Original Research Article

A study of the correlation of non-motor symptoms of Parkinson's disease and Parkinson plus syndrome with duration of the disease

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Abstract

Introduction: Depression is common in PD, occurring in up to one-half of the patients. Anxiety disorders may be as common as depression and the two are frequently co-existent. Parkinson plus syndrome (PPS) is a group of sporadic, neurodegenerative diseases of the central nervous system, less common and usually more severe than Parkinson's disease. They are characterised by relatively rapid disease progression and the presence of features that are atypical for PD, such as early postural instability and dementia, severe autonomic failure, or pyramidal and cerebellar signs. **Material and Methods:** The study was conducted to assess the effect of duration in non-motor dysfunction in 60 patients with Parkinsonism including idiopathic Parkinson's disease and Parkinson plus syndrome who attended either the outdoor services, or were admitted in the Neurology ward of our tertiary care centre, PGIMER & Dr. RML Hospital, New Delhi, India. **Results:** PD patients had no correlation between cognition and duration of disease (p=0.079 with MMSE and p=0.145 with SCOPA COG) but had significant correlation between depression, sleep problems, pain and autonomic dysfunction with duration of disease (p=0.027, 0.008, 0.010 and 0.042 respectively). **Conclusion:** Early recognition and diagnosis of PD and PPS is important as treatment may improve quality of life in patients. Co-existence of non-motor dysfunctions in the disease significantly adds to the burden of disease and affects the quality of life.

Keywords: Parkinson's disease, Parkinson plus syndrome, Non motor symptoms, Neuropsychiatric symptoms.

Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder second only to Alzheimer's disease [1]. The cardinal clinical features of PD include asymmetric onset bradykinesia, rigidity and rest tremor [2]. The peak age of onset of PD is in the early 60s (range 35-85 years), and the course of illness ranges from 10 to 25 years [3].

The Parkinson's disease result from the loss of dopaminergic neurons in substantia nigra pars compacta [4]. Among the subjects with clinical features of Parkinsonism, approximately 80-85% have PD and the rest are Parkinson Plus Syndrome and secondary Parkinsonism [5]. Disorders of mood and affect, though receiving less attention than motor aspects of the disease, have long been recognized as a part of PD. Depression is common in PD, occurring in up to one-half of the patients. Anxiety disorders may be as common as depression [6, 7] and the two are frequently co-existent. Apathy, may overlap, but is usually distinct from depression.

In addition, suicidal ideations, hallucinations, and delusions may occur [8, 9] When PD patients are carefully questioned, it becomes evident that fatigue, sleepiness, and sleep disturbances are major problems independent of any medication and motor disability.

Parkinson plus syndrome (PPS) is a group of sporadic, neurodegenerative diseases of the central

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nervous system, less common and usually more severe than Parkinson's disease. They are characterised by relatively rapid disease progression and the presence of features that are atypical for PD, such as early postural instability and dementia, severe autonomic failure, or pyramidal and cerebellar signs. Survival time is shorter and more complications occur in earlier stages and with higher degree of severity than in PD [10].

We conducted the present study to assess the non-motor dysfunction in idiopathic PD and PPS, and to find if these symptoms associated with the duration of the disease.

Material and Methods

Study design: It was a cross-sectional study.

Study population: The study was conducted to assess the effect of duration in non-motor dysfunction in 60 patients with Parkinsonism including idiopathic Parkinson's disease and Parkinson plus syndrome who attended either the outdoor services, or were admitted in the Neurology ward of our tertiary care centre, PGIMER & Dr. RML Hospital, New Delhi, India.

Inclusion criteria: Patients with Parkinsonism disease.

Exclusion Criteria

1. Systemic conditions known to be associated with autonomic dysfunction including diabetes, chronic alcoholism, chronic renal failure, chronic liver disease.
2. Patients with essential tremor
3. Patients with secondary parkinsonism
4. Severe cognitive dysfunction such that the relevant questionnaires for assessment cannot be undertaken by the patient
5. Refusal to give consent for study

Methodology

1. The study was approved by the Institutional Review Board of PGIMER & Dr. RML Hospital, New Delhi, India.
2. A written informed consent was taken from all subjects before inclusion in the study.
3. After collecting the demographic data, all patients were subjected to comprehensive workup including history, general physical examination, and neurological examination.
4. They underwent routine investigations including complete blood counts, blood sugar (Fasting & Postprandial), serum creatinine, total serum bilirubin, serum transaminases, serum electrolytes (sodium, potassium, and calcium), resting electrocardiogram, and neuroimaging (CT Scan Head and / or MRI Brain).
5. The patients were classified as Parkinson disease and Parkinson plus syndrome based on their clinical presentation.
6. Diagnosis of PD was made as per UK Brain Bank criteria [11].
7. Psychiatric and behavioural disorder was assessed by BDI-II (Beck Depression Inventory-II) [12] and NPI (Neuropsychiatric Inventory). [13].
8. Patients were classified into two groups based on age at onset (≤40 years and >40 years), three groups based on disease duration (<2 years, 2-5 years and ≥5 years) and three groups based on disease severity (mild, moderate and severe) [14].

