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FOR TECHNICIANS**

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Premenstrual syndrome

By Christine Stewart, B.Sc.Pharm, R.Ph.

Statement of objectives

Upon completion of this lesson, the pharmacy technician should be able to:

1. Recognize the symptoms of premenstrual syndrome.
2. Understand the available treatments for premenstrual syndrome.
3. Identify patients who would benefit from a pharmacist consultation, to assess possible treatments, provide additional information about premenstrual syndrome or make an appropriate referral.

Introduction

Premenstrual syndrome (PMS) refers to a group of symptoms that occur in relation to the menstrual cycle. Symptoms usually begin 10 to 14 days before the menstrual cycle starts and subside when menstruation begins. Symptoms affect almost 40% of women, with 5% of these women experiencing severe impairment.¹ This severe subtype of PMS, known as premenstrual dysphoric disorder, is characterized by significant impairment of normal function and pronounced mood changes. The cause of PMS is unclear; however, it appears to be related to fluctuations in hormone levels. While stress does not directly cause PMS, it may make it worse.

Symptoms

PMS symptoms only occur during the luteal phase of the menstrual cycle (the time between ovulation and the onset of menses). The severity, pattern and number of symptoms vary widely from woman to woman and cycle to cycle. Symptoms may range from

mild to severe and tend to get worse during times of emotional and/or physical stress. Researchers have identified over 100 different PMS symptoms. See Table 1 for the more common symptoms.

Diagnosis

Since a diagnostic test for premenstrual syndrome does not currently exist, conditions that may mimic PMS must be ruled out. These conditions could include thyroid disorders, diabetes, anemia, endometriosis and a number of psychiatric disorders.

Several factors must be considered to make a diagnosis of PMS. The symptoms must occur only during the luteal phase of the menstrual cycle, reach a peak shortly before menstruation begins and subside at the onset of menses (or shortly thereafter). Symptoms must be severe enough to interfere with daily functioning. There will also be a symptom-free period during the follicular phase of the menstrual cycle (the first day of menstruation until ovulation). To aid in diagnosis, women are often asked

to keep a symptom diary for two to three cycles to help track ovulation dates and menstrual bleeding, and to record daily symptoms and severity. Since ovulation dates can vary during a woman's cycle, it may be necessary to track basal body temperature, monitor cervical mucus or use ovulation predictor kits to accurately record ovulation. For a sample of a symptom diary, consult the Canadian Pharmacists Association publication *Patient Self-Care*.²

Treatment

A variety of treatment options exist for patients dealing with PMS symptoms. Because symptoms vary widely from woman to woman, as a pharmacy technician, you should be familiar with all treatment options.

Nonpharmacological therapy

Once it's determined that a woman is suffering from PMS symptoms, nonpharmacological measures represent a good starting point for treatment. Promoting a healthy lifestyle to improve general health can

Table 1: Common symptoms of PMS³

Physical	Emotional	Behavioural
Water retention	Sadness	Withdrawal from family and friends
Weight gain	Crying spells	Physical/verbal aggression
Breast swelling and tenderness	Irritability	
Lack of energy	Anxiety	
Acne	Mood swings	
Food cravings	Forgetfulness	
Migraine headaches	Difficulty concentrating	
Low back pain	Depression	
Abdominal cramps		
Aching joints		
Sleep changes		
Upset stomach		
Constipation or diarrhea		

help alleviate many symptoms. Women who do moderate aerobic exercise regularly (3 to 4 times a week) have significantly fewer PMS symptoms than sedentary women.⁴ One possible reason is that regular exercise increases endorphin levels which, in turn, have a positive effect on mood. Given the overall benefits of exercise in the treatment and prevention of numerous disease states, encouraging women to increase their activity level is generally a good idea.

Sleep disturbances, such as insomnia or excessive sleep, are common in women with PMS. A well-structured sleep schedule with consistent sleep and wake times can be helpful in managing this symptom. Caffeine restriction, by reducing or eliminating tea, coffee and cola beverages,

can assist with insomnia management, as well as help to reduce premenstrual irritability.

Dietary modifications may also be necessary to manage PMS symptoms. Common recommendations include reducing sugar intake and increasing complex carbohydrates, such as fruits, vegetables and whole grains. Restricting sodium intake may minimize the effects of bloating, fluid retention, weight gain, and breast swelling and tenderness. Eating smaller, more frequent meals may also help to reduce bloating. Women should be encouraged to choose calcium-rich foods as part of a well-balanced diet. As well, eliminating alcohol and quitting smoking can be helpful in improving general health and well-being.

While stress is not a cause of PMS, it may aggravate

PMS symptoms. Taking steps to reduce stress, using time-management techniques, deep breathing exercises, yoga, massage therapy and by getting adequate rest, may improve overall symptoms of PMS. While none of these practices have been well studied, nor have they been recommended as 'stand alone' treatment for PMS, they are generally regarded as safe, well tolerated and helpful.

