Original Article

An Evaluation of Neuropsychiatric Symptoms in Parkinson's Disease Patients

S Oruç, G Gülseren[1], OY Kusbecı, O Özbulut[1]

Departments of Neurology and [1]Psychiatry, Faculty of Medicine, Afyon Kocatepe University, Afyonkarahisar, Turkey

ABSTRACT

Objective: We aimed to examine neuropsychiatric symptoms of patients with early and advanced stage Parkinson's disease (PD). **Materials and Methods:** The study was performed at Kocatepe University Neurology Department in Turkey, comprised 46 PD patients and 46 controls. Hoehn-Yahr (HY) scale was used to evaluate the clinical stages of PD and Unified Parkinson's Disease Rating Scale (UPDRS) was used to evaluate the severity of clinical signs. Cognitive functions were evaluated by Mini-Mental State Examination (MMSE) and neuropsychiatric findings were evaluated by Beck Depression Inventory (BDI), Scale for the Assessment of Positive Symptoms (SAPS), and Scale for the Assessment of Negative Symptoms (SANS). **Results:** Significant difference was determined between BDI values of patients (13.28 ± 9.04) and control group (9.71 ± 5.19) (P = 0.02). Significant difference was determined with SANS (23.84 ± 15.42, 2.58 ± 3.13, $P < 0.001$) but not with SAPS (1.36 ± 4.16, 0.15 ± 0.43, P = 0.07). The patients were evaluated according to the HY stages and there was no significant difference between mild and severe symptom groups in respect of BDI, SAPS, and SANS values (P = 0.91, P = 0.31, and P = 0.29). According to gender, no significant difference was found between groups in respect of BDI, SAPS, and SANS values (P = 0.60, P = 0.54, and P = 0.67). No correlation was found between BDI, SAPS, SANS values, and HY stages. **Conclusion:** Higher rates of depression and negative symptoms were observed in patients with PD compared with healthy individuals. Results did not differ with different stages of PD. Therefore, it should be kept in mind that neuropsychiatric symptoms can be seen from the early stages of the disease and should be treated earlier.

Keywords: *Depression, Parkinson's disease, psychosis*

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Introduction

Parkinson's disease (PD) is a chronic, progressive, and neurodegenerative disease which may present with complaints of tremor, bradykinesia, rigidity, and postural imbalance. Besides motor symptoms, neuropsychiatric symptoms such as depression, hallucination, anxiety, sleep disorders, and psychosis are often encountered in affected individuals.[1] In a study of 139 PD patients over a 4-year observation period, 61% had at least one psychiatric symptom, while 45% had two or more psychiatric symptoms.[2] In the aforementioned study, depression was the most common neuropsychiatric symptom with hallucinations, whereas anxiety was seen less often. Vegetative, affective, and cognitive dysfunction symptoms often seen in PD may mask depression symptoms and pose several challenges in the estimation of the frequency of depression in PD. Therefore, different results are found in different community-based studies on the frequency of PD. Furthermore, rates varying from 4% to 75% have been reported in several studies evaluating the frequency of depression in PD.[3-5]

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Address for correspondence: Assist Prof. S Oruç, Department of Neurology, Faculty of Medicine, Afyon Kocatepe University, Afyonkarahisar, Turkey.
E-mail: drserdaroruc@gmail.com

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Psychosis is also common in PD.[6] Risk factors include dementia, cognitive impairment, >65 years of age, prolonged disease duration, presence of sleep disorders, depression, visual disturbances, and the use of drugs to treat motor symptoms of PD.[7]

In this study, we aimed to evaluate the neuropsychiatric symptoms caused by depression and to assess positive and negative psychotic symptoms in early and late stage PD without dementia.

Materials and Methods

This study included Caucasian subjects enrolled in Turkey. Approval for the study was granted by the local Ethics Committee and an informed consent was obtained from each participant. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The study included a total of 46 patients who were clinically diagnosed with PD according to the British PD Association Brain Bank Criteria[8] and who were being followed at Turkey, Kocatepe University, Faculty of Medicine, Neurology Department, Movement Disorder outpatient clinic. In 2 months, the total number of patients with PD who attended the clinic were 68, only 46 patients were included in the study. The control group consisted of a total of 46 consecutive age- and sex-matched healthy individuals (They were the relatives of the patients who attended to neurology clinic).

The exclusion criterias were as followed: [1] dementia (MMSE score <28) [2] patients with a history of neurological, psychiatric, or chronic medical condition, such as renal and hepatic insufficiencies, vascular diseases, and cancer. [3] Patients on treatment with special medications such as anti-depressants or neuroleptic therapy, glucocorticoids, thyroid hormone replacements, anticonvulsive drugs, lithium, blood glucose-reducing agents were excluded from the study.

