DOI: 10.14744/DAJPNS.2019.00053
Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2019;32:365-367

CASE REPORT

Pathological gambling in a patient with Parkinson's Disease and valproate response

Yildiz Degirmenci[1], Hulusi Kececi[1]

[1]Duzce University, Faculty of Medicine, Department of Neurology, Duzce - Turkey

ABSTRACT

Sodium valproate is a well-known antiepileptic agent with multiple mechanisms of action such as sodium channel blockage and gamma-aminobutyric acid activity induction. Despite its well-described anxiolytic and mood stabilization effects, its mechanism of action in pathological gambling is not clear. However, it has been reported as an effective treatment option in pathological gambling for patients without Parkinson's disease (PD). We presented a male patient with a diagnosis of PD suffering from pathological gambling as an impulse control disorder due to antiparkinsonian drugs who did not respond to drug adjustments but showed complete improvement with sodium valproate, without any worsening in PD symptoms.

Keywords: Parkinson's disease, pathological gambling, impulse control disorders, sodium valproate

INTRODUCTION

Idiopathic Parkinson's disease (PD) is a chronic, neurodegenerative, progressive disorder caused by the dysfunction of dopaminergic transmission in the basal ganglia and characterized with cardinal motor symptoms including bradykinesia, rest tremor, rigidity, and postural instability, as well as non-motor symptoms such as hyposmia, mood disorders, cognitive and autonomic dysfunction, sleep problems, and many others. As the disease progresses, patients are prone to show dopaminergic therapy-induced complications including motor fluctuations, levodopa-induced dyskinesia, and impulse control disorders (ICDs) (1).

Impulse control disorders include a number of repetitive and reward-based behaviors, which are reported to occur with a prevalence of 8.1 to 35% among patients with PD (2). Hypersexuality, compulsive shopping, binge eating are known as the major ICDs, however it is important to emphasize that pathological gambling was in the classification of ICDs previously, but is considered as behavioral addiction recently. Hobbysim, punding, hoarding, and dopamine dysregulation syndrome, which are common in patients with PD in the course of disease are also classified in the broad spectrum of ICDs (3). The pathophysiology of ICDs is thought to be associated with the use of antiparkinsonian dopaminergic drugs, affecting the mesocorticolimbic dopamine system in particular, although the role played by possible genetic predisposition and neural alterations due to the disease that may lead to neurobiological sensitivity is not clear (4).

While the primary treatment of ICDs is the cessation of the offending antiparkinsonian drugs, dopamine agonists in particular and levodopa to a lesser extent, some patients cannot tolerate this discontinuation due

How to cite this article: Degirmenci Y, Kececi H. Pathological gambling in a patient with Parkinson's Disease and valproate response. Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2019;32:365-367.

Correspondence: Yildiz Degirmenci, Duzce University, Faculty of Medicine, Department of Neurology, Duzce - Turkey
Phone: +90 380 542 13 90 **E-mail:** ydegir@gmail.com

Received: March 29, 2019; **Revised:** July 11, 2019; **Accepted:** July 24, 2019

to the worsening motor syndrome or withdrawal syndrome. Since some patients may be unresponsive to dopaminergic treatment modification, other drugs, including antidepressants and antiepileptic agents, may be helpful in addition to dopaminergic drug modification (5).

Since there is a limited number of reports assessing topiramate and fluvoxamine in the treatment of ICDs in IPD patients and sodium valproate in patients without PD (5,6), we here reported a PD patient suffering from pathological gambling who was unresponsive to dopaminergic treatment modification but showed a complete recovery with sodium valproate treatment.

