Case Report / Olgu Sunumu
doi: 10.5606/phhb.dergisi.2025.40

OPEN ACCESS

Balancing motor control and psychiatric stability: A five-year experience with apomorphine infusion in Parkinson's disease and bipolar disorder

Motor kontrol ve psikiyatrik dengenin sağlanması: Parkinson hastalığı ve bipolar bozuklukta apomorfin infüzyonunun beş yıllık deneyimi

Nilüfer Büyükkoyuncu Pekel, Demet Yıldız

Department of Neurology, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Türkiye

ABSTRACT

Although uncommon, the coexistence of Parkinson's disease and bipolar disorder presents unique therapeutic challenges in both oral pharmacological treatments and the selection of device-aided interventions. Herein, we reported a 60-year-old male patient with both bipolar disorder and Parkinson's disease. Apomorphine infusion therapy was initiated after motor symptoms remained uncontrolled despite optimized medical management. During a five-year follow-up, motor symptoms were effectively managed without any worsening of psychiatric status. Apomorphine infusion therapy may be considered a safe and effective treatment option for patients with advanced Parkinson's disease and comorbid bipolar disorder.

Keywords: Apomorphine, bipolar disorder, Parkinson's disease.

ÖZ

Nadir olmakla birlikte, Parkinson hastalığı ve bipolar bozukluğun birlikte görülmesi hem oral farmakolojik tedavilerde hem de cihaz destekli tedavi seçeneklerinin seçiminde özgün terapötik zorluklar sunmaktadır. Bu yazıda, hem bipolar bozukluk hem de Parkinson hastalığı tanısı bulunan 60 yaşında erkek bir hasta sunuldu. Optimum medikal tedaviye rağmen motor semptomları kontrol altına alınamayan hastada apomorfin infüzyon tedavisi başlandı. Beş yıllık takip süresince motor semptomlar, psikiyatrik durumda herhangi bir kötüleşme olmaksızın etkili bir şekilde yönetildi. Apomorfin infüzyon tedavisi, ileri evre Parkinson hastalığı ile birlikte bipolar bozukluğu olan hastalarda güvenli ve etkili bir tedavi seçeneği olarak değerlendirilebilir.

Anahtar Sözcükler: Apomorfin, bipolar bozukluk, Parkinson hastalığı.

It is known that patients diagnosed with bipolar disorder have a higher risk of developing Parkinson's disease compared to the general population.[1] In this comorbid condition, there are no guideline-based recommendations regarding medical

Correspondence: / İletişim adresi: Nilüfer Büyükkoyuncu Pekel, MD. SBÜ, Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, 16310 Yıldırım, Bursa, Türkiye.
E-mail *(e-posta):* niluferbuyuk@hotmail.com

Received / *Geliş tarihi: August 23, 2025* Accepted: / *Kabul tarihi: September 16, 2025* Published online: / *Online yayın tarihi:* 19 Eylül 2025

Presented at the 16th National Congress on Parkinson's Disease and Movement Disorders, Before Sleep: Video Case Discussions Session (April 27 – May 1, 2023, Bodrum, Türkiye).

Citation:
Büyükkoyuncu Pekel N, Yıldız D. Balancing motor control and psychiatric stability: A five-year experience with apomorphine infusion in Parkinson's disease and bipolar disorder. Parkinson Hast Harek Boz Derg 2025;28(1):9-12. doi: 10.5606/phhb.dergisi.2025.40.

treatment or device-aided therapy options, and the available data are limited to case reports. Antipsychotic agents and mood stabilizers, such as lithium and valproic acid, commonly used in the treatment of bipolar disorder may adversely affect patients with Parkinson's disease.[2-4] Conversely, dopaminergic treatments used in Parkinson's disease can trigger mania in bipolar patients, while dopamine agonists may lead to impulse control disorders (ICDs).[5,6]Device-aided treatment options are also limited in this patient group. Deep brain stimulation (DBS) is generally not preferred in cases with active psychiatric symptoms; apomorphine, as a dopamine agonist, carries the risk of triggering mania; and the use of levodopa-carbidopa intestinal gel (LCIG) in psychiatric patients presents challenges, all of which restrict device-aided therapy options for this population.[7-10]

In this report, we presented a patient with comorbid bipolar disorder and Parkinson's disease, whose motor symptoms could not be adequately controlled despite optimal medical therapy. The patient was followed for five years under apomorphine infusion therapy, during which motor symptoms were successfully managed without the occurrence of manic episodes or any worsening of the psychiatric condition.

