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Interaction Between Oxcarbazepine and Long-Acting Aripiprazole Leading to Relapse of Bipolar Disorder

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Bipolar disorder is a chronic psychiatric condition characterized by alternating episodes of mania and depression. Long-acting injectable antipsychotics, such as aripiprazole, are increasingly used for mood stabilization in bipolar disorder due to their ability to ensure medication adherence and provide consistent therapeutic levels.[1] Aripiprazole is approved by the US Food and Drug Administration (FDA) for the treatment of bipolar I disorder, providing a valuable option for managing this condition.[1] However, its metabolism by cytochrome P450 (CYP) enzymes 2D6 and 3A4 can be influenced by concomitant medications that induce or inhibit these enzymes.[2] This case report highlights the interaction between aripiprazole and oxcarbazepine, a known inducer of CYP3A4, resulting in subtherapeutic levels of aripiprazole and recurrence of manic symptoms in a patient with bipolar I disorder.

Case Report

A 45-year-old woman with a history of bipolar I disorder presented to the inpatient unit with manic and depressive symptoms, including suicidal ideation. The patient's clinical history revealed longstanding treatment with long-acting paliperidone for mood stabilization, which was discontinued 3 months prior due to side effects. Subsequently, aripiprazole 400-mg monthly injections were initiated in the outpatient setting, including completion of the required oral overlap period. However, the patient was admitted for mania after the administration of the long-acting injection. The patient was also on oxcarbazepine 1,200 mg/d, which was part of her home medication regimen for mood stabilization.

Upon admission, the patient exhibited symptoms of mania, including distractibility, irritability, flight of ideas, pressured speech, and hyperverbal communication. Laboratory investigations, including liver and kidney function tests, were within normal limits. The patient's medication compliance was verified through pharmacy records and patient self-report.

The patient's aripiprazole levels were measured and found to be 54 ng/mL, significantly below the therapeutic range of 150–300 ng/mL.[2] Considering the known interaction between oxcarbazepine and aripiprazole metabolism, oxcarbazepine was tapered and discontinued during the hospital stay.[3] Despite this adjustment, the patient continued to exhibit manic symptoms. Given the long half-life of aripiprazole and the time needed to reach steady-state levels after discontinuation of oxcarbazepine, lithium was introduced for its acute antimanic effects.[4] Upon discharge, the patient's mood had stabilized, and she was discharged with plans for outpatient follow-up, serum level monitoring, adjustment of medications, and a long-term treatment plan involving either lithium or long-acting aripiprazole.

Discussion

This case underscores the importance of considering drug-drug interactions in patients with bipolar disorder receiving long-acting injectable aripiprazole. The induction of CYP3A4 by oxcarbazepine significantly reduced aripiprazole levels, leading to a recurrence of manic symptoms.[5] Clinicians must be vigilant about potential interactions and monitor therapeutic drug levels to ensure efficacy. For oral aripiprazole, the FDA recommends doubling the dosage of this medication in patients who are taking strong CYP3A4 inducers.[6] Additionally, the introduction of lithium was necessary due to the time required for aripiprazole levels to normalize, given its long half-life. Lithium remains a cornerstone treatment in bipolar disorder despite its limited immediate benefits, highlighting its clinical utility in managing acute manic episodes while waiting for other medications to reach therapeutic levels.[4]

Moreover, oxcarbazepine could potentially be used to manage adverse effects from supratherapeutic levels of medications metabolized by CYP3A4. However, careful monitoring and individualized treatment plans are essential to optimize patient outcomes and avoid adverse interactions.[7] Future studies should investigate the prevalence of such interactions in larger populations and explore strategies for managing drug interactions to optimize treatment outcomes in bipolar disorder. Additionally, research should focus on developing guidelines for the monitoring and adjustment of antipsychotic doses in the presence of enzyme-inducing medications.

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