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Evaluation of patients with Parkinson's disease in terms of psychiatric diseases and related clinical features

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Abstract

Aim: In this article, we aimed to evaluate patients with Parkinson' s disease (PD) in terms of psychiatric diseases and related clinical features.

Materials and Methods: 101 patients diagnosed with PD and 101 randomly selected control cases who applied to general internal medicine and endocrine outpatient clinics were included in the study. All subjects were administered a questionnaire including questions about their sociodemographic and clinical features, and were evaluated by the psychiatrist.

Results: The rate of psychiatric disease (42.6%) in the PD group was significantly higher than the control group. Anxiety disorders and depression were the most common among these diseases. Also the use of antidepressant in the PD group was higher than the control group.

Conclusion: Psychiatric disorders are seen more frequently in patients with PD than in patients with other physical diseases. Considering that quality of life in patients with PD is associated with psychiatric well-being, psychiatric symptoms in patients are of high clinical importance. The physician' s awareness of psychiatric symptoms and taking necessary precautions will contribute positively to the treatment of the disease.

Introduction

Parkinson's disease (PD) is a slowly progressive neurodegenerative disease that affects 7-10 million people worldwide and is more common in the elderly. It is a central nervous system disorder and is mainly characterized by slow dopaminergic neuron loss in substantia nigra [1-3]. In PD, psychiatric complaints occur in about 60% of patients [4]. The most common psychiatric disorders are depression and anxiety [5]. There are various studies evaluating psychiatric comorbidities in patients with PD. In the study conducted by Aksoy et al., in which psychiatric disorders were examined in patients with PD, 55 patients with idiopathic PD were compared with 40 patients with degenerative arthrosis, and the Symptom Checklist 90 Revized were applied to all participants. It was observed that the participants in the Parkinson group had higher depression, anxiety, somatization and obsessive compulsive disorder subscale scores compared to the participants in the control group [6]. It has been reported that depression in PD is associated with impaired quality of life, decreased functionality, cognitive decline, increased mortality and caregiver burden [7]. It is well known that some symptoms of depressive disorders overlap with other non-motor symptoms in PD [8]. Neurovegetative symptoms such as anhedonia, apathy, difficulty concentrating, fatigue, and insomnia are often seen in depression in patients with PD. Therefore, it can be difficult to define clinical depression in patients with PD [9]. Depression can occur anytime from the stage when motor symptoms are not yet developed to the last stages of the disease [10]. In some studies, depression have been shown to exist about 5 years before the disease begins [11]. In the study of Eser et al., which included 55 patients with PD, the relationship between PD and depression were evaluated, depression was reported as the most common psychiatric comorbidity. The lifetime depression rate was reported as 45.5%, and the rate of depression before PD started was reported as 20% [12]. These findings suggest that depression may be an early non-motor symptom in PD [13]. Anxiety is more common in patients with

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PD than in the general population and those with other chronic physical diseases. About 1/3 of patients have a diagnosable anxiety disorder [14]. Levels of anxiety increase with with the onset of freezing or off periods, and motor fluctuations, which are associated with periods of low dopamine levels [10]. Anxiety in patients with PD can not be adequately diagnosed due to the overlapping of Parkinson' s with its motor and cognitive symptoms, complexity of diagnosis, and underreporting of symptoms by the patient and caregiver [15]. Studies show that patients with PD have a higher risk of developing an anxiety disorder before diagnosed with PD [16]. These findings also suggest that anxiety, similar to depression, may be an early nonmotor symptom of PD [13,15]. In addition, impulsive and compulsive behaviors, psychotic symptoms, and cognitive dysfunction are observed in most of the patients. Quality of life of patients with PD are thought to be associated with psychiatric well-being [17]. In this research, we aimed to evaluate patients with PD in terms of psychiatric diseases and related clinical features. The hypothesis of the research is that psychiatric diseases will be found higher in patients with PD than in patients with other physical diseases. We think that our research will shed light on further studies examining psychiatric comorbidity in PD and contribute to the literature in this regard.

