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"It's been a long time since I drank like that": A case report of binge drinking associated with aripiprazole

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Abstract

Aripiprazole has been linked to the development of impulse control problems (ICPs), most commonly gambling. Aripiprazole's effect on serotonergic and dopaminergic pathways has had mixed results on drinking behaviors. A male patient receiving outpatient psychiatric care presented with ongoing symptoms of depression on his current regimen of mirtazapine and gabapentin. Aripiprazole was chosen for augmentation after multiple failed trials of alternative medications. Within 3 weeks the patient discontinued the medication due to escalating binge-drinking behavior. This behavior resolved within 3 days after discontinuing aripiprazole. Individuals who engage in binge drinking demonstrate consistent impulse control deficits that are unrelated to the rewarding effects of alcohol. Aripiprazole may be related to this patient's return to binge drinking from an ICP standpoint rather than driven by alcohol cravings as other psychosocial factors remained stable throughout this time.

Keywords: aripiprazole, binge drinking, impulse control disorders

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Background

Aripiprazole is a second-generation antipsychotic indicated for schizophrenia and bipolar disorder; it is also used as adjunct treatment in major depressive disorder, Tourette syndrome, and irritability with autism spectrum disorders.[1] In 2016, a safety communication was released by the US Food and Drug Administration warning about the association between aripiprazole and new onset impulse control problems (ICPs), most commonly gambling, seen in 184 reported cases.[2]

Therapeutically, aripiprazole is a partial agonist at the dopamine D2 and D3 receptors and an antagonist at the serotonin 5-HT2A receptors in the frontal cortical and subcortical areas of the brain.[3] These regions regulate motor activity and behavior and are involved in decision making, complex behaviors, and neuropsychiatric symptoms.[4,5] Dopaminergic pathways are linked to motivation, reward, and reinforcement; notably, there is D3 receptor upregulation found in people with substance use disorders.[6] Whereas not often cited as an ICP, substance use is included within some ICP literature.[7] The following case demonstrates the potential impact of aripiprazole's mixed mechanism on binge drinking in the context of impaired impulse control.

Case Report

A 29-year-old male patient with posttraumatic stress disorder, major depressive disorder, and a history of heavy alcohol use was seen in the outpatient mental health clinic via telehealth (video to home) for medication management, being followed

by the same provider since February 2020. Between 2018 and 2020, he was seen by other mental health providers within the same health care system. Social history is significant for military service prior to 2018. His past known medication trials included bupropion, buspirone, clonazepam, doxazosin, dronabinol, duloxetine, escitalopram, gabapentin, mirtazapine, prazosin, quetiapine, and risperidone. Although some of these medications were not tolerated or effective, he denies that any previous trials were related to significant changes in drinking behavior.

At his visit in April 2023, the patient reported ongoing symptoms of depression with his current regimen of mirtazapine 30 mg at bedtime and gabapentin 100 mg twice daily as needed for anxiety. Regarding his drinking history, in the year 2017 and prior, he would drink 12 to 18 beers plus undisclosed amounts of hard liquor 3 to 4 times per week, resulting in blackouts. After residential substance use treatment in 2017, while still serving in the military, he reported a decrease from heavy drinking to once monthly or less during the years of 2018 to 2020. He later limited alcohol even further to once per semester in 2021 as he started the process to complete an undergraduate degree. The patient denies excursions from his described drinking habits, and prior to aripiprazole, he would be considered low-risk, drinking within recommended limits per the US dietary guidelines.[8] These guidelines define moderate drinking limits for men to be 2 or fewer in a day and no heavy drinking days (5 or more drinks in 1 day or 15 or more drinks in a week). After discussion of risks and benefits of adjunctive medication treatment, particularly how it may affect his academic performance, it was decided to trial aripiprazole, an FDA-approved adjunctive treatment in major depressive disorder, at 2.5 mg daily to treat ongoing symptoms of depression.

