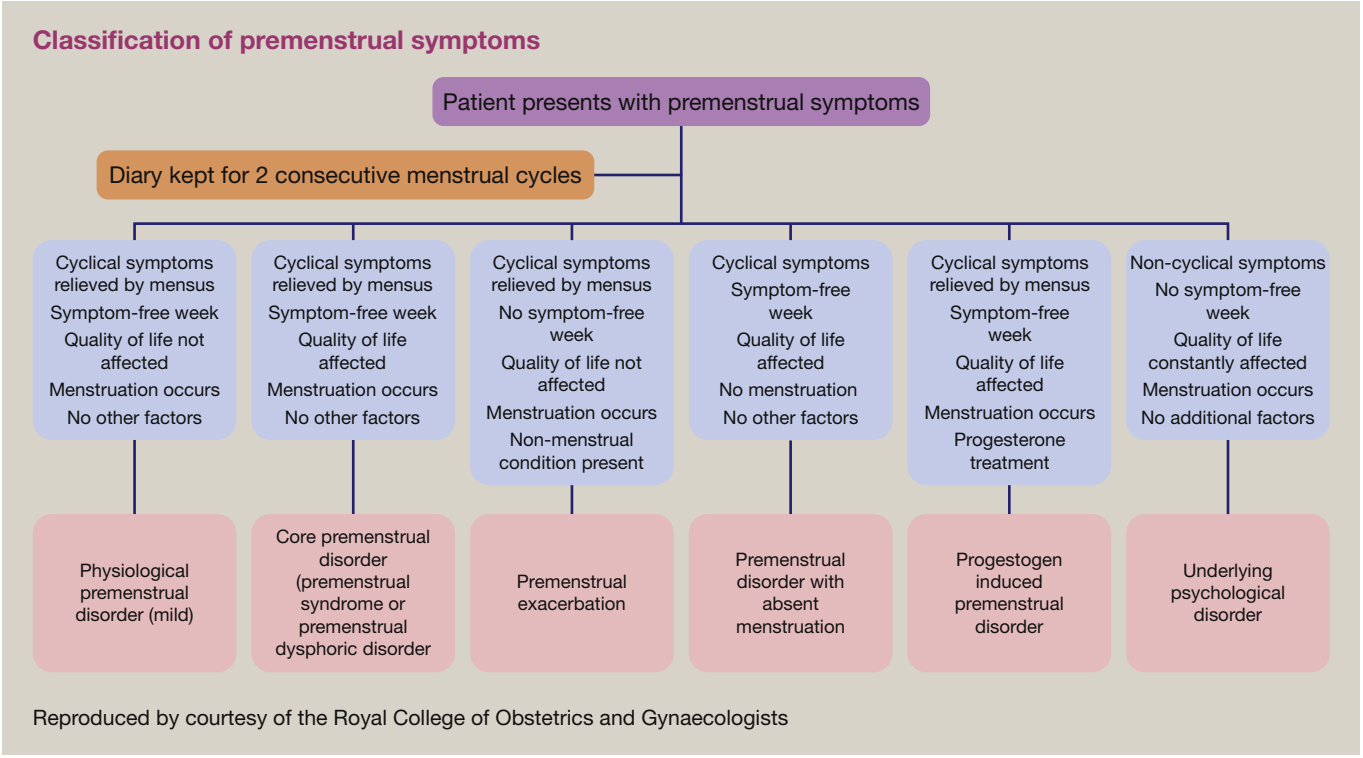

Figure 1

Diagnosing PMS

A prospective diary of symptoms over two menstrual cycles is essential to help diagnose PMS. The Daily Record of Severity of Problems (DRSP), shown in Table 1, is a well-validated scale used by health professionals to diagnose of PMS. Patients score each symptom on each day using a scale (1–6: 1 = not at all, 2 = minimal, 3 = mild, 4 = moderate, 5 = severe, 6 = extreme). The scores are added in the column for the first day of menses. A total score less than 50, indicates a diagnosis other than pre-menstrual syndrome. If there is a total score greater than 50, record two cycles of symptoms. If more than three items have an average score of more than 3 (mild) during the luteal phase, add the scores of five-day intervals during the luteal and follicular phases. A luteal phase score, 30% greater than the follicular phase score signposts premenstrual syndrome. Other tools, such as the Premenstrual Symptoms Screening Tool (PSST) and various new telephone apps are available, whilst these are accessible they have not been validated to diagnose the condition.

