








Case Report

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ACUTE HICCUPS FOLLOWING ARIPIPRAZOLE TREATMENT IN A PATIENT WITH AUTISM SPECTRUM DISORDER AND CATATONIA: A DETAILED CASE REPORT AND MANAGEMENT CHALLENGES

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Abstract

Aripiprazole is a widely used second-generation antipsychotic known for its favourable side effect profile. Although generally well-tolerated, rare adverse reactions, such as hiccups, have been documented. We present the case of a 28-year-old male with autism spectrum disorder and psychosis with catatonic features who developed acute, persistent hiccups shortly after starting aripiprazole treatment. The patient, hospitalised for catatonia and psychotic symptoms, was initially treated with benzodiazepines and later with aripiprazole. Within 24 hours of the dose increase to 10 mg/day, he developed continuous hiccups that significantly interfered with oral intake. Aripiprazole was identified as the most likely cause; thus, the medication was discontinued, and chlorpromazine 25 mg twice daily was administered for symptomatic relief. The hiccups completely resolved within 48 hours. This case highlights that hiccups may occur across a range of aripiprazole doses and typically subside after discontinuation. Young male patients with developmental disorders and those concurrently receiving benzodiazepines may be at greater risk. Chlorpromazine may serve as an effective symptomatic option for managing aripiprazole-induced hiccups when benzodiazepine dose reduction is not feasible.

Keywords: Aripiprazole, autism spectrum disorder, catatonia, hiccup.

Introduction

Aripiprazole is a second-generation antipsychotic with partial agonist activity at dopamine D2 and serotonin 5-HT_{1A} receptors and antagonism at 5-HT_{2A} receptors. Its tolerability profile is generally favourable compared with other antipsychotics, with lower rates of metabolic adverse effects, extrapyramidal symptoms, and hyperprolactinemia.¹

Hiccups, defined as involuntary, spasmodic contractions of the diaphragm and intercostal muscles, are usually benign and self-limiting; however, they can become persistent or intractable when centrally mediated. Several pharmacological agents, including corticosteroids, benzodiazepines, and antipsychotics, have been implicated as potential causes.² Aripiprazole-induced hiccups case series have been reported in the literature, but the patients' characteristics and treatment methods vary.³

Here, we present a detailed case of a young male patient with autism spectrum disorder and psychosis who developed acute hiccups after aripiprazole treatment. We discuss diagnostic considerations, potential mechanisms, and management strategies.

Case Report

A 28-year-old single male, high-school graduate, unemployed, living with his mother, was followed for autism spectrum disorder and atypical psychosis. He was admitted to our psychiatric inpatient unit after abruptly discontinuing clozapine 500 mg/day within one week because of frequent falls resulting in multiple lower extremity fractures. On admission, he presented with catatonic symptoms, which were mutism, generalised muscular rigidity, refusal of oral intake, and posturing.

The initial work-up, including complete blood count, renal and thyroid function tests, electrolytes, electroencephalography (EEG), and cranial computerised tomography (CT), revealed no abnormalities. Brain magnetic resonance imaging (MRI) could not be performed due to orthopaedic implants from previous surgeries. The Bush-Francis Catatonia Rating Scale (BFCRS) score was 19, and the Clinical Global Impression (CGI) severity score was 7. Because lorazepam was unavailable in the market, diazepam 20 mg/day was initiated and titrated up to 40 mg/day. His catatonic symptoms were partially remitted.

By day 7, he developed psychotic symptoms, including talking to himself, staring at a fixed point, and stating he was "searching for himself on Google." Olanzapine 10 mg/day was added, and diazepam dosage decreased to 30 mg/day as catatonia improved. By day 15, however, he developed sedation, psychomotor slowing, mutism, posturing, and urinary incontinence. BFCRS score rose to 21, and olanzapine was discontinued.

Electroconvulsive therapy (ECT) was considered but deferred by the orthopedist because of active, unstable lower extremity fractures. Diazepam was replaced with lorazepam, titrated up to 12 mg/day.

Approximately 15 days later, catatonic symptoms resolved, but psychotic symptoms reemerged, including visual hallucinations and mystical delusions as “communicating with angels and paradise”. Given the history of recurrent falls under clozapine treatment, lack of response to risperidone and paliperidone, and limited response to olanzapine, aripiprazole 5 mg/day was started and increased to 10 mg/day after three days.

Soon after increasing aripiprazole treatment to 10 mg/day, he developed acute, day-long hiccups that impaired oral intake. Cardiac, pulmonary, and neurological evaluations were unremarkable, and repeat cranial CT remained normal. In addition, gastrointestinal etiologies (reflux-related symptoms and abdominal discomfort), metabolic abnormalities (electrolyte imbalance, renal/hepatic dysfunction), infectious signs (fever, inflammatory markers), and other non-drug-related triggers were systematically considered and not supported by clinical assessment or laboratory results. Based on the temporal association and exclusion of other possible causes, aripiprazole-induced hiccups were suspected, and the drug was discontinued on the second day of symptoms. Chlorpromazine 25 mg was administered twice daily for symptomatic relief, and the hiccups resolved completely within 48 hours.

He remained clinically stable and continued on lorazepam 4 mg/day for three weeks. The plan was to reduce the benzodiazepine dose gradually. During his follow-up, olanzapine was administered again due to ongoing psychotic symptoms. No recurrence of hiccups was observed. His final CGI severity score was 5, and global improvement was rated as 2. The patient was discharged with olanzapine 5 mg/day and lorazepam 3 mg/day, and continues to be followed as an outpatient.

Discussion

Aripiprazole-related hiccups, though rare, are clinically important because they may interfere with nutrition, hydration, and medication adherence. In a systematic review of 29 cases, it was reported that hiccups most frequently appeared within 1–2 days of starting or increasing aripiprazole and resolved within 1–4 days after discontinuation, regardless of dose (2.5–30 mg/day).³ Our patient’s presentation, onset shortly after starting aripiprazole treatment, and complete remission within 48 hours of discontinuation, align with these findings.

Young age, male sex, and neurodevelopmental disorder may increase susceptibility.³ Additionally, benzodiazepine co-administration has been associated with a marked increase in hiccup risk. Benzodiazepines enhance GABA(A) receptor activity, which may facilitate activation of the medullary “hiccup reflex arc.” A retrospective study reported a 70-fold increased risk in patients receiving both aripiprazole and

benzodiazepines, particularly in men.^{4,5} In our case, the benzodiazepine dose could not be reduced due to ongoing catatonic symptoms, which may have augmented the risk of hiccups.

The most effective management strategy is the reduction or discontinuation of aripiprazole, leading to resolution in most cases within a few days.^{6,7} Adjunctive pharmacological measures, such as chlorpromazine, gabapentin, or baclofen, can be used when symptoms are severe or persistent.^{5,8,9} In our patient, discontinuation of aripiprazole combined with chlorpromazine administration resulted in rapid improvement.

Persistent hiccups (>48 h) in primary care should prompt a brief structured assessment, including symptom severity, impact on oral intake, and a focused medication review, with particular attention to recently initiated or dose-escalated antipsychotics and concomitant benzodiazepines. Red flags such as focal neurological findings, cardiopulmonary symptoms, fever, persistent vomiting, weight loss, or inability to maintain oral intake should warrant urgent referral. Supportive measures and empiric treatment for possible gastroesophageal reflux with a proton pump inhibitor or an H2-receptor antagonist may be considered when clinically appropriate, and chlorpromazine can be used for severe symptoms, along with discontinuation of the suspected causative medication.

This case emphasises that hiccups should be considered as a potential adverse effect, particularly in male patients on benzodiazepines, during aripiprazole titration. Prompt recognition and discontinuation of aripiprazole can prevent complications such as dehydration and aspiration risk and improve treatment adherence. Additionally, chlorpromazine may be considered as an effective symptomatic option for managing acute hiccups in these patients.

Ethical Considerations: Written informed consent was obtained from the patient, and all personal information has been kept confidential.

Conflict of Interest: The authors declare no conflict of interest.

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