

Axial symptom resistance to levodopa in Parkinson's disease: a study of patients treated with continuous infusion of levodopa-carbidopa intestinal gel

Domiziana Rinaldi^{2*}, G. Imbalzano^{1,2*}, G. Calandra Buonauro^{4,5}, M. Contin^{4,5}, F. Amato⁶, G. Giannini^{4,5}, L. Sambati^{4,5}, C. Ledda, A. Romagnolo, G. Olmo⁶, P. Cortelli^{4,5}, M. Zibetti^{1,2}, L. Lopiano^{1,2}, C.A. Artusi^{1,2}

*These authors equally contributed to the manuscript

¹Department of Neuroscience "Rita Levi Montalcini", University of Torino, Torino, Italy

²SC Neurologia 2U, AOU Città della Salute e della Scienza, Torino, Italy

³Department of Neuroscience, Mental Health and Sense Organs (NESMOS), Sapienza University of Roma, Roma, Italy

⁴IRCCS, Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

⁵Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy

⁶Department of Control and Computer Engineering, Politecnico di Torino, Torino, Italy

Background: The treatment of freezing gait (FoG) and other axial symptoms of Parkinson's disease (PD) is currently an unresolved challenge for clinicians. While these symptoms appear to be unresponsive to levodopa, there are no systematic evaluations of axial symptoms at progressively increasing doses of levodopa. We sought to analyze the response to high levodopa doses of FoG, posture, gait parameters, and speech occurring in a daily-ON therapeutic condition.

Methods: We performed an interventional study in PD patients treated with continuous infusion of levodopa/carbidopa-intestinal gel (LCIG) presenting FoG in daily-ON condition. Subjects were evaluated by quantitative outcome measures at their usual LCIG infusion rate (T1), and one hour after 1.5x (T2) and 2x (T3) increase of the LCIG infusion rate. Two blinded raters evaluated the number of FoG episodes (primary outcome), posture, speech, and gait parameters. We also analyzed any changes in motor symptoms, dyskinesia, and plasma levodopa concentrations.

Results: We enrolled sixteen patients (mean age of 69±9.4 years) treated with LCIG for a mean of 2.2±2.1 years. FoG improved in 83.3% of patients and the number of FoG episodes significantly decreased (mean 2.3 at T1, 1.7 at T2, 1.2 at T3; p:0.013). Posture and speech parameters did not significantly change; stride length, turn duration, and turn velocity significantly improved (p: 0.049; p: 0.001; p: 0.024) after doubling the levodopa dose.

Conclusions: Increasing the dose of levodopa dose acutely may improve 'dopa-resistant' FoG and gait parameters PD patients presenting optimal control of motor symptoms and fluctuation in the absence of significant dyskinesia worsening.