A thorough history is essential when seeing these patients, and when symptoms appear during the luteal phase, and resolve during or at the end of menstruation, the diagnosis is confirmed. A third cycle of a symptom diary may be required if the diagnosis is unclear.

Where symptom diaries can give confusing results, especially in patients with variant PMDs, GnRH analogues should be used for 3 months to differentiate those with and without PMS, by inhibiting cyclical ovarian function. The first month allows the agonist to suppress the hormone effect, as well as providing 2 months' worth of symptom diaries.

Daily record of severity of problems (DRSP)

1a Felt depressed, sad, 'down,' or 'blue'
1b Felt hopeless
1c Felt worthless, or guilty
2 Felt anxious, tense, 'keyed up' or 'on edge'
3a Had mood swings (e.g., suddenly felt sad or tearful)
3b Was more sensitive to rejection or my feelings were easily hurt
4a Felt angry, irritable
4b Had conflicts or problems with people
5 Had less interest in usual activities (e.g., work, school, friends, hobbies)
6 Had difficulty concentrating
7 Felt lethargic, tired, fatigued, or had a lack of energy
8a Had increased appetite or over-ate
8b Had cravings for specific foods
9a Slept more, took naps, found it hard to get up when intended
9b Had trouble getting to sleep or staying asleep
10a Felt overwhelmed or that I could not cope
10b Felt out of control
11a Had breast tenderness
11b Had breast swelling, felt 'bloated', or had weight gain
11c Had headache
11d Had joint or muscle pain
At work, at school, at home, or in daily routine, at least one of the problems noted above caused reduction of productivity or inefficiency.
At least one of the problems noted above interfered with hobbies or social activities (e.g., avoid or do less).
At least one of the problems noted above interfered with relationships with others.

Table 1

Management

General practitioners (GPs) are the first point of care for these women, therefore awareness of the condition and up-to-date information on its management is essential. Where simple measures implemented by GPs have failed to relieve symptoms, symptom diaries demonstrate noncyclical symptoms, or an underlying psychiatric or somatic disorder is considered, referral to a secondary-care physician is required, i.e. a gynaecologist or psychiatrist. A multidisciplinary team can implement a unique patient care-plan, using a variety of treatments.

Management is implemented in a step-wise manner, from non-pharmacological treatment (including discussion of complementary therapies), anti-depressant medications, hormonal medications, with surgical options being the last resort (see Figure 2).

Non-pharmacological therapy

Complementary therapies, although there is limited evidence about their efficacy, can be considered in women where hormonal treatments are contraindicated. Table 2 outlines the current holistic therapies available and the evidence of benefit to PMS symptoms from research, that should always be discussed with the patient.

Evening primrose oil has been shown, in one prospective randomised controlled trial (RCT), to improve menstrual symptoms compared with placebo, at both 1 g per day and 2 g per day

Summarises current research into the benefits of selected complementary therapies for the treatment of PMS

Complementary therapy	Benet
Exercise	Some benefit
Refiexology	Some benefit
Vitamin B6	Mixed results
Magnesium	Mixed results
Multivitamins	Unknown
Calcium/vitamin D	Yes
Isoflavones	Mixed results
Vitex agnus castus L	Yes- Inadequate safety data
St John's Wort	Mixed results
Ginkgo biloba	Some benefit
Saffron	Yes
Evening primrose oil	Some benefit
Acupuncture	Some benefit
Lemon balm	Some benefit
Curcumin	Some benefit
Wheat germ	Some benefit

