

Pathological Gambling Due to Aripiprazole: Two Cases
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ABSTRACT

Aripiprazole is an atypical antipsychotic agent which has partial agonistic effect on dopamine D2 and D3 receptor. It is effective in the treatment of schizophrenia and bipolar disorder. Due 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 two case reports with a tendency to gambling and alcohol abuse under treatment of aripiprazole who show pathological gambling behavior are reported. Cases have a history of gambling in the past. Due to the use of aripiprazole, pathological gambling behavior occurs quickly and with discontinuation of aripiprazole it ended completely. In spite of its very low therapeutic drug monitorization (TDM) level, aripiprazole may cause this. Aripiprazole causes pathological gambling by forming hyperdopaminergic condition in the mesolimbic dopaminergic pathway. Aripiprazole should be recommended carefully to the patients who are impulsive and have a history of alcohol / substance abuse.

Keywords: Aripiprazole, dopamine partial agonist, pathological gambling

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INTRODUCTION

Aripiprazole is an atypical antipsychotic which has partial agonistic effects on dopamine receptors. In contrast to other atypical antipsychotics which have antagonistic effect on the dopamine receptors fully, dopamine is unique due to have partial agonistic effect on D2 and D3 receptors. It is effective in the treatment of schizophrenia and bipolar disorder (1). Aripiprazol may cause pathological gambling due to its act as a partial dopamine agonist in 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 behavior due to their treatment of aripiprazol.

CASE 1

Fifty-four year old, male patient applied to the clinic with complaints of alcohol abuse. He has been using alcohol for ten years. He used to play card games such as poker but he has not been gambling for couple of years. Aripiprazole 5 mg/day and valproic acid 500 mg/day treatment was started to patient. After two weeks, therapeutic drug monitorization (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 (ug/ml) (Therapeutic reference range: 50-100 (ug/ml) (2). In the fourth week of his treatment, he had intense desire to gamble; he lost 400 thousand dollars in two weeks. Therefore aripiprazole treatment was terminated. Hypomanic symptoms such as sleep and appetite were not observed. His Young Mania Rating Scale total score was 2. The dose of valproic acid has been increased to 1000 mg / day. Gambling behavior was not observed in the subsequent period.

CASE 2

Thirty-eight year old male patient was applied 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 to patient. Therapeutic drug monitorization (TDM) 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 (ug/ml) (Therapeutic reference range: 50-100 (ug/ml) (2). Three weeks later he was discharged from the hospital. In following 2 months, his desire to bet has increased excessively and he started betting every day. He lost 400 thousand dollars in these two months; his family and work life was 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 about pathological gambling due to aripiprazole have been reported. The first case was presented in 2010 by Raxonas. After changing the treatment of a 64-year-old female patient with schizophrenia from pimozide to aripiprazole 15 mg/day, she showed pathological gambling behavior and compulsive eating behavior. One month later of the aripiprazole treatment, Ziprasidone treatment started and later her pathological gambling ended (3). Gavaudun et al. reported two cases with schizophrenia (4). A few weeks after changing the treatment from haloperidol and amisulpride to aripiprazole, they started showing gambling behavior and have criminal behaviors. These patients had no history of gambling in their pasts. A few weeks after the termination of the aripiprazole treatment, their gambling and criminal behaviors have ended completely. Cohen et al reported a case series of three

about pathological gambling due to aripiprazole (5). These patients, of whose is with schizoaffective disorder and the others are with schizophrenia, showed pathological gambling behavior after (one of them and the others 4 weeks after) the initiation of aripiprazole treatment 15 mg/day. Two patients for 9 months and the other one for one month have lost thousands of dollars in gambling during their treatment with aripiprazole. In 7-25 days pathological gambling behavior has disappeared due to termination of the aripiprazole treatment. In the article, it is stated that these three cases have no gambling history in their past. The same year, Smith and colleagues reported series of three cases (6). Two patients with schizophrenia and one patient with schizoaffective disorder, who have a history of gambling in their pasts started to think about gambling repeatedly and increased significantly their gambling behavior due to 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 behaviors decreased after the termination of aripiprazole treatment. Gaboriau et al have recently published a series of eight cases (7). 166 people who admitted to the clinic for the treatment of pathological gambling were examined. Gambling tendencies and behaviors of these 8 patients with schizophrenia, bipolar disorder and major depressive disorder were increased due to aripiprazole treatment (5 mg/day to 30 mg/day). Pathological gambling behavior could be controlled in five of these cases even the aripiprazole treatment continued. In the other three cases, gambling has ended a few weeks after the termination of aripiprazole. The authors claimed that aripiprazole 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 have not diagnosis of schizophrenia or bipolar disorder. One of them had alcohol abuse. Due to his gambling behaviors it was suggested that the other one had impulsive and reward-seeking behaviors. Dopamine hyperactivity in the mesolimbic pathway which occurs due to the use of

aripiprazole may activate the reward system. With the two cases that were presented in this article, 19 cases were examined in total. So, we can conclude that patients with psychosis or not, have a history of gambling behavior or not might show gambling behaviors or increase the existing gambling behaviors due the use of lower (5 mg/day) or high (30 mg/day) doses of aripiprazole. It can be said that the risk is high, even at low doses. TDM levels have not been measured in previous reports. As in the first case we presented, pathological gambling may occur despite very low level of TDM. Therefore aripiprazole should be recommended carefully to the patients who diagnosed with schizophrenia and bipolar disorder or not, have a history of alcohol / substance abuse and gambling and have impulsive behaviors. Gambling behaviors should be always investigated in patients who use aripiprazole in their follow-up examinations.

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