

Abuse of Sinemet® (Levodopa/Carbidopa Combination) in a Patient with Schizophrenia

Şizofreni Tanılı Hastada Sinemet® (Levodopa/Karbidopa Kombinasyonu) Kötüye Kullanımı

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ABSTRACT

Sinemet® is a combination of carbidopa and levodopa (L-dopa) that is used to treat Parkinson's disease and syndrome. L-dopa is considered the gold standard of drug therapies for the treatment of Parkinson's disease because it is the metabolic precursor of dopamine, crosses the blood-brain barrier, and is presumably converted to dopamine in the brain. Drug abuse is the patterned use of a substance (drug) in which the user consumes the substance in amounts or through methods not supported by the advice of medical professionals. Patients with Parkinson's disease require escalations in the dose of the dopamine agonists that are used to treat this disease as it progresses, and it is possible that this may lead to psychological dependence and abuse as the dose increases. The abuse potential of anticholinergic drugs is well known, but there is limited research regarding the abuse potential of dopamine agonists in the medical literature. Thus, in this case report, it was aimed to discuss abuse of Sinemet® in a patient with schizophrenia.

Key Words: Sinemet®, schizophrenia, drug abuse, antiparkinsonian drugs, levodopa/carbidopa.

ÖZET

Sinemet®, içeriği levodopa/karbidopa kombinasyonu olan, Parkinson hastalığı ve Parkinson sendromunun tedavisinde kullanılan bir ilaçtır. Levodopa (L-dopa) Parkinson hastalığının tedavisinde altın standart olarak bilinir. Levodopa, dopaminin metabolik bir öncü molekülü olup, kan-beyin bariyerini geçtikten sonra dopamine dönüşür. İlaç kötüye kullanımı ise, kullanıcının hekim önerisi ve tıbbi kullanımlar dışında, birçok farklı yolla, madde (ilaç) kullanım şeklidir. Parkinson hastalığının seyri boyunca, hastalar doz artırımına ihtiyaç duyarlar. Bu hastalarda psikolojik bağımlılık ve antiparkinson ilaçların kötüye kullanımı, doz artırımları sonrası ortaya çıkar. Literatürde antikolinerjik ilaçların kötüye kullanım potansiyeli ile ilgili çok sayıda çalışma ve olgu bildirimi olmasına karşın, dopamin agonisti olan diğer ilaçların kötüye kullanımları ile ilgili çalışmalar kısıtlı sayıdadır. Bu olgu bildiriminde Sinemet® kötüye kullanımı olan şizofreni tanılı bir hastanın ele alınması amaçlanmıştır.

Anahtar Kelimeler: Sinemet®, şizofreni, madde kötüye kullanımı, antiparkinson ilaçlar, levodopa/karbidopa.

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INTRODUCTION

Antiparkinsonian drugs are typically used to ameliorate the extrapyramidal movement disorders that often manifest as a side effect of treatment with antipsychotic drugs (1). Conversely, anticholinergic and dopamine agonist drugs are commonly used to treat the extrapyramidal side effects associated with the use of antipsychotics (2).

Sinemet® is a combination of carbidopa and levodopa (L-dopa) that is used for the treatment of Parkinson's disease and syndrome. Patients with Parkinson's disease suffer from a variety of cognitive and motor symptoms, including tremor, dyskinesia, stiffness, and slowness of movement, that are generally considered to result from dopaminergic deficiencies (1). A substance (drug) use disorder is defined as a cluster of cognitive, behavioral, and physiological symptoms indicating that an individual continues to use a substance despite significant substance-related problems (3). L-dopa is considered the gold standard drug therapy for Parkinson's disease because it is a metabolic precursor of dopamine, crosses the blood-brain barrier, and is presumably converted to dopamine in the brain (4). However, patients with Parkinson's disease require escalating doses of the dopamine agonists that are used to treat this disorder as it progresses. It has been reported that psychological dependence on and the abuse of antiparkinsonian drugs may develop as the dose escalates (5). While the risk of abuse of anticholinergic drugs is well known, little research has been conducted regarding the abuse potential of dopamine agonist drugs. Thus, the present study aimed to determine whether a patient with schizophrenia exhibited Sinemet® use disorder.

CASE REPORT

Approximately 15 years after the initiation of follow-up assessments for a diagnosis of schizophrenia, a 46-year-old male patient presented at our hospital with exacerbated positive psychotic symptoms, including auditory and visual hallucinations and delusions, and negative symptoms that included anhedonia, avolition, and introversion, which were predominant. The patient had discontinued use of his prescribed antipsychotic treatment 6 months prior to the current admission.

