

Pathological Gambling Due to Aripiprazole: Two Cases

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ABSTRACT

Aripiprazole is an atypical antipsychotic agent which has a partial agonistic effect on dopamine D2 and D3 receptors. It is effective in the treatment of schizophrenia and bipolar disorder. Owing to its partial agonistic effect, hyperactivity of dopamine may occur in the mesolimbic pathway. In the literature, there are few case reports about pathological gambling due to aripiprazole. In this article, there are two case reports of patients who showed pathological gambling behaviour and alcohol abuse and who were under treatment with aripiprazole. The patient had a history of gambling in the past. With the use of aripiprazole, pathological gambling behaviour occurred quickly and with discontinuation of aripiprazole it ended completely. Aripiprazole causes pathological gambling by forming a hyperdopaminergic condition in the mesolimbic dopaminergic pathway. Aripiprazole should be recommended cautiously and carefully to patients who are impulsive and have a history of alcohol/substance abuse.

Keywords: Aripiprazole, dopamine partial agonist, pathological gambling

INTRODUCTION

Aripiprazole is an atypical antipsychotic which has partial agonistic effects on dopamine receptors. In contrast to other atypical antipsychotics that have antagonistic effects on the dopamine receptors fully, Aripiprazole is unique having a partial agonistic effect on the D2 and D3 receptors. It is effective in the treatment of schizophrenia and bipolar disorders (1). Aripiprazole may cause pathological gambling due to its action as a partial dopamine agonist in the mesolimbic pathway. In the literature, some case series of aripiprazole-induced pathological gambling have been reported. In this article, two cases that show pathological gambling behaviour due to their treatment with Aripiprazole are reported.

CASE 1

A 54-year-old male patient presented to the clinic with complaints of alcohol abuse. He has been using alcohol for 10 years. He used to play card games such as poker but had not done so for two years. Aripiprazole 5 mg/day and valproic acid 500 mg/day treatment was started for the patient. After two weeks, therapeutic drug monitoring (TDM) level of aripiprazole was determined

as 13–14 ng/ml [therapeutic reference range: 150–500 (ng/ml)] and TDM level of valproic acid was determined as 15, 70 (µg/ml) (therapeutic reference range: 50–100 (µg/ml)) (2). In the fourth week of his treatment, he had the intense desire to gamble; he lost 400 000 dollars in two weeks. Therefore aripiprazole treatment was terminated. Hypomanic symptoms such as sleep and poor appetite were not observed. His Young Mania Rating Scale total score was 2. The dose of valproic acid was increased to 1000 mg/day. Gambling behaviour was not observed in the subsequent period.

CASE 2

A 38-year-old male patient came to the clinic because of his gambling problem. For eight years, he has been betting on the Internet two or three times a week. He has a regular job and a family life. He was hospitalized and aripiprazole 20 mg/day and valproic acid 1000 mg/day treatment was started. Therapeutic drug monitoring level of aripiprazole was determined as 228, 28 (ng/ml) [therapeutic reference range: 150–500 (ng/ml)] and TDM level of valproic acid was determined as 76, 34 (µg/ml) [therapeutic reference range: 50–100 (µg/ml)]

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(2). Three weeks later, he was discharged from the hospital. In the following two months, his desire to bet has increased excessively and he started betting every day. He lost 400 000 dollars in these two months; his family and work life were affected negatively. Aripiprazole treatment was terminated and valproic acid treatment started. Approximately four weeks later, his gambling trend decreased.

