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Motor and non-motor symptoms of 1453 patients with Parkinson's disease: Prevalence and risks

Asako Yoritaka [a,b,*], Yasushi Shimo [a], Masashi Takanashi [a], Jiro Fukae [a,c], Taku Hatano [a], Toshiki Nakahara [a], Nobukazu Miyamato [a], Takao Urabe [a,d], Hideo Mori [a,b], Nobutaka Hattori [a]

[a] Department of Neurology, Juntendo University School of Medicine, Japan
[b] Department of Neurology, Juntendo University Koshigaya Hospital, Japan
[c] Department of Neurology, Fukuoka University Hospital, Japan
[d] Department of Neurology, Juntendo University Urayasu Hospital, Japan

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ABSTRACT

Purpose: We examined the prevalence and risk of clinical symptoms in a large number of Japanese patients with Parkinson's disease (PD) ($n = 1453$; 650 males).
Methods: Events were analyzed using Kaplan–Meier survival curves, logistic regression, and Cox proportional-hazards models.
Results: The mean age (SD) was 67.7 (10.0), age of onset was 58.0 (11.5), and disease duration was 9.7 (6.6) years. The mean modified Hoehn and Yahr stage was 2.8 (1.2). Most patients (88.9%) received levodopa (547.7 (257.6) mg/day). A large proportion (81.3%) received dopamine agonists (136.2 (140.7) mg/day). About 23.4% received pain treatment 6.9 (5.1) years after the onset; females ($p < 0.05$) and patients with late-onset PD (≥60 years, $p < 0.001$) were more likely to be affected. About 44.7% of patients had wearing-off 7.5 (4.7) years after the onset, and it was more common in females ($p < 0.001$) and patients with early-onset PD ($p < 0.001$). Camptocormia was found in 9.5% of patients 8.1 (6.2) years after the onset, and it was more common in females ($p < 0.05$) and patients with late-onset PD ($p < 0.05$). About 28.6% of patients developed psychosis 9.0 (5.4) years after the onset, and it was more likely to occur in patients with late-onset PD ($p < 0.001$). Late-onset PD and cerebrovascular disease were also associated with increased risk of pneumonia.
Conclusions: Considering that very few studies have assessed numerous clinical symptoms in the same report, these data provide a useful reference for the clinical course of PD.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease. Dopamine replacement with levodopa or dopamine agonists (DA) results in marked improvement of motor symptoms and alleviation of disability; these treatments have also improved patient survival [1,2]. However, levodopa use is also associated with the development of motor complications that substantially contribute to disability in patients with advanced PD. Various motor and non-motor symptoms (NMS) and side effects of anti-parkinsonian drugs limit the medication dose and the ability to prescribe other drugs. Here, we have described the prevalence and risk of clinical symptoms in a large number of Japanese patients with PD.

2. Patients and methods

Between January and June 2010, we retrospectively reviewed the charts of patients who had visited our outpatient neurology clinic at Juntendo Hospital in Tokyo, and had been diagnosed with PD by a board-certified neurologist. Diagnoses were based on the UK Brain Bank diagnostic criteria for PD [3], and patients with dementia with Lewy bodies [4], progressive supranuclear palsy, corticobasal degeneration, vascular parkinsonism, and other forms of parkinsonism were excluded. Hospital charts were systematically reviewed by A.Y. This study was approved by the Juntendo Hospital institutional ethics committee, and informed consent was obtained.

The following data were collected from patients: sex; date of birth, first visit, and onset; initial symptoms, side of initial symptoms, order of medications taken from the time of initial medication, approximate date of start or stop of each medication, and modified Hoehn and Yahr (H & Y) stage for the initial and final evaluations; and dates of important events (pain, wearing-off, camptocormia, sleep attack, orthostatic hypotension, psychosis, electrical convulsive therapy [ECT] for

* Corresponding author. Department of Neurology, Juntendo University Koshigaya Hospital, Fukuroyama 560, Saitama 343-0032, Japan. Tel.: +81 48 975 0321; fax: +81 48 975 0346.
E-mail addresses: ayori@juntendo.ac.jp, yyykoro@yahoo.co.jp (A. Yoritaka).

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Table 1
Baseline demographic and clinical characteristics of patients with Parkinson's disease.

