EFFECTS OF SUBCUTANEOUS FOSLEVODOPA-FOSCARBIDOPA ON MOTOR AND NONMOTOR SYMPTOMS IN PARKINSON'S DISEASE: A PROSPECTIVE LONGITUDINAL STUDY

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OBJECTIVES. Foslevodopa/foscarbidopa is a novel, soluble prodrug combination administered as a 24-hour continuous subcutaneous infusion (CSCI) for the treatment of patients with advanced Parkinson's disease (PD). The aim of this study was to evaluate the effect of switching from oral levodopa therapy to continuous subcutaneous infusion of foslevodopa/foscarbidopa on motor and nonmotor symptoms in patients with Parkinson's disease over 3-month treatment period.

MATERIALS. From April 2024 to September 2025, 55 patients with fluctuating PD, not adequately controlled by oral dopaminergic therapy, were initiated on continuous subcutaneous infusion (CSCI) at our Center. Longitudinal 3-month follow-up data were available for 38 patients.

METHODS. Motor symptoms were assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) part III. Nonmotor symptoms burden was evaluated by the NonMotor Symptom Scale (NMSS). Presence of treatment-related motor and nonmotor complications were assessed by means of the UPDRS part IV and Nonmotor Fluctuation Assessment questionnaire (NoMoFa), respectively. Parkinson's Disease Sleep Scale 2 (PDSS-2) was used to evaluate sleep quality. We also registered patient-reported quality of life using the Parkinson's Disease Questionnaire 8 (PDQ-8). At baseline and at 3-month follow-up visit, the total levodopa equivalent daily dose (LEDD) was calculated. Within-subject longitudinal differences on demographic and clinical variables between the two timepoints were assessed by means of one-way repeated-measures ANOVA analyses.

VARIABLE	pre-CSCI (mean ± SD) n=38	post-CSCI (mean ± SD) n=38	p-value
Age	66.5 ± 9.1	-	-
Sex (F/M)	7/31	-	-
Age at onset	66.6 ± 8.8	-	-
Disease duration (years)	12.1 ± 6.2	-	-
mH&Y stage	2.4 ± 0.4	-	-
Total LEDD (mg)	1282 ± 372.1	1347 ± 345.0	0.141

Table 1. Demographic and clinical characteristics of the study population.

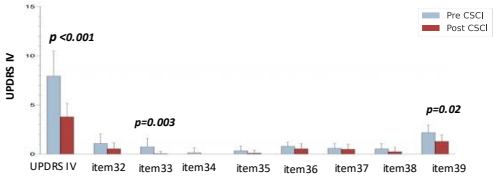

Figure 1. Longitudinal assessment of total UPDRS Part IV and related subscores before and after 3 months of treatment with continuous subcutaneous infusion. P-values are reported only for significant longitudinal differences.

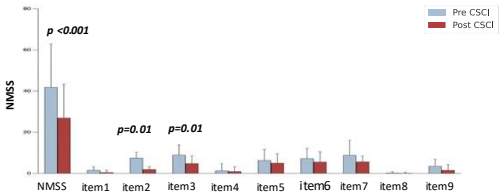

Figure 2. Longitudinal assessment of total and domain-specific subscores of Non-Motor Symptoms Scale (NMSS) before and after 3 months of treatment with continuous subcutaneous infusion. P-values are reported only for significant longitudinal differences.

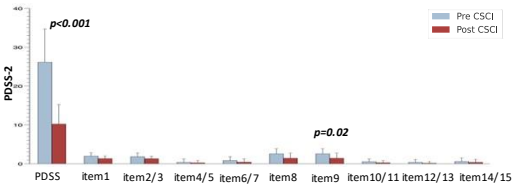

Figure 3. Longitudinal assessment of total and domain-specific subscores of Parkinson's Disease Sleep Scale (PDSS-2) before and after 3 months of treatment with continuous subcutaneous infusion. P-values are reported only for significant longitudinal differences.

RESULTS. As expected, after 3 months of CSCI treatment, total wake-up time spent in the OFF state significantly decreased, along with significant reduction in troublesome dyskinesia severity (Figure 1). Moreover, at follow-up significant improvements were observed in the NMSS sleep and mood/cognition domains as compared to baseline (Figure 2). Significant improvements were also found in PDSS-2 (Figure 3) and PDQ-8 scores (data not shown). No significant differences were found in total LEDD between oral and CSCI treatment. Infusion site-related adverse events were common but generally well tolerated after 3 months of treatment.

DISCUSSION. Our findings support the clinical effectiveness of CSCI in patients with PD who respond inadequately to oral therapy. The treatment improved motor fluctuations, dyskinesia, sleep quality and mood/cognition, leading to a clinically significant improvement in patients' quality of life. These benefits were achieved without significant increase in LEDD, indicating efficacy without additional dopaminergic load.

CONCLUSION. This study confirm preliminary observations in multicentric cohorts showing that CSCI may significantly reduce the burden of nonmotor symptoms in patients with PD.

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