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Abstract:

Many patients who have undiagnosed Seasonal Affective Disorder (SAD) may come into the pharmacy to try to self-treat their symptoms with over-the-counter and herbal drugs. Often, patients do not recognize their symptoms as a true depressive disorder since they are not constant. The pharmacist has the opportunity to talk to these patients, educate them on the disease state and explain that they do have options, both pharmacologic and non-pharmacologic. It also is important for pharmacists to point out any interactions that the herbal or over-the-counter medications may have with other medications and to refer patients to their physician for further treatment. Currently, the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV does not recognize SAD as a separate disorder but rather a specifier of Major Depressive Disorder (MDD). However, there are currently recommendations to include SAD as a distinct disorder in the DSM V, which is to be released in May 2013.

Etiology

Seasonal Affective Disorder, commonly referred to as SAD, is a mental health disorder that affects 4-6 percent of the general population; however, certain studies have found that the latitude of the individual's residence may affect these numbers.^{2,3} A person living in a colder climate with drastic weather changes between seasons is more likely to develop SAD than an individual who lives in a more temperate climate.⁴ It also is believed to affect women more than men, but this can be due to the interpretation of depression symptoms.³ Men oftentimes have different coping mechanisms than women, which can manifest in ways such as escapist behavior, substance abuse, and abusive or risky behavior. Because these symptoms are not readily recognized as signs of depression, the prevalence of SAD may be skewed in the direction of women. The etiology of SAD is presently unknown, but the current hypotheses include a circadian phase shift, melatonin imbalance, and the influence of neurotransmitters.⁴ A circadian phase shift can affect an individual's timing of physiological processes, which then can lead to widespread variance of normal patterns. The circadian phase shift has been found to lead to an imbalance of certain hormones, such as serotonin and dopamine, which regulate mood, making the patient more prone to a depressed feeling. An increase in melatonin secretion due to an altered circadian rhythm and lack of light exposure also may lead to symptoms. Finally, a decrease in the amount of serotonin from lack of light exposure in the brain may cause depression.⁵

SAD vs. Depression

The general feeling of unhappiness makes SAD resemble a major depressive episode, but there are important differences. Typically, depressed patients have decreased appetite, weight loss, and a lack of sleep. However, SAD depressive episodes are often atypical and include

reversed vegetative symptoms such as weight gain due to increased appetite, carbohydrate craving, morning fatigue, and hypersomnia.^{4,6,7} Additionally, SAD differs from major depressive disorder in that these symptoms are only present in the patient during the autumn and winter months, and patients are typically symptom-free during the spring and summer months. Although the etiology of SAD is unknown, the seasonal pattern is recognized by the DSM-IV as a specifier of major depressive disorder (MDD).⁸ The requirements for diagnosis are as follows: recurrent major depressive episodes with regular seasonal patterns, two consecutive years of symptoms, history of major affective disorder, and absence of other DSM-IV disorders.

Treatment

The most common and most effective non-pharmacological treatment for SAD is light therapy, which helps alleviate symptoms in around 80 percent of patients.⁹ It is recommended for a patient to sit in front of a light box for around 30 minutes a day, generally in the morning, in order to achieve the best results; however, it may require longer than 30 minutes in order for a patient to see a benefit.⁴ The current theory is that light therapy increases different neurotransmitters, such as serotonin, which works to improve mood. Also, bright light therapy can reset a patient's circadian rhythm, which has been found to be altered in SAD patients. The use of light therapy can help reduce the production of melatonin in SAD patients, which is higher than the general population's levels.³ Currently, more research is being done regarding the level of brightness of the light used in this therapy technique. It is possible that a different level of light brightness will produce more positive effects in SAD patients, making light therapy more beneficial. For example, a study by Strong et al. showed that blue-light therapy using narrow-band LED panels was superior to red-light therapy and equal to the current recommendation of 3,000-5,000 lux-hr/day of bright light.³ Also, a study by Anderson et al. showed similar results with a lower lux measurement from a short-wavelength LED light.¹⁰ Patients can use therapy standards that are currently in place, even though ongoing research is still being done for better outcomes. While this is the most commonly used treatment for SAD, some patients do not find success and need alternative therapy.

Patients who find light therapy too time intensive, or those who fail this therapy, may look for a different treatment strategy. A common supplement patients may use to help with depression symptoms is St. John's Wort. This herbal supplement has been found to have antidepressant effects similar to imipramine, citalopram and amitriptyline.¹¹ It works through nonselective inhibition of serotonin, dopamine, and norepinephrine uptake and increases dopaminergic activity in the prefrontal cortex. While all these effects sound promising and helpful for patients suffering with SAD, St. John's Wort should not be a first-line recommendation to patients due to its induction of the CYP3A4 enzyme and increase in p-glycoprotein levels. This increase in enzymatic activity can

lead to lower levels of concurrently used medications that are metabolized by CYP3A4 or are highly protein bound. Such substances include certain benzodiazepines, antidepressants, anticoagulants, antibiotics and hormone-based medications. These lower levels can lead to decreased efficacy of medications the patient may be on. It is important to discuss any herbal supplements a patient may be taking because of such interactions.

