High-Dose Olanzapine for Bipolar Depression: Proceed With Caution

To the Editor: High-dose olanzapine has gained momentum as an effective pharmacotherapy in individuals diagnosed with treatment-resistant schizophrenia, yet there is little evidence regarding its safety.[1–4] Olanzapine is also indicated for the treatment of bipolar disorder; however, few guidelines are available regarding dosing of olanzapine for individuals with treatment-resistant bipolar disorder. The following case report highlights the need for increased guidance in the management of treatment-resistant bipolar disorder.

Case report. Mr A is a white man with a long history of psychiatric disorders, specifically bipolar I disorder (*DSM-IV-TR* criteria). He also has a diagnosis of posttraumatic stress disorder and a history of alcohol dependence and cannabis use (*DSM-IV-TR* criteria); however, he is reported to have not used cannabis for over 2 years. Mr A complained of severe mood swings including daily anxiety and panic attacks several times weekly and paranoia. After failing treatment with several other mood stabilizers and antipsychotic medications and declining treatment with clozapine, olanzapine was prescribed by his primary care provider. Olanzapine was increased over the course of 4 weeks to 80 mg/d (40 mg oral twice a day) to control his symptoms. Mr A reported that the anxiety and panic attacks did not occur as frequently; however, he was now experiencing erectile dysfunction, which was believed to be due to high-dose olanzapine. Despite the erectile dysfunction, Mr A asked to maintain high-dose olanzapine, as he felt the benefits outweighed the risks. Over the following 2 weeks, his depressive symptoms fluctuated, and Mr A reported that he was still struggling with posttraumatic stress disorder but managing better with other symptoms.

At the time of his presentation to the inpatient psychiatry ward, 5 weeks after the prescription of high-dose olanzapine, Mr A reported increasing anxiety, depression, paranoid delusions, guilt, and suicidal ideation. He also described symptoms similar to hyperreligiosity. Mr A denied use of any illicit drugs or alcohol prior to arriving at the hospital. The olanzapine dose was reduced to 40 mg/d (20 mg oral twice a day). Following this reduction, he showed immediate improvement in symptoms and felt significantly better. Mr A was provided with education regarding the benefits and risks of high-dose olanzapine and reported that this was "new information," and he had not been adequately told of the dangers. At discharge, Mr A was stable on 40 mg/d of olanzapine.

Although some studies have indicated the benefits of high-dose olanzapine, the dose is typically in the range of 20–60 mg/d rather than 80-mg/d, as was prescribed to Mr A.[1,2] Greater guidance is needed to clarify procedures involved in dose escalation of olanzapine and monitoring of side effects. Further clinical trials highlighting the benefits and risks of high-dose olanzapine with a foundation on understanding mechanisms of treatment resistance should be a priority.

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