Pharmacological therapy: OTC remedies

Calcium: Evidence indicates that taking 1200 mg/day of calcium carbonate can reduce the severity of PMS symptoms such as mood swings, fluid retention, cravings and pain by about 50% after three continuous cycles of use.⁵ Since calcium is relatively inexpensive and is important for the prevention

of osteoporosis, it is recommended as a primary treatment for PMS.

Researchers have also investigated whether calcium and vitamin D from dietary sources could prevent the initial development of PMS and they found that the participants who ranked highest in calcium and vitamin D intake had a reduced risk for the onset of PMS.⁶

Magnesium: Magnesium deficiency has been suggested as a factor contributing to PMS symptoms. Magnesium is thought to be beneficial because it's involved in the activity of serotonin and other neurotransmitters that play a role in improving mood. Taking 200 to 400 mg of magnesium daily may help reduce fluid retention, breast tenderness, bloating and premenstrual migraine.⁷ Higher doses of magnesium are not recommended and may cause a mild laxative effect.

Vitamin B₆: Pyridoxine (vitamin B₆) is perhaps one of the most widely used treatments for PMS; however, there is controversy over its effectiveness. Vitamin B₆ is used in the metabolic synthesis of serotonin and dopamine. In theory, low levels of vitamin B₆ lead to high levels of prolactin, which in turn produce fluid retention and some of the psychological symptoms associated with PMS. In a review of nine controlled trials, researchers concluded that while the studies were poor in design,

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there does appear to be 'some' benefit of treatment with vitamin B₆.⁸ Lower doses (50-100 mg/day) appear to be as effective as higher doses (200-500 mg/day), with fewer side effects. High doses of vitamin B₆ have been associated with nausea and peripheral neuropathy.

Combination OTC Remedies: A variety of nonprescription PMS remedies exist on the market. They contain a combination of ingredients that include acetaminophen, caffeine, pamabrom (a diuretic) and pyrilamine (an antihistamine). While acetaminophen may provide some relief from headaches and pain, it can be purchased more economically as a single-entity product. Pamabrom and pyrilamine may offer some relief, and their effects appear to be mild. There is no evidence to support the superiority of these agents over an analgesic alone.

Natural remedies

Chasteberry: Chasteberry (*Vitex agnus-castus*) has been evaluated in several studies for PMS. It seems to work best on physical symptoms, such as breast tenderness and constipation, which may improve by as much as 50%, but it doesn't appear to be as helpful for bloating. Some improvement in mood, anger and headache may also occur.⁹ The exact mechanism of action is not known and adverse effects are rare. Based on the evidence to date, chasteberry is promising, but its use should be limited until further research establishes its place in therapy.

Evening primrose: Evening primrose (*Oenothera biennis*) contains two essential fatty acids, linoleic acid and gamma-linolenic acid, which are needed for prostaglandin synthesis. While a number of studies have explored the use of evening primrose in the management of premenstrual

syndrome, most are of too poor quality to draw any firm conclusions. A systematic review of clinical trials concluded that evening primrose oil offers no benefit.¹⁰ While evening primrose is generally well tolerated, it is expensive and long-term use may be associated with an increased risk of inflammation, thrombosis and immunosuppression.¹¹

Other natural remedies: Black cohosh (*Actaea racemosa*), red clover (*Trifolium pratense*) and soy (*Glycine max*) are well-known herbs found in a variety of menopause remedies. However, there is no reliable evidence that these treatments are effective for PMS symptoms.

Prescription therapy

Pain Reliever: Nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen, ibuprofen and mefenamic acid can be used to reduce the pain caused by prostaglandins and therefore help to relieve PMS symptoms such as headache, cramps, breast pain and lower back pain. NSAIDs should be used in the lowest effective dose and for short-term use only, in order to minimize the side effect of stomach upset. Treatment should begin seven to 10 days prior to the onset of menses.

Antidepressants: Selective serotonin reuptake inhibitors (SSRIs) can be used to treat mood-related and physical symptoms of PMS. These medications work by improving the brain's use of the neurotransmitter serotonin, thus helping to relieve symptoms of anxiety, depression, irritability and aggression. They may be administered on a continuous basis or during the two weeks leading up to menstruation. Side effects such as headache, drowsiness, insomnia, fatigue, sexual dysfunction and gastrointestinal complaints may limit their

usefulness in some patients. SSRIs are therefore only used in women who have severe symptoms for which other measures have failed.