Materials and Methods

Study sample

The research was conducted in a university hospital between July 2018 and February 2019. The research was approved by the local ethics committee (27.06.2018-2018/101), all participants were informed about the research and written informed consents were obtained. Schrag reported in her study that psychiatric complaints occur in about 60% of patients with PD [4]. In the epidemiological field study conducted in the United Stated of America, it was determined that the one-month prevalence of mental illnesses in the society was 15.4% [18]. Based on these studies while planning this study, it was estimated that the prevalance of psychiatric disease would be 30% in PD group and 13% in control group, the difference between groups (PD and control groups) in prevalance of psychiatric disease would be 17%, the power analysis based on these data showed that at least 90 subjects were required in each group to obtain a difference of 17% in prevalance of psychiatric disease with $\alpha = 0.05$ and power $(1\text{-}\beta) = 0.80$. 110 patients diagnosed with PD in the neurology outpatient clinic were included in the study. Exclusion criteria were determined as the following conditions: Vascular parkinsonism, PD due to neuroleptic drug use, surgery for PD, severe cognitive impairment, and being unable to answer questions. Five patients were excluded from the research because their cognitive functions were not sufficient for filling the forms, and four patients were missing the forms. A total of 101 patients with PD were evaluated. The diagnosis of PD was made according to the criteria of "United Kingdom Parkinson' s Disease Society Brain Bank". According to these criteria, in addition to bradykinesia, at least one of rigidity, resting tremor and postural instability must accompany the clinic for the diagnosis of PD [19]. The control group consisted of 101 age-matched randomly selected volunteer participants who applied to general internal medicine and endocrine outpatient clinics and were not diagnosed with PD. Those diagnosed with alcohol-substance addiction and mental retardation were excluded from the study. All the participants from PD and control groups were referred to the psychiatry outpatient clinic after their evaluation in the outpatient clinic, where they were interviewed by the same psychiatrist using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) Dısorders Clinical Version (SCID-5-CV).

Structured clinical interview for DSM-5 disorders clinical version (SCID-5-CV)

It is a semi-structured interview guide developed to diagnose mental illness according to DSM-5 [20]. Turkish adaptation and reliability study was conducted by Elbir et al. [21].

Sociodemographic data form

A sociodemographic data form prepared by clinicians was applied to the PD and control groups. This form is a questionnaire which includes questions about the clinical and demographic features of the participants. This form was used to collect information such as age, gender, marital status, psychiatric drug usage, and history of physical disease.

Statistical analysis

"SPSS (Statistical Package for Social Sciences) for Windows 17.0" package program was used for statistical analysis of the findings obtained in the research. Since the number of subjects was over 50, the suitability of variables to normal distribution was examined using the Kolmogorov-Smirnov test. It was determined that the numerical data (age, total antidepressant usage duration) in the study showed a normal distribution and the student' t test was used in the statistical analysis of these data. The chi-square test was used to compare categorical variables. Value of $p<0.05$ was accepted as statistically significant.

Results

Our study included 101 patients with PD and 101 controls who applied to general internal medicine and endocrine outpatient clinics. Of the PD group, 43 were women (42.6%), 58 (57.4%) were men, and 52 of the control group were women (46.8%) and 59 (53.2%) were men. The mean age of the PD group was 64.51 ± 10.97, and the mean age of the control group was 64.66 ± 9.02. The groups were similar in terms of gender and age (p=0.532, p=0.916, respectively). The mean disease duration of the PD group was 6.32 ± 5.10. The rate of psychiatric disease was 42.6% in the PD group and 24.8% in the control group, and the difference between the groups in terms of psychiatric disease was statistically significant (p=0.007). Anxiety disorder was the most common, and depression was the second most common psychiatric disease in the PD and control groups. Depression and anxiety disorder rates were higher in the PD group than in the controls, but this difference was not statistically significant

Table 1. Demographic and clinical features of the PD and control groups.