Statistical Analysis: Statistical analysis in the study was done using SPSS software for the variables under study. The correlation of presence of non motor symptoms with severity and duration of disease was done by using appropriate statistical tests. Statistical significance level was considered at a p-value <0.05.

Results

In our study, out of 40 patients with Parkinson's disease, twenty-five (62.50%) were males and 15 (37.50%) were females with mean age of 55.02 (SD ±13.56) years as shown in table 1. Among patients with MSA, six (66.70%) were male and 3 (33.33%) were female with mean age of 62.00 (SD ±11.38) years. Among patients with PSP, four (50.00%) were male and 4 (50.00%) were female with mean age of 62.37 (SD ±10.25) years while all the three patients with DLB were male having mean age of 65.33 (SD ±12.34) years.

Table-1: Clinical profile of sample population.

		PD (n=40)	DLB (n=3)	MSA (n=9)	PSP (n=8)	PPS (n=20)	p value (PD vs PPS)
Age at onset [Frequency (%)]	≤40 Yrs	5 (12.50)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	>40 Yrs	35 (87.50%)	3 (100%)	9 (100%)	8 (100%)	20 (100%)	
Duration of Disease [Mean ± SD]		2.09 ± 1.82	3.17 ± 0.29	2.67 ± 1.52	1.90 ± 1.11	2.43 ± 1.29	0.455
Duration of Disease [Frequency (%)]	< 2 yrs	19 (47.5%)	0 (0%)	4 (44.4%)	3 (37.5%)	7 (35%)	
	2 - 5 yrs	19 (47.5%)	3 (100%)	5 (55.6%)	5 (62.5%)	13 (65%)	
	> 5 yrs	2 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
UPDRS (III)		22.10 ±5.83	27.00 ±3.00	22.88 ±9.78	26.00 ±4.50	24.75 ±7.20	0.131

PD patients had mean disease duration of 2.09(SD ±1.82) years. Thirty-eight (95%) PD patients had less than 5 years of disease duration and only 2 (5%) subjects had disease duration of more than 5 years. The mean duration of disease in MSA patients was 2.67 (SD ±1.52) years with 4 (44.44%) and 5 (55.56%) subjects having <2 years and 2-5 years duration of disease respectively. Patients with PSP had mean disease duration of 1.90 (SD ±1.11) years with 3 (37.50%) and 5 (62.50%) subjects having <2 years and 2-5 years duration of disease respectively. Amongst DLB patients, the mean duration of illness was 3.17(SD ±0.29) years with all the subjects in 2-5 years disease duration range. The mean UPDRS-III score of PD and Parkinson plus syndrome patients was 22.10 (SD ±5.83) and 24.75(SD ±7.20) respectively **(Table No. 1).**

Table No.-2: Relation of non motor symptoms scales score with duration of disease in Parkinson's disease

Name of scale	< 2 yrs (n=19) Mean (SD)	2 - 5 yrs (n=19) Mean (SD)	> 5 yrs (n=2) Mean (SD)	(n=40) Mean (SD)	P value
MMSE	25.68(±3.667)	23.68(±5.121)	30.00(±0.0)	24.95(±4.546)	0.079
SCOPA-COG	23.84(±5.263)	22.84(±5.550)	29.50 (±3.536)	23.65(±5.423)	0.145
DBI-II	7.95(±8.784)	15.16(±8.952)	15.50 (±13.43)	11.75(±9.521)	0.027
PDSS	132.16 (±35.059)	122.53(±20.034)	108.50 (±6.364)	126.40 (±28.169)	0.008
PAIN	3.11(±2.079)	5.58(±2.714)	6.00 (±0.00)	4.42(±2.650)	0.010
SCOPA-AUT	11.05 ± 6.51	15.42 ± 5.20	16.50 ± 0.71	13.40 ± 6.10	0.042

PD patients had no correlation between cognition and duration of disease (p=0.079 with MMSE and p=0.145 with SCOPA COG) but had significant correlation between depression, sleep problems, pain and autonomic dysfunction with duration of disease (p=0.027, 0.008, 0.010 and 0.042 respectively) **(table no. 2).**

Table No.-3: Relation of non motor symptoms scales score with duration of disease in Parkinson plus Syndrome.

Name of Scale	Duration of disease			p value
	<2 Yrs (n=7)	2-5 Yrs (n=13)	>5 Yrs (n=0)	
MMSE	24.57 ± 4.58	20.69 ± 6.81	0.0 ± 0.0	0.176
SCOPA-COG	25.57 ± 5.91	22.69 ± 5.14	0.0 ± 0.0	0.176
BDI-II	5.29 ± 4.68	11.62 ± 9.41	0.0 ± 0.0	0.163
PDSS	138.00 ± 9.68	132.31 ± 12.21	0.0 ± 0.0	0.302
VAS	2.43 ± 2.15	2.46 ± 1.94	0.0 ± 0.0	0.799
SCOPA-AUT	13.71 ± 7.04	17.77 ± 4.93	0.0 ± 0.0	0.190

Parkinson plus Syndrome patients had correlation between cognition impairment, depression, sleep problems, pain and autonomic dysfunction with duration of disease but not statistically significant (p=0.176 with MMSE, p=0.176 with SCOPA-COG, p=0.163 with BDI, p=0.302 with PDSS, P=0.799 with VAS and p=0.190 with SCOPA-AUT) **(Table No. 3).**

Discussion

The mean duration of illness was 2.09 (SD ± 1.82) years for subjects with PD and 2.43 (SD± 1.29) years for subjects with PPS. Most of patients of PPS had moderate to severe disease (19 out of 20 patients) while around 60% (24patients) of PD were of the similar severity.

The mean UPDRS-III score of PPS patients was higher than that of PD patients (Mean ± SD: 24.75 ± 7.20) than PD (Mean ± SD: 22.10 ± 5.83).

Using MMSE, cognitive impairment was observed in 12 (30%) cases of PD in which 9 (22.50%) had mild and 3 (7.50%) had moderate cognitive impairment. On the SCOPA-COG scale, cognitive impairment was observed in 9 (22.5%) patients. We did not find any significant correlation between cognitive impairment and duration of disease in PD.

(MMSE P value=0.079 with duration and P value =0.925 with Modified H & Y and 0.791 with UPDRS-III, SCOPA. COG P value =0.145 with duration and P value =0.978 with Modified H & Y and P value =0.785 with UPDRS-III.

Earlier estimates of prevalence of dementia in PD have been highly variable, ranging from 20% to 81% [15]. This might be due to different assessment techniques and different study populations.

Depression was observed in all the PD patients using BDI-II. There was significant correlation of depression with duration (p=0.027) of illness. Statistically significant correlation was found between depression and duration of disease when assessed by UPDRS-III (p= 0.003).

Our finding is in concordance with previous literature. Reijnders JSAM et al. and Tan LCS reported major depressive disorder in 17%, minor depressive disorder in 22%, and dysthymia in 13% of their PD patients. They observed clinically significant depressive symptoms in 35% of PD patients [16, 17]

The sleep problems significantly correlated with duration and severity of disease in PD (p=0.008, p=0.015 and p<0.001 correlation with duration, Modified H & Y and UPDRS-III respectively). Using NPI, 62.5% patients had night behaviours problems with sleep fragmentation,early awakening and excessive naps during day time.

Our findings were similar to that reported by other authors. Tandberg Ert al. reported sleep problems in 60% [18]. Behari M et al reported sleep problems in 42% in which 32% insomnia, 32% nightmares and 15% excessive day time sleepiness [19].

In PPS patients, 45% reported having pain. In individual groups, pain was present in 44.44%, 50% and 33.33% of MSA, PSP and DLB patients respectively. This finding is similar to other studies. Tison F et al. found that 47% had pain in MSA [20]. In our study PPS patients had no statistically significant correlation of pain with duration (p=0.799) and severity (p=0.698 with Modified H& Y and 0.105 with UPDRS) of disease.

In PD, autonomic dysfunctions were significantly increased with duration and severity of disease (p=0.042 with duration and p<0.001 with mod. H & Y staging and UPDRS-III). The autonomic dysfunctions in PD patients were similar to previous studies. Visser Visser M. et al. reported that the prevalence of autonomic disturbances ranged between 14% and 80%, and these symptoms were better evaluated with the SCOPA-AUT scale [21].

Conclusion

Non-motor symptoms are a frequent cause of hospitalisation which can increase the cost of care of patients with PD by four times. Early recognition and diagnosis of PD and PPS is important as treatment may improve quality of life in patients. Co-existence of non-motor dysfunctions in the disease significantly adds to the burden of disease and affects the quality of life.

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