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Short communication

Prevalence and treatment strategies of dyskinesia in patients with Parkinson's disease

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Summary A study into the prevalence and treatment of dyskinesia in Parkinson's disease (PD) patients was performed with 380 PD specialists' completed interviews relating to PD and retrospectively completed 1900 patient record forms for patients with dyskinesia. Physicians reported, that 34% of their PD patients experience dyskinesia, 57% of dyskinetic PD patients were affected by moderately-to-completely disabling dyskinesia. Treatment of dyskinesia was looked upon as not satisfactory, fractionating of levodopa dose was used as first choice therapeutic option of dyskinesia.

Keywords: Parkinson's disease, dyskinesia, levodopa, patient disability, physician satisfaction

Introduction

Levodopa is well tolerated and highly effective in controlling motor symptoms in patients with Parkinson's disease (PD). It is common opinion, that onset of complications such as fluctuations in motor response and/or dyskinesia are predominantly associated with levodopa intake (Fahn et al., 2004). There is considerable variability in the reported prevalence of dyskinesia in PD patients, ranging from 30–45% of the overall PD population, with a distinct impact on quality of life (Schrag and Quinn, 2000; Ahlskog and Muenter, 2001; Chapuis et al., 2005). Beside treatment recommendations, little is known about how dyskinesia are managed in clinical practice and how satisfied physicians are with current treatment options (Olanow et al., 2001; Pahwa et al., 2006). Here we report the findings from a survey into the prevalence and conventional treatment strategies of dyskinesia in daily clinical practice in PD patients.

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Participants

This survey was performed in seven countries with 380 physicians (50 from each of France, Germany, Italy, Japan, Spain and the UK, and 80 from the USA). Participants were screened to ensure that they fulfilled the following criteria: to have practiced as a PD specialist between 5 and 30 years, routinely treating $\geq$50 patients each week and $\geq$15 PD patients each month. Physicians had to confirm that they were responsible for initiating treatment in PD patients and were involved directly in treatment decisions for PD patients with dyskinesia.

Interview

Each physician participated in a 25-minute structured interview. They were asked to estimate: the proportion of their PD patients who were newly diagnosed or visiting for repeat consultations; the treatments they used for patients at different stages of PD; the proportion of their PD patients with dyskinesia; who and how they manage patients with dyskinesia; and their satisfaction with the outcome of the treatments they use for these patients.

Patient record form

Physicians were also asked to complete retrospective patient record forms for their last five PD patients with dys-

kinesia (total 1900; 250 [France, Germany, Italy, Japan, Spain, UK]; 400 [USA]). These forms included information on: patient demographics; PD treatment at onset of dyskinesia; the proportion of the waking day with dyskinesia (0%, 1–25%, 26–50%, 51–75%, 76–100%) before any action was taken to reduce dyskinesia; the disability caused by dyskinesia before any action was taken (not/mildly/moderately/severely/completely disabling); the number of times the patient was seen by the physician in the past year; length of time from diagnosis of dyskinesia to first action taken; actions ever taken to reduce dyskinesia; and satisfaction with the current outcome achieved with regard to dyskinesia (very satisfactory/satisfactory/borderline/unsatisfactory/very unsatisfactory).

Statistics

Descriptive statistics and Pearson Product correlation for correlation analysis were employed.

Results

Treatment conditions of PD patients

In most countries, PD specialists are solely responsible for the ongoing management of the majority of patients with PD (72–88% across all countries surveyed). In France and the UK, however, approximately 50% of PD patients receive ongoing management from their general practitioner and visit specialists as required, while the other 50% are managed solely by PD specialists. At all stages of PD, physicians estimated that most of their PD patients receive dopaminergic therapy, either as monotherapy with levodopa or a dopamine agonist, or as combination therapy with levodopa and a dopamine agonist (Table 1). As the severity of PD increases, more physicians use combination therapy to treat their patients and fewer use dopamine agonist monotherapy. Overall, physicians believed that >80% of their patients at Hoehn and Yahr stage III would be receiving levodopa, either as monotherapy or in combination with a dopamine agonist, and this increased to >90% for patients at stages IV and V.

Table 1. *Demographics of PD patients with dyskinesia (from patient record-forms)*

	N (%)
Male	1064 (56)
Female	836 (44)
Mean age, years (range)	69 (25–93)
Mean time with PD, years (standard deviation)	8.9 (5.1)
Hoehn and Yahr stage	
1	67 (3.5)
1.5	126 (6.6)
2	262 (13.8)
2.5	260 (13.7)
3	662 (34.8)
4	403 (21.2)
5	120 (6.3)
Treatment regimen at onset of dyskinesia	
Levodopa monotherapy	726 (38.2)
Combination therapy	1068 (56.2)
Dopamine agonist monotherapy	97 (5.1)
Not stated	9 (0.5)

PD Parkinson's disease, *N* number of subjects.

Prevalence of dyskinesia

Physicians estimated that approximately 34% of their PD patients experienced dyskinesia, although there was marked regional variation as physicians in Japan and the USA estimated lower incidences of dyskinesia among their PD patients (24 and 26%, respectively), while physicians in Italy estimated that 51% of their patients suffered dyskinesia. Physicians in Germany, France, Spain and the UK estimated that 31, 35, 38 and 40% of their PD patients, respectively, experienced dyskinesia.

