Review (Derleme)

Neuropsychiatric Symptoms in Parkinson's Disease Patients

Parkinson Hastalarında Nöropsikiyatrik Semptomlar

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Özet

Nörolojik hastalıklarda birçok fiziksel, bilişsel ve ruhsal belirtiler kendini gösterebilmektedir. Parkinson hastalığı (PH) nöronların dejenerasyonundan kaynaklanan, motor ve non-motor semptomlar ile karakterize olan nörolojik bir rahatsızlıktır. PH'da da motor semptomlarla beraber, non-motor semptomlar içerisine dahil olan psikiyatrik belirtiler görülebilmektedir. PH semptomları, genetik yatkınlık, uygulanan farmakolojik tedavilerin yan etkileri, psikososyal faktörler; anksiyete, depresyon, dürtü kontrol bozukluğu, psikoz gibi psikiyatrik durumların ortaya çıkmasına neden olabilmektedir. PH'de en sık görülen psikiyatrik bozukluğun depresyon olduğu, onu takip eden psikiyatrik bozukluğun ise anksiyete olduğu saptanmıştır. PH'de psikiyatrik komorbitelerin varlığı yüksek oranda olmasına rağmen, tanı ve tedavi sürecinde çoğunlukla klinisyenlerin gözünden kaçmaktadır. Tanı sürecinde bu faktörler dikkate alınmalı ve Parkinson Hastalarının tedavi stratejileri multifaktöriyel bir şekilde yapılandırılmalıdır.

Anahtar kelimeler: Parkinson hastalığı, Nöropsikiyatrik semptomlar, Anksiyete, Depresyon, İmpuls kontrol bozukluğu, Psikoz

Abstract

Many physical, cognitive and psychological symptoms can be seen in neurological diseases. Parkinson's disease (PD) is a neurological disorder arising from the degeneration of neurons, is characterized by motor and non-motor symptoms. Along with motor symptoms, psychiatric symptoms that are included in non-motor symptoms can also be seen in PD. PD symptoms, genetic predisposition, side effects of pharmacological treatments, psychosocial factors; can cause psychiatric conditions such as anxiety, depression, impulse control disorder, and psychosis. It has been determined that the most common psychiatric disorder in PD is depression, followed by anxiety. Although the presence of psychiatric comorbidities in PD is high, it is often overlooked by clinicians during the diagnosis and treatment process. These factors should be taken into account in the diagnosis process and treatment strategies of Parkinson's patients should be structured in a multifactorial manner.

Keywords: Parkinson's Disease, Neuropsychiatric symptoms, Anxiety, Depression, Impulse control disorder, Psychosis

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INTRODUCTION

Parkinson's disease (PD) is a neurological disorder arising from the degeneration of neurons, is characterized by motor and non-motor symptoms; chronic, genetic and environmental factors are effective in the pathophysiology of the disease and finally resulting in disability. PD is the most common neurodegenerative disorder after Alzheimer's Disease (1). In addition to the fact that the disease is seen in both sexes, it is supported by studies that men are affected more than women, and that the age of onset of the disease in men is earlier than in women (2,3). While the average age of onset of PD symptoms is 60-65 years, it has been reported as a result of numerous studies that the incidence is highest at the age of 70-79 (2).

While the resulting motor symptoms are thought to be related to the low amount of dopamine in the nigrostriatal pathway, the low dopaminergic neurons in the mesolimbic and mesocortical pathways reveal conditions called non-motor symptoms in addition to motor symptoms in patients (4). Although PD is known as movement dysregulation, non-motor symptoms constitute an essential part of the clinical presentation. Patients often do not report the present non-motor symptoms as a bothersome complaint. If the detailed history of the patient is not adequately taken by the physician, this important factor that negatively affects the quality of life of the patients will be ignored (5). Non-motor symptoms, also called "premotor symptoms", including cognitive dysfunction, depression, pain, fatigue, anxiety, apathy, psychosis, and sleep disturbances constitute an important cause of morbidity in all stages of the disease and appear 10 years before diagnosis or even before the onset of motor symptoms (6).

It is aimed to correct the impaired dopamine level in patients with levodopa or dopamine agonists used for treatment. However, Dopamine Replacement Therapy (DRT) not only has an effect on the movement control of the brain, but also stimulates the reward mechanism in the brain by triggering non-motor symptoms (7). Patients, on the other hand, may increase the use of dopaminergic drugs without a doctor's follow-up in order to relieve the aforementioned non-motor symptoms or to prevent limitation in motor movements (8). As a result of this, dopamine dysregulation is observed due to the use of drugs above the required dose despite the harmful physical, psychiatric and social sequelae. In the following process, punding that includes repetitive and stereotypical motor movements (9) and impulse control disorders (ICD), which are described as the inability to prevent the urge to act that harm oneself or others, are added to this picture (10).

DEPRESSION

Depression is an emotional disorder characterized by symptoms such as depressed mood, fatigue, decreased interest in daily activities, and recurrent thoughts of death for at least two weeks (10). As a result of an international study, lifetime prevalence estimates of depression ranged from 1% (Czech Republic) to 16.9% (United States), while 1-year prevalence estimates were found as 4.5% (Mexico) and 5.2% (West Germany) (11). The International Classification of Diseases (ICD-10) provided information on the major depressive episode: The 1-year prevalence was reported as 3.2% in individuals without comorbid physical disease and 9.3-23% in those with chronic disease (12).

In a meta-analysis, the prevalence of depression in Parkinson's patients was reported as 31% (13). In a more recent review, it is reported that in population-based studies compared to clinical PD data, there are lower rates of major depression (14). It is also advocated that the reason for the development of depression in PD is a reaction developed as a result of the chronic disease. However, depressive symptoms may occur before the onset of motor symptoms as well (15). Therefore, it has been suggested that changes in neurochemicals such as dopamine, serotonin, and norepinephrine in PD are responsible for depression (16). In a study by Marshal, L., it was shown that depressive disorders, in addition to causing inherent emotional distress, negatively affect quality of life, motor and cognitive deficits, functional disability, and other psychiatric comorbidities in PD (17). Concomitant depression causes patients to perceive their existing motor symptoms as worse, and this is seen as the most important factor that reduces the quality of life of patients (18).

ANXIETY

Anxiety is the second most common nonmotor symptom after depression, which is characterized by persistent anxiety, loss of attention, muscle tension, headache, and sleep dysregulation (19). Anxiety is present in an average of 25%-49% of Parkinson's patients, and it is the second neuropsychiatric disorder with a higher incidence in individuals with PD compared to individuals in the same population without a diagnosis (20,21). The source of anxiety symptoms in the PD patient group has not been fully clarified. However, as a result of numerous studies, it supports the view that these pathologies, including the dopaminergic system and other structures with which it interacts, result from abnormalities in noradenergic and serotonergic mechanisms. (22,23). Although L-Dopa treatment is

considered the gold standard treatment for PD disease, it also triggers many neuropsychiatric complications such as anxiety and depression as a result of increasing the dopamine level in the brain (24-26). Serotonin is an important neurotransmitter that has serious effects on mood, fear and anxiety (27,28). Anxiety symptoms emerge as a result of damage or loss of serotonergic neurons (29). 5-HT1A is one of the receptors that play a role in the etiology of serotonin and may cause psychiatric complications in PD patients as a result of modulating dopamine release (30,31).

OBSESSIVE COMPULSIVE DISORDER

Obsessive-compulsive disorder (OCD) is a heterogeneous disorder characterized by the emergence of obsessions, compulsive rituals, or most commonly both (10). Obsessions, which cause anxiety are repetitive and persistent, mostly involving order, cleanliness, doubt, and religious issues; are intrusive and unwantedthