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CASE REPORT

Effectiveness of vortioxetine for winter depression in bipolar disorder: A case report

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Abstract

Background: We present a case report on the efficacy of the short-term application of vortioxetine in managing winter depression in patients with seasonal bipolar disorder (BP). Standard treatment strategies for BP may not adequately address seasonal depressive symptoms during winter in patients with seasonal BP patterns. Depressive symptoms during winter may be linked to seasonal changes in serotonin transporter binding, such as a decrease in synaptic serotonin levels, necessitating alternative approaches. Although antidepressants, including vortioxetine, are effective in treating seasonal monopolar depression, their efficacy and safety in treating depression in patients with seasonal BP patterns remain unclear.

Case Presentation: This case report focuses on a 44-year-old male patient diagnosed with seasonal BP who had recurrent depressive episodes, specifically during winter. Notably, the patient had a significant decrease in recurrent episodes after short-term seasonal vortioxetine use without inducing mania or rapid cycling.

Conclusion: Our study highlights the potential effectiveness of a seasonal, short-term treatment strategy with antidepressants, including vortioxetine, for winter depression in individuals with BP.

KEYWORDS
SAD, seasonal affective disorder, SSRI, winter depression, vortioxetine

BACKGROUND

Bipolar disorder (BP) exhibits a distinct seasonal pattern, with approximately 25% of patients having symptoms that correlate with seasonal changes.[1] This pattern is often characterized by depressive symptoms, with the highest occurrence of seasonality-associated depressive episodes during winter.[1] Winter depression management in patients with BP with seasonal patterns poses a challenge and is difficult to prevent with standard strategies. In fact, a study showed that patients with BP exhibiting seasonal patterns are twice as likely to present with rapid cycling compared to those without such patterns.[2]

In addition, winter depression in patients with BP does not typically respond to standard treatments for bipolar depression.[1] One contributing factor may be the increased serotonin transporter binding observed during autumn and winter compared to spring and summer. This suggests that extracellular serotonin is more readily depleted during winter, potentially leading to depression.[3] These findings highlight the limitations of current therapeutic approaches, necessitating the exploration of alternative treatments for managing

depressive symptoms in winter in patients with BP with seasonal patterns.

Selective serotonin reuptake inhibitors (SSRIs) have been utilized in large randomized controlled trials to treat seasonal depression,[4] but their effectiveness and safety for seasonal depressive symptoms in individuals with BP remain to be demonstrated. Vortioxetine is an antidepressant with effects equivalent to those of SSRIs (e.g., escitalopram). Specifically, vortioxetine inhibits the serotonin transporter (SERT) and modulates a range of serotonin receptors, including serotonin-1A (5-HT1A), serotonin-1B (5-HT1B), serotonin-3 (5-HT3), and serotonin-7 (5-HT7). This action elevates extracellular serotonin (5-HT) levels in mood disorder-related brain regions, paralleling the effects of SSRIs (e.g., escitalopram).[5] In this report, we present a case of BP with a seasonal pattern in which limited use of vortioxetine during the winter months effectively prevented relapse without inducing manic symptoms.

CASE PRESENTATION

A 44-year-old man was diagnosed with Bipolar I Disorder after being hospitalized for a severe manic episode at the age of 20 years. After discharge, the patient had depressive symptoms annually, predominantly during winter. Despite treatment with a moderate dose of lithium carbonate and aripiprazole, with subsequent supplementation of lamotrigine, winter depression remained unmitigated. These recurrent depressive episodes significantly affected the patient's ability to work, leading to frequent absences and biennial job loss. The use of antidepressant medications was strictly avoided due to the risk of manic episode recurrence or rapid cycling. At the age of 40 years, medication dosages were increased to their maximum levels to ameliorate winter depressive symptoms: lithium carbonate to 1200 mg (serum concentration 0.66 mEq/L), aripiprazole to 30 mg, and lamotrigine to 200 mg (serum concentration 4.4 μg/ml). Nevertheless, the patient continued to have depressive episodes during winter and subsequently lost his job the following year.

Considering these challenges, vortioxetine (10 mg) was added exclusively during winter and was administered shortly before the onset of depressive symptoms, that is, depressed mood, inappropriate guilt, and loss of energy. Due to the recurrence of depressive states during a fixed period in winter, the timing of administration was determined based on the course of past episodes. The duration of treatment was based on randomized controlled trials for fluoxetine, which showed significant improvement in depressive symptoms after 5 weeks of treatment.[6] Before the initiation of treatment with vortioxetine, patients and medical institutions are informed that the prophylactic use of vortioxetine is off-label in Japan, and its administration was carried out only after obtaining their informed consent. Although light therapy was deliberated as a potential treatment option, it was ultimately not chosen due to cost constraints and challenges associated with procuring the necessary equipment.

In this case, winter depression was successfully managed with 4-week administration of vortioxetine. Given the potential for a manic transition, we opted to discontinue the administration. No adverse effects were observed on initiation, maintenance, or discontinuation of vortioxetine administration. After an annual 4-week administration of vortioxetine, the recurrence of winter-related episodes was averted completely. Notably, the patient did not exhibit any signs of mania or rapid cycling, indicating favorable tolerance and effectiveness of vortioxetine. The clinical course of the present case, including the details of pharmacotherapy, is shown in Figure 1.

