Lacosamide Precipitated Neutropenia in a Patient with Bipolar Disorder and Comorbid Epilepsy

Sir,

Epilepsy is common in patients with bipolar disorder.[1] While anti-epileptic agents are commonly used for the treatment of bipolar disorder, one needs to be cautious about their side effects when they are used in combination with other psychotropic medications, due to the possibility of additive side effects. In this case report, we describe a patient with bipolar disorder and complex partial seizures, on treatment with clozapine, who developed neutropenia after initiating lacosamide.

CASE REPORT

Mr. A, a 20-year-old male, had a global developmental delay and was diagnosed as having mild intellectual developmental disorder. From the age of 13 years, he had multiple episodes of mania and was diagnosed as having bipolar affective disorder (International Classification of Disorders-10). In view of treatment resistance, he was on treatment with clozapine 200 mg/day for 2 years and had achieved partial remission of symptoms. He also had poorly controlled complex partial seizures with secondary generalization since the age of 5 years. He had a poor response to phenytoin, carbamazepine, and levetiracetam and was on valproate 1000 mg/day and clobazam 10 mg/day with a partial response. In view of the poor control of epilepsy, lacosamide was considered as add-on treatment and was started at 100 mg/day.

As Mr. A was on treatment with clozapine, his total and differential white blood cell counts were regularly monitored. After 10 days of initiation of lacosamide, he developed neutropenia with absolute neutrophil count (ANC) of 1300 cells/μl. As neutropenia is a known adverse effect of clozapine, it was stopped. However, even after 15 days of stopping clozapine, his ANC remained persistently low, reaching a nadir of 1000 cells/microliter as the dose of lacosamide was increased to 200 mg/day. Suspecting lacosamide to be the causal agent, it was tapered and stopped. After 2 days of stopping lacosamide, the ANC returned to normal and remained so (>3000) for 6 months. Naranjo Adverse Drug Reaction Probability Scale[2] score was 6, indicating probable causality of lacosamide

having precipitated neutropenia. He was started on valproate 1000 mg/day and haloperidol 20 mg/day. He did not have significant worsening of symptoms with the change of medication.

To the best of our knowledge, this is the first case report suggesting lacosamide precipitated neutropenia in a patient with bipolar disorder. He developed neutropenia following treatment with lacosamide, which reversed after it was stopped. While one cannot rule out the confounding effect of clozapine or valproate, it is important to note that he was on treatment with these medications for 2 years, and hence, the neutropenia is less likely to be due to these medications as clozapine-induced agranulocytosis is less prevalent after 2 years of therapy.[3] Due to the serious nature of the side effect, we did not attempt re-challenge with lacosamide. As patient did not have significant worsening of symptoms when clozapine was stopped, he was maintained on haloperidol and valproate, and we did not restart clozapine.

Neuropsychiatric side effects are reported with lacosamide,[4,5] but neutropenia and agranulocytosis are uncommon. Lacosamide is being added to the Food and Drug Administration Adverse Event Reporting System watch list for agranulocytosis,[6] and our report adds to the existing literature. As patient improved after stopping lacosamide and drug-induced neutropenia is the most common cause of idiopathic neutropenia,[7] we did not evaluate for other causes of neutropenia using invasive measures such as bone marrow examination. Hence, one cannot rule out the possibility of other causes co-occurring at the same time.

To conclude, one needs to be cautious while using lacosamide in patients with comorbid epilepsy and psychiatric disorders as psychotropics also carry the risk of neutropenia. When using lacosamide along with other psychotropics which can cause neutropenia, such as clozapine or valproate, one needs to be careful and regular monitoring is advised in such situations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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