Patients with dyskinesia: assessment of patient record-forms

On average, patients at Hoehn and Yahr stages I–II had suffered PD for 6.9 years, those at stage III for 9.2 years, while those at stages IV and V had been diagnosed with PD for an average of 11.0 and 12.4 years, respectively. Almost all patients (94%) were receiving levodopa at the onset of dyskinesia, either as monotherapy (38%) or in combination with a dopamine agonist (56%) (Table 1). Only 5% of patients were receiving dopamine agonist monotherapy at the onset of dyskinesia. The incidence of dyskinesia was unrelated to the length of time that patients had been treated with levodopa. Among the 1794 patients who were receiving levodopa at the time that dyskinesia was first diagnosed, 12% had been treated with levodopa for $\leq$1 year, 60% of patients had received levodopa for 1–6 years, while in 28% of patients, dyskinesia was not diagnosed until after 6 or more years of levodopa treatment. Daily doses of levodopa at dyskinesia diagnosis were 531 ± 473 ([mean $\pm$ standard deviation] mg/day) among patients diagnosed with dyskinesia within 1 year of beginning levodopa treatment, compared with $634 \pm$

Table 2. *Impact of dyskinesia on patients' lives before any action was taken to reduce dyskinesia*

	N (%)
Proportion of the waking day with dyskinesia	
None	42 (2.2)
1–25%	857 (45.2)
26–50%	661 (34.8)
51–75%	255 (13.4)
76–100%	83 (4.4)
Disability caused by dyskinesia	
Not disabling	167 (8.8)
Mildly disabling	642 (34.0)
Moderately disabling	769 (40.7)
Severely disabling	287 (15.2)
Completely disabling	26 (1.4)

N Number of subjects.

283 mg/day among patients diagnosed after >10 years of treatment. Dyskinesia caused distinct patient disability. On average, before any action was taken to reduce dyskinesia, 53% of patients suffered dyskinesia for >25% of the waking day and 18% for >50% of the waking day. Overall, 57% of dyskinetic PD patients were affected by moderately-to-completely disabling dyskinesia, while fewer than 10% of patients with dyskinesia experienced no disability (Table 2).

Treatment of dyskinesia: physician perceptions

Physicians estimated that approximately 60% of treatment interventions were made as soon as the patient presented with dyskinesia, and >80% of patients received a change in treatment within 1 year of diagnosis. The physicians reported that patients whose treatment remained unchanged were mostly (90%) those in whom dyskinesia was either 'not disabling' or 'only mildly disabling'. Physicians claimed that, in the majority of cases, the decision to change treatment in response to dyskinesia is made in conjunction with the patient. The main strategies used for managing dyskinesia in patients with PD were fractionating the levodopa dose (86%), lowering the overall dose of levodopa (82%) as further treatment option and lowering the levodopa dose while adding a dopamine agonist (86%). Other treatment strategies used less commonly included application of levodopa retard formulations; adding a catechol-O-methyltransferase inhibitor and lowering the dose of levodopa concomitantly; addition of a *N*-methyl-D-aspartate antagonist, i.e. amantadine; or use of an apomorphine pump. Brain surgery was used to treat dyskinesia in just 3% of patients but was discussed with >20% of patients.

Physicians reported that the measures they took achieved satisfactory control of dyskinesia in only 54% of their patients. The level of physician dissatisfaction with treatment increased with the level of disability caused by dyskinesia ($r = 0.212$, $P < 0.01$; $N = 1891$). A significant correlation was observed between physician dissatisfaction with the treatment outcome achieved in individual patients and the length of time between dyskinesia diagnosis and action being taken to reduce it ($r = 0.117$, $P < 0.01$; $N = 1849$). Physicians felt that dyskinesia outweighed the benefits of levodopa in 26% of patients.

Discussion

The results of our survey confirm that dyskinesia is a common problem, affecting approximately 34% of PD patients (Schrag et al., 2000; Ahlskog et al., 2001).

We show, that the majority of PD patients (approximately 95%) were receiving levodopa at the onset of dyskinesia, either as monotherapy or in combination with dopamine agonists, but we also report on 97 dyskinetic PD patients with dopamine agonist monotherapy. Thus we provide further circumstantial evidence, that initiating treatment with dopamine agonist monotherapy in early PD may delay the onset of dyskinesia primarily through a levodopa-delaying effect, but cannot prevent them (Rascol et al., 2006). We confirm, that dyskinesia in PD patients are mostly moderately-to-completely disabling and thus impact quality of life (Chapuis et al., 2005). We show, that physicians are dissatisfied with current options available for managing dyskinesia. The use commonly recommended treatment approaches with predominant fractionating of the levodopa dose as first choice (Pahwa et al., 2006). Interestingly, the administration of NMDA antagonists, i.e. amantadine, does not play a major therapeutic role in the real life situation outside the study world (Silva-Junior et al., 2005). Limitations of this work are, that selection of neurologists is only based on their initial answers on their experience with PD in the interview, that the employed questions were not validated, that used patient record-forms were filled out in a retrospective fashion.

In conclusion our interview based survey and retrospective analysis of patient records show, that occurrence of dyskinesia affects about 34% of PD patients, but therapeutic options are not satisfactory, to date.

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