Is Quetiapine the Best Option for Patients With Antipsychotic-Induced Disorders of Extrinsic Ocular Motricity?

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Antipsychotic medications (APs) can provoke antipsychotic-induced disorders of extrinsic ocular motricity (AIDEOM) such as oculogyric crisis (OGC) and blepharospasm (BS) due to an interference in the extrapyramidal system, mediated by dopamine receptor D_2 (DRD2) antagonism. OGC is an acute dystonic deviation of the eye bulbs, commonly upward, lasting minutes to hours. BS is a repetitive, persistent spasm of the orbicularis oculi muscle. AIDEOM are more common in young males taking high doses of high-potency first-generation APs (FGAs).[1] The association with atypical APs remains loose, with no systematic studies available but only case reports on olanzapine,[2] quetiapine,[3] aripiprazole,[4–6] amisulpride,[7] ziprasidone,[8] risperidone,[9] and sertindole[10] for OGC and with olanzapine[11,12] or combined olanzapine-quetiapine[13] for BS.

The management of AIDEOM is uncertain, especially when provoked by atypical APs, and includes anticholinergic medications (eg, biperiden, procyclidine diphenhydramine, trihexyphenidyl), AP switching (toward a low-potency FGA or an atypical AP), and dose reduction.[1]

Here, 3 cases of AIDEOM in schizophrenia, remitting after switch to a quetiapine monotherapy, are reported. Per the World Health Organization–Uppsala Monitoring Centre[14] causality assessment system, the causal relationship between AP treatment and AIDEOM was probable. Diagnoses of AIDEOM were confirmed with ophthalmologic and neurologic evaluations, including brain magnetic resonance imaging.

Case 1

Mr A is a 27-year-old African man, presenting sporadic commentating voices, executive deficits, abulia, and emotional flattening, with no delusions. When hospitalized for the first and only time upon disease onset, an oral treatment with aripiprazole was started, and he developed OGC once a week lasting 30 seconds each. OGC worsened in intensity, frequency, and duration after switching to long-acting injectable formulation (400 mg/4 weeks), lasting several minutes and occurring 3 to 4 times/week. Biperiden 8 mg/day was ineffective, and no spontaneous remission of OGC was observed. After 4 months, the dose was reduced to 300 mg/4 weeks, leaving OGC unchanged. Quetiapine extended release, titrated to 200 mg/day resolved OGC with no relapse of psychotic symptoms or body mass index increase.

Case 2

A 25-year-old White man, known for episodes of paranoid delusions with congruent auditory hallucinations and obsessive-compulsive symptoms, developed parossistic BS while well stabilized with amisulpride 200 mg. The treatment was changed for lurasidone 60 mg, with persistence of the same phenomenon. BS resolved after switching to quetiapine extended release titrated to 200 mg. Because of a low-severity relapse of paranoid thinking, quetiapine was effectively uptitrated to 400 mg/day without BS relapse.

Case 3

A 20-year-old man, presenting abulia, anhedonia, social retirement, and mystic delusions, developed OGC lasting 2 minutes each several times per week with amisulpride 800 mg, persisting after down-titration to 400 mg. He was previously treated with risperidone 8 mg/day, not tolerated for loss of libido; aripiprazole 30 mg/day, ineffective on positive and negative symptoms; and clozapine (400 mg/day), not tolerated for sedation and sialorrhea. Quetiapine 600 mg was effective for a complete resolution of OGC, but low-severity positive and negative symptoms remained.

Discussion

AIDEOM are often neglected but can compromise quality of life and adherence to treatment. The cases presented here are in line with past evidence that AIDEOM can occur with atypical APs, more commonly

in young men.[1] High-potency DRD2 antagonists such as amisulpride[7] and lurasidone and the partial agonist aripiprazole[4–6] were more often responsible for AIDEOM in previous literature and in the patients presented here. Quetiapine could represent the first choice for patients with AIDEOM, because mechanism of action relies more on 5-HT_{2A} receptor and 5-HT_{1A} receptor binding than on DRD2 antagonism, in line with another case report.[15] Moreover dosage, mirroring the occupancy of DRD2, is relevant, and a high dose of quetiapine provoked AIDEOM in previous reports.[3,13]

Our experience suggests that anticholinergics are not effective (notwithstanding the impact on cognition and vigilance), and that once AIDEOM ensues, switching to a different AP is a better strategy compared to dose reduction. Sedation and metabolic syndrome are a concern with quetiapine but can be tempered using a low dose, especially in the maintenance phase. Clozapine is a suitable alternative to quetiapine, which should be relegated to second-line treatment due to the unfavorable side effects profile.

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