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Long-term retention rate of pramipexole in the treatment of Parkinson's disease

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To the editor:

In a recent retrospective study, Arbouw et al. [1] reported that 60% of patients treated with pramipexole (PRX) due to Parkinson's disease (PD) discontinued the drug within 3 years. The patients were identified from a neurology department of a large teaching hospital in The Netherlands, and the discontinuation rates were based on prescription data from community pharmacies. We have assessed long-term retention rate of patients on PRX therapy based on hospital records and sought to identify risk factors underlying the discontinuation of PRX.

Using the patient records of Tampere University Hospital (Finland), we retrospectively identified all patients with idiopathic PD treated either as in- or outpatients at the Department of Neurology between 1 January 1999 and 31 December 2005. We included patients who had been prescribed PRX and for whom data were available from at least one follow-up visit. From the hospital records on patient demographics, age at onset and duration of PD, we obtained information on possible motor (treatment-related fluctuations, dyski-

nesia) and non-motor complications (e.g. orthostatic hypotension, hallucinations etc.) and previous concomitant PD drugs and their doses prior to and during PRX treatment. The cause and time of possible discontinuation of PRX was recorded. The retention rate (i.e. the proportion of patients continuing on PRX medication) was estimated using the Kaplan–Meyer method [2]. Follow-up commenced at the introduction of PRX into the treatment program and ended at the discontinuation of treatment or closing date. The effect of different factors on retention rate was examined using Cox regression analysis [3].

A total of 94 patients (33 women, 61 men) fulfilled the study criteria. The mean age of the patient cohort at the onset of PD was 59 (standard deviation 11) years, and the duration of the disorder before the initiation of PRX therapy was 6.5 (SD 6) years. Motor fluctuations prior to the introduction of PRX were recorded in 37 patients (39%). At the initiation of PRX treatment, 66 patients (70%) were on levodopa, 30 (32%) used selegiline, 19 (20%) used entacapone and 15 (16%) used other antiparkinsonian drugs. At the last follow-up, 72 patients were still using PRX. Figure 1 shows the estimated rate of patient continuation on PRX. At 1 year, 76% of the patients were still on PRX; the rate at 3 and 6 years was 63%. The mean maintenance dose of PRX was 1.05 mg/day (as base; corresponding approximately to 1.5 mg as salt). Of the 94 patients, 14 (15%) discontinued PRX due to adverse effects, and eight (9%) discontinued due to insufficient therapeutic effects. The most common adverse effects leading to discontinuation were confusion (three patients), hallucinations (three patients) and nausea (two patients). Other reasons of discontinuation included dyskinesia, orthostatic hypotension and miscellaneous symptoms.

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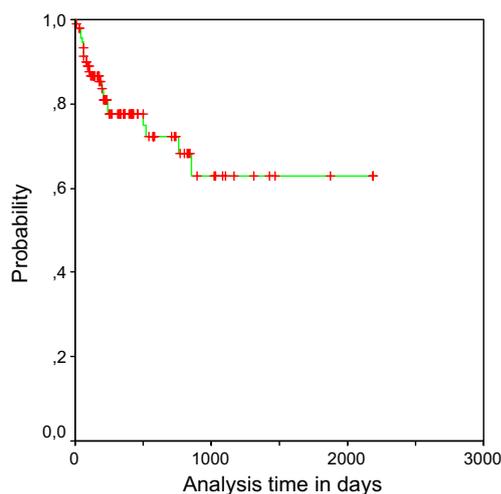


Fig. 1 Estimated retention rate for pramipexole in the treatment of patients with Parkinson's disease, as determined by Kaplan–Meyer analysis

Statistically significant predictors for an increased risk of discontinuation of PRX were orthostatic hypotension ($p=0.002$) and entacapone treatment ($p=0.38$) prior to the introduction of PRX. None of the other possible risk factors analyzed (age, sex, duration of PD, presence of motor fluctuations, dyskinesia, hallucinations or confusion at the initiation of PRX) predicted discontinuation of PRX treatment.

Retention rate of PRX among our PD patients was much higher than that found by Arbouw et al. in their clinic-based cohort [1]. The cause for the discrepancy in the findings remains unclear. Several characteristics of these two patient groups, including the duration of PD as well as the use of other antiparkinsonian drugs, especially levodopa and selegiline, were comparable. However, the mean daily dose of PRX in our patients was lower than that in the patients of Arbouw et al. (2.0 g) [1]. Different study methods may also contribute to the variation in

findings: Arbouw and co-workers [1] assessed the continuation of PRX treatment by retrieving prescription data from pharmacies, whereas we relied on records of physicians treating the patients.

Our study methodology allowed us to assess risk factors for the discontinuation of PRX. Two long-term clinical trials [4, 5] reported that the main reasons for discontinuation are dopaminergic adverse effects, hallucinations, confusion and nausea. Dyskinesia was an uncommon cause of withdrawal of PRX in our patients. Multivariate analysis of the risk factors showed that orthostatic hypotension and entacapone treatment prior to the start of PRX predicted a higher risk of discontinuation of the medication. Concomitant entacapone treatment has probably predisposed patients to a high dopaminergic tone, thus increasing the risk of adverse effects and discontinuation of PRX.

In conclusion, our findings suggest that PRX is a useful and well-tolerated adjunct to levodopa in the long-term treatment of advanced PD.

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