		PD group n=101 Mean (SD)	Control group n=101 Mean (SD)	p value
Age		64.51 (10.97)	64.66 (9.02)	0.916*
Disease duration		6.32 (5.10)	-	-
Total antidepressant usage duration		3.30 (3.69)	2.88 (2.97)	0.375*
		n (%)	n (%)	
Gender				
	Female	43 (42.6)	49 (48.5)	0.532**
	Male	58 (57.4)	52 (51.5)	
Marital status				
	Married	83 (82.2)	82 (81.2)	0.844**
	Single	1 (1.0)	2 (2.0)	
	Divorced or widow	17 (16.8)	17 (16.8)	
Education level				
	Primary school	30_a (29.7)	14_b (13.9)	0.002**
	Secondary school	60_a (59.4)	59_a (58.4)	
	High school	4_a (4.0)	18_b (17.8)	
	College	7_a (6.9)	10_a (9.9)	
Residency				
	Rural	21 (20.8)	26 (25.7)	0.405**
	Urban	80 (79.2)	75 (74.3)	
Physical disease				
	No	49 (48.5)	27 (26.7)	0.001**
	Yes	52 (51.5)	74 (73.3)	
Physical disease subtypes				
	Diabetes	17 (16.8)	21 (20.8)	
	Cardiac disorders	5 (5.0)	5 (5.0)	
	Hypertension	13 (12.9)	19 (18.8)	
	Other	17 (16.8)	29 (28.7)	
	None	49 (48.5)	27 (26.7)	
Psychiatric disease				
	No	58 (57.4)	76 (75.2)	0.007**
	Yes	43 (42.6)	25 (24.8)	
Psychiatric disease subtypes				
	Depression	14 (13.9)	10 (9.9)	
	Anxiety disorders	21 (20.7)	13 (12.9)	
	Psychosis	5 (5.0)	0 (0)	
	Bipolar affective disorder	2 (2.0)	1 (1.0)	
	Other	1 (1.0)	1 (1.0)	
	None	58 (57.4)	76 (75.2)	
Antidepressant use				
	No	58 (57.4)	76 (75.2)	0.007**
	Yes	43 (42.6)	25 (24.8)	
Drug groups				
	Fluoxetin	1 (2.3)	3 (12.0)	
	Sertralin	18 (41.9)	6 (24.0)	
	Escitalopram	15 (34.9)	13 (52.0)	
	Paroxetin	2 (4.7)	0 (0.0)	
	SNRI (Duloxetin or Venlafaxin)	4 (9.3)	1 (4.0)	
	Mirtazapin	1 (2.3)	0 (0.0)	
	Unknown	2 (4.6)	2 (8.0)	

There is a statistically significant difference in group categories which have multinomial variables that do not contain the same letter. SD: Standart deviation, PD: Parkinson' s disease, SNRI: Serotonin Norepinephrine Reuptake Inhibitor, *: p value for student' s t test, **: p value for chi-square test, $p<0.05$.

(p=0.384, p=0.132 respectively). The rate of antidepressant use in PD group was 42.6%, and that of the control group was 24.8%, and the difference between them in terms of antidepressant use was statistically significant (p=0.007). Among the patients with PD, the most used antidepressant was sertraline with a rate of 41.9%. There was no statistical difference between the total antidepressant usage durations of the groups (p=0.375) (Table 1).

