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Pathological Gambling In A Patient With Parkinson’s Disease And Valproate Response

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PATHOLOGICAL GAMBLING IN A PATIENT WITH PARKINSON’S DISEASE AND VALPROATE RESPONSE

ABSTRACT

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

**Key-words:** Parkinson’s disease, impulse control disorders, pathological gambling, sodium valproate.

**BIR PARKINSON HASTASINDA PATOLOJIK KUMAR OYNAMA VE SODYUM VALPROAT CEVABI**

**ÖZET**

Sodyum valproat, sodyum kanal blokaji, gama-aminobütyrik asit aktivitesi indüksiyonu gibi çoklu etki mekanizması olan iyi bilinen bir antiepileptic ajandır. İyi tanımlanmış anksiyolitik ve duygudurum düzenleyici etkisine rağmen, patolojik kumar oynamanın üzerindeki etki mekanizması açık değildir. Bununla birlikte, Parkinson hastalığı (PH) olmayan hastalarda patolojik kumar oynamanın üzerine etkin bir tedavi seçeneği olarak bildirilmiştir. Biz PH tanısı almış, anti-parkinson ilaçlara bağlı dürtü kontrol bozukluğu olarak patolojik kumar oynamadan yakınan, ilaç ayarlamalarına cevap vermeyen fakat sodium valproat ile; PH semptomlarında herhangi bir kötüleşme olmadıkça tam düzeltme gösteren genç bir erkek hastayı sunduk.

**Anahtar Kelimeler:** Parkinson hastalığı, dürtü kontrol bozukluğu, patolojik kumar oynamaya, sodium valproate.

**INTRODUCTION**

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

Impulse control disorders are a number of repetitive and reward-based behaviours, which are reported to occur in a prevalence of 8.1 % and 35 % among patients with PD (2). Hypersexuality, compulsive shopping, binge eating and pathological gambling are known as the major ICDs, however hobbyism, punding, hoarding, and dopamine dysregulation syndrome are also classified in the broad spectrum of ICDs, which are common in patients with PD, in the course of the disease (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 possible genetic predisposition and neural alterations due to the disease that may lead to neurobiological sensitivity are not clear (4).

Although 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 can’t tolerate this discontinuation due to the worsening of 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 limited number of reports revealing topiramate, fluvoxamine in the treatment of ICDs in IPD patients and sodium valproate in patients without PD (5, 6), we here reported a young PD patient suffering from pathological gambling which was unresponsive to dopaminergic treatment modification, but showed a complete recovery with sodium valproate treatment.

CASE REPORT

A 52-year old, right handed man presented to our movement disorders outpatient clinic with the complaint of inappropriate behaviours such as compulsive shopping, selling household goods, and pathological gambling which gradually worsened within last 6 months. He was suffering from terrifying visual hallucinations that were marked at nights but also exist in the day time. He had the diagnosis of IPD based on the clinical findings of asymmetrical Parkinsonism with resting tremor of the limbs, and gradually worsened slowing which began 3 years ago, and he was under dopaminergic treatment since then. His medical records revealed that he was taking combined levodopa (Levodopa+carbidopa+enthacapone, © Stalevo) 100 mg three times a day, 1 mg rasagiline once daily, and 2 different types of dopaminergic agonists (50 mg pribedile three times a day, and 1mg pramipexole three times a day) simultaneously since 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 deteriorating gate. Psychiatric assessment of the patient was consistent with anxiety, psychosis, and impulsive behaviours including the irresistible urge to spend all the money he has, and pathological gambling. The pathological gambling habit of the patient existed since 6 months, with day to night gambling in internet, horse race bets, and cards. He began to lose increasing amounts of money leading to a marked deterioration in the family’s income, as well as the relationships of the family members. Since these impulsive behaviours were attributed to the inappropriate and excessive amount of dopaminergic treatment, pribedile and rasagiline were discontinued and in the follow-ups, pramipexole dose was gradually lowered to 1 mg once a day, and discontinued within 4 weeks. As a consequence of dopaminergic drug management, compulsive shopping, selling household goods, and spending excessive money symptoms were found to be improved but pathological gambling was resistant. Additionally, his Parkinsonism symptoms were gradually worsened. Therefore, the combined LD doses were titrated up to 125 mg three times a day, and 25 mg quetiapine at night time was introduced for hallucinations and psychosis. These changes in treatment regimen led to an improvement in the motor symptoms of Parkinsonism and the psychosis. However, he was still gambling in internet, and betting on horse races, and loosing increasing amounts of money. Thus extended-release sodium valproate (©Depakin Chrono BT) was introduced 500 mg per day for the resistant pathological gambling behaviour. In the second-week of follow up visit, the patient and his wife reported that the urge of the patient for gambling began to decrease, and completely dissolved within 1 month.

DISCUSSION

Pathological gambling is an important ICD with a prevalence of 3.4-6.1 % among patients with PD, and defined as an excessive, uncontrolled gambling despite financial losses and social problems in International classification of diseases-10 (7, 8).
Pathophysiology of pathological gambling is still a myth with the potential involvement of serotonergic, dopaminergic and opioid dysfunction. However, there is a growing interest to the neural pathways underlying motivation, reward, decision-making and impulsivity. Among these, dysregulation of the mesocorticollimbic dopamine system is thought to be the major neurobiological factor as for other ICDs in PD (9, 10).

Despite the lack of definite and clarified aetiology of pathological gambling in patients with PD, the most causative agents reported are dopaminergic agents, dopaminergic agonists in particular (11). However, short-acting levodopa, monoamine oxidase-B inhibitors, amantadine have also 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 in which careful monitorization is mandatory to avoid withdrawal syndrome or the worsening of PD symptoms. In addition to behavioural therapy, pharmacological agents shown to be effective in the treatment of ICDs including pathological gambling are selective serotonin reuptake inhibitors as fluvoxamine, citalopram and mood stabilizers as carbamazepine, lithium that are thought to be effective due to their effects on noradrenergic system or limbic antikindling effects (12-15).

Sodium valproate is a well-known antiepileptic drug with multiple mechanism of action including sodium channel blockage, increasing the release of inhibitory neurotransmitter GABA, and block T-type Ca2+ channels (16). Beyond its’ antiepileptic effects, sodium valproate is an effective mood stabilizer that is also shown to improve pathological gambling in patients without PD (14, 16).

According to our knowledge and literature review, there is no report of sodium valproate as a therapeutic option on pathological gambling in patients with PD. Besides, it has been known as a drug that in encountered in the list of drugs inducing parkinsonism (12). However, we here reported a young patient with PD experiencing pathological gambling that 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 an only 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.

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REFERENCES


