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Non-motor symptoms in Indian patients with Parkinson's disease

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ABSTRACT

Non-motor symptoms (NMS) are increasingly recognised as important determinants of disability and quality of life in patients with Parkinson's disease (PD). This is a cross-sectional study on NMS in Indian patients with PD, describing their relationship to motor function and other NMS. Consecutive patients with PD were administered a detailed questionnaire by a neurologist. 171 patients (*M* – 59.6%, mean age 67.1years) recruited over six months. Median duration of PD was 4 years (range, 1–22) with mean age of onset 62.5 (range, 37–91). 16.2% were <50 years old at PD onset. 75.6% were in H&Y stages 1–2.5. 91.8% reported NMS; the number of NMS ranged 0–8 (median, 3). Anxiety, urinary urgency, constipation and rapid-eye movement sleep behaviour disorder were the commonest NMS, each seen in >35% of patients. 8.2% reported NMS antedating onset of motor symptoms. Anxiety was commoner in females, while males reported more urinary frequency and nocturia. The number of NMS was related to H&Y stage, age >70 and later onset of PD, but not to PD duration. Anxiety and depression were commoner in the earlier stages, while psychosis and memory impairment were prevalent in advanced PD. Pedal oedema was commoner in patients <50 years old, but most other NMS were prevalent in older patients and those with later onset or longer duration of PD. NMS are common in Indian patients with PD, and may antedate motor symptoms. NMS number increases with H&Y stage, age >70 years, PD duration and later onset. Mood symptoms and pedal oedema are prevalent in younger patients, other NMS being commoner in older patients.

1. Introduction

Initially characterised as the archetypal "movement disorder", Parkinson's disease (PD) has a number of non-motor symptoms (NMS) in addition to the motor symptoms of tremor, rigidity and bradykinesia [1]. NMS are associated with significant disability, worsen quality of life, and complicate treatment with dopaminergic drugs [2,3]. Despite their importance in holistic patient management, they are missed by neurologists in 50% of visits [4]. We present a cross-sectional study on NMS in Indian patients with PD, and describe the relationship of NMS to demographic parameters and motor function.

2. Methods

Consecutive patients with PD attending the neurology clinic or patient support group meetings in Goa, India were prospectively enrolled in this single-centre, cross-sectional, observational study after obtaining informed consent. The diagnosis of "probable" PD was based on UKPDS Brain Bank criteria and patients with other forms of parkinsonism or with a mini-mental state examination (MMSE) score <24 were excluded. All patients were examined by at least one neurologist to ascertain the diagnosis and had imaging of the brain. A detailed questionnaire was administered by a single neurologist (A.S.) to each patient. Patients were assessed in the 'on' state, while severity of PD was measured in the "off" state using the Höhn and Yahr (H&Y) scale. In cases where NMS were considered likely due to drug use or intercurrent medical illness, the offending drug(s) were stopped, the possible medical precipitant was treated, and the patient was re-assessed after at least three weeks. Depression, anxiety, hallucinations and apathy were defined according to the neuropsychiatric inventory [5]; constipation was defined as <3 bowel movements per week; memory dysfunction was deemed to be present if the patient had persistent complaints of forgetfulness and/or deficits on the MMSE; frequent micturition and nocturia were defined as urinating >1 time every two hours and >2 times/night respectively; and orthostatic hypotension was defined as a fall in measured systolic blood pressure of >20 mm of mercury or in diastolic blood pressure of >10 mm of mercury after standing for three minutes.

Data on non-motor symptoms were coded as "yes" or "no" and entered into a simple spreadsheet. Statistical analysis was carried

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out using SPSS version 15 (SPSS Inc., Chicago IL, USA). Descriptive statistics such as mean, standard deviation, frequencies and percentages were used to express data. The prevalence of each non-motor symptom was assessed by calculating the total number of positive responses. Comparisons between various groups were carried out using the Students' *t*-test or univariate analysis of variance for continuous variables and Chi square tests for categorical variables. One-way analysis of variance followed by post hoc tests was carried out to compare mean values when the number of groups was more than two. A p value of <0.05 was considered significant.

3. Results

Over six months from September 2012 to February 2013, 171 patients with a diagnosis of Parkinson's disease were administered the questionnaire. 102 (59.6%) were males. The patients' ages ranged between 42 and 92 years, with a mean age of 67.1 years (standard deviation (SD) 9.7). 18.2% were younger than 60 years old, and one-fourth (24.8%) were over 75. The patients had had symptoms of PD for a mean of 4.69 years (SD 3.74, range, 1–22 years). The age of onset of PD ranged from 37 to 91 years (mean 62.5), with 16.2% being <50 years old at disease onset. Table 1 describes the overall occurrence of non-motor and motor symptoms in this cohort of patients with Parkinson's disease. A median of 3 NMS were reported (range 0–8). At least one NMS was seen in 91.8% of patients. As many as 41.4% of patients reported anxiety, 39.7% urinary urgency, 37.9% constipation and 35.5% rapid eye movement sleep behaviour disorder (RBD). Cognitive or behavioural symptoms were seen in as many as 118 patients (69%), while autonomic dysfunction was seen in 121 patients (70.8%). Sleep disorders (insomnia or daytime somnolence) were present in 17 patients (10%). Although present in 31 patients, in only two was anosmia noticed to antedate the onset of motor symptoms. RBD antedated motor symptoms in two patients, constipation in six, and anxiety or depression in four. The "on" phase in 49 patients with wearing off lasted 3.6 hours on average (SD 1.1). All patients with urinary frequency/nocturia and with excessive daytime somnolence as well as the lone patient reporting sexual dysfunction were male. Anxiety was commoner in females (32 of 69 females, 37 of 102 males, $p = 0.048$).

Table 1
Motor and non-motor symptoms in 171 patients with Parkinson's disease.

Parameter	*N*	%		
		All patients (*N* = 171)	Males (*N* = 102)	Females (*N* = 69)
Motor symptoms				
Postural dysfunction	73	43.2	38.6	50.8
Wearing off	49	29	28.7	29.9
Peak-dose dyskinesia	34	20.1	14.9	28.4
Off-phase dyskinesia	4	2.4	4	0
Diphasic dyskinesia	3	1.8	3	0
Cognitive/behavioural symptoms				
Anxiety	70	41.4	36.3	47.8
Depression	42	24.6	21.6	29.4
Apathy	2	1.2	1	0.7
Vivid dreams	27	16	13.9	19.4
RBD	60	35.5	36.6	32.8
Hallucinations	41	24.4	24	23.9
Memory difficulties	38	22.5	24.8	19.3
Insomnia	11	6.5	5.9	7.4
Daytime somnolence	6	3.5	5.9	0
Autonomic symptoms				
Urinary urgency	67	39.7	35.6	44.8
Urinary frequency/nocturia	12	7	11.8	0
Sexual dysfunction	1	0.6	1	0
Pedal oedema	21	12.4	10.9	14.9
Orthostatic hypotension	44	26	27.8	22.4
Constipation	64	37.9	39.6	35.8
Bloating/anorexia	5	2.9	3.9	0.7
Anosmia	31	18.3	18.8	17.9

3.1. Correlation of the H&Y stage with NMS

Most patients were in earlier stages of PD, with only 24.4% being in stages 3 and 4 (Table 2). No patient was in stage 5, as recruitment was done at an out-patient clinic. In a linear regression model, the number of NMS was significantly related to the H&Y stage ($p = 0.04$) but not to duration of PD. Patients in stages 1 and 2 had a mean of 2.4 and 1.4 fewer NMS respectively than those in stage 4. Anxiety and depression were significantly commoner in patients with earlier disease stages ($p = 0.043$ and 0.007 respectively). Conversely, psychosis and memory impairment were more common in patients with advanced disease ($p < 0.001$ for each). When patients in stages 1 or 2 were compared with patients with more advanced disease, patients in the later stages were significantly older, had longer duration of PD, and were more likely to have postural dysfunction, urinary urgency, psychosis, memory dysfunction, wearing off (with shorter "on" time), and peak-dose dyskinesias. The presence of postural dysfunction was significantly related to the H&Y stage ($p < 0.001$).

3.2. Effect of age

Older patients were more likely to be in later stages of PD (H&Y stages 3 or 4, $p = 0.022$), with more NMS. They also reported vivid dreams more often ($p = 0.05$). Table 3 shows that while diphasic dyskinesias and pedal oedema were more frequent in patients <50 years of age, older patients had a higher incidence of other NMS, and more NMS overall.

Patients with later age at onset of PD had significantly more NMS overall ($p = 0.045$), more cognitive/behavioural symptoms ($p = 0.003$), daytime somnolence ($p = 0.01$), and memory difficulties ($p = 0.024$). Table 3 shows symptoms analysed separately in patients with age of onset of PD <50 and >50 years. Although the early-onset group had longer disease duration ($p = 0.023$), with worse motor fluctuations, NMS were commoner in patients with later onset. Patients whose PD symptoms began after age 70 years had a shorter duration of PD (mean ± SD, 3.44 ± 2.2 years), fewer motor fluctuations overall with less wearing off ($p = 0.001$) and less "off" dyskinesias ($p = 0.045$) than those patients with earlier onset whose mean disease duration was 5.02 ± 4.0 years.

Table 2
Correlation of Hoehn & Yahr disease stage with selected motor and non-motor symptoms.

Parameter	Hoehn & Yahr stage						*p* value
	1	1.5	2	2.5	3	4	
Whole cohort (%)	23.8	2.4	31.5	17.9	19.6	4.8	–
All motor fluctuations (%)	2.5	0	22.6	40	72.7	87.5	<0.001
Wearing off (%)	2.5	0	18.9	30.3	63.6	87.5	<0.001
Peak-dose dyskinesia (%)	0	0	11.3	20	51.5	62.5	<0.001
Anxiety (%)	40	50	50.9	26.7	42.4	25	0.043
Depression (%)	30	25	26.4	16.7	24.2	12.5	0.007
Psychosis (%)	10	0	23.1	23.3	36.4	75	<0.001
Memory difficulties (%)	12.5	25	17	20	27.3	100	<0.001
All autonomic symptoms (%)	62.5	50	67.9	70	84.8	100	0.007
Urinary urgency (%)	22.5	50	39.6	40	51.5	62.5	0.004
Orthostatic hypotension (%)	15	25	24.5	26.7	36.4	50	0.016
Anosmia (%)	5	0	20.8	30	24.2	12.5	0.044