Treatment of Acute Mania With Aripiprazole in an Older Adult With Noted Improvement in Coexisting Parkinson's Disease

Sir: We describe a patient in a skilled nursing facility who had symptom exacerbation of bipolar disorder while taking divalproex and olanzapine. The patient was treated with a combination of aripiprazole and divalproex after discontinuation of olanzapine.

Case report. Ms. A, a 64-year-old single, white, female resident of a skilled nursing facility, was admitted to the inpatient psychiatric unit due to psychotic symptoms characterized by delusions (claims that she had been sexually active in the nursing facility and was pregnant) and impaired judgment. The patient had a DSM-IV diagnosis of bipolar affective disorder with psychotic symptoms. Her past medical history was significant for hypertension, hypothyroidism, obesity, and Parkinson's disease (still had tremor and akinesia). Her past psychiatric history was significant for multiple previous psychiatric admissions due to psychotic symptoms, and she attended a continuing day treatment program prior to admission to the skilled nursing facility. At admission, her medications included olanzapine, 5 mg, at bedtime; a daily multivitamin; acetylsalicylic acid, 81 mg/day; ranitidine, 150 mg/day; docusate sodium, 100 mg, twice daily; tolcapone, 100 mg, 3 times daily; pramipexole dihydrochloride, 0.25 mg, 4 times daily; carbidopa-levodopa, 25/100 mg, 1 tablet 4 times daily, and 50/200 mg, 1 tablet every 8 hours; divalproex, 500 mg, twice daily; and levothyroxine sodium, 50 µg/day.

On the mental status examination, Ms. A was alert and oriented in all spheres with clear, rapid speech. Her psychomotor activity was increased. She had manic features, including grandiose delusions with sexual preoccupation. She had circumstantiality and flight of ideas. Her attention span was limited, and her concentration, judgment, and insight were impaired. Her Mini-Mental Status Examination[1] revealed a score of 21 out of 30. Ms. A's vital signs revealed elevated systolic blood pressure and tachycardia with a heart rate of 112 beats/min. The results of the laboratory tests, which included a complete blood count and electrolyte and thyroid-stimulating hormone levels, were within normal limits.

Olanzapine was discontinued, and the patient began taking aripiprazole starting at 7.5 mg/day, which was subsequently increased to 30 mg/day. After gradual titration, the patient began taking a dosage of 40 mg/day of aripiprazole. A trial of discontinuation of divalproex did not help, resulting in the patient's continuing to take divalproex, 500 mg, twice daily. Ms. A's psychotic symptoms completely remitted; she became more hopeful and was discharged back to the skilled nursing facility. She continues to do well on these medications. In addition, there was noted improvement in Ms. A's Parkinson's disease, specifically tremor and akinesia, without adjustment of her antiparkinsonian medications. The patient has continued to be free of manic symptoms for the last 13 months.

Studies document the presence of manic symptoms in 6.5% to 18% of elderly depressed individuals.[2] There is an increasing awareness among primary care physicians about the importance of screening for and treating bipolar disorder in patients who present with depressive symptoms. This case highlights the use of agents other than divalproex, lithium, and olanzapine in the treatment of bipolar illness. Aripiprazole, referred to as a dopamine system stabilizer (D_2 partial agonist/antagonist), is one such agent that may be used. Although the drug has not yet received approval for treatment of bipolar illness from the U.S. Food and Drug Administration (FDA), clinical trials have demonstrated efficacy in young adults.[3,4] Studies in older adults are usually done as a follow-up to studies in younger adults.

In a phase 3, multicenter, double-blind study (study 1),[5] 262 patients with acute mania were randomized to treatment with aripiprazole, 30 mg, (N = 130) or placebo (N = 132) for 3 weeks. Aripiprazole produced a statistically significant improvement in Young Mania Rating Scale scores beginning on day 4 ($p < .005$), which was maintained throughout the 3-week study. Twice as many aripiprazole-treated patients responded to treatment compared with placebo-treated patients (40% vs. 19%, respectively;

p = .01).[5] Discontinuations due to adverse events were similar between the aripiprazole and placebo groups (11% and 13%, respectively). Aripiprazole was efficacious, safe, and well tolerated in patients with bipolar disorder experiencing an acute manic or mixed episode. Additional trials have been conducted but have not yet been published in the peer-reviewed literature. The improvement in Ms. A's Parkinson's disease symptoms was an incidental finding. The improvement in parkinsonian symptoms may be the result of partial agonist activity of aripiprazole at the dopamine receptor.

Recently, risperidone and quetiapine were granted FDA approval for the treatment of acute mania. Olanzapine has received FDA approval for maintenance treatment in addition to the acute mania indication. It is probable that aripiprazole might have an acute mania indication, thus increasing the number of safe treatment options available in the primary care setting for geriatric patients with bipolar disorder. Aripiprazole is not a sedating medication and has not been noted to worsen cognition. Aripiprazole is well tolerated, and there are no clinically significant drug-drug interactions of concern with the combination of multiple medications Ms. A was taking either prior to or after the switch to aripiprazole. In addition, it is our opinion that drug-drug interactions were not a reason for lack of efficacy of olanzapine. In older adults taking multiple medications, drug-drug interactions are a potential concern, as these medications for bipolar disorder are prescribed long-term. Bipolar disorder is a lifelong condition and requires long-term medication treatment. Otherwise, there is a high risk of relapse.

This clinical case demonstrates that there are now newer agents available for the management of bipolar disorder, although some are being used off-label at this time.

Dr. Madhusoodanan has served as a consultant for and on the speakers or advisory boards of Eli Lilly, Bristol-Myers Squibb, AstraZeneca, and Janssen. Dr. Gupta and Ms. Chohan report no financial affiliation or other relationship relevant to the subject matter of this letter.

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