Int. j. adv. multidisc. res. stud. 2026; 6(4):1497-1498

Received: 01-08-2026
Accepted: 11-08-2026

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

Does Levodopa / Carbidopa Intestinal Gel Actually Increase the Risk of Neuropathy in Patients with Parkinson's Disease?

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DOI: https://doi.org/10.62225/2583049X.2026.6.4.6759

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Letter to the Editor

We read with interest the article by Erdem *et al*. on a prospective study investigating whether levodopa/carbidopa intestinal gel (LCIG) actually increases the risk of neuropathy compared to oral dopaminergic therapy (ODT) in patients with Parkinson's disease (PD) diagnosed at least five years prior [1]. The study showed that levodopa levels, levodopa equivalent daily doses, and homocysteine levels were higher in the LCIG group compared to the ODT group, that compound muscle action potentials and sensory nerve conduction velocities were reduced in all nerves examined, and that F-wave latencies were prolonged in the LCIG cohort [1]. It was concluded that LCIG increases the risk of polyneuropathy in PD patients [1]. While the study is interesting, some points warrant further discussion.

First, the other ingredients besides levodopa/carbidopa in the preparations taken by the included patients were not reported. Knowledge of the full spectrum of ingredients is crucial, as there is evidence that other components, not levodopa/carbidopa, are responsible for the development of neuropathy [2]. In addition to hyperhomocysteinemia, vitamin-B deficiency, and high doses of levodopa, reduced vitamin-D levels, duodenal tube material, gel components, and additional malnutrition can also cause neuropathy [2].

Second, elevated serum homocysteine levels can have various causes [3]. These include low levels of vitamin-B12, vitamin-B6, and folic acid; renal insufficiency; MTHFR mutations; smoking; high caffeine consumption; alcohol abuse; low thyroid hormone levels; malabsorption syndromes; psoriasis; homocystinuria; methotrexate; antiepileptic drugs; antidiuretics; male sex; and advanced age [3]. Were these factors actually ruled out as alternative causes of elevated homocysteine levels?

Third, it was not reported whether the nerve conduction studies (NCS) were performed by the same or different examiners in all patients [1]. Information on whether one, two, or more examiners performed the NCS is crucial, as interobserver variability may exist, which could significantly affect the results [4]. It was also not reported whether the NCS were performed once or repeatedly [1]. In the case of repeated NCS, the variability between examinations should be reported.

Fourth, the mean age in both groups was relatively high, suggesting that at least some patients suffered not only from PD but also from other comorbidities [1]. Therefore, it is essential to state whether the included patients in both groups received only levodopa/carbidopa or whether they also took other medications. In cases of polypharmacy, it should be investigated whether these additional medications could have influenced the NCS results and levodopa blood levels.

Fifth, the family history is not mentioned. To determine whether the included patients had a hereditary disease, including hereditary neuropathy, it is crucial to indicate whether or not first-degree relatives suffered from such a disease.

Finally, the study design, with only small cohorts and data from just one center, is not ideal for drawing general conclusions about the neurotoxicity of LCIG.

Declarations
Ethical Approval: Not applicable.

Consent to Participation: Not applicable.

Consent for Publication: Not applicable.

Funding: None received.

Availability of Data and Material: All data are available from the corresponding author.

Completing Interests: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contribution: JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. CS and FS: contributed to literature search, discussion, correction, and final approval.

Acknowledgements: None.

Keywords: Parkinson's Disease, Levodopa, Carbidopa, Intestinal Gel, Secondary Neuropathy

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