Variable	Category	*n* or mean	SD	Median
Total		1453		
Age		67.7	10.0	68.5
Age at onset		58.0	11.5	59.3
Sex	Male	650 (44.7%)		
	Female	803 (55.3%)		
Disease duration	Mean	9.7	6.6	8.5
Hoehn and Yahr stage on		First visit	Enrollment	
	0	10 (0.7%)	48 (3.3%)	
	0.5 and 1.0	241 (16.6%)	101 (7.0%)	
	1.5 and 2.0	685 (47.1%)	428 (29.5%)	
	2.5 and 3.0	414 (28.5%)	438 (30.1%)	
	4	68 (4.7%)	294 (20.2%)	
	5	10 (0.7%)	99 (6.8%)	
	Not described	25 (1.7%)	45 (3.1%)	
Hypertension		258 (17.8%)		
Dyslipidemia		174 (12.0%)		
Diabetes mellitus		79 (5.4%)		
Cerebral vessel disease		86 (5.9%)		
Malignant tumor		87 (6.0%)		
Therapy in another hospital before our hospital		802 (55.2%)		
Anti-parkinsonian drugs				
Levodopa		1292 (88.9%)		
Duration from onset to start of treatment	Years	2.9	3.2	2.0
Daily dose at enrollment day	mg	547.7	257.6	600.0
Cumulative dose	g	1259.2	1190.0	933.4
Pramipexole		900 (61.9%)		
Duration from onset to start of treatment	Years	6.4	5.6	5.0
Daily dose ($n = 900$)	mg	2.1	2.6	1.7
Ropinirole		212 (14.6%)		
Duration from onset to start of treatment	Years	7.5	6.1	6.0
Daily dose ($n = 212$)	mg	7.5	4.7	3.3
Pergolide		414 (28.5%)		
Duration from onset to start of treatment	Years	4.9	4.9	3.5
Daily dose ($n = 414$)	mg	941.4	2.0	1.6
Cabergoline		405 (27.9%)		
Duration from onset to start of treatment	Years	4.9	5.2	3.3
Daily dose ($n = 405$)	mg	2.3	1.3	2.0
Bromocriptine		99 (6.8%)		
Duration from onset to start of treatment	Years	4.3	4.2	3.4
Daily dose ($n = 99$)	mg	16.2		7.5
Dopamine agonist		1182 (81.3%)		
Duration from onset to start of treatment	Years	4.0	4.4	2.6
Daily dose ($n = 1453$)	mg	136.2	140.7	120.0
Entacapone		314 (21.6%)		
Duration from onset to start of treatment	Years	10.3	5.8	9.3
Daily dose ($n = 314$)	mg	490.3	249.3	400.0
Trihexyphenidyl		561 (38.6%)		
Duration from onset to start of treatment	Years	4.0	4.0	2.7
Daily dose ($n = 561$)	mg	3.3	1.6	3.0
Amantadine		598 (41.2%)		
Duration from onset to start of treatment	Years	5.6	5.8	3.9
Daily dose ($n = 598$)	mg	166.0	63.6	150.0
Zonisamide		98 (6.7%)		
Duration from onset to start of treatment	Years	9.9	7.2	8.2
Daily dose ($n = 98$)	mg	47.3	34.9	25.0
Droxidopa		134 (9.2%)		
Duration from onset to start of treatment	Years	7.0	5.1	5.9
Daily dose ($n = 134$)	mg	380.6	178.7	300.0
Selegiline		620 (42.7%)		
Duration from onset to start of treatment	Years	6.7	5.0	5.6
Daily dose ($n = 620$)	mg	7.2	6.0	5.0

severe psychosis, neuroleptic malignant syndrome, pneumonia, and tube feeding). "Onset" was defined as the date of appearance of the first symptoms of parkinsonism (bradykinesia, rest tremor, and/or rigidity). "Pain" was defined as pain that required treatment, including pain related to wearing-off and excluding pain related to bone fracture, myocardial infarction, respiratory disease, and abdominal disease. "Camptocormia" was defined as marked anterior flexion of the thoracolumbar spine in the recumbent position without evidence of fixed kyphosis. "Sleep Attack" was an acute and irresistible episode of sleep occurring without warning signs [5]. "Orthostatic hypotension" was defined as a greater than 20 mmHg decrease in systolic pressure. "Psychosis" included reports of illusion, false sense of presence, hallucinations, or delusions that continued or recurred for at least 1 month [6]. Diagnosis of "neuroleptic malignant syndrome" was based on Levenson's criteria [7]. Other NMS like depression, cognition, apathy, and excessive daytime sleepiness were not selected, because their onset was not clear, and the patients were not regularly examined using tools like the NMS questionnaire (NMSQuest) [8], Scale for Outcomes in Parkinson's Disease-Psychiatric Complications (SCOPA-PC) [9], or SCOPA-Cognition (SCOPA-COG) [10]. NMS in early PD like REM sleep behavior disorder (RBD), olfactory dysfunctions, or constipation were not analyzed.

The daily levodopa equivalent dose was calculated on the basis of the following equivalences: 100 mg standard levodopa = 10 mg bromocriptine = 1 mg pergolide = 5 mg ropinirole = 1 mg pramipexole [11].

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