At the next follow-up visit in May 2023, the patient reported that he only took the aripiprazole for 3 weeks. He reports that, during this time, within days after starting the aripiprazole, he drank to blackout most days due to an "urge," that he did not feel like himself, and he was feeling internally restless. He denies psychosocial stressors or an increase in pain worsening during this time frame. He then stopped the aripiprazole on his own and states that the reported symptoms (restlessness, alcohol use) resolved completely over the next 3 days. At this appointment, it was decided to return to a medication that was previously beneficial, bupropion, as adjunctive treatment with the mirtazapine. During the appointment, risks and benefits of bupropion were discussed, including theoretical risks of reduced seizure threshold in the setting of acute alcohol intoxication and withdrawal. At follow-up in July 2023 mood symptoms were improving, and he denied any further excessive drinking behavior and a return to his plan to only drink once per semester (ie, 2 to 3 times per year). Per the Naranjo Adverse Drug Reaction Probability Score, the occurrence of drinking is considered "probable" (score of 5 points) related to aripiprazole based on the drinking occurring after the aripiprazole was given, resolving upon discontinuation, and the lack of known alternative causes (ie, other psychosocial stressors or pain).[9]

Discussion

This case presents a unique finding among aripiprazole-related ICPs and exposes more questions regarding its proposed mechanism on dopaminergic pathways. Among second-generation antipsychotics with partial dopamine agonism, aripiprazole is most frequently implicated in ICPs.[10] Aripiprazole may increase compulsive gambling, shopping, and sexual behaviors, but an increase in gambling behaviors appears to be the most common presentation.[11,12] In each case, these ICP behaviors resolved within weeks following aripiprazole discontinuation, similarly in our case.[11]

A literature review was conducted using the following search terms in PubMed: aripiprazole, binge drinking, impulse control problems and disorders, alcohol use associated with aripiprazole. Articles containing data on human subjects and written in English were further reviewed for relevance. No published reports were identified on the aripiprazole-induced binge drinking using these search criteria. Current evidence describes aripiprazole-induced behaviors in patients with no previous history of those ICPs. We present a case with a history of heavy drinking behavior that was currently reduced to 1 drink per month, ultimately exacerbated to binge drinking when taking aripiprazole.

Dopamine-blocking medications, such as olanzapine, demonstrate effectiveness in reducing alcohol consumption.[13] Conversely, dopamine agonists, such as pramipexole, have been associated with an increase in compulsive behaviors, such as gambling and shopping as well as hypersexuality.[6] As aripiprazole is a partial dopamine agonist, this raises the question as to what effects it may have on impulsive behaviors, including alcohol consumption. Given that dopamine antagonism reduces alcohol consumption, we wonder if dopamine agonism could increase the desire for alcohol.

Aripiprazole is linked to both negative and positive impacts on alcohol consumption (eg, alcohol use disorder [AUD] and binge drinking), but the scales remain unbalanced.[13–19] Aripiprazole has been reported to reduce alcohol-seeking behavior and promote abstinence among individuals with AUD.[15] Psychiatrists report cases in which aripiprazole was successfully used in combination with other psychoactive medications to reduce impulsivity and stop binge drinking.[14,18] It is hypothesized that this is due to aripiprazole-induced delays in drinking reward and reduced euphoric effects of alcohol.[19] This hypothesis for aripiprazole's efficacy as potential pharmacotherapy for AUD is consistent with the mechanism of naltrexone, a first-line recommended medication

for AUD.[20] Alternatively, aripiprazole showed no significant impact on drinking behavior at doses of 15 mg over 8 days or 5 weeks in 2 studies.[16,18] Randomized controlled trials are required to fully support this therapeutic use for aripiprazole as the case we present here appears to contradict the efficacy of aripiprazole in reducing alcohol consumption.[19,21]

The patient presented here endorsed prior binge drinking behaviors though alcohol use had been below recommended daily and weekly limits for approximately 5 years preceding the initiation of aripiprazole per US dietary guidelines.[8] Aripiprazole's partial dopamine agonism at D2 and D3 receptors may reduce drinking through alterations of reward pathways and also lead to the development of ICPs; this may indicate that the mechanisms underlying these 2 effects differ.[3] Individuals who engage in binge drinking demonstrate consistent impulse control deficits that are unrelated to the rewarding effects of alcohol.[18] We believe aripiprazole may be related to our patient's return to binge drinking from an ICP standpoint and not driven by alcohol cravings. More research is needed to further elucidate the relationship between aripiprazole and binge drinking behaviors, particularly the relationship between upregulation of D3 receptors in individuals with SUDs and aripiprazole's partial agonism of the D3 receptor.

Conclusion

Suspected aripiprazole-induced ICPs typically include gambling, shopping, and sexual behaviors and, until now, have lacked publication around binge drinking. This case highlights binge drinking behavior in an individual beginning within days after initiation of aripiprazole and subsiding 3 days after its discontinuation. Aripiprazole's partial dopamine agonism may play a role in exacerbating drinking behavior in an individual with previous heavy drinking from an ICP perspective rather than alcohol craving.

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