Age, sex, education status, duration of disease, medications used, and clinical history of the patients were recorded. The Beck Depression Inventory (BDI)[9] was used in the evaluation of depressive symptoms. In addition, cognitive functions were measured using the Mini-Mental State Examination (MMSE),[10] and neuropsychiatric symptoms were measured with the Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS).[11] Although SANS is not recommended by the Movement Disorders Society Task Force on psychosis scales for PD, SAPS fulfils the criteria as a recommended scale for rating PD psychosis.[12] However, both scales have not been validated.

The patients were divided into two groups as mild and severe according to the Hoehn-Yahr (HY) scale.[13] This scale is commonly used to evaluate the progress of PD. Based on the literature data, there are mainly two classifications ranging from 1 to 5 and modified scale including seven stages. In several studies, HY scale is divided into three or two categories[14] as HY score <2 and >2 based on the structure of sample and research design. To be consistent with the literature data, we also divided the patients into two groups as mild (HY stage 1 or 2) and severe (HY stage 3 or 4) groups.

The severity of clinical findings was defined according to the Unified PD Rating Scale (UPDRS),[15] while HY and UPDRS scales were used to evaluate the clinical stages of PD by neurologists.

In this comparative study, a group of PD patients who did not have dementia were compared with a control group in respect of the values recorded on depression scales and the positive-negative symptom scales. It was also investigated whether the relationship was the same in early and late stage PD. The difference between the genders was also included in the scales and the correlations were examined within the scales.

Statistical Analysis

SPSS for Windows 17.0 programme was used for data analysis. Numerical data were compared using the *t*-test, while nonparametric tests were used to compare the scale scores. The Pearson's correlation analysis was used to analyze the correlations. A *P*-value of <0.05 was considered statistically significant.

Results

Of the study group, 13 (18.3%) were females and 33 (71.7%) were males. The mean age of the patients was 69.60 ± 9.49 years. The mean disease duration was 72.91 ± 55.43 months. The mean UPDRS points were calculated as 32.21 ± 14.61. According to the HY grading, the patients were divided into two groups with 14 (30.4%) patients in the mild symptom group and 32 (69.6%) in the severe symptom group. Medical treatment for PD was administered to 38 (82.6%) patients, while 8 (17.4%) patients were not under any medical treatment. The medications used were L-DOPA alone in 7 (15.2%) patients, dopamine agonist alone in 8 (17.3%) patients, and combined anti-PD medication in 23 (50%) patients [Table 1].

Table 1: Clinical and demographic characteristics of PD patients (mean ± SD)

Sex (M/F)	33/13
Age (y)	69,60 ± 9,49
Duration of PD (month)	72,91 ± 55,43
Severity of PD (mild/severe)	14/32
UPDRS scores	
Mild PD	17.92 ± 4.98
Severe PD	48.46 ± 12.91
Medical treatment (yes/no)	38/8
Treatment (n)	
L-DOPA (only)	7
Dopamine agonist (only)	8
Combined	23

UPDRS=Unified Parkinson's Disease Rating Scale; PD=Parkinson's disease

Table 2: Comparison of BDI, SAPS, and SANS scores between the PD patients and healthy controls (mean ± SD)

	PD Patients (n = 46)	Control (n = 46)	P
BDI	13.28 ± 9.04	9.71 ± 5.19	0.02
SAPS	1.36 ± 4.16	0.15 ± 0.43	0.07
SANS	23.84 ± 15.42	2.58 ± 3.13	<0.001

BDI=Beck Depression Inventory; SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms

Table 3: Comparison of BDI, SAPS, and SANS scores between the mild and severe symptom groups (mean ± SD)

	Mild (n= 14)	Severe (n = 32)	P
BDI	13.50 ± 8.28	13.18 ± 9.48	0.91
SAPS	0.42 ± 1.08	1.78 ± 4.90	0.31
SANS	20.92 ± 9.46	25.12 ± 17.38	0.29

BDI=Beck Depression Inventory; SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms

No statistically significant difference was found between the patient and control groups in terms of age (69.60 ± 9.49 years, 68.02 ± 10.36 years, respectively; P = 0.446). The BDI scores were 13.28 ± 9.04 in the patient group and 9.71 ± 5.19 in the control group, indicating a statistically significant difference (P = 0.02). The SANS scores were 23.84 ± 15.42 in the patient group and 2.58 ± 3.13 in the control group, indicating a statistically significant difference (P < 0.001). There was no significant difference according to the SAPS scores (1.36 ± 4.16, 0.15 ± 0.43, respectively; P = 0.07) [Table 2].