A second option that patients may use to self-treat is melatonin. This may seem counter-intuitive, since melatonin seems to produce atypical depressive symptoms such as hyperphagia and hypersomnia in patients, but the purpose of melatonin administration is attempting to alter the circadian rhythm back to a normal pattern.¹² Melatonin should be taken by patients in the afternoon or evening so levels will rise during the early stages of sleep instead of during the later stages and daytime. While this treatment option may work for some, it is not first-line therapy. It seems that the best results with melatonin are achieved in combination with sleep deprivation for a few nights. This may be difficult for patients to complete on their own outside of an experimental design and could cause more harm than benefit.

Another non-pharmacologic option that influences melatonin production is exercise. While this seems like an easy option for patients to alleviate their SAD symptoms, there is conflicting evidence regarding whether exercise increases or decreases melatonin production.⁴ Studying the benefits of exercise in the treatment of major depression, as well as SAD, is difficult because exercise cannot be isolated or studied in a tightly controlled manner. For example, varying amounts of endorphins are released, which can have differing impacts on each individual. Additionally, patients may benefit from the distraction that exercise provides as well as the social interaction. The timing of an exercise regimen does not seem to be directly correlated with the outcome of antidepressant effects. In various studies, patients participating in an exercise regimen at different times of the day had the same range of therapeutic outcomes. An outdoors aerobic exercise program, such as walking around the neighborhood, may be the best option for patients since it would not require equipment and does not need to be extremely strenuous. Additionally, this type of exercise can be done outside to receive the added benefit of natural sunlight.

The prescription pharmacologic treatment options for treatment of SAD are somewhat limited. These options may be tried in patients who have not benefited from light therapy or those who have eye diseases, such as macular degeneration, because the bright light exposure can cause further damage to the already injured or diseased eye.¹³ Those with other depressive disorders, or who have had previous success with antidepressants, also may benefit from pharmacologic treatments. Only one medication, bupropion, is approved for treatment of SAD, but other anti-depressants are used as off-label treatments. Psychotherapy is recommended to accompany any administration of these anti-depressants as well as light therapy.

Bupropion HCl extended release, brand name Wellbutrin XL®, is the only drug currently offered that is approved by the Food and Drug Administration (FDA) for the treatment of SAD.^{14,15} This dopamine reuptake inhibitor

also is approved for treatment in other psychological disorders such as MDD. The treatment regimen for SAD patients is usually 150 mg daily in the morning and may be titrated to 300 mg if needed. Prophylactic, or year-round treatment, of SAD with bupropion is usually reserved for patients with frequent episodes or those whose lives are significantly impaired by symptoms. Treatment is to be initiated in the autumn prior to the onset of SAD symptoms and continued through spring, when it is discontinued via tapered dosing. It is a pregnancy category C and should be avoided in pregnant or nursing women if possible. A black box warning advises that it may increase suicidal thoughts in patients aged 18-24 and should not be used in children. Bupropion should not be taken with ethanol, St. John's Wort, SAMe or kava kava, so pharmacists should be careful to make patients aware of these serious drug interactions. Adverse effects commonly (>10%) associated with bupropion HCl XL include headache, insomnia, dry mouth, nausea and nasopharyngitis.

Though not approved by the FDA for use in SAD therapy, selective serotonin reuptake inhibitors (SSRIs) also are commonly used as treatment. This drug class, however, does share the same black box warning as bupropion, stating that these drugs may increase suicidal thoughts in patients aged 18-24 and should not be used in children. A placebo-controlled multicenter trial investigated the effectiveness of sertraline as treatment for SAD. A total of 187 patients on doses of 50-200 mg daily were evaluated using physician and patient scales to measure SAD symptoms.⁶ Sertraline was shown to be significantly more effective than placebo and was overall fairly well-tolerated. The main side effects that patients experienced included nausea, diarrhea, insomnia and dry mouth. This study helped to suggest a role for sertraline and other SSRIs in SAD therapy. Based on the fact that SAD is symptomatically similar to MDD, it seems reasonable to test other anti-depressant medications for its treatment; however, SSRIs are used more commonly than monoamine oxidase inhibitors (MAOIs) or tricyclic antidepressants (TCAs) because of their less severe side-effect profiles.

Conclusion

Seasonal Affective Disorder is a relevant issue for many Americans. Pharmacists can play an important role in helping patients recognize and manage this disease state by working with patients and physicians to help determine the best individual treatment regimen, whether it be pharmacologic or non-pharmacologic. Because of the serious nature of the disorder and of the medications that may be used to treat SAD, it is very important for patients to take their medication exactly as prescribed. Additionally, it is important to discuss any herbal supplements a patient may be taking because many of these supplements have drug interactions of which the patient may not be aware. There is a vital role for the pharmacist in any disease state but especially in mental disorders because of the temptation for self-treatment in an attempt to alleviate symptoms. Such self-treatment measures have the potential to interfere with prescribed therapies, and quality of life can be negatively impacted. Patients also may be unwilling to discuss mental health problems with other health care professionals because of embarrassment or concerns about privacy. Pharmacists can use this as an opportunity to be accessible, understanding and helping patients suffering from Seasonal Affective Disorder.

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