Diuretics: Spironolactone (Aldactone[®]) is the only diuretic that has shown efficacy in the treatment of PMS. It relieves symptoms such as breast tenderness and fluid retention. Thiazide diuretics, while sometimes prescribed, have not been found to be beneficial in patients with PMS.¹²

Contraceptives: Oral contraceptives have been tried in patients with PMS in order to suppress ovulation and correct hormonal fluctuations. Since many women who suffer from PMS also require a reliable form of contraception, this treatment option offers a combined advantage. When oral contraceptives are first initiated, however, the side effects of breast tenderness, headache, bloating and depression may actually make PMS symptoms worse. While trials have concluded that contraceptives are useful in reducing the physical symptoms of PMS, further studies are needed to determine the best formulation to control mood abnormalities, i.e., triphasic (progesterin to estrogen ratio varies in three phases of the cycle) or monophasic (progesterin to estrogen ratio remains the same throughout the cycle). One study demonstrated that a monophasic regimen was less likely to cause adverse mood changes than a triphasic formulation.¹³ Additional studies are required to determine whether continuous pill intake over a three-month (or longer) time frame will further assist by limiting the rise and fall of hormones associated with the typical monthly cyclic regimens. Yasmin[®], a new oral contraceptive containing ethinyl estradiol and drospirenone, an analog of

spironolactone, is showing initial promise for treatment of PMS symptoms.

The technician's role

A personalized approach is necessary for effective management of PMS, since it presents with a variety of symptoms and its cause has not been clearly defined. The pharmacy technician can play a key role in identifying patients who may benefit from consultation with the pharmacist. Successful interventions can assist women in alleviating or eliminating symptoms, reducing the impact of PMS on daily activities and relationships, and maximizing the benefits of treatment while minimizing adverse effects.

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QUESTIONS

- 1. Which of the following statements is TRUE?**
- a. The severe subtype of PMS is known as premenopausal dysphoric disorder
 - b. Premenstrual symptoms only occur during menses
 - c. Symptoms are consistent from cycle to cycle
 - d. Up to 40% of women may suffer symptoms that affect daily activity
 - e. PMS is caused by stress
- 2. Which of the following is NOT one of the symptoms of premenstrual syndrome?**
- a. Crying spells
 - b. Dizziness
 - c. Lack of energy
 - d. Withdrawal from family and friends
 - e. Food cravings
- 3. Carly is a 35-year-old businesswoman whose busy schedule requires many late meetings, irregular meals and little leisure time. She has recently been diagnosed as suffering from PMS. She would like to consult with the pharmacist about nonpharmacological approaches to manage her symptoms. Which of the following nonpharmacological approaches may help Carly?**
- a. Establishing a regular sleep pattern
 - b. Decreasing caffeine intake
 - c. Increasing complex carbohydrates
 - d. Aerobic exercise
 - e. All of the above
- 4. Which of the following symptoms can be relieved by nonsteroidal anti-inflammatory drugs?**
- a. Headache
 - b. Aggression
 - c. Insomnia
 - d. Mood swings
 - e. Stomach upset
- 5. Marilyn, a 23-year-old student, has been advised by her physician to increase her intake of calcium. She thought she was being treated for PMS but she read in a textbook that calcium is used in the elderly to prevent osteoporosis. Sensing her confusion, you refer her to the pharmacist for consultation. What advice might the pharmacist provide to Marilyn?**
- a. Marilyn has osteoporosis and needs to take calcium
 - b. Calcium is a recognized treatment for PMS
 - c. Calcium will be effective during her first menstrual cycle
 - d. Calcium may help reduce fluid retention, food cravings and pain
 - e. b) and d) are correct
- 6. Which of the following statements regarding SSRIs is INCORRECT?**
- a. SSRIs are useful in treating mood-related symptoms of PMS
 - b. SSRIs must be used on a continuous basis
 - c. Side effects of SSRIs include headache, drowsiness, and insomnia
 - d. SSRIs are only used in women who have severe symptoms of PMS
 - e. SSRIs are useful in treating the diuretic spironolactone
- 7. Jennifer is browsing in your OTC section. You offer to assist her with locating a product. She indicates that she would like to buy vitamin B₆ to treat her PMS symptoms. Which of the following statements is TRUE?**
- a. Thiamine is another name for vitamin B₆
 - b. She should take 500 mg/day
 - c. Vitamin B₆ is used in the synthesis of dopamine and estrogen
 - d. High doses of vitamin B₆ are not associated with any side effects
 - e. None of the above
- 8. Which of the following statements regarding contraceptives is INCORRECT?**
- a. Many women who suffer from PMS also need a reliable method of contraception
 - b. The monophasic formulation is more likely to cause adverse mood changes
 - c. Drospirenone is an analog of the diuretic spironolactone
 - d. Studies are needed to determine the optimum dosing cycle for treating PMS
 - e. Side effects of contraceptives may worsen PMS symptoms
- 9. Which of the following statements is TRUE?**
- a. Chasteberry doesn't appear to be helpful for bloating
 - b. Chasteberry works best on physical symptoms such as breast tenderness
 - c. The exact mechanism is unknown
 - d. Chasteberry is also known as Vitex agnus-castus
 - e. All of the above
- 10. The pharmacy technician has a valuable role to play in identifying patients with PMS who would benefit from a consultation with a pharmacist. Which of the following statements are CORRECT?**
- a. Successful interventions can assist women with PMS in reducing their symptoms
 - b. Benefits of treatment can be maximized
 - c. Adverse effects can be minimized
 - d. The impact of PMS on daily activities can be improved.
 - e. All of the above

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