Table 2

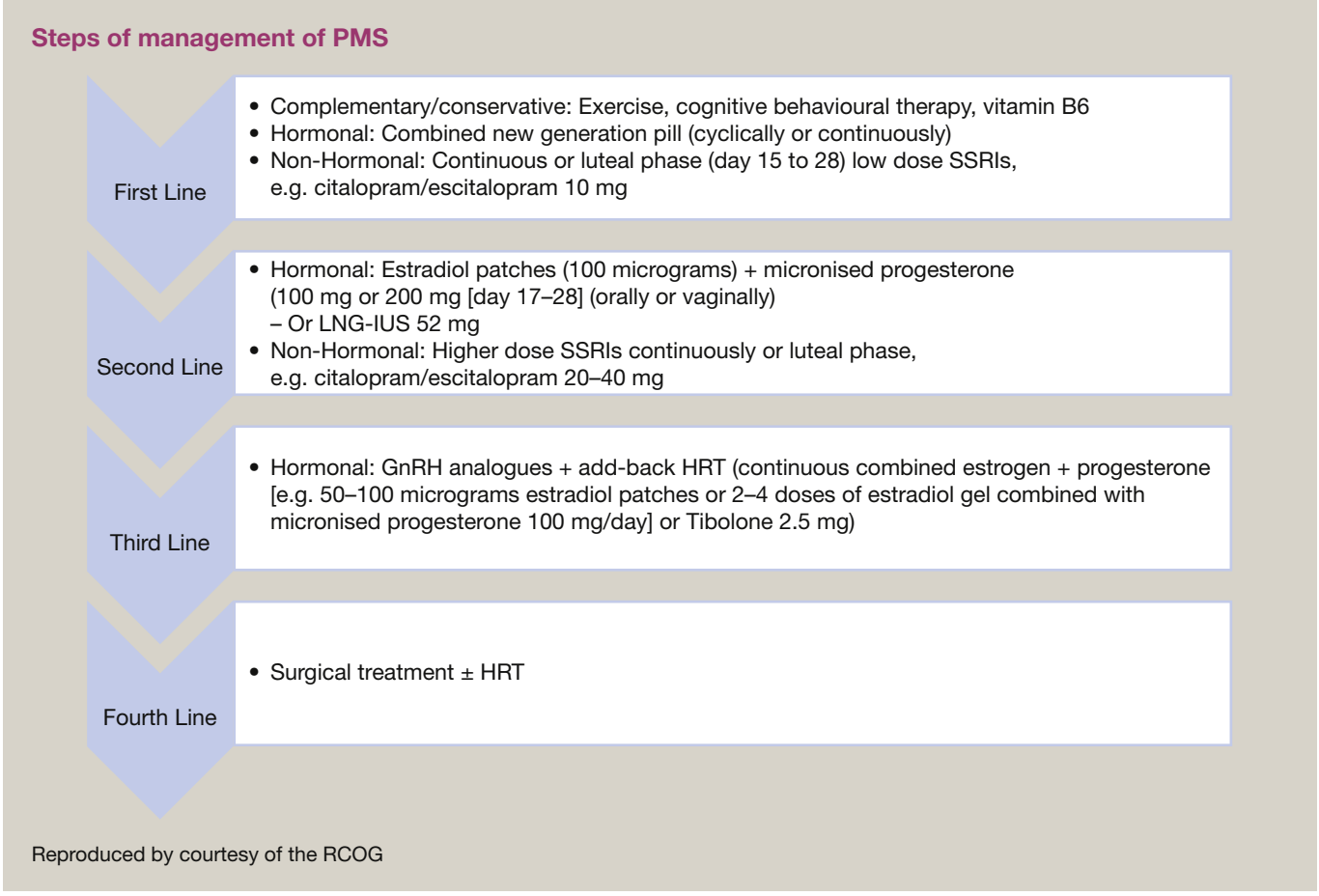

Figure 2

dosages. A systematic review of 29 RCTs showed evidence of calcium alleviating physical and psychological symptoms in PMS. St John's Wort showed conflicting results in RCTs, with mild PMS showing improvement in physical and behavioral symptoms but no improvement in mood or pain symptoms. St John's Wort also interacts with other medications, such as SSRIs and can make low dose COCs ineffective. All of the above needs discussion with the patient, highlighting the fact that there is little conclusive evidence to support their use.

In mild PMS, a course of cognitive behavioural therapy (CBT) to help with relaxation, stress management, and assertiveness training, has been shown to be effective. If successful, this could avoid pharmacotherapy and associated side-effects, but has shown a less rapid response compared with SSRIs, but better maintenance.

Hormonal treatment

In hormonal treatment, newer combined contraceptives, such as drospirenone 3 mg and ethinyl estradiol 20 μg, with anti-mineralocorticoid and antiandrogenic progestogens are shown to suppress ovulation, without generating progestogen related PMS symptoms. It should be considered first-line pharmaceutical therapy (if not contraindicated in the patient), especially if the patient requires contraception as well. It is also suggested that continuous therapy has a better effect on mood, headache and pelvic pain scores, compared with cyclical therapy.

