EDITORIAL

Recent Advancements in Parkinson's Disease

Sahil Mehta

Journal of Postgraduate Medicine, Education and Research (2024): 10.5005/jp-journals-10028-1652

Parkinson's disease (PD) is a neurodegenerative disorder characterized by cardinal motor symptoms of tremor, bradykinesia, and rigidity.[1] Pathologically, it involves loss of dopaminergic neurons in the substantia nigra with deposition of eosinophilic inclusions named "Lewy bodies." This chronic progressive disorder affects the quality of life not only due to motor disability but also a plethora of nonmotor symptoms ranging from sleep disturbances, constipation, urinary dysfunction, dementia, and psychosis. Treatment of this disorder is multidisciplinary, with the predominant role of a movement disorder specialist and the team efforts of neurosurgeon, rehabilitation expert, psychiatrist, and neuropsychologist. Pharmacotherapy includes the use of levodopa (still the gold standard), dopamine agonists, monoamine oxidase B (MAOB) inhibitors, catechol-O-methyltransferase (COMT) inhibitors, amantadine, and safinamide.[2] The onset of motor fluctuations and dyskinesias with the advancement of the disease course warrants the use of advanced therapies in the form of deep brain stimulation (DBS), apomorphine infusion therapy, and levodopa carbidopa intestinal gel.

Although breakthrough disease-modifying therapies in PD are still awaited, novel formulations of dopaminergic drugs with newer modes of delivery, advancements in device-aided therapies, and new drug targets have further increased the scope of providing improvised care in PD. For example, opicapone, a longer-acting COMT inhibitor has recently been approved by United States Food and Drug Administration (US FDA) to treat off periods.[3] Inhaled levodopa and sublingual apomorphine are also available in the West as rescue therapy.[4] Istradefylline, adenosine A2A receptor antagonist was approved in 2019 to treat motor fluctuations.[5] Regarding invasive therapies, levodopa–carbidopa–entacapone jejunal infusion and continuous subcutaneous levodopa carbidopa infusion are being studied in various clinical trials for efficacy in treating motor symptoms.

Recent technological advancements have paved the way for the improvisation of DBS by introducing directional electrodes, current steering, and bidirectional systems capable of sensing neural activity while simultaneously delivering therapeutic stimulation and adaptive DBS, among others.[6] Recently, the US FDA approved noninvasive magnetic resonance (MR)—guided focused ultrasound for tremor-predominant PD in December 2018 and gained additional approval for bradykinesia, rigidity, and dyskinesia in November 2021.[7] This procedure involves focused high-intensity ultrasound with MR thermography to cause thermocoagulative lesioning of the target without the risk of open surgery. However, it is approved only for unilateral treatment as bilateral treatment can result in dysphagia and speech worsening. Spinal cord stimulation is also being tested in clinical trials to alleviate freezing of gait with promising results.

Department of Neurology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Corresponding Author: Sahil Mehta, Department of Neurology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, Phone: +91 7087008270, e-mail: mehtasahilpgi@gmail.com

How to cite this article: Mehta S. Recent Advancements in Parkinson's Disease. J Postgrad Med Edu Res 2024;58(1):1–2.

Source of support: Nil

Conflict of interest: None

Another critical development in PD is the implication of the gut–brain axis in its pathogenesis, development, and progression; it even has therapeutic potential. The dysbiotic gut microbiome can influence the progression and onset of PD *via* numerous mechanisms, such as altered intestinal permeability, neuroinflammation, α-synuclein deposition, oxidative stress, and decreased neurotransmitter functions. Elevated fecal calprotectin levels, a marker of intestinal inflammation have been found to be elevated in PD. Several therapeutic approaches are being tried, such as probiotics, prebiotics, and fecal microbiota transplantation.[8] However, evidence is still scarce in the form of case reports or series and warrants high-quality clinical trials with larger sample sizes.

Device-assisted digital and remote sensor-based assessments are gaining popularity for more objective evaluation and measurement of response to treatment. Most wearable sensors contain accelerometers and gyroscopes to measure bradykinesia, tremor, dyskinesia, and spatiotemporal gait parameters.

Much needed progress has occurred in the development of various biomarkers. Real-time quaking-induced conversion (RT-QuIC) can detect α-synuclein aggregation in patients with high sensitivity and specificity in cerebrospinal fluid (CSF) and is also being studied in nasal swab samples.[9] This will enable molecular diagnosis and be essential to monitor the response of various synucleinopathy-targeted treatments. These α-synuclein-targeted treatments include inhibiting α-synuclein aggregation, promoting extracellular degradation through active and passive immunization, gene replacement, inhibiting lysosomal glucocerebrosidase activity, enhancing intracellular degradation and decreasing its production *via* ribonucleic acid (RNA) interference.[10]

Parkinson's disease (PD) is not a single disorder but is considered a multisystem disease owing to its clinical, genetic and molecular heterogeneity. Hence, treating this syndrome cannot be a "one size fits all" approach and highlights the importance of precision medicine. The treatment armamentarium for PD is expanding with every passing year, and we hope to find a cure for this progressive degenerative disorder in the near future.

References

1. Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet 2021;397(10291):2284–2303. DOI: 10.1016/S0140-6736(21)00218-X
2. Armstrong MJ, Okun MS. Diagnosis and treatment of parkinson disease: a review. JAMA 2020;323(6):548–560. DOI: 10.1001/jama.2019.22360
3. Scott LJ. Opicapone: a review in Parkinson's disease. CNS Drugs 2021;35(1):121–131. DOI: 10.1007/s40263-020-00778-6
4. Jost WH, Kulisevsky J, LeWitt PA. Inhaled levodopa for threatening impending OFF episodes in managing Parkinson's disease. J Neural Transm (Vienna) 2023;130(6):821–826. DOI: 10.1007/s00702-023-02636-3
5. Müller T. The role of istradefylline in the Parkinson's disease armamentarium. Expert Opin Pharmacother 2023;24(7):863–871. DOI: 10.1080/14656566.2023.2201374
6. Aleid A, Aleid M, Alehaiwi G, et al. Advancements in the clinical outcomes of functional neurosurgery with deep brain stimulation for movement disorders: a literature review. Cureus 2023;15(6):e40350. DOI: 10.7759/cureus.4035
7. Martínez-Fernández R, Natera-Villalba E, Máñez Miró JU, et al. Prospective long-term follow-up of focused ultrasound unilateral subthalamotomy for Parkinson disease. Neurology 2023;100(13):e1395–e1405. DOI: 10.1212/WNL.0000000000206771
8. Cheng Y, Tan G, Zhu Q, et al. Efficacy of fecal microbiota transplantation in patients with Parkinson's disease: clinical trial results from a randomized, placebo-controlled design. Gut Microbes 2023;15(2):2284247. DOI: 10.1080/19490976.2023.2284247
9. Vivacqua G, Mason M, De Bartolo MI, et al. Salivary α-synuclein RT-QuIC correlates with disease severity in de novo Parkinson's disease. Mov Disord 2023;38(1):153–155. DOI: 10.1002/mds.29246
10. Menon S, Armstrong S, Hamzeh A, et al. Alpha-synuclein targeting therapeutics for Parkinson's disease and related synucleinopathies. Front Neurol 2022;13:852003. DOI: 10.3389/fneur.2022.852003