Discussion

The most important findings of our research in which we investigated patients with PD in terms of psychiatric diseases and related clinical features; 1) The rate of psychiatric disease (42.6%) in the PD group was significantly higher than the control group. Anxiety disorders and depression were the most common among these diseases. 2) The use of antidepressant in the PD group was higher than the control group. Depressive disorders and anxiety disorders can directly or indirectly increase the risk of PD. Direct effects; It is the neurochemical changes that occur in PD may be related to depression and anxiety. Neurotransmitters such as dopamine, norepinephrine, gamma aminobutyric acid and serotonin which are involved in the pathogenesis of depression and anxiety, also play a role in the pathophysiology of PD [22]. The relationship between the dopamine system and the norepinephrine and serotonin systems in anxiety disorders can be hypothesized in the causal relationship between the two diseases. Similarly, it has been suggested that the main factors contributing to the development of depression in PD are the depletion of brain catecholamine, acetylcholine and serotonin and the irregularity of fronto-subcortical connections that regulate mood [23, 24]. However, further studies are required to prove this causal relationship and understand the circuits responsible for the occurrence of these diseases. Although PD and depressive or anxiety disorders have different etiologies, they tend to occur as comorbidities. There seems to be a special relationship between depression and anxiety in PD. Patients with PD have significantly higher depression and anxiety scale scores than control group [25,26] . Menza et al. found depression in 92% of patients with PD with anxiety disorder, and found anxiety disorder in 67% of patients with PD with depressive disorder [27]. Anxiety disorders and depressive disorders may be the early non-motor signs of PD' s process. Henderson et al. found a high correlation between PD and depression and anxiety. Twenty percent of these patients reported that depression and / or anxiety began before the onset of physical symptoms [28]. Gonera et al. reported that motor symptoms of PD start after a prodromal phase, which usually lasts 4-6 years [29]. This period corresponds to the 4.7-year period, from the onset of neuronal loss to the 60% loss required for the appearance of motor symptoms in the substantia nigra [30]. However, due to the cross-sectional nature of our research, a possible interpretation could not be made on these issues. Drugs used in the treatment of anxiety disorders or depressive disorders can also be an indirect factor that increases the risk of PD. Selective serotonin reuptake inhibitors (SSRIs) are used in increasing proportions due to their low side effects and good tolerability. Side effects related to extrapyramidal system (EPS) are encountered with the use of SSRI [31]. The incidence of EPS is 1-2 per 1000 people per year [32]. Akathisia, dystonia and parkinsonism are the most common [33], most emphasized explanation about the relationship of parkinsonism symptoms known to be associated with dopaminergic system with SSRI is the suppressive effect of serotonin on the central dopaminergic system [34]. It is emphasized that the drug may increase the serotonin levels and prevent the production and release of dopamine in the nuclei [35]. There are case reports in the literature that develop parkinsonism with the use of paroxetine, escitalopram and sertraline [36, 37]. In a retrospective study, Richard et al. reported that in 10% of patients with PD using SSRI, motor symptoms worsened [38]. Latorre et al. reported that in a case of Parkinsonism developing due to sertraline, the symptoms regressed 3 months after stopping the drug, but despite a 14-month drug-free period, the patient developed PD and responded to levodopa [39]. In our study, the rate of SSRI use in the PD group was higher than the control group. But due to the cross-sectional nature of our study and methodological limitations, analysis on the use of SSRI and the development of PD could not be made. In some of the studies in the literature evaluating PD and psychiatric comorbidities, psychiatric evaluation was performed by using scales. In our study, patients were interviewed by a psychiatrist using SCID-5-CV. This feature made our research different from these studies. The results of our research should be interpreted carefully due to its cross-sectional nature and small sample size. The limitations inherent in this approach include selection or identification, interpretation, and reporting biases. In addition, the presence of PD' s motor symptoms at the time of the interview may be difficult to remember events and symptoms. As a result, comparing the information provided by patients with PD with those of the control subjects is a limitation that may affect the results of our research. In conclusion, psychiatric diseases are seen more frequently in patients with PD than in patients with other physical diseases. Considering that quality of life of patients with PD is associated with psychiatric well-being, psychiatric symptoms in patients are of high clinical importance. In this context, the physician' s awareness of psychiatric symptoms and taking necessary precautions will contribute positively to the treatment of the disease. Longitudinal, prospective studies with larger samples are required to contribute to the elucidation of the PD-psychiatric disease relationship.

Ethics approval

The study was approved by the Clinical Research Ethics Committee of Inonu University (Approval Date: 27.06.2018, Approval Number: 2018/102).

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