CASE REPORT

A 60-year-old male patient was diagnosed with bipolar disorder in 2004 and was hospitalized in the psychiatry clinic for treatment due to a mixed episode that developed two years after the initial diagnosis. In 2015, the patient presented with complaints of hand tremor and bradykinesia and was diagnosed with Parkinson's disease at an external center. At that time, he was receiving valproic acid 1500 mg/day, quetiapine 100 mg/day, and trifluoperazine 5 mg/day, to which levodopa+benserazide 125 mg tablet (three times daily), pramipexole 1.5 mg/day, and rasagiline 1 mg/day were added sequentially. Written informed consent was obtained from patient.

In 2019, the patient was admitted to the psychiatry ward with symptoms such as excessive spending, increased activity, excessive talking, and suspiciousness and was diagnosed with a manic episode. During this period, sodium valproate and pramipexole were discontinued, and lithium 600 mg (twice daily) was initiated.

In 2020, the patient presented to our movement disorders center with a Unified Parkinson's Disease Rating Scale (UPDRS) score of 32. Neurological examination revealed resting and postural tremor in both upper extremities, decreased finger tapping amplitude more prominent on the left side, anteflexion posture, short-stepped gait, and reduced associated movements. Following psychiatric consultation, the antipsychotic regimen was revised, and anticholinergic agents were added. However, as motor symptoms did not sufficiently improve, the dose of levodopa+benserazide was increased to 125 mg (five times daily). After the dose escalation, the patient experienced worsening hallucinations, and the regimen was reverted to the previous dose.

As the patient had become dependent in activities of daily living, an apomorphine challenge test was performed. A significant response was observed at a dose of 7 mg, with a 50% reduction in off periods and a decrease in the UPDRS score from 32 to 7. Consequently, continuous apomorphine infusion therapy was initiated at 7 mg/h for 14 h per day. During a five-year follow-up period, motor symptoms remained well controlled, and no worsening of psychiatric status or development of manic episodes was observed.

DISCUSSION

Parkinson's disease is characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta, with the main therapeutic goal being the replacement of dopamine.[11] Bipolar disorder, on the other hand, is marked by manic and depressive episodes. Dopaminergic activity is thought to play a role in the pathogenesis of manic episodes.[12] Dopamine replacement, which

forms the basis of treatment in Parkinson's disease, is known to potentially trigger manic episodes, while dopamine agonists may lead to ICDs.[5,6] These interactions between therapeutic agents complicate medical management. Another critical aspect is the selection of device-aided therapies in cases with comorbid Parkinson's disease and bipolar disorder.

In patients with Parkinson's disease whose symptoms cannot be adequately controlled despite optimal medical treatment, device-aided therapies are considered. Apomorphine infusion therapy may be applied in individuals who have experienced side effects such as psychosis or ICDs during treatment with other dopamine agonists. However, its use is recommended with caution in patients with Parkinson's disease with a prior diagnosis of psychosis who are under treatment and follow-up.[13] Apomorphine exerts its effects through dopaminergic, alpha-adrenergic, and serotonergic receptors. The D3 receptors in the limbic system have been associated with ICDs, while 5-hydroxytryptamine (5-HT)2A receptors have been linked to hallucinations. The low affinity of apomorphine for both D3 and 5-HT2A receptors may explain why it causes fewer ICDs and hallucinations compared to other dopamine agonists.[6,7]

In one reported case of comorbid Parkinson's disease and bipolar disorder, even doses of pramipexole exceeding 1 mg/day were found to trigger mania.[14] Similarly, in our patient, a manic episode developed during treatment with pramipexole 1.5 mg/day, leading to the discontinuation of oral dopamine agonist therapy. Following the initiation of continuous apomorphine infusion, no manic episodes were observed throughout the five-year follow-up period.

Another device-aided treatment option is DBS. As a general principle, DBS is not preferred in patients with movement disorders who have active psychiatric symptoms. Nevertheless, case-based reports exist on the potential use of DBS in such patients. The absence of comparative groups, the low level of evidence, and the heterogeneity of the reported outcomes make clinical decision-making challenging. While the subthalamic nucleus is the most common DBS target in Parkinson's disease, it is known that globus pallidus internus is associated with fewer neuropsychiatric side effects.[15] Therefore, globus pallidus internus DBS may represent a potential treatment option in appropriately selected patients with comorbid Parkinson's disease and bipolar disorder.

Another device-aided therapy is LCIG infusion. In a three-year follow-up study of patients with advanced Parkinson's disease receiving infusion therapy, both apomorphine and LCIG were found to be safe in Parkinson's disease with ICDs. Furthermore, delivering Parkinson's disease medications in infusion form was reported to carry a lower risk of ICD development.[9] Moreover, LCIG therapy was not only considered safe but also found to be associated with improvement in ICD symptoms.[16]

In conclusion, the comorbidity of Parkinson's disease and bipolar disorder poses significant challenges in both pharmacological and device-aided therapeutic approaches. The bidirectional interactions between these two disorders necessitate a cautious and individualized treatment strategy in terms of both efficacy and safety. Although case reports and clinical experience are gradually increasing, the current body of knowledge remains limited. Large-scale, long-term studies are needed to develop evidence-based guidelines that can provide clinicians with a clearer direction in managing such comorbid conditions.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Contributed to case management, manuscript drafting, and correspondence: N.B.P.; Contributed to literature review and critical revision. Both authors approved the final version of the manuscript: D.Y.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Faustino PR, Duarte GS, Chendo I, Castro Caldas A, Reimão S, Fernandes RM, et al. Risk of developing Parkinson disease in bipolar disorder: A systematic review and meta-analysis. JAMA Neurol 2020;77:192-8. doi: 10.1001/jamaneurol.2019.3446.
2. Kavasoglu T, Ahmad A, Khan A. Lithium induced Parkinsonism: A case report. BJPsych Open 2022;8:S120. doi: 10.1192/bjo.2022.358.
3. Zhang CQ, He BM, Hu ML, Sun HB. Risk of valproic acid-related tremor: A systematic review and meta-analysis. Front Neurol 2020;11:576579. doi: 10.3389/fneur.2020.576579.
4. Rose O, Huber S, Trinka E, Pachmayr J, Clemens S. Treatment of Parkinson's disease psychosis-a systematic review and multi-methods approach. Biomedicines 2024;12:2317. doi: 10.3390/biomedicines12102317.
5. Maier F, Merkl J, Ellereit AL, Lewis CJ, Eggers C, Pedrosa DJ, et al. Hypomania and mania related to dopamine replacement therapy in Parkinson's disease. Parkinsonism Relat Disord 2014;20:421-7. doi: 10.1016/j.parkreldis.2014.01.001.
6. Isaacson SH, Hauser RA, Pahwa R, Gray D, Duvvuri S. Dopamine agonists in Parkinson's disease: Impact of D1-like or D2-like dopamine receptor subtype selectivity and avenues for future treatment. Clin Park Relat Disord 2023;9:100212. doi: 10.1016/j.prdoa.2023.100212.
7. Monreal JA, Duval F, González-Rodríguez A, Seeman MV. Apomorphine probe: A synthesis of studies with implications for affective and psychotic disorders. 2022. Available at: https://www.researchgate.net/publication/360089528_Apomorphine_probe_A_synthesis_of_studies_with_implications_for_affective_and_psychotic_disorders
8. Gelman K, Melott J, Thakur V, Tarabishy AR, Brandt A, Konrad P, et al. MR-guided focused ultrasound thalamotomy for lithium-induced tremor: A case report and literature review. Front Neurol 2024;14:1331241. doi: 10.3389/fneur.2023.1331241.
9. Todorova A, Samuel M, Brown RG, Chaudhuri KR. Infusion therapies and development of impulse control disorders in advanced Parkinson disease: Clinical experience after 3 years' follow-up. Clin Neuropharmacol 2015;38:132-4. doi: 10.1097/WNF.0000000000000091.
10. Hartmann CJ, Fliegen S, Groiss SJ, Wojtecki L, Schnitzler A. An update on best practice of deep brain stimulation in Parkinson's disease. Ther Adv Neurol Disord 2019;12:1756286419838096. doi: 10.1177/1756286419838096
11. Zhou ZD, Yi LX, Wang DQ, Lim TM, Tan EK. Role of dopamine in the pathophysiology of Parkinson's disease. Transl Neurodegener 2023;12:44. doi: 10.1186/s40035-023-00378-6.
12. Ashok AH, Marques TR, Jauhar S, Nour MM, Goodwin GM, Young AH, et al. The dopamine hypothesis of bipolar affective disorder: The state of the art and implications for treatment. Mol Psychiatry 2017;22:666-79. doi: 10.1038/mp.2017.16.
13. Özkan S, Erer S, Elibol B, Özkaynak SS, Akbostancı MC, Çakmur R, et al. Apomorphine in the treatment of Parkinson's disease. Turk J Neurol 2021;27:358-65. doi: 10.4274/tnd.70293.
14. Tanrıtanır B. Bipolar bozukluk ve Parkinson hastalığı birlikteliğinde farmakoterapi ikilemi: Bir olgu sunumu. Süleyman Demirel Üniversitesi Sağlık Bilimleri Dergisi 2021;12:233-6.
15. Accolla EA, Pollo C. Mood Effects After deep brain stimulation for Parkinson's disease: An update. Front Neurol 2019;10:617. doi: 10.3389/fneur.2019.00617.
16. Catalan MJ, Molina-Arjona JA, Mir P, Cubo E, Arbelo JM, Martinez-Martin P, et al. Improvement of impulse control disorders associated with levodopa-carbidopa intestinal gel treatment in advanced Parkinson's disease. J Neurol 2018;265:1279-87. doi: 10.1007/s00415-018-8803-1.