# Levodopa-carbidopa intestinal gel treatment: focus on troublesome dyskinesias

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## Introduction

- Levodopa-carbidopa intestinal gel (LCIG) has shown an optimal efficacy in the reduction of motor fluctuations among advanced Parkinson' disease (PD) patients [1].
- Conversely, results on dyskinesias can be heterogeneous, with **some patients showing even a significant increase of dyskinesias within the first years of treatment and other patients presenting de novo by-phasic dyskinesias** [2,3].
- No study has specifically investigated the clinical prognostic factors for a better outcome in terms of dyskinesias management under LCIG treatment;
- **Objective**: To identify a sub-group of advanced PD patients who are more likely to have troublesome dyskinesias, under continuous LCIG.

## Material and methods

- A **retrospective and cross-sectional** study, including idiopathic PD patients under continuous LCIG treatment during at least six months;
- Patients were assessed for the Movement Disorder Society-Sponsored revision (MDS) of the Unified Parkinson disease rating scale (UPDRS) part I-II-III and UPDRS-IV, Hoehn & Yahr (H&Y) scale, Schwab and England score (S&E), Mini Mental State Examination (MMSE), body weight (BW), L-dopa equivalent daily dose (LEDD) and LEDD/kg, at two time-points, one week before starting LCIG treatment **(T0)** and at last outpatient visit on LCIG therapy **(T1)**.
- Statistical analysis were performed stratifying patients based on the **presence/absence or development/not development of troublesome dyskinesias** (UPDRS-IV, item 33 ≥2) at T1.

| | T0 (n=47) | T1 (n=47) |
|---|---|---|
| **Gender (Female, n/%)** | 16 / 34% | 16 / 34% |
| **Age, yrs** | 66.1±6.5 | 71±8.3 |
| **Age at PD onset, yrs** | 52.8 ± 7.8 | / |
| **Disease duration, yrs** | 14.5± 6.5 | 18.8 ± 7 |
| **LCIG treatment duration, months** | / | 51.7 ± 34.1 |
| **Body Weight, Kg** | 70.4 ±14.3 | 65.4 ±13.2 [a] |
| **BMI (Kg/m²)** | 25.7 ± 4.8 | 23.8 ± 4.1 [a] |
| **H&Y** | 2.8 ±0.9 | 3.1 ±1.2 [a] |
| **S&E** | 66.3 ± 14.3 | 55.1 ±21.9 [a] |
| **MMSE** | 27.5 ± 2 | 24 ± 4.6 [a] |
| **MDS-UPDRS I** | NA | 13.8 ±6.6 |
| **MDS-UPDRS II total** | 17.8± 8.2 | 27.6 ±11.1 [a] |
| **MDS-UPDRS III total** | | |
| **Off** | 49.1 ± 21 | NA |
| **On** | 31.7 ± 13.5 | 43.1 ± 20 [a] |
| **UPDRS IV total** | 9.3 ± 3.3 | 4.9 ± 2.9 [a] |
| **UPDRS IV – item 32 (dyskinesia duration)** | 1.6 ± 0.9 | 1.5 ± 0.9 |
| **UPDRS IV – item 33 (dyskinesia disability)** | 1.2 ± 1 | 0.9 ± 0.9 |
| **UPDRS IV – item 39 (Off-duration)** | 2 ± 0.5 | 0.9 ± 0.6 [a] |
| **Pts with troublesome dyskinesias (%)** | 17 | 29[a]<br>21 - disappear<br>19 - new<br>10 - unchanged |
| **LEDD** | 1426.5 ± 481.8 | 1558.1± 414.4 [a] |
| **LEDD/Kg** | 20.3 ± 8.4 | 24.4 ± 7.6 [a] |

**Table 1. Demographic, clinical, therapeutic data of the patients at baseline (T0) and follow-up (T1).**
Values are expressed as mean ± SD, if nor otherwise specified.
H&Y: Hoehn & Yahr scale; S&E: Schwab and England score; LEDD: levodopa equivalent daily dose; MMSE: Mini Mental State examination. Troublesome dyskinesias:
[a] $p < 0.05$ comparison of baseline (T0) vs. follow-up (T1);
[b] $p < 0.05$ comparison of Med-Off vs. Med-On scores.

## Results

- We included **47 PD patients** (34% female) with a mean (SD) age and disease duration at of 71.1 (8.3) and 18.8 (7) years, respectively.
- **After a mean of 51.7 (34.1) months** of LCIG treatment, MDS-UPDRS-II/III, SE, MMSE and HY significantly worsened. UPDRS-IV improved ($p< 0.01$), with a significant improvement of "Off-time", in spite of a not significant change of dyskinesias severity and duration (Table 1).
- **At T0, 17% of the patients had troublesome dyskinesias**. The percentage increases up to **29% at T1, with 19% developing new troublesome dyskinesias**, 21% in which troublesome dyskinesias disappeared and 10% in which they endured.
- **Being female was the only clinical variable significantly associated both to the presence or development of troublesome dyskinesias at T1**, while a **lower BW at T0** was relevant only for having troublesome dyskinesias at T1. At a binary logistic regression, adjusted for LCIG treatment, disease duration and ΔLEDD/kg, **being female** continued to be significant **for having or developing troublesome dyskinesias** at T1 (**Hazard Ratio: 7.45** and 6.3, respectively).

## Conclusions

- **Being female and having a lower BW** can be significantly associated with a poor outcome in terms of dyskinesias management under chronic LCIG treatment.
- This sub-group of advanced PD patients should be carefully monitored once submitted to this device-aided therapy.

**References**

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