DISCUSSION

In the literature, few cases on pathological gambling due to aripiprazole have been reported. The first case was presented by Raxonas in 2010. After changing the treatment of a 64-year-old female patient with schizophrenia from pimozide to aripiprazole 15 mg/day, she showed pathological gambling behaviour and compulsive eating. One month after the aripiprazole treatment, Ziprasidone treatment started and her pathological gambling ended (3). Gavaudun *et al* (4) reported two cases with schizophrenia. A few weeks after changing the treatment from haloperidol and amisulpride to aripiprazole, they started exhibiting gambling and had criminal behaviours. These patients had no history of gambling in their pasts. A few weeks after the termination of the aripiprazole treatment, their gambling and criminal behaviours ended completely. Cohen *et al* (5) reported a case series of three patients with pathological gambling due to aripiprazole. These patients, one of whom had a schizoaffective disorder and the others had schizophrenia, showed pathological gambling behaviour after 4 weeks of the initiation of aripiprazole treatment 15 mg/day. Two patients over nine months and the other one over one month had lost thousands of dollars in gambling during their treatment with aripiprazole. After the termination of the aripiprazole treatment pathological gambling behaviour disappeared 7–25 redplate. In the article, it is stated that these three cases had no gambling history in their past. In the same year, Smith *et al* (6) reported a series of three cases. Two patients with schizophrenia and one patient with a schizoaffective disorder, who had a history of gambling in their past, started to think about gambling repeatedly and increased significantly their gambling behaviour on aripiprazole. One of these patients lost huge amounts of money due to the aripiprazole 5 mg/day and the other two patients lost huge amounts of money due to the aripiprazole 15 mg/day. Their gambling behaviours decreased after the termination of the aripiprazole treatment. Gaboriau *et al* (7) have recently published a series of eight cases. One hundred and sixty-six people who were admitted to the

clinic for the treatment of pathological gambling were examined. Gambling tendencies and behaviours of these eight patients with schizophrenia, bipolar disorder and major depressive disorder were increased on aripiprazole treatment (5–30 mg/day). Pathological gambling behaviour could be controlled in five of these cases even with the continuation of the aripiprazole treatment. In the other three cases, gambling ended a few weeks after the termination of aripiprazole. The authors claimed that aripiprazole was a new risk factor for pathological gambling considering nine cases that were reported before them. Our cases had a history of gambling in the past. However, unlike the previous cases they had no diagnosis of schizophrenia or bipolar disorder. One of them had alcohol abuse. Owing to his gambling behaviours it was suggested that the other one had impulsive and reward-seeking behaviours. Dopamine hyperactivity in the mesolimbic pathway which occurs due to the use of aripiprazole may activate the reward system. With the two cases that are presented in this article, 19 cases were examined in total. So, we can conclude that patients with psychosis or not, with or without a history of gambling behaviour, might show gambling behaviours or increase the existing gambling behaviours due to the use of lower (5 mg/day) or higher (30 mg/day) doses of aripiprazole. It can be said that the risk is high, even at low doses. Therapeutic drug monitoring levels have not been measured in previous reports. As in the first case we presented, pathological gambling may occur despite very low levels of TDM. Therefore, aripiprazole should be recommended carefully to the patients who are diagnosed with schizophrenia and bipolar disorder (or not), have a history of alcohol/substance abuse and gambling and have impulsive behaviours. Gambling behaviours should be always investigated in patients who use aripiprazole in their follow-up examinations.

REFERENCES

1. Lieberman JA. Dopamine partial agonists: a new class of antipsychotic. *CNS Drugs* 2004; **18**: 251–67.
2. Hiemke C, Baumann P, Bergemann N, Conca A, Dietmaier O, Egberts K et al. AGNP consensus guidelines for therapeutic drug monitoring in psychiatry: update 2011. *Pharmacopsychiatry* 2011; **44**: 195–235.
3. Roxanas MG. Pathological gambling and compulsive eating associated with aripiprazole. *Aust N Z J Psychiatry* 2010; **44**: 291.
4. Gavaudun G, Magalon D, Cohen J, Lancon C, Leonetti G, Pelissier-Alicot et al. Partial agonist therapy in schizophrenia: relevance to diminished criminal responsibility. *J Forensic Sci* 2010; **55**: 1659–62.
5. Cohen J, Magalon D, Boyer L, Simon N, Christophe L. Aripiprazole-induced pathological gambling: a report of 3 cases. *Curr Drug Saf* 2011; **6**: 51–3.
6. Smith N, Kitchenham N, Bowden-Jones H. Pathological gambling and the treatment of psychosis with aripiprazole: case reports. *Br J Psychiatry* 2011; **199**: 158–9.

7. Gaboriau L, Victorri-Vigneau C, Gérardin M, Allain-Veyrac G, Jolliet-Evin P, Grall-Bronnec M. Aripiprazole: a new risk factor for pathological gambling? A report of 8 case reports. *Addict Behav* 2014; **39**: 562–5.

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