Based on the HY grading, no statistically significant difference in the BDI, PSS, and NSS scores was found between the mild and severe symptom groups (P = 0.91, P = 0.31, P = 0.29, respectively) [Table 3].

According to sex analysis, no statistically significant difference was found in the BDI, SAPS, and SANS scores between the groups (P = 0.60, P = 0.54, P = 0.67, respectively) [Table 4].

Table 4: Comparison of BDI, SAPS, and SANS scores according to the sex (mean ± SD)

	Male (n = 33)	Female (n = 13)	P
BDI	12.84 ± 9.79	14.38 ± 7.00	0.60
SAPS	1.60 ± 4.82	0.76 ± 1.48	0.54
SANS	23.24 ± 16.05	25.38 ± 14.16	0.67

BDI=Beck Depression Inventory; SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms

Table 5: Correlation of clinic stage, BDI, SAPS, and SANS scores

		HY	BDI	SAPS	SANS
BDI	R	0.01	1		
	P	0.91			
SAPS	R	0.15	0.59**	1	
	P	0.31	<0.001		
SANS	R	0.12	0.40**	0.17	1
	P	0.40	0.006	0.25	

HY=Hoehn and Yahr; BDI=Beck Depression Inventory; SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms. **: P<0,01

In addition, there was no statistically significant correlation was found between BDI, SAPS, and SANS scores and the HY grading (R = 0.01, P = 0.91; R = 0.15 P = 0.31; R = 0.12, P = 0.40, respectively). There was a statistically significant positive correlation between the BDI and SAPS and SANS scores (R = 0.59, P = 0.00; R = 0.40, P = 0.00, respectively) [Table 5].

Discussion

In this study, statistically the BDI scores of the PD patients were significantly higher compared with the control group. This finding supports the view that PD patients are in an increased risk of depression.[16] However, we found no statistically significant difference between the scores of the mild and severe symptom patient groups.

Previous studies investigated the relationship between depression and the severity of PD reported conflicting results. In a study by Wichowicz *et al*.,[17] a significant relationship was reported between depression and high-HY grade, high UPDRS points, and longer duration of disease. On the other hand, several studies did not find a relationship between the PD grade and severity and the development of depression.[18] In our study, we also found that PD grade was not associated with the BDI scores.

The development of depression in the two sexes of PD patients is another matter of debate. While Kuopio *et al*.[19] reported that depressive symptoms were more common in female PD patients and Ketharanathan *et al*.[20] found no significant difference in the rate of depression between the two sexes. Consistent with the findings of the latter study, we found no statistically significant difference in the BDI scores between the males and females.

Furthermore, neuropsychiatric findings such as psychosis, dementia, and depression present in PD patients in the early stage are of utmost importance, this may lead to mortality.[21,22] In this study, the negative symptom scale scores used to identify psychotic findings were found to be statistically higher in the PD patients than in the control group. However, these scores did not significantly differ between the PD patients with mild or severe symptoms. Previous studies also reported the frequency of psychotic findings with PD as 20%-40%.[23] In those with a tendency to the persistent or progressive forms, the most commonly reported symptoms are visual hallucinations, particularly in the evenings.[24] In previous studies, a strong relationship was also found between PD and psychosis associated with advanced age, duration and severity of the disease, cognitive failure, and increased depression.[7,25] In addition, several epidemiological studies and extensive case series reported a relationship between the psychotic findings and the use of L-DOPA and dopamine agonists, while other studies did not establish a link between the use of anti-PD drugs and psychosis.[26-28]

Moreover, in this study, no statistically significant difference in the positive and negative symptom scale scores between the early and late stage PD patients was found. However, there are different views on the relationship of the disease stage and psychotic findings. In a study by Graham *et al*.[29] hallucinations reached a peak within the first 5 years, indicating no relationship with the motor status, cognitive dysfunction, or depression. In another study by Bugalho *et al*.,[30] hallucinations were found at a high rate in the early stage PD patients, however these findings were not associated with impaired cognitive functions or anti-PD drugs at therapeutic doses. Fenelon *et al*.[31] also reported that hallucinations in PD patients were related to cognitive dysfunction only in the advanced stages of the disease.

This study has some limitations. First one is the small sample size. Second, the scales used to evaluate psychosis in PD were not validated and SANS was not a recommended scale for this indication. Third, since the statistical significance of the data is limited, the power of this small sample size is evidently low and some differences might have been overlooked.

Conclusion

In conclusion, during the early stage of the disease itself, physicians should actively look for the presence of neuropsychiatric symptoms in PD patients and should treat as early as possible. Therefore, it might prevent further adverse effects on the quality of life, which is already impaired by the symptoms of PD.

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Conflicts of interest

There are no conflicts of interest.

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