Lurasidone-Induced Dystonia

To the Editor: Lurasidone is a novel antipsychotic that differs from other atypical antipsychotics in having a potent 5-hydroxytryptamine 7 (5-HT_7) and 5-HT_{1A} receptor activity.[1,2] Dystonic reactions have not been commonly described, with only 1 report[3] of glossopharyngeal dystonia with lurasidone-fluoxetine combination. We present the case of a patient who developed episodes of recurrent oculogyric crises with lurasidone use.

Case report. Ms A is a 28-year-old woman with a 12-year history of schizophrenia (*DSM-5* criteria). She has had several hospital admissions with acute psychosis related to partial compliance with antipsychotics following intolerance of side effects. Ms A has received trials of risperidone, quetiapine, aripiprazole, and amisulpride. While taking amisulpride, Ms A experienced jaw stiffness and oculogyric crisis, so the medication was stopped, and lurasidone 40 mg/d was initiated. Her psychotic symptoms subsequently worsened with increased auditory hallucinations and paranoia, so the lurasidone dose was increased to 80 mg/d. Three weeks after the increased dose was initiated, Ms A presented to the emergency department with an oculogyric crisis. She was administered benztropine 2 mg with good effect and was admitted to the hospital for further monitoring and treatment of her psychosis. Ms A requested to remain on lurasidone and was maintained on 80 mg for 7 days with no recurrence of dystonia.

The lurasidone dose was uptitrated, aiming for a better antipsychotic response. With each dose increment of 40 mg, Ms A experienced a mild episode of oculogyric crisis within 3 to 4 days, which resolved rapidly with benztropine 2 mg. Given that each oculogyric episode resolved rapidly and the patient preferred to keep taking lurasidone, the dose increment increase continued. On a dose of 160 mg/d, Ms A experienced the most severe episode, which resolved 45 minutes after she was given benztropine 2 mg. As a consequence of the recurrent oculogyric crises, lurasidone was stopped, and she was started on monthly depot aripiprazole (after establishing tolerability) with no further dystonic reactions and good antipsychotic response.

Oculogyric crisis is an acute dystonic reaction characterized by conjugate upward eye deviation usually associated with antipsychotic medications. Drug-related risk factors include high potency, high doses, and rapid dose increments. The pathophysiology of acute dystonia is poorly understood. Hyperdopaminergic mechanisms are widely supported; research[4] has suggested that compensatory increase in dopamine turnover in response to the antipsychotic-induced dopamine blockade contributes to the pathogenesis of acute dystonic reactions. This increase in dopamine is short lived and is replaced by postsynaptic supersensitivity[4] and reduction of dystonic episodes. However, hypodopaminergic mechanisms have also been implicated, as other studies[5] have suggested that acute dystonic reactions occur due to dopamine hypofunction, leading to a relative hyperactivity of cholinergic mechanisms.

Ms A's first episode of oculogyric crisis occurred 3 weeks after increasing lurasidone from 40 mg to 80 mg orally, with further episodes occurring with each dose increase. The most severe episode occurred at the highest dose of 160 mg/d. Each episode was responsive to benztropine, and the episodes resolved completely when lurasidone was stopped. The reaction scored an 8 on the Naranjo Adverse Drug Reaction Probability Scale,[6] indicating that lurasidone was the probable cause of Ms A's oculogyric crises.

Ms A was subsequently stabilized on aripiprazole depot with no further dystonic episodes, despite that aripiprazole has similarly low anticholinergic properties and is known to cause acute dystonias.[5] We postulate that her dystonic reactions were due to rapid dose increment and lurasidone's additional proserotonergic effects, as high serotonin levels are also implicated in dystonia.[7]

Conventionally, first-generation antipsychotics are more implicated in acute dystonia. However, newer second-generation antipsychotics like lurasidone can also cause dystonia, and clinicians should be aware of this, especially when serious dystonic reactions have occurred in the same patient with previous antipsychotic use.

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