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Levodopa/carbidopa intestinal gel infusion can improve camptocormia in Parkinson's disease

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Camptocormia in Parkinson's disease (PD) is an involuntary flexion of the thoracolumbar spine evident during standing or walking which resolves when supine or leaning against a wall. It can be classified as upper (≥45° thoracic spine flexion) or lower (≥30° hip flexion) based on the inflexion point [1]. Camptocormia is reported in 3–17% of PD patients and is associated with disease progression, a higher burden of non-motor symptoms and reduced quality of life [2,3]. Oral levodopa, botulinum toxin injections and deep brain stimulation (DBS) provide variable or limited benefit [2]. We report two patients with camptocormia that improved after levodopa/carbidopa intestinal gel (LCIG) infusion. Signed consent for online publication and dissemination of all persons visible on the videos were obtained.

Patient 1. The patient was diagnosed with PD at age 62. His Parkinsonism was well-controlled with rasagiline, levodopa/carbidopa and CR pramipexole 4.5 mg (total LED 1150 mg) but he eventually developed troublesome motor fluctuations. At age 70, over a period of 6-months, he developed epigastric pulling and painless progressive truncal flexion, especially after prolonged walking. He had occasional falls due to freezing of gait (FOG). His dose of pramipexole had been stable for seven years. The patient underwent an acute levodopa challenge with 150/37.5 mg which resulted in a good 'on'. He had mild residual bradykinesia and rigidity, postural instability but no tremor. However, there was a persistent 75° thoracic flexion (malleolus method) both pre- and post-levodopa that was almost completely reduced by extending his back against the wall. There was no truncal weakness. Because of our experience with 24-h LCIG treatment in 16-h treatment-resistant dyskinesias, 24-h LCIG was introduced 8-months after the onset of his camptocormia. All other dopaminergic treatment was ceased the day he commenced LCIG. After 3-months, re-assessment with the same methods the patient had 45° thoracic flexion, and at 1-year, there was a 15–30° flexion and a substantial improvement of FOG (Table 1). After 25-months, the camptocormia ranged between 10 and 30° and his final LED was 3010 mg.

Patient 2. This 74-year-old was diagnosed with idiopathic PD at age 64. He had disabling motor fluctuations treated with oral levodopa, rasagiline and pramipexole CR 2.25mg (LED 775 mg) but over 12 months developed progressive truncal flexion. After a levodopa challenge using 300 mg, at which time he reported a good 'on', he had moderate bradykinesia and rigidity, impaired postural reflexes, 45° thoracic flexion (malleolus method) and 20° right truncal tilt (Pisa syndrome). There was no back pain and no truncal weakness. Pramipexole was weaned 5-months before LCIG, but his camptocormia did not improve. He commenced 16-h LCIG and nocturnal oral levodopa. At 6-months, there was a substantial improvement of motor symptoms, FOG and camptocormia (Table 1). The examination 10-months, after starting LCIG showed a 10–30° thoracic flexion, but Pisa syndrome was not changed.

Camptocormia in PD is frequently associated with disease progression, and as few as ~20% of patients may experience benefit from oral levodopa [4]. In addition, STN or GPi DBS, can improve symptoms in ~60% of patients, particularly when the camptocormia is levodopa responsive [2,5]. Our patients had progressive camptocormia despite modification to their oral medication regimens and did not respond to an acute levodopa challenge. Despite this, they improved with continuous levodopa infusion therapy, providing evidence for a novel treatment strategy. The mechanism of improvement with LCIG could potentially be due to both pharmacokinetic and pharmacodynamics effects due to an optimized levodopa/carbidopa delivery.

Axial myopathic and musculoskeletal mechanisms have been postulated in PD camptocormia [2] but was excluded on clinical grounds in our cases, as there was no truncal weakness on specific examination and also due to the dissociation between their ability to extend their back when leaning against a wall as opposed to without the use of this sensory trick. Dopamine agonists have also been rarely implicated in camptocormia but was unlikely to be the cause in our patients because in Patient 1, pramipexole had been at a stable dose for seven years, and in Patient 2, pramipexole was ceased 5-months before LCIG without improvement.

It is of interest that in Patient 2, camptocormia improved but Pisa syndrome did not. Axial musculoskeletal abnormalities are implicated in both Pisa syndrome and camptocormia, whereas disordered sensorimotor integration of posture, as well as both dopaminergic and non-dopaminergic mechanisms, have been postulated in the former. The lack of improvement in his Pisa syndrome suggests that non-dopaminergic mechanisms were predominant.

In conclusion, 16-h or 24-h LCIG may reduce camptocormia in PD. Confirmation of this finding in a larger group of patients is required.

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Table 1
Baseline and follow-up assessments of Parkinson's disease patients with camptocormia.

	Patient 1*	Patient 2**
PD age of onset	62 years	64 years
Age of LCIG commencement	72 years	74 years
Time with camptocormia symptoms before LCIG therapy	8 months	12 months
MoCA score	28 points	27 points
UPDRS-MDS Part 3 Baseline	39 points	41 points
UPDRS-MDS Part 3 Follow-up	31 points	22 points
UPDRS-MDS Part 4 Baseline	10 points	13 points
UPDRS-MDS Part 4 Follow-up	3 points	4 points
Hoehn and Yahr Baseline	3	3
Hoehn and Yahr Follow-up	2	2
NFOG-Q Baseline	27 points	28 points
NFOG-Q Follow-up	0 points	0 points
Degree of truncal flexion Baseline	75°	45°
Degree of truncal flexion Follow-up	30°	10°
Dopaminergic medications immediately prior to LCIG therapy	Pramipexole ER 4.5 mg (stable dose for 7-years) Levodopa/Carbidopa 600 mg/day Rasagiline 1 mg (total LED 1150 mg)	Pramipexole ER 2.25 mg (stable dose for 2-years) Levodopa/Carbidopa 450 mg/day Rasagiline 1 mg (total LED 775 mg)
LCIG and concomitant dopaminergic medications	Morning dose 2.3 mL Daytime continuous rate 6.8 mL/hr Nocturnal continuous rate 4.8 mL/hr (total LED 3010 mg)	Morning dose 11 ml Continuous rate 4.9 mL/hr Levodopa/Carbidopa CR 200/50 mg (at night) (total LED 2167 mg)
Therapy complications ***	None	None

Abbreviations: NFOG-Q: new freezing of gait questionnaire; MoCA: Montreal Cognitive Assessment.
*Follow-up assessment after 12-months of LCIG therapy.
**Follow-up assessment after 10-months of LCIG therapy.
***Therapy complications included neuropathy, vitamin B6, B12, B1 deficiency, tube complications, dopamine agonist withdrawal syndrome, troublesome dyskinesia and hallucinations.

Author contributions

Hugo Morales: Study design, collection of data, writing the first draft, and final version of the manuscript. Stephen Duma, Andrew Martin, Jane Griffith, David Tsui: Study design, collection of data, review of the final version of the manuscript. Neil Mahant and Victor SC Fung: Study design, collection of data, study supervision, and review of the final version of the manuscript.

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Potential conflict of interest

None'

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.06.010.

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