CASE

A 52-year-old, right-handed man presented to our movement disorders outpatient clinic with the complaint of inappropriate behaviors such as compulsive shopping, selling off household goods, and pathological gambling, which had gradually worsened within the last 6 months. He was suffering from terrifying visual hallucinations that were marked at nights but also existed in the daytime. He had a diagnosis of IPD based on the clinical findings of asymmetrical Parkinsonism with resting tremor of the limbs and gradually worsened slowing that began 3 years ago, and he had been under dopaminergic treatment since then. His medical records revealed that he had been taking combined levodopa (Levodopa +carbidopa+enthacapone, Stalevo) 100mg three times per day, 1mg rasagiline once daily, and 2 different types of dopaminergic agonists (50mg piribedil three times per day, and 1mg pramipexole three times per day) simultaneously for the last 1 year. His medical and family history was unremarkable otherwise. He had no medical comorbidities. His neurological examination revealed a marked resting tremor in his left hand, bilateral rigidity and bradykinesia, pronounced in the left side, anteflexion posture, and deteriorating gait. Psychiatric assessment of the patient was consistent with anxiety, psychosis, and impulsive behaviors, including the irresistible urge to spend all the money he had, and pathological gambling. The patient's pathological gambling habit had existed for 6 months, with day-and-night gambling on the internet, horse race bets, and card games. He began to lose increasing amounts of money, leading to a marked deterioration in the family's income as well as the relationships with the family members. Since these impulsive behaviors were attributed to the inappropriate and excessive amount of dopaminergic treatment, piribedil and rasagiline were discontinued, and in the follow-ups, the pramipexole dose was gradually lowered to 1mg once per day and discontinued within 4 weeks. As a consequence of dopaminergic drug management, the symptoms of compulsive shopping, selling household goods, and spending excessive money were found to be improved, but pathological gambling was resistant. Additionally, the patient's Parkinsonism symptoms gradually worsened. Therefore, the combined LD doses were titrated up to 125mg three times per day, and 25mg quetiapine at night was introduced for hallucinations and psychosis. These changes in the treatment regimen led to an improvement in the motor symptoms of Parkinsonism and in the psychosis. However, the patient was still gambling on the internet and betting on horse racing, losing increasing amounts of money. Thus extended-release sodium valproate (Depakine Chrono BT) 500mg per day was introduced for the resistant pathological gambling behavior. In the second-week follow-up visit, the patient and his wife reported that the patient's urge for gambling began to decrease, and it completely dissolved within 1 month.

DISCUSSION

Pathological gambling defined in the ICD-10 as excessive, uncontrolled gambling despite financial losses and social problems, is an important ICD with a prevalence of 3.4-6.1% among patients with PD (7,8).

The pathophysiology of pathological gambling is still unclear, potentially involving serotonergic, dopaminergic, and opioid dysfunction. However, there is a growing interest in the neural pathways underlying motivation, reward, decision-making, and impulsivity. Among these, dysregulation of the mesocorticolimbic dopamine system is thought to be the major neurobiological factor as for other ICDs in PD (9,10).

Despite the lack of a definite and clarified etiology of pathological gambling in patients with PD, the causative agents most reported are dopaminergic agents, in particular dopaminergic agonists (11). However, short-acting levodopa, monoamine oxidase-B inhibitors, and amantadine have also been shown to be responsible (10). As a gold standard approach, the first-line treatment of ICDs in PD is the discontinuation of the inducing drugs, where careful monitorization is mandatory to avoid withdrawal syndrome or the worsening of PD symptoms. In

addition to behavioral therapy, pharmacological agents shown to be effective in the treatment of ICDS including pathological gambling are selective serotonin reuptake inhibitors such as fluvoxamine and citalopram and mood stabilizers like carbamazepine and lithium, which are thought to be effective due to their effects on the noradrenergic system or limbic antikindling effects (6,12-14).

Sodium valproate is a well-known antiepileptic drug with multiple mechanisms of action including sodium channel blockage, increasing the release of the inhibitory neurotransmitter GABA, and blocking T-type Ca^{2+} channels (15). Beyond its antiepileptic effects, sodium valproate is an effective mood stabilizer that is also shown to improve pathological gambling in patients without PD (6,15).

According to our knowledge and the literature review, there is no report of sodium valproate as a therapeutic option in pathological gambling for patients with PD. Besides, this substance is encountered in the list of drugs inducing Parkinsonism (12). However, we here reported a patient with PD experiencing pathological gambling who was unresponsive to the drug adjustments but responded well to sodium valproate with complete recovery and without any worsening of PD symptoms. Since this is a single case report, further studies in the future with larger number of PD patients should be helpful to clarify the effects of sodium valproate on pathological gambling in PD.

