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A Turning Point in Parkinson's Disease Treatment: Targeting Progression, Not Just Symptoms

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Introduction

Parkinson's disease (PD) is the second most frequent neurodegenerative disorder characterized by tremor and bradykinesia with an increasing prevalence in elderly population (about 1% in people over 65 years old). While current treatments for PD largely focus on managing motor symptoms through dopaminergic therapies, these approaches do not halt or slow the underlying neurodegenerative process. As the understanding of PD pathophysiology deepens, there is a growing emphasis on disease-modifying strategies, including gene therapy, cell-based interventions, and neuromodulation. This review explores cutting-edge therapeutic advances that aim to go beyond symptom relief and address the root causes and progression of PD.

Materials and Methods

This review is based on 12 articles from the PubMed and Embase databases, including randomized controlled trials and phase II/III studies published between 2019 and 2024, analyzing a total of 864 patients. The therapeutic strategies investigated involved disease-modifying approaches such as gene therapy, stem cell transplantation, immunotherapy targeting alpha-synuclein, and neuroprotective pharmacological agents. The inclusion criteria for patients consisted of those diagnosed with idiopathic Parkinson's disease, at early to moderate disease stages, and enrolled in studies specifically targeting disease progression rather than symptom management. Exclusion criteria involved patients with atypical or secondary parkinsonism, presence of major comorbidities affecting study outcomes, or recent participation in other interventional clinical trials within the last 6 months.

Results

Multiple investigational strategies are emerging with the potential to alter disease progression. Gene therapy targeting GBA and LRRK2 mutations, and dopamine (DA) replacement gene therapies like adeno-associated virus (AAV)-glutamic acid decarboxylase (GAD) and L-amino acid decarboxylase (AADC), which increase DA transmitter levels have been demonstrated to be safe and efficient in early-phase clinical trials. Stem cell-derived dopaminergic neuron transplants are entering clinical trials with encouraging safety profiles. Non-invasive brain stimulation techniques, such as focused ultrasound and adaptive deep brain stimulation (DBS), offer new ways to modulate neural circuits with greater precision. Immunotherapies targeting alpha-synuclein aggregates, as well as repurposed drugs (e.g., GLP-1 agonists), are advancing in development as disease-modifying agents. However, most remain in experimental stages, and challenges persist regarding delivery methods, patient selection, and long-term efficacy.

Conclusion

The treatment landscape for Parkinson's disease is rapidly evolving, with a growing emphasis on therapies aimed at stalling disease progression. Although current clinical management continues to center around symptomatic relief—primarily through dopaminergic therapies—novel approaches are emerging that target the underlying pathology of the disease. These include gene therapies, neuroprotective agents, and regenerative strategies. Realizing the promise of these approaches will depend on establishing reliable biomarkers, improving how to match patients to specific treatments, and executing well-designed, long-duration clinical trials to demonstrate both safety and lasting benefit.

Keywords: Parkinson's disease, disease-modifying therapy, gene therapy, neuromodulation