Additionally, the patient had begun treatment with Biperiden, an anticholinergic drug, 2 years earlier for the treatment of extrapyramidal symptoms that developed secondary to amisulpride therapy, which is prescribed for the treatment of positive psychotic symptoms. Despite the Biperiden treatment, the patient's extrapyramidal symptoms did not diminish, and he was prescribed add-on treatment with Sinemet® (30 mg/day), an antiparkinsonian agent that acts as a dopamine agonist. Following the initiation of Sinemet® therapy, the patient's extrapyramidal symptoms dramatically diminished, and he discontinued the use of all prescribed drugs except Sinemet®. He continued to use Sinemet® (90 mg/day) for 3 months, but over time, the dose increased to 180 mg daily until he was hospitalized. In the time period in which he was free of antipsychotics but was using Sinemet®, the positive psychotic symptoms re-emerged.

During the patient's psychiatric examination, he was cooperative unless he was distracted by hallucinations. His speech and attitude were childish, he sometimes smiled inappropriately, and he exhibited conceptual disorganization, unusual thought content, blunted affect, psychomotor agitation, and choreiform movements of his extremities. Additionally, he could not sleep at night for over 1 month. This constellation of symptoms was indicative of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for schizophrenia. His score on the Positive and Negative Syndrome Scale (PANSS) was 163 at his first psychiatric examination; as a result, the patient was immediately assessed by the consultant neurologist. The neurologist ruled out a diagnosis of Parkinson's disease and concluded that the choreiform movements were quite likely linked to treatment with Sinemet®. Ultimately, the neurologist recommended the discontinuation of Sinemet® and the initiation of valproic acid (1000 mg/day) to treat the choreiform movement disorder and, if necessary, an antipsychotic that was less associated with movement disorders. Subsequently, olanzapine (10 mg/day) was prescribed for the patient's psychotic symptoms, and the dose was increased to 20 mg/day within 15 days. After 1 month, the choreiform movement disorder fully resolved, and the patient's PANSS score decreased to 97. Currently, the patient is in remission and

continues his follow-up visits at the outpatient clinic.

DISCUSSION

Anticholinergic and dopamine agonist drugs are widely used to treat the extrapyramidal motor symptoms caused by antipsychotic or other antidopaminergic drugs. However, these drugs may be abused due to their stimulant effects, and this abuse is most commonly observed in patients taking antipsychotic treatments (6).

It is generally assumed that patients with Parkinson's disease perceive their need for antiparkinsonian drugs based on emergent motor symptoms. However, abstinence from dopaminergic drugs results in drug-seeking behavior. Psychological dependence to L-dopa was reported in a small subset of Parkinson patients in 1985 (7). In the present case, treatment with Sinemet® (30 mg/day) was initiated in a patient with schizophrenia to ameliorate extrapyramidal motor symptoms caused by antipsychotic drugs over 2 years. Eventually, the patient discontinued the antipsychotic treatment but did not stop using Sinemet®, despite the fact that the extrapyramidal symptoms disappeared. Ultimately, the patient had a psychotic episode with predominant positive symptoms that continued for 2 months.

In patients with Parkinson's disease, dopamine replacement therapy is the standard treatment for motor symptoms such as tremors, rigidity, and bradykinesia and for neuropsychiatric symptoms such as dysphoria, anhedonia, fatigue, irritability, and anxiety (8, 9). The compulsive use of dopamine agonists is associated with a pattern of addiction or drug abuse that is a side effect of dopamine replacement therapy (10). Compulsive users experience withdrawal symptoms such as anxiety, panic attacks, depression, dysphoria, agitation, insomnia, dizziness, nausea, irritability, fatigue, and drug cravings if the dose of the dopamine agonist is decreased or withdrawn (3,11). On the other hand, malfunctions within the reward system may result from the degeneration of the dopaminergic system and long-term exposure to dopamine agonists, which can lead the compulsive use of L-dopa (12). To date, many case reports in the medical literature have described L-dopa addiction and impulsive behavior disorder in patients with Parkinson's disease, but there is limited information regarding L-dopa abuse,

except in patients with Parkinson's disease (13-23).

The present case is different from others in the literature because this patient was diagnosed with schizophrenia rather than Parkinson's disease and predominantly exhibited negative symptoms such as anhedonia, avolition, and introversion. The patient compulsively used Sinemet®, although his only complaint was extrapyramidal side effects of antipsychotic treatment, and he continued use of this drug even when the motor symptoms disappeared. Dopamine plays a major role as the "reward" neurotransmitter in the brain (24), and dysfunction of this reward system may underlie the negative symptoms of schizophrenia, including anhedonia, apathy, and the loss of motivation (25). Dopaminergic drugs trigger the risk of abuse and addictive use patterns from the very first dose, even if prescribed for treatment. Thus, care is needed when determining which patients require these types of therapy.

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