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The use of entacapone in patients with advanced Parkinson's disease: 2 years' experience

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Abstract Since January 2000 we have administered entacapone (200 mg) to 75 patients with severe Parkinson's disease in combination with their routine levodopa dose. At baseline the mean UPDRS (item III) score was 38±6. After 3 months of entacapone therapy the patients presented a significant improvement of motor fluctuations; the mean UPDRS score (item III) was 20±4. This improvement was also statistically significant after 2 years of entacapone therapy.

Short Report

Parkinson's disease (PD) is a chronic neurodegenerative disease with the principal pathological abnormality of progressive loss of dopaminergic neurones projecting from the substantia nigra to the striatum [1]. During the first years of levodopa therapy, the patient experiences marked improvement in parkinsonian symptoms, functional capacity, and quality of life. However, after an initial period of good and continuous response to levodopa, levodopa dose-related motor complications, end-of-dose wearing-off, and dyskinesias emerge [2, 3].

To further smooth the response to levodopa and diminish the dose and frequency of administration of levodopa needed by PD patients, a second class of enzyme inhibitors has been used as an adjunct to levodopa therapy, the catechol-O-methytransferase (COMT) inhibitors [4]. Entacapone, used as an adjunct to each daily levodopa/DDC inhibitor dose, inhibits the formation of 3-O-methyldopa in the periphery, thereby increasing the bioavailibility and half-life of levodopa without affecting the peak plasma concentration (Cmax) or the time taken to reach Cmax (tmax) [5].

Since January 2000 we have administered entacapone to 75 patients with advanced Parkinson's disease in our neurological outpatient department. They presented marcate motor fluctuations characterized by sudden on and off states with frequency and media duration of 4±1 and 1±0.5 h daily, respectively. To confirm their symptoms, all patients were asked to fill in hourly diaries of their disturbances, reporting motor fluctuations, off and on periods with and without dyskinesias during the last week prior to administration of entacapone. The patients had been treated for 6±2 years with levodopa (800±100 mg daily) and dopaminoagonists (ropinirole 15±3 mg and pramipexole 2.1±0.18 mg). We utilized the UPDRS [6] to evaluate motor fluctuations. Statistical analyses were performed with Wilcoxon's signed rank test and Student's *t*-test.

At baseline the mean UPDRS (item III) score was 38±6. All patients started entacapone (200 mg) in combination with their routine levodopa dose. After 3 months they returned to our laboratory for follow-up. The patients showed a large significant reduction of motor fluctuations, the mean UPDRS (item III) score was 20±4. This value was statistically significant at 6, 12, 18, and 24 months after the introduction of entacapone therapy ($p<0.001$) (Table 1).

We also observed a mild increase of dyskinesias in 20 patients after 3 months of entacapone treatment. For this reason we decided to reduce levodopa (200±50 mg). Within 10 days of entacapone introduction, 3 patients experienced severe dyskinesias, so we reduced the levodopa dose (300±25 mg). However, patients continued to present marked dyskinesias and so after 1 month of entacapone treatment the drug was withdrawn. Furthermore, 20 patients presented with discoloration of the urine; 6 patients reported reversible and mild nausea, but they continued to take entacapone.

Our short report confirms the efficacy and safety of entacapone therapy in severe PD. Patients presented a significant reduction and severity of motor fluctuations, and this benefit was confirmed after 2 years of entacapone therapy.

References

1. Hornykiewicz O (1982) Brain neurotransimtter changes in Parkinson's disease. In: Marsden CD, Fahn S (eds) Movement disorders. Butterworth, London, pp 41–58

Table 1 Mean UPDRS (item III) score during entacapone therapy

Time (months)	0	3	6	12	18	24
Score mean value	38±6	20±4	19±2	21.5±3	20.7±3	21.3±5
p versus baseline		<0.001	<0.001	<0.001	<0.001	<0.001

2. Rinne UK, Larsen JP, Siden A, Worm-Petersen J, and the NONECOMT Study Group (1998) Entacapone enhances the response to levodopa in parkinsonian patients with motor fluctuations. Neurology 51:1309–1314
3. Myllyla VV, Kultalahati ER, Haapaniemi H, Leinonen M, and the FILOMEN Study Group (2001) Twelve-month safety of entacapone in patients with Parkinson'd disease. Eur J Neurol 8:53–60
4. Mannista PT, Kaakkola S (1990) Rationale for selective COMT inhibitors as adjuncts in the drug treatment of Parkinson's disease. Phamarcol Toxicol 66:317–323
5. Keranen T, Gordin A, Hariola VP et al (1993) The effect of catechol-O-methyl transferase inhibition by entacapone on the pharmacokinetics and metabolism of levodopa in healthy volunteers. Clin Neurophamacol 16:145–156
6. Fahn S, Elton RL, Members of the UPDRS Development Committee (1987) In: Fahn S, Marsden CD, Calne DB, Goldstein M (eds) Recent developments in Parkinson's disease, vol. 2. Mcmillan Health Care Information, Florham Park, NJ, pp 153–164