

Clinical Management of Drug-Induced Dyskinesia in Parkinson's Disease: Why Current Approaches May Need to Be Changed to Optimize Quality of Life

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Introduction:

Parkinson's Disease is a complex degenerative disorder which includes both motor and non-motor symptoms. Many patients who take dopamine replacement therapies to treat the motor symptoms of Parkinson's Disease experience drug-induced dyskinesia.

- **Dyskinesia:** random, uncontrolled, involuntary muscle movements that are a common side effect of long-term use of dopamine replacement therapies with the most common type occurring when the medication reaches its peak (peak-dose dyskinesia).

Research has shown that 30-50% of patients report experiencing dyskinesia within 5 years of starting treatment for PD and 60-100% of patients report dyskinesia within 10 years.

Current approaches to dyskinesia management

- Modify medication dosage or administration
 - o Reduce medication dosage; Can lead to PD symptoms reappearing
 - o Change medication administration by taking the same dose but in smaller doses throughout the day; Effective for a limited time only and not helpful to all
- Add another dopamine agent (not very supported by research)
- Continuous drug delivery system
 - o Duodenal infusion of levodopa or continuous subcutaneous apomorphine infusion can reduce dyskinesias
- Amantadine (NMDA receptor antagonist)
 - o Significantly reduces the duration of dyskinesia while providing a mild anti-parkinsonian effect
 - o For some, it only provides a temporary relief, which can be prolonged with extended release formulation
- Serotonergic Agents
 - o Some agents have been successful at reducing dyskinesia (e.g., Clozapine); Can have severe side effects
 - o Other medications have not been successful and have led to worsening PD symptoms (e.g., Buspirone, Sarizotan)

- Surgical Interventions
 - o Deep Brain Stimulation has been shown to reduce dyskinesia by 80% or more, which may be due to reduced medication following surgery.
 - o Appropriateness for DBS is determined by assessments conducted by neurologists, neuropsychologists (to assess risk factors related to cognition and mood), and a neurosurgeon.

Novel approach - Is it always clinically necessary to treat dyskinesia?

Dyskinesias affect patients differently and research shows that dyskinesias are not always related to a decrease in quality of life or increase in caregiver burden. However, dyskinesias do impact quality of life when they disturb the daily activities performed by the patient, which relies on the specific “motor repertoire” used by each patient. Functional limitations in PD patients can in turn result in increased caregiver burden. Therefore, taking a tailored and personalized approach to treating dyskinesia calls for new evaluation methods to capture each patient’s motor repertoire and the extent to which they are impacting their daily life and activity engagement.

Example: A seamstress might be more impacted by dyskinesia than someone who does not rely on very fine movements throughout their work day.

Implementation of the proposed approach

1. Use validated scales to assess dyskinesia and activities of daily living as well as scales specifically addressing the impact of dyskinesia on daily activities.
2. Use a combination of objective measures and subjective patient perceptions to improve treatment decisions and best capture changes in treatment.
3. Work toward the development of new scales assessing the entire motor repertoire of patients with PD.
4. Use wearable technology to complete data collection over longer time periods, clarify duration and severity of dyskinesia, and eventually provide real time feedback to patients and physicians to personalize treatment.

Conclusion

Implementing medication changes in Parkinson’s patients based on the impact of dyskinesia on their daily activities, by considering their entire motor repertoire, may lead to better quality of life of both patients and their caregivers. It is important to obtain the “patient’s perspective” about dyskinesias when tailoring treatment to his or her specific needs. Personalized treatments should be implemented to improve management of drug-induced dyskinesia, which will require further developments in how patients are evaluated.