Introduction:

Women of reproductive age experience symptoms during the late luteal phase of menstrual cycle, which remits within 4-5 days after menses & collectively these complaints are termed pre-menstrual syndrome or pre-menstrual tension. Nearly 300 different symptoms have been reported, both psychiatric & physical. Premenstrual dysphoric disorder [PMDD] is considered a severe form of PMS & is listed as a mental disorder by American Psychiatric Association.

Prevalence:

40% of women experience some or other symptoms but 5-8% have severe PMS.
Aetiology & patho-physiology:

The cause is unknown; it revolves around the ovarian hormones as symptom begins with ovulation & resolve with menses. It is further reaffirmed by absence of PMS prior to puberty & after menopause.

Estrogen & progestogens are neuroactive steroids & influence the CNS neurotransmitters, Serotonin, Nor-adrenaline & GABA. Progesterone metabolites allopregnanolone is a potent modulator of GABA receptor.

Decreased serotonergic activity has been seen in luteal phase.

Sex steroids also interact with Renin- Angiotensin- Aldosterone system [RAAS] to alter electrolyte & fluid balance. The anti-mineralocorticoid properties of progesterone & possible estrogen activation of RAAS explains PMS symptoms of bloating & weight gain.

Diagnosis & Symptoms:

It is the timing, rather than the symptoms & degree of impact on daily routine, that supports the diagnosis of PMS.

To diagnose it must be demonstrated that the symptoms cause significant impairment to individual during luteal phase of menstrual cycle.

A symptom diary for at least 2-3 cycle should be maintained & reviewed to make a diagnosis.

Gonadotrophin releasing hormone analogue may be used for 3 months for a definitive diagnosis if compiled symptom diary alone is inconclusive.

<table>
<thead>
<tr>
<th>Physical Symptoms</th>
<th>Psychological Symptoms</th>
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<tbody>
<tr>
<td>Bloating &amp; weight gain</td>
<td>Mood swings</td>
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<tr>
<td>Constipation / diarrhea cramps</td>
<td>Irritability</td>
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<tr>
<td>Tender breasts</td>
<td>Depressed</td>
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<tr>
<td>Headache / back-ache</td>
<td>Bad temper</td>
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<tr>
<td>Low tolerance to noise / light</td>
<td>Tiredness / Troubled sleeping</td>
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<td>Appetite change</td>
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Symptoms can vary from month to month, although they form a pattern over months.
Various presentation with PMS:

1. Mild PMS: Patient with cyclical symptoms during luteal phase with complete remission of symptoms & no interference with daily life.
2. Moderate PMS: Symptoms in luteal phase but with some interference with social/professional life & symptom free weeks.
3. Severe PMS: severe symptoms affecting day to day activity with symptom free week.
4. Severe symptoms of PMS affecting daily activity with no symptom free week, also called pre-menstrual exaggeration. This can be associated with underlying pathology medical, physical or psychiatric.
5. Pre-menstrual dysphoric disorder: This is independent clinical condition that are identified by an accompanying psycho-social or functional impairment.

Treatment:

The treatment is focused on either symptom reduction or modification of underlying hormonal dysregulation. Various treatment options are there for mild to moderate PMS which are continued for 2-3 cycles for their efficacy, but if there are no benefits or symptoms are severe, then psychiatric referral will be required.

Integrated holistic approach should be used for the treatment.

Lifestyle changes:

1) Regular exercises
2) Balanced / healthy diet: rich in Vitamin B, calcium, magnesium and complex carbohydrates
3) Avoid salt, sugar, caffeine and alcohol
4) Managing stress with yoga, meditation & mindfulness

Medical Treatment:
Hormonal: COCP with drospirenone is more effective as compared to levonorgesteral / desogestral.

Regimen: continuous therapy is more effective rather than cyclical regime.

Percutaneous estradiol with cyclical progesterone has been effective in managing physical & psychological symptoms.

Both implant & patch can be used & lowest possible dose of progesterone is recommended to minimize progestogenic side effect.

Micronized progesterone is preferred.

Women should be informed of long-term effects of estradiol on breast & endometrium. Treatment of PMS should be on individual basis taking into account the risk & benefits.

GnRH are highly effective in treating PMS but is not routinely recommended & is reserved for severe symptoms or to diagnose inconclusive cases.

If using GnRH analogue for more than 6 months, ‘add back therapy’ should be used and continuous combined HRT or tibolone is recommended.

BMD should be measured yearly.

There is no evidence to support the use of LNG-IUD alone to treat PMS.

Non-Hormonal treatment:

SSRIs should be the first line of treatment in severe PMS. Either luteal or continuous dosing with SSRI is recommended & it should be discontinued gradually, to avoid withdrawal symptom in continuous regimen.

Side effects are nausea, insomnia, somnolence, fatigue & reduction in libido. Citalopram & Escitalopram show good resolution of symptoms with good tolerability. Women with PMS who conceive, while on SSRIs, should be aware of possible though unproven association with congenital malformation.

Spironolactone a diuretic can be used to treat physical symptoms like fluid retention & bloating.

**Surgical Management:**

Hysterectomy with B/L salpingo-oophorectomy can benefit when medical management fails or any other gynecological condition indicates surgery.

Efficacy of surgery should be predicted by prior use of GnRH. HRT is recommended post-surgery especially for women less than 45 years.

**Summarizing the treatment:**
1. Mild symptoms: lifestyle modification

2. Moderate symptoms: lifestyle modification with medical therapy
   - COC pill with drospirenone (preferably continuous regimen) OR estradiol patch / implant with micronized progesterone from 15-25th day of cycle can be used
   - SSRI (fluoxetine, sertraline, citalopram / escitalopram)

3. Severe PMS: GnRH analogues with add back HRT is recommended (estrogen orally or patch with micronized progesterone)

4. Severe symptoms not responding to medical treatment Surgical option TAH with BSO can be considered with HRT post-surgery.

Summary:
Most of the women experience PMS in absence of organic or underlying psychiatric disorder.

Timing of symptom is important for the diagnosis.

Treatment depends on the severity & type of symptoms.

Mild symptoms may be treated with lifestyle changes.

Moderate to severe symptoms need medical management.

Hormonal & non-hormonal treatment can be initiated depending on the type & severity of symptoms.
References:


Acknowledgments:

1. William’s Gynecology

2. RCOG Green Top Guidelines