Safinamide versus Entacapone in Parkinson disease
Results from a prospective multicentre study

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BACKGROUND

- Safinamide is a novel drug for Parkinson's disease (PD) whose pharmacological profile includes reversible MAO-B inhibition, blockage of voltage-dependent sodium channels, modulation of calcium channels and abnormal glutamate release (FIGURE 1).
- Entacapone is a selective reversible COMT inhibitor that, when co-administered with LDopa, increases its AUC and plasma concentration.
- Both drugs are used as add on therapy in PD patients with motor fluctuations treated with Ldopa but there aren't any comparison studies between the two inhibitors.

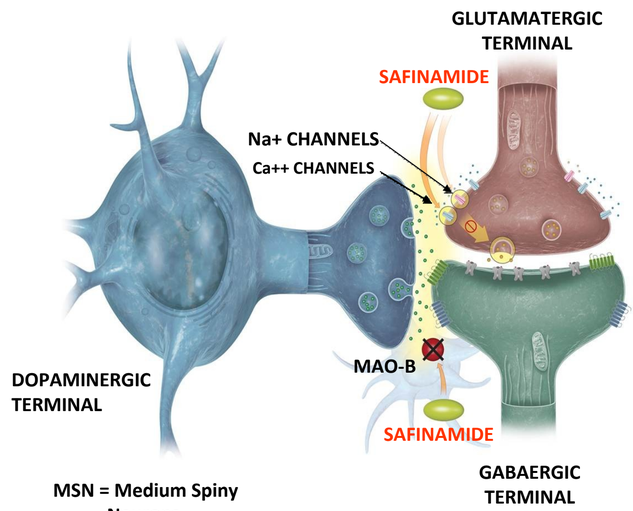


FIGURE 1

METHODS

Objective: To compare Safinamide versus Entacapone treatment in PD patients with motor fluctuations

Study design: ***open label multicentre prospective trial***

Group A (n. 25): safinamide 50 mg add on therapy

T0 *(homogeneous for age, gender and clinical features)* **Tf = 8 months**

Group B (n. 25): entacapone 200 mg add on therapy

Group C (n. 12): switch overnight Entacapone/Safinamide

Statistical analysis:

t-test group A versus B (T_f evaluation)

t test Tf versus T0 group C

Inclusion criteria

Motor fluctuations (wearing off)

Absence of cognitive impairment

Absence of psychiatric complications (ICD, psychosis)

Absence of dyskinesia (groups A and B)

Patients in Ldopa/DA treatment

No IMA-B treatment in the previous 3 months

Group C: *patients treated with Entacapone and with moderate/severe dyskinesia*

Primary outcome

- change in total daily off-time (minutes)

Secondary outcome:

- clinical global improvement (CGI) score,
- UPDRS total score
- UPDRS Part II score
- UPDRS Part III score
- Dyskinesia score (UPDRS subitems 32+33+34)
- PFS-16

RESULTS

- There were no significant differences in demographic features between the three groups (TABLE 1)
- 6 patients (3 assigned to GROUP B, 2 assigned to GROUP A, and 1 to GROUP C) did not complete the study (change of PD medication)
- No serious side effects were shown in the three groups
- Both Safinamide and Entacapone reduced significantly mean daily off time and improved CGI and UPDRS scores but no significant differences were showed between the two treatments (TABLE 2, FIGURE 2).
- Dyskinesia, when present, worsened in both groups (GROUP A and B) but significantly more in patients treated with Entacapone (FIGURE 2).
- Patients in GROUP C didn't change significantly in mean daily off time and UPDRS whereas dyskinesia improved significantly between T_0 and T_f (TABLE 2, FIGURE 2).

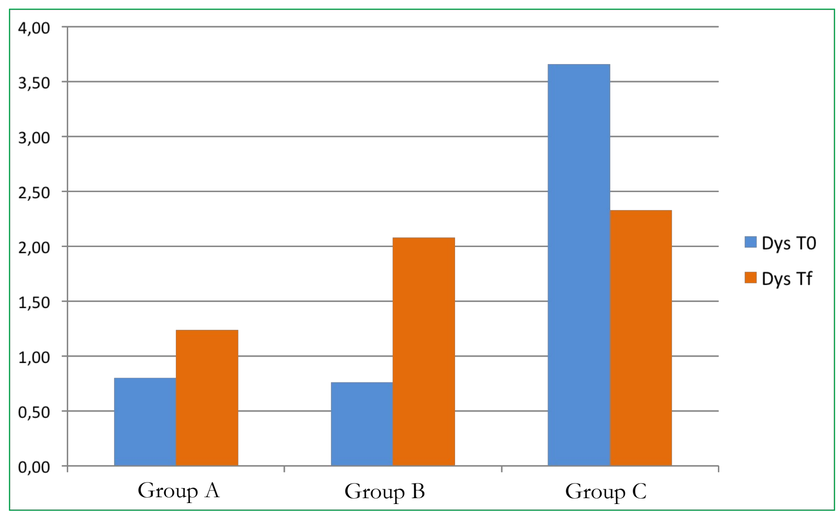
TABLE 1

	M/F	Age (years)	H&Y	Dis duration (years)	LEDD (mg)
GROUP A	15/10	68.16±9.95	2.1±1.1	8.28±2.73	686±254
GROUP B	16/9	69.96±5.55	2.0±1.0	8.64±2.77	740±315
GROUP C	6/6	69.58±4.96	2.1±0.9	10.42±2.78	683±224

TABLE 2

		UPDRS II	UPDRS III	UPDRS tot	Dysk	CGI-I	OFF time(min)	PFS-16
GROUP A	T0	11.5±3.5	21.8±7.8	33.4±10.2	0.8±0.9		109±48	20.1±6.7
	Tf	*10.6±3.1*	*20.4±7.0*	*31.0±8.8*	*1.3±0.9*	***2.2±0.9***	*71±52*	19.4±6.3
GROUP B	T0	10.5±4.2	17.8±8.7	28.3±12.4	0.7±0.7		122±54	20.8±5.1
	Tf	*9.3±3.1*	*17.0±7.7*	*26.4±10.1*	*2.1±1.0*	***2.3±0.9***	*69±52*	*20.3±5.0*
GROUP C	T0	9.4±2.6	16.7±5.3	26.1±6.7	3.7±0.9		55±35	17.8±3.6
	Tf	9.3±2.6	16.1±5.9	25.3±7.1	***2.3±0.7***	***3.2±0.7***	58±33	17.3±3.7

FIGURE 2



CONCLUSIONS

Once-daily Safinamide reduces mean daily off-time and improves symptoms of PD in Ldopa-treated patients with motor fluctuations, an effect similar to that of Entacapone. Our study showed less dyskinesia score in patients treated with Safinamide compared to Entacapone. These results may be related to Safinamide non dopaminergic (glutamatergic) properties and are unlikely due to reduced dopaminergic stimulation. The open-label design and the small sample size of our study represent a limitation and the results must be confirmed with double blind randomized clinical trials.

References

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