

# Premenstrual syndrome- a short review

## Abstract

The Premenstrual Syndrome is a very common cause of psychological and physical changes. Despite of the difficulty to establish a definitive diagnosis, a lot of different treatments were proposed. The objective of this short review is recapitulate current available approaches.

**Keywords:** Premenstrual syndrome, Premenstrual dysphoric disease

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## Introduction

The Premenstrual Syndrome (PMS) is a common cause of psychological and physical changes in women in their reproductive years. It is a condition that manifests as behavioral and psychological symptoms in the absence of organic or psychiatric diseases.<sup>1</sup> In general it occurs in the luteal phase of every menstrual cycle and disappears or regresses significantly with the end of menstruation. The intensity and pattern of symptoms varies individually and differ to normal premenstrual psychological symptoms to significant changes of patients' daily lives. Epidemiological studies estimates that 75% of women at reproductive age lives with symptoms attributed to the premenstrual phase. The prevalence of severe PMS varies between 3-30% and seems to be more prevalent in obese and sedentary women.<sup>2</sup> In some cases, when there is no symptoms relief, the working, social and domestic life are extremely impaired every month, frequently over years.<sup>3</sup> This pattern of emotional and behavioral symptoms may be so intense that a series of diagnostic criteria for this situation was developed, the Premenstrual Dysphoric Disease (PMDD).<sup>4</sup>

## Etiology

The exact etiology remains unknown, but the cyclic ovarian activity and the estradiol and progesterone effects in the serotonin (5-HT) and gammaaminobutyric acid (GABA) neurotransmission appears to play an important role.<sup>5</sup> Studies have shown simultaneity between ovarian hormones fluctuating levels and central serotonergic function showing that it can be influenced by estrogen and progesterone. In the hypothalamus, estrogen induces a cyclic diurnal fluctuation in 5-HT whereas progesterone increases the turnover of dopamine. In addition, a reduction of 5-HT leads to a low impulse control, depressed mood, irritability and carbohydrate cravings, behavioral and mood symptoms associated with PMDD. Studies also suggest that women with PMS and PMDD can be behavioral or biochemically sub or even oversensitive to the serotonergic changes.<sup>6</sup>

## Diagnosis

There is no objective diagnostic test for PMS or PMDD and prospective evaluation of symptoms is essential to make the diagnosis. Analysis of symptoms for at least two consecutive cycles should be performed. The most common psychological symptoms are mood swings, irritability, depression and the feeling of losing control. The main physical symptoms may include breast tenderness, increased premenstrual headache and behavioral symptoms associated with a higher propensity to accidents.<sup>7</sup> A woman with PMDD must be

evaluated at least once in each stage of the cycle to ensure that there is a real relationship between the worsening of symptoms and menstrual phase. The symptoms should follow the luteal phase and interfere or alter her social, working and personal relationships. The assessment should show clear worsening of premenstrual symptoms and improve a few days after the onset of menses. After proper evaluation, the diagnostic possibilities include:

1. PMS or PMDD
2. Another psychiatric/ psychological condition isolated
3. PMS or PMDD coexisting with other psychiatric / psychological condition
4. Exacerbation or premenstrual magnification other psychiatric / psychological condition
5. No related diagnosis (only psychosocial or situational stressors)

In women who have other psychological or psychiatric conditions, premenstrual symptoms are different from symptoms of these conditions, appearing in the luteal phase and disappearing in the follicular phase. Patients may also experience premenstrual exacerbations or magnifications of other mental health conditions. Dysphoria, fatigue, panic, anxiety, bulimia and substance abuse, for example, symptoms can be shared between PMS / PMDD and other conditions. In premenstrual magnification of these pictures, the symptoms exist throughout the cycle, but worse in the premenstrual phase. Some women have persistent symptoms (such as dysthymia) or cyclic symptoms not related to the menstrual phase (such as cyclothymia). These patients may experience changes in their mental conditions as a direct consequence of social or situational stressors such as family status, marital or working problems.<sup>8</sup>

## Treatment

### Behavioral treatments

A wide range of treatments for PMS have been proposed. In all possible scenarios, the use of treatments that involve behavioral changes (such as regular exercise, decreased contact with stressors and techniques agents relaxation) or dietary adjustments (reduction of caffeine consumption, chocolate, alcohol and salt) are encouraged.<sup>3</sup>

### Low risk pharmacological treatments

**Calcium:** a multicentric study (12 centers) involving 466 women with moderate to severe PMS diagnoses were randomized into a

placebo group and another group receiving 1200 mg/day of calcium carbonate. After the third cycle, in the calcium-users group, there was a 48% reduction of symptoms intensity compared to the initial symptoms severity and to placebo group ( $p < 0.01$ ). Due to this study sample size, its methodology and the positive impact on treatment, these findings generate good evidence for inclusion of calcium as a additional PMS treatment.<sup>9</sup>

**Vitamin B6:** A systematic review evaluated vitamin B6 use in PMS treatment. In general, the selected trials quality was considered poor. There also were problems regarding subjects' inclusion and exclusion criteria. The results of the meta-analysis revealed that there is some benefit in the use of Vit. B6 for this purpose (OR 2.12; CI 1.8 to 2.48) but there is no level of evidence that shows the quality of this treatment to recommend it.<sup>10</sup>

**Agnus Castus:** Multicentric study (6 centers), double-blind, randomized, placebo-controlled trial involving 170 women showed statistically significant reduction in PMS symptoms by the end of 3 cycles.<sup>11</sup>

**Evening Primrose Oil (PO):** A systematic review of PO use in the treatment of PMS was carried out aiming to establish a meta-analysis. Only 7 placebo-controlled trials were found, but only 5 randomization criteria were clear. The only two studies with better design and forms of control had not enough evidence to recommend beneficial effects of PO use in the treatment of PMS. Interesting fact is the improvement of reported breast tenderness in these patients.<sup>12</sup>

**Hypericum perforatum:** Only an observational study with a low number of participants noted improvement in symptoms. There is no evidence supporting recommendation.<sup>13</sup>

## Hormonal treatments

**Combined oral contraceptives (COC):** They are widely used to control the symptoms of PMS. Despite its popularity, the trials demonstrates that the quality of symptoms relief varies due to different progestins used in COCs.<sup>14</sup> The widespread use of drospirenone, chlormadinone and norgestrel in small observational and randomized trials have demonstrated their effectiveness.<sup>15</sup> Despite the theoretical logical association to PMS physiopathology, there are limited clinical data showing the increased effectiveness of continuous administration of COC in relation to cyclic administration.<sup>16</sup>

**Progestins:** Despite new perspectives with the use of bio-identical progesterone, a literature systematic review failed to present evidence supporting the use of Progestins in the treatment of TPM.<sup>17</sup>

**GnRH analogs:** GnRH Analogs are successfully used for ovarian suppression. Despite the effectiveness in this arena, there is no recommendation for the its use in PMS treatment, unless the adverse effects are justified in cases of severe PMS or PMDD. Still, one must exclude other alternatives.<sup>18</sup>

**Levonorgestrel-releasing IUDs:** The clinical widespread use for this purpose still need specific data to justify its use.<sup>19</sup>

**Selective serotonin reuptake inhibitors (SSRIs):** There is broad evidence of the role of serotonin in the genesis of PMS. Therefore, a variety of SSRI has been successfully used. There is evidence level A to frame them as first-line treatments, in both cyclical and continuous use (Evidence level 1b).<sup>20</sup>

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## Conflicts of interest

None.

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