DISCUSSION

In this case report, the administration of seasonal and short-term vortioxetine effectively prevented the recurrence of winter depression in a patient with BP. Although short-term use of antidepressants

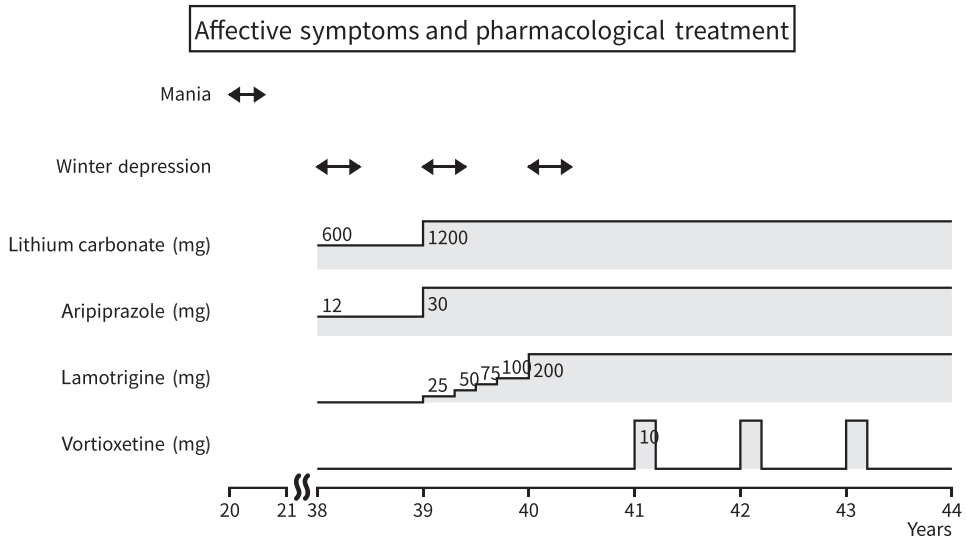

FIGURE 1 Clinical course of the present case. The graph shows the drug dosage in relation to affective symptoms.

could benefit BP depression without seasonal change,[7] general prescription guidelines discourage the use of antidepressant medications, including SSRIs, in the treatment of depression in patients with BP because of the risk of inducing manic episodes or rapid cycling.[8] However, the case presented here suggests that seasonal and short-term vortioxetine can be safely administered as a treatment approach for recurrent winter depression in patients with BP without inducing manic symptoms or rapid cycling.

The pronounced effect and safety of this approach may be due to significant diurnal and seasonal fluctuations in the serotonergic transporter function of patients with BP with winter depression. Studies have shown increased serotonin transporter binding in various brain regions during autumn and winter compared to that during spring and summer, with a negative correlation with average daily sunlight exposure.[3,9,10] This elevated serotonin transporter binding suggests a reduced serotonin level at the synaptic level.[3] Vortioxetine should compensate for this reduced serotonin level at the synaptic cleft to prevent depression without inducing mania or rapid cycling. Considering these findings, the use of vortioxetine to mitigate the reduction in serotonin levels during winter months may have supported the therapeutic outcomes in our patient. Vortioxetine has multimodal action, which includes a range of mechanisms contributing to its therapeutic effects. Its 5-HT1A agonist effect accelerates desensitization, and the combination of full or partial simultaneous antagonism of 5-HT1B, 5-HT1D, and 5-HT7 receptors inhibits negative feedback, thereby promoting the release of 5-HT.[11] Antagonism of 5-HT3 receptors releases glutamate in the midbrain, stimulating the release of 5-HT.[12] In addition, vortioxetine also increases norepinephrine and dopamine in the ventral hippocampus and nucleus accumbens. Beyond the extracellular serotonin hypothesis, these effects may also contribute to the improvement of winter depression.[5]

Administration of vortioxetine beyond winter may potentially induce manic states. This is because serotonin levels outside winter in patients with BP with a seasonal pattern are not reduced. Studies examining seasonal hospitalization rates for bipolar disorder have reported peaks of manic episodes in spring and summer, and depressive episodes in autumn and winter.[11–13] These imply that the risk of manic shifts due to antidepressants may be lower in winter compared to spring and summer. Consequently, we propose that long-term continuous vortioxetine use should be avoided.

In summary, with careful clinical surveillance of potential manic or hypomanic episodes, the administration of seasonal and short-term vortioxetine has emerged as a viable treatment strategy for seasonal bipolar depression during winter.

AUTHOR CONTRIBUTIONS

Y.Y. managed the literature search, and wrote and revised the first draft of the manuscript. S.K. interviewed and treated the patient, and rewrote and revised the manuscript. H.K. and G.S. wrote and revised parts of the manuscript. All authors contributed to and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The author declares no conflict of interest.

DATA AVAILABILITY STATEMENT

N/A.

ETHICS APPROVAL STATEMENT

This study was conducted according to the principles of the Declaration of Helsinki.

PATIENT CONSENT STATEMENT

Written informed consent for presentation of the patient's clinical course was given by the patient.

CLINICAL TRIAL REGISTRATION

N/A.

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