Contribution Categories		Author Initials
Category 1	Concept/Design	Y.D.
	Literature review	Y.D.
	Data analysis/Interpretation	Y.D.
	Case follow-up (if applicable)	Y.D.
Category 2	Drafting manuscript	Y.D., H.K.
	Critical revision of manuscript	Y.D., H.K.
Category 3	Final approval and accountability	Y.D., H.K.
Other	Technical or material support	None
	Supervision	None

Acknowledgements: The manuscript was presented as a poster at the 52th National Neurology Congress, November 25-December 1, 2016, Antalya, Turkey.

Informed Consent: Written consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan, Lang AE, Halliday G, Goetz CG, Gasser T, Dubois B, Chan P, Bloem BR, Adler CH, Deuschl G. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord 2015; 30:1591-1601. [CrossRef]
2. Maloney EM, Djamshidian A, O'Sullivan SS. Phenomenology and epidemiology of impulsive compulsive behaviours in Parkinson's disease, atypical Parkinsonian disorders and non-Parkinsonian populations. J Neurol Sci 2017; 374:47-52. [CrossRef]
3. Voon V, Fox SH. Medication-related impulse control and repetitive behaviors in Parkinson disease. Arch Neurol 2017; 64:1089-1096. [CrossRef]
4. Vriend C. The neurobiology of impulse control disorders in Parkinson's disease: from neurotransmitters to neural networks. Cell Tissue Res 2018; 373:327-336. [CrossRef]
5. Ramirez-Zamora A, Gee L, Boyd J, Biller J. Treatment of impulse control disorders in Parkinson's disease: practical considerations and future directions. Expert Rev Neurother 2016; 16:389-399. [CrossRef]
6. Pallanti S, Quercioli L, Sood E, Hollander E. Lithium and valproate treatment of pathological gambling: a randomized single-blind study. J Clin Psychiatry 2002; 63:559-564. [CrossRef]
7. World Health Organization. International Classification of Diseases (ICD-10). Clinical descriptions and diagnostic guidelines. Geneva: World Health Organization, 1992.
8. Avanzi M, Baratti M, Cabrini S, Uber E, Brighetti G, Bonfa F. Prevalence of pathological gambling in patients with Parkinson's disease. Mov Disord 2006; 21:2068-2072. [CrossRef]
9. Zurowski M, O'Brien JD. Developments in impulse control behaviours of Parkinson's disease. Curr Opin Neurol 2015; 28:387-392. [CrossRef]
10. Weintraub D, Claassen DO. Impulse control and related disorders in Parkinson's disease. Int Rev Neurobiol 2017; 133:679-717. [CrossRef]
11. Iancu I, Lowengrub K, Dembinsky Y, Kotler M, Dannon PN. Pathological gambling: an update on neuropathophysiology and pharmacotherapy. CNS Drugs 2008; 22:123-138. [CrossRef]
12. Montastruc JL, Sommet A, Olivier P, Bagheri H, Gony M, Lapeyre-Mestre M, Brefel-Courbon C, Ferreira J, Schmitt L, Senard JM, Rascol O. Drugs, Parkinson's disease and Parkinsonian syndroms: recent advances in pharmacovigilance. Therapie 2006; 61:29-38. (French) [CrossRef]
13. Goodman WK, Ward H, Kablinger A, Murphy T. Fluvoxamine in the treatment of obsessive-compulsive disorder and related conditions. J Clin Psychiatry 1997; 58(Suppl.5):32-49.
14. Zimmerman M, Breen RB, Posternak MA. An open-label study of citalopram in the treatment of pathological gambling. J Clin Psychiatry 2002; 63:44-48. [CrossRef]
15. Deshmukh R, Thakur AS, Dewangan D. Mechanism of action of anticonvulsant drugs: a review. Int J Pharm Sci Res 2011; 2:225-236.