Estrogen therapy has also been suggested as a method of inhibiting ovulation in PMS. Transdermal patches are usually used rather than an implant. However, patients need progestogen therapy to oppose the estrogen and prevent endometrial hyperplasia, unless a hysterectomy has been performed. The lowest dose for the shortest time (micronized progesterone, 100 or 200 mg) should be used to prevent progestogen-induced PMS symptoms. Alternatively, use of the levonorgestrel-containing intrauterine system, LNG-IUS (to directly work on the endometrium), can reduce recurrence of progesterone-induced PMS symptoms. Patients should be advised that initially PMS like symptoms may occur. The treatment combinations suggested includes percutaneous estradiol, and either a cyclical 10–12 day course of oral or vaginal progesterone or LNG-IUS 52 mg. A low threshold for investigating unscheduled bleeding is needed when low-doses of progesterone are used. Women should also be advised that there is little evidence on the long-term effects on the endometrium and breast tissue when using estradiol treatments.

Long-acting GnRH analogues are highly effective in treating severe PMS. They work by suppressing ovarian functioning and therefore inhibiting the menstrual cycle. While in the long-term this is a good option, in the short term the treatment causes hot flushes, night sweats, low mood and insomnia. In the long term, the estrogen deficiency can also cause vaginal atrophy, increased cardiovascular risk and osteoporosis, therefore treatment without add–back therapy should only be given for 6 months. If add–back therapy from 6 months is used on a long-term basis, bone mineral density should also be assessed yearly using DEXA scanning. Although hormone replacement therapy (HRT) can decrease the side-effects of estrogen deficiency, it can cause PMS like symptoms. Due to the problems outlined, GnRH analogues, should be reserved for the most severe symptoms, or if other treatments have failed. If patients fail to respond to GnRH analogues, then the diagnosis of PMS should be reconsidered. Although not licenced, GnRH analogues are used to aid diagnosis where 2-month diaries do not reveal PMS.

Non-hormonal treatment

Selective SSRIs (fluoxetine 20–60 mg, citalopram 20–40 mg and sertraline 50–150 mg) need to be considered along with GnRH analogues as first-line treatment in severe PMS. They have shown an effect on the emotional, behavioural and physical symptoms in the treatment of core PMD. SSRIs work quickly, meaning they can be taken sequentially in the luteal phase, as well as continuously. Patients should be informed of side effects (nausea, fatigue, insomnia and sexual dysfunction) that can present with the use of SSRIs, which are reduced with intermittent use. Unfortunately, PMS symptoms recur when SSRIs are stopped. The dose should be tapered off to prevent withdrawal symptoms, if they are taken continuously. This is not a problem if taking luteal-phase SSRIs. Women should also be given adequate pre-pregnancy counselling. They should be told that PMS symptoms will stop during pregnancy and so SSRIs should be discontinued before and during pregnancy. There is a possible, but unproven, association with congenital malformations, and women should be made aware of this. This risk is likely to be extremely small when compared to the general population. Women who fail two or more SSRI treatment regimes, should try hormonal treatment.

The use of diuretics, such as spironolactone 100 mg, has been shown to have an effect on physical symptoms, weight gain and mood.

Surgical treatment

Hysterectomy and bilateral salpingo-oophorectomy is the permanent method of stopping ovulation and consequently removing the ovarian cycle. As the endometrium is also removed, estrogen can be given without progesterone opposition. This surgical option can be justfied for women in whom medical treatment has failed, where long-term GnRH analogue medication is needed, or other gynaecological pathologies require a hysterectomy. However, this must be considered in severe cases only, after careful discussion with the patient, given the reproductive consequences of a hysterectomy in an often young age group.

Preoperative GnRH analogues should be used as a test of cure, to be certain that HRT will be tolerated, especially in women under 45 years old considering surgery for PMS alone. Following surgery, estrogen-only HRT should be advised. Avoiding progestogen treatment prevents reintroduction of PMS-type symptoms. Replacing testosterone is also important, as the ovaries produce 50% of it and a deficiency causes decreased libido.

Conclusion

PMS is debilitating to women and although not considered obviously life-threatening, it can have a massive impact on a woman's quality of life. If a woman has not responded to more than one pharmacological treatment, they should be reassessed

for psychiatric or medical disorders. This highlights the role of regular assessment of women with PMS symptoms. ◆

Practice Points

- A thorough history, including a prospective diary over a minimum two month period is essential for diagnosis
- Ensure underlying psychological or medical diseases are always ruled out
- Discuss management options with the patient and always consider the step-wise approach suggested
- Always outline current research, guidelines and supportive evidence-based medicine
- Regular follow-up is key when treating such women

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