Continuous subcutaneous infusion of Foslevodopa/Foscarbidopa in patients with idiopathic Parkinson's Disease: understanding psychiatric adverse effect

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BACKGROUND

Foslevodopa/Foscarbidopa (fLD/fCD) is a recently developed formulation of levodopa/carbidopa designed for continuous subcutaneous infusion, aiming to provide more stable plasma levels, hence reducing motor fluctuations.

While clinical benefits are increasingly recognized, less is known about the incidence and characteristics of psychiatric adverse effects associated with this treatment.

OBJECTIVE

To assess the frequency, severity, and predictive factors of psychiatric adverse effects (PAEs) associated with continuous subcutaneous Foslevodopa/Foscarbidopa (fLD/fCD) infusion in patients with Parkinson's disease (PD).

MATHERIALS and METHODS

Thirty-one PD patients (M = 17, F = 14; mean age 64.48±10.99 y; BMI 24.65±3.70 kg/m²) were hospitalized for fLD/fCD pump implantation.

Sex, age, BMI, age at onset, disease duration, RBD, MDS-UPDRS III–IV, MOCA, MMSE, PD Mild Cognitive Impairment (PD-MCI), Oral LEDD were collected at baseline. fLD/fCD LEDD was determined at two timepoints: at implantation and at discharge.

Variable	mean ± SD or frequency
Age (y)	64.48 ± 10.99
Age at PD onset (y)	53.16 ± 11.67
BMI (Kg/m2)	24.65 ± 3.70
Disease duration (y)	11.06 ± 6.29
Sesso (M/F)	17/14
RBD (y/n)	17/14
PD-MCI (y/n)	14/17
Mood disorders (y/n)	16/15
UPDRS III	41.06 ± 12.71
UPDRS IV	9.74 ± 3.57
MoCA	20.94 ± 4.42
MMSE	27.45 ± 2.98
LEDD oral (mg)	1145.59 ± 367.53
LEDD I-COMT(mg)	347.56 ± 183.39
LEDD I-MAO (mg)	100.00 ± 0.00
LEDD Da (mg)	275.38 ± 362.74
fLD/fCD LEDD Admission (mg)	1234.34 ± 339.17
fLD/fCD day dose admission (mg)	1250.69 ± 394.27
fLD/fCD night dose admission (mg)	361.94 ± 99.89
fLD/fCD LEDD discharge (mg)	1378.86 ± 493.27
fLD/fCD day dose discharge (mg)	1371.93 ± 420.46
fLD/fCD night dose discharge (mg)	395.52 ± 127.97

Table 1.
Patients had long disease duration (11.06 y±6.29) and moderate motor impairment (UPDRSIII: 41.06±12.71). PD-MCI was present in 45% (14/31), and 51% (16/31) had a pre-existing mood disorder. Oral LEDD at baseline was 1145.59 ± 367.53; implantation fLD/fCD LEDD was 1234.34 ± 339.17, while discharge LEDD was 1378.86 ± 493.27.

*Doses were calculated using a 24 mg fLD = 17 mg LD conversion factor. Infusion hours: 16 h daily dose and 8 h nighttime dose. Conversion factor (ml/h to mg): infusion velocity*infusion hours* 240*

RESULTS

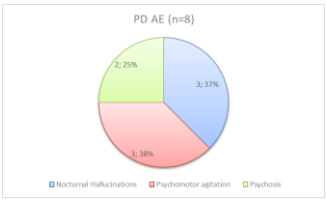

Fig. 1

Figure 1 and 2
Eight patients (8/31, 26%) developed PAEs (3 nocturnal hallucinations, 3 psychomotor agitation, 2 psychosis), mostly within the first two nights of infusion. Symptoms resolved either with night-time dose reduction (4/8) or spontaneously (4/8); only one patient required antipsychotic therapy. No discontinuations occurred.

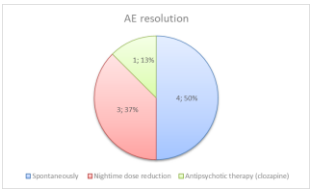

Fig. 2

Table 2
Based on occurrence of PAE, patients were categorized as PD-AE (n = 8) or PD-noAE (n = 23). No significant demographic or baseline clinical differences were observed between the two groups.

Variable	AE Group (mean ± SD)	NO AE Group (mean ± SD)	p-value
Age (y)	63.25 ± 16.68	64.91 ± 8.68	ns
Age at PD onset (y)	52.62 ± 17.48	53.35 ± 9.40	ns
BMI (Kg/m2)	25.02 ± 4.59	24.52 ± 3.44	ns
Disease duration (y)	10.75 ± 3.77	11.17 ± 7.02	ns
UPDRS3 T0	40.38 ± 13.89	41.30 ± 12.60	ns
UPDRS4 T0	7.62 ± 3.96	10.48 ± 3.19	ns
MoCA al T0	20.25 ± 5.28	21.17 ± 4.18	ns
MMSE al T0	26.25 ± 3.65	27.87 ± 2.67	ns
LEDD oral (mg)	1288.03 ± 393.46	1096.04 ± 353.55	ns
LEDD I-COMT(mg)	376.85 ± 110.83	337.80 ± 204.27	ns
LEDD I-MAO (mg)	100.00 ± 0.00	100.00 ± 0.00	ns
LEDD Da (mg)	660.00 ± 784.89	220.43 ± 280.05	ns
fLD/fCD LEDD Admission (mg)	1483.46 ± 258.67	1147.69 ± 324.29	*0,012*
fLD/fCD day dose admission (mg)	1469.03 ± 314.21	1174.75 ± 396.48	*0,078*
fLD/fCD night dose admission (mg)	440.10 ± 81.63	334.75 ± 92.15	*0,006*
fLD/fCD LEDD discharge (mg)	1632.92 ± 710.55	1290.49 ± 373.51	ns
fLD/fCD day dose discharge (mg)	1531.72 ± 463.39	1316.35 ± 400.29	ns
fLD/fCD night dose discharge (mg)	434.70 ± 135.00	381.89 ± 125.62	ns

Variable	AE Group (n=8	NO AE Group (n=2	p
Sex (Male freq)	75%	47,8%	ns
RBD (yes freq)	75%	48%	ns
Mood disorders (yes freq	63%	48%	ns
PD-MCI (yes feq)	63%	39%	ns

Figure 3 and 4
However, PD-AE patients had significantly higher implantation fLD/fCD LEDD (1483.46 mg±258.67 vs 1147.69 mg±324.29; p = 0.012), especially for night-time dosing (440.10 mg±81.63 vs 334.75 mg±92.15; p = 0.006).

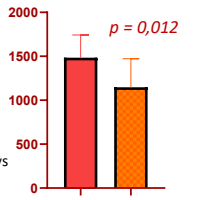

Fig. 3

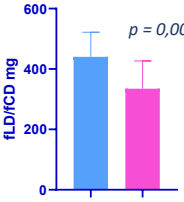

Fig. 4

fLD/fCD LEDD Admission fLD/fCD night dose admission

DISCUSSION

26% of patients showed mild AE (nocturnal hallucinations, psychomotor agitation).
A reduction in night-time dose resulted in symptom resolution.
No associations were found with other known risk factors.

CONCLUSION

In our cohort, although PAEs were observed in a subset of patients, they were generally mild, transient, and associated with higher night-time dosing. Careful titration facilitated prompt management and resolution of symptoms. Further studies are needed to better understand the incidence and predictive factors of PAEs in PD patients receiving fLD/fCD infusion.

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