



A Case Report: Is There a Drug-Induced Gambling Disorder?

Afrendi Akbar^(✉) and Mustafa M. Amin

Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
akbarafrendi@gmail.com, mustafa.mahmud@usu.ac.id

Abstract. Gambling disorder (GD) has been identified as a rare but serious adverse reaction to dopaminergic drugs that are widely used to treat mental problems. It is characterized as a recurrent and persistent sickness that results in clinically substantial pain or disability and threatens the patient's capacity to maintain stability in both their personal and professional lives. Mr. TL, a 35 years old unmarried man who works as an employee, has been receiving aripiprazole treatment for three years and complained about a preoccupation with online gambling. The patient also admitted to being unable to control or stop gambling and the proclivity to place large bets until he is deeply in debt. Medical professionals should always consider the possibility of pathological gambling when administering aripiprazole and other dopamine agonists. Patients having a history of impulse control disorder and gambling behavior should be assessed for an elevated risk of pathological gambling prior to obtaining therapy with drugs that induce DG.

Keywords: Drug-induced gambling disorder · aripiprazole · dopamine agonist

1 Introduction

A persistent, maladaptive gaming pattern that results in clinically substantial discomfort is known as gambling disorder (GD). A person must display at least four out of the nine symptoms over the course of a year in order to meet the diagnostic requirements. Based on the intensity of the symptoms, GD is categorized as mild (4–5 symptoms), moderate (6–7 symptoms), or severe (8–9 symptoms). It can also appear as episodic or chronic symptoms. Pathological gambling is now referred to as GD and reclassified from an impulse control disorder to an addiction-related illness in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), underscoring the long-standing conceptualization of GD as an addiction. Numerous factors, such as manual diagnosis criteria, high rates of comorbidity, a shared genetic origin, comparable neurobiological consequences, and standard treatment methods, are associated with GD, alcoholism, and drug use disorders [1–3].

The DSM-5 Criteria for pathological gambling, which are largely based on earlier editions, include: 1) the need to place larger bets; 2) feeling restless or irritable when restricted to gambling; 3) failure to manage or quit gambling on multiple occasions; 4) dependence on gambling; 5) gambling as a coping mechanism for unpleasant stimuli;

6) gambling to make up for losses; 7) faking a gambling habit; and 8) jeopardized relationships, employment, or educational opportunities due to gambling and 9) relying on financial bailouts from other parties to relieve gambling-related financial stress. A GD diagnosis is complete when at least four of these criteria are present in 12 months [4, 5]. Pathological gambling is still included in the habit and impulse disorder in ICD-10, with the essential feature being persistent gambling that is repeated and often worsens despite adverse social consequences such as poverty, household failures, and personal chaos. Furthermore, in the ICD-10, there is no mention of a specific time frame that must be fulfilled [6].

Pathological gambling affects between 0.4 and 1 percent of people in the general population over their lifetimes (0.6 percent of males and 0.2 percent of women), and the risk factors are as follows [7, 8]:

1. Factors of temperament (including disorders of antisocial personality, depression, bipolar disorder, and substance or alcohol abuse);
2. Variables that are genetic, environmental, and physiological (Monozygotic twins are more likely to have GD than dizygotic twins, and first-degree relatives of people with moderate to severe alcohol use disorders are more likely to get GD than the general population.); and
3. The use of dopamine receptor agonists (pramipexole, ropinirole) and partial dopamine agonists (aripiprazole).

Parkinson's disease patients are more likely than the general population to have GD, with estimates ranging from 2.2 to 7 percent (1.4 percent). Although the precise source of this condition is uncertain, it has been connected to a mesolimbic system dysfunction that affects how risks and rewards are evaluated. Additionally, GD has been identified as a side effect of parkinsonism medications, notably dopaminergic agonists (such pramipexole), particularly when administered at high doses. In recent years, cases utilizing antipsychotic medications, such as aripiprazole, have also been documented [9].

2 Case Report

Mr. TL, a 35 years old unmarried man with schizoid personality traits who works as an employee in a company, has received aripiprazole as an antipsychotic medication regularly for the past three years and complained of preoccupation with online gambling. He claimed to be unable to control or stop gambling and placed large bets until he was in a debt of 10 million rupiahs. Mr. TL also admitted to often gambling online but usually having a specific target to stop. However, his gambling desire became uncontrollable after using aripiprazole.

Mr. TL was diagnosed with schizophrenia three years ago and given aripiprazole at an initial dose of 10 mg, which was later increased to 15 mg because the treatment goal was not achieved. After receiving this dose, he admitted that he could gradually return to normal and work again. The complaints of GD started within eight months, and the aripiprazole was discontinued two months ago. The desire to gamble was said

to have reduced drastically upon discontinuation, and he required consultation for a replacement drug. Despite not taking medication, psychotic symptoms did not appear during these two months. The result of the neurological examination was still within normal limits. Furthermore, no significant abnormality was found during the composites, awareness, and mental status examination.

3 Discussion

In recent years, dopamine agonists, a common drug used to treat Parkinson's disease, have also been shown to have the direct side effect of pathological gambling. Dopamine agonists for Parkinson's disease, restless legs syndrome, and endocrine disorders have been linked to an increased risk of impulse control disorders like pathological gambling, increased libido, compulsive shopping, and overeating, according to a public statement from the Italian Medicine Agency (AIFA). The EU Pharmacovigilance Working Party conducted an evaluation that led to the discovery of this information. According to recent research, drugs including apomorphine, bromocriptine, pramipexole, levodopa, and its derivatives linked to carbidopa increase the likelihood of developing impulsive behavior disorders. Furthermore, the development of GD was linked to subsequent aripiprazole, sertraline, citalopram, and lamotrigine therapy [10].

