Schizophrenia With Decompensation on Clozapine With Pramipexole

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Clozapine is an atypical antipsychotic accepted as the medication of choice for individuals with treatment-resistant schizophrenia. The primary actions of clozapine include antagonizing effects on dopamine and serotonin receptors.[1] In contrast, dopamine agonists represent a medication class used to treat neurologic disorders, including restless leg syndrome (RLS). There are case reports[2,3] in the literature describing first-time episodes of psychosis in patients taking dopamine agonists; however, literature about the concurrent use of a dopamine agonist with an antipsychotic is scarce.

Case Report

A 56-year-old woman with a history of schizophrenia previously well controlled on clozapine for 30 years presented to a community hospital with acute paranoia, religious and somatic preoccupation, and erratic behavior. Three months prior to her psychiatric decompensation, she was started on pramipexole 0.5 mg daily to treat symptoms of RLS. Previous psychiatric history was significant for multiple hospitalizations and past failed medication trials; however, after initiating treatment with clozapine, she had no further hospitalizations over the past 30 years until this admission.

Initial laboratory tests included blood cell count, serum electrolytes, liver and renal function, thyroid-stimulating hormone, urinalysis, ammonia, urine drug screen, inflammatory markers, syphilis and HIV antibody, and magnesium levels. A head computed tomography scan and electrocardiogram were also performed. The medical workup and physical examination were unremarkable for a cause of her acute decompensation. Clozapine and norclozapine levels were found to be 392 mcg/L and 216 mcg/L, respectively, at the time of admission (clozapine therapeutic level range, 350–1,000 mcg/L; norclozapine reference range, 25–400 mcg/L). It was theorized that the addition of pramipexole contributed to the patient's psychosis, as there were no other recent medication changes, acute stressors, or changes to her daily living routine, and medical issues were effectively ruled out. Accordingly, pramipexole was discontinued. There was minimal report of RLS nocturnally while hospitalized, and these symptoms did not appear to worsen acutely.

At the beginning of the hospital course, the patient's symptoms failed to improve and required several medication interventions. On day 5 of her hospitalization, valproic acid 250 mg 3 times daily was initiated to target impulsivity, distractibility, and disorganized thought processes. The valproic acid level obtained 3 days after initiation was 89 μ/mL (reference range, 50–100 μ/mL). Additionally, the patient continued to have symptoms despite titration of clozapine to 350 mg, a higher dose than what she was taking prior to admission. Due to the possibility of a reduced efficacy of clozapine as well as the risk of agranulocytosis with rapid dose escalation, fluphenazine 2 mg nightly was added to target her residual psychotic symptoms. The patient demonstrated no further signs of psychosis on clozapine, valproic acid, and fluphenazine and was discharged home to her family after 17 days of hospitalization.

Discussion

There is limited literature on the use of dopamine agonists in patients with a history of a psychotic disorder while successfully stabilized on an antipsychotic. Interestingly, a small pilot study[4] concluded that the addition of pramipexole to an antipsychotic medication in schizophrenia and schizoaffective disorder may decrease positive and negative symptoms. Another small study[5] suggests a dopamine agonist, bromocriptine, can be safely used in patients at risk for psychotic illnesses if they are clinically stable and maintained on an antipsychotic. However, there remains a general paucity of research regarding this topic to guide providers in the treatment of patients for whom both classes of medications may be indicated. Although pramipexole was the only medication trialed in our case, it may be safer to begin with alternative non–dopamine agonist medications in patients with schizophrenia. Additionally, communication between primary care providers and specialists is imperative to identify and decrease the risk of medication interactions.

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