LETTER TO THE EDITOR

To the Editor

Deep Brain Stimulation as a Rescue When Duodenal Levodopa Infusion Fails

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Patients with advanced Parkinson's disease (PD) often experience motor fluctuations and dyskinesias with escalating doses of dopaminergic medications. When medication-induced motor complications become disabling, device-based therapies are considered. Currently available options in Canada include duodenal levodopa infusion, also known as levodopa-carbidopa intestinal gel (LCIG) infusion,[1] and deep brain stimulation (DBS). LCIG works well for motor fluctuations and troublesome dyskinesias overall; in some cases, though, it may not provide sustained benefit for dyskinesias.[2] DBS is an effective treatment for both motor fluctuations and dyskinesia. Here, we describe a patient who underwent bilateral subthalamic nucleus (STN) DBS after initially being treated with LCIG. To our knowledge, using DBS as a form of rescue therapy for insufficient symptom control with LCIG has not been reported in the literature.

The patient is a 63-year-old male with an 18-year history of PD. Levodopa was titrated to 800 mg/day from 2006 to 2012, and initially controlled motor symptoms, but with time, he experienced significant motor fluctuations, as well as severe dyskinesia impacting gait and balance. Amantadine provided minimal anti-dyskinetic benefit. His unified PD rating scale (UPDRS-III) motor score was 38. His Hoehn and Yahr score was 4. At that time, he chose LCIG treatment rather than DBS because of its less invasive nature. Initially, motor fluctuations and dyskinesias improved significantly and his Hoehn and Yahr score was 2.5. After being on LCIG for 2 years, he was OFF about 25% of waking hours, and suffered increasing dyskinesia and gait abnormalities. At that point, his Hoehn and Yahr score was 3–4. He was subsequently evaluated for DBS because of severity and inadequate control of dyskinesia by LCIG.

Levodopa equivalent daily dose (LEDD) at initiation of LCIG was 1050 mg (LCIG monotherapy during the day, oral levodopa 200–300 mg at night). UPDRS-III was 30 when ON medications (on LCIG). Levodopa challenge with a supra-ON dose improved the UPDRS-III from 49 (practically defined OFF LCIG) to 32, and Hoehn and Yahr score was 4 when OFF. Severe generalized peak dose dyskinesia was seen (Supplementary Video 1). Given severe dyskinesias poorly controlled by LCIG, continued good motor response to levodopa, and persistent motor fluctuations, he was deemed to be a suitable candidate for DBS and underwent bilateral STN-DBS with no surgical complications. STN was chosen as opposed to globus pallidus interna because the patient had significant motor fluctuations (in addition to dyskinesias), and one of the additional goals was to decrease the LEDD. Neuropsychology testing revealed preserved cognitive function, and his Montreal cognitive assessment score was 29/30.

Perioperatively, it was decided to maintain the patient on LCIG before programming was optimized, and to see if there was a need for "dual" therapy. Deep brain stimulation programming started 4 weeks after surgery. Dyskinesia improved significantly (Supplementary Video 1) and LCIG was discontinued, with a decrease in LEDD by 40% initially. However, he remained extremely sensitive to regular levodopa-carbidopa: even low doses (50 mg) resulted in axial dyskinesia. Therefore, combination of a controlled release formula (CR 200/50 mg, five times/day) with rotigotine transdermal patch (4–8 mg/24 hours) was used and adjusted over the next 4 months. Although the initial decrease in LEDD was not sustained, the patient eventually experienced minimal motor fluctuations or freezing of gait, and dyskinesias were well-controlled. Five months after DBS, when DBS was optimized, his UPDRS-III score was 14. This is lower than the UPDRS-III ON pre-DBS, which may be explained by dyskinesias negatively affecting gait, fine motor movements, and potentially tone as well. At that point, his Hoehn and Yahr score was 2-2.5.

To our knowledge, this is the first report that DBS is used to improve insufficient symptom control in a patient treated with LCIG. On the other hand, using LCIG for refractory symptoms after long-term STN-DBS has been reported.[3] Both LCIG and DBS have good efficacy in controlling motor fluctuations and reducing troublesome dyskinesia in advanced PD.[4] However, DBS is usually considered first in younger patients who can remain independent for many years. In those with severe dyskinesia, patient preference is an important consideration. Dyskinesias can worsen with LCIG,[2,4] and, in fact, have been reported as a reason to stop LCIG therapy.[5] For patients not optimized on LCIG, our case suggests that DBS can be reconsidered if no contraindications exist.

Literature is lacking on transitioning from LCIG to oral levodopa peri- or post-DBS surgery. As it often takes a few months to optimize programming for DBS, it may be reasonable to continue LCIG until DBS settings have been optimized. Although we were ultimately unable to reduce LEDD with a combination of levodopa CR and rotigotine transdermal patch, motor symptom control was satisfying to the patient and bothersome dyskinesias were significantly reduced. Although our patient was concerned about the invasive nature of DBS and initially chose LCIG, with consultation and support, he coped well with both the peri-operative DBS period and programming.

In summary, this report highlights the need for re-evaluating patients for alternative treatment options if symptom control is not optimized even when they are already on continuous dopaminergic stimulation.

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Patient Consent

The patient provided informed written consent for this case report including the video.

Statement of Authorship

NN and FB drafted the manuscript. NN, TS, OS, and FB critically reviewed and edited the manuscript. TS, OS, and FB were involved in the medical management of the patient. All authors approved the final version of the manuscript.

Supplementary Material

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