Due to its partial agonist properties at the brain's dopamine D2 (striatum, mesolimbic) and D3 (mesolimbic) receptor regions, the second-generation antipsychotic medication aripiprazole is unique. Since aripiprazole causes a hyperdopaminergic state at the D3 receptor, which is mostly found in the mesolimbic pathway (reward system) and has agonist properties, it has been theorized that this receptor contributes to the emergence of compulsive gambling. This theory is backed by the observation that whereas other dopamine receptor agonists, such as bromocriptine, cabergoline, rotigotine, and apomorphine, which are not selective for D3 receptors, are not, pramipexole and ropinirole, which have a higher affinity for the D3 receptor, are. Other neurotransmitter systems, such as the serotonin, norepinephrine, opioid, and glutamate systems, have also been shown to contribute to pathological gambling in addition to the dopamine system. Numerous case studies and case series have been published, highlighting the potential of a link between a considerable loss of demand for gambling after the conclusion of treatment or while using a specific medication in conjunction with psychotherapy while taking aripiprazole [7, 11].

Despite D3 agonists being more closely linked to gambling and related behavioral issues, aripiprazole, an atypical antipsychotic that works as a partial agonist at D2, 5HT1a, and serotonin 5-HT2 receptors, has also been linked to pathological gambling. Aripiprazole may lead to gambling because of its agonist effect in the mesocortical pathway, where low dopamine activity appears to be connected to cognitive impairments. Similar to this, other case studies detailed the occurrence of GD in patients receiving aripiprazole treatment for mood, depression, and schizoaffective disorders. The majority of these occurrences start anywhere between a few days and a year after beginning aripiprazole treatment, and they usually go away after the medication is stopped. Between 2003 and 2012, reports sent to the FDA Adverse Event Reporting System contained 1580 instances of impulse control disorders. Among the involved medications, pramipexole and aripiprazole showed the strongest correlation with impaired impulse control [10].

Despite the fact that dopamine agonists are known to cause behavioral disorders, it's crucial to remember that Parkinson's disease and several psychiatric diseases have a number of symptoms with pathological gambling, compulsive shopping, and eating disorders. Without eliminating changes in serotonin and opioid transmission, disruption of the dopamine receptor system or function may be a key neurobiological mechanism generating compulsive gambling associations or mental problems in this scenario. These signs and symptoms typically develop early in the illness and worsen the patient's quality of life. In a similar vein, people with mood and bipolar illnesses frequently experience addictions of any kind, including pathological gambling [10].

4 Conclusion

Aripiprazole and other dopamine agonists may cause pathological gambling, thus medical practitioners should constantly take this into account. Patients with a history of poor impulse control and gambling behavior should be assessed for an increased risk of compulsive gambling prior to therapy with drugs that produce GD. Serious outcomes could be avoided with early detection and appropriate care, such as dose reduction or the administration of medications with different mechanisms of action. Therefore, it is important to constantly evaluate treated individuals for impulse control issues and gambling behavior at each appointment. Patients may also gain from psychotherapy and psychoeducation that target impulsive conduct. Although the study suggested a link between pathological gambling, aripiprazole, and other dopamine agonists, more research is needed to fully understand the mechanisms at play.

References

1. Mathieu S, Varescon I. When gambling with derivative products can become problematic: a case report of excessive trading. *Int J Psychol Res Rev.* 2021;50.
2. Rash C, Weinstock J, Van Patten R. A review of gambling disorder and substance use disorders. *Subst Abuse Rehabil.* 2016;3.
3. Martinotti G, Chillemi E, Lupi M, De Risio L, Pettorruso M, Di Giannantonio M. Gambling disorder and bilateral transcranial direct current stimulation: A case report. *J Behav Addict.* 2018;7(3):834–7.
4. Rash CJ, Petry NM. Psychological treatments for gambling disorder. 2014;285–95.
5. American Psychiatric Association. DSM-5 Diagnostic Classification. In: *Diagnostic and Statistical Manual of Mental Disorders.* 2013.
6. World Health Organization. International Classification of Diseases (ICD-10) Version:2016. Who. 2016.
7. Giri YR, Peteru SR. Escalation of gambling associated with aripiprazole: A case report and literature review. *J Psychiatr Pract.* 2019;25(2):139–45.
8. Yau YHC, Potenza MN. Gambling disorder and other behavioral addictions: Recognition and treatment. *Harv Rev Psychiatry.* 2015;23(2):134–46.
9. Lanteri PF, Leguía A, Doladé NG, García GC, Figueras A. Drug-induced gambling disorder: A not so rare but underreported condition. *Psychiatry Res [Internet].* 2018;269(July):593–5. Available from: <https://doi.org/10.1016/j.psychres.2018.09.008>

10. Scavone C, Stelitano B, Rafaniello C, Rossi F, Sportiello L, Capuano A. Drugs-Induced Pathological Gambling: An Analysis of Italian Spontaneous Reporting System. *J Gambl Stud* [Internet]. 2020;36(1):85–96. Available from: <https://doi.org/10.1007/s10899-019-09828-1>
11. Von Hammerstein C, Miranda R, Aubin HJ, Romo L, Khazaal Y, Benyamina A, et al. Mindfulness and Cognitive Training in a CBT-resistant Patient With Gambling Disorder: A Combined Therapy to Enhance Self-control. *J Addict Med*. 2018;12(6):484–9.

Open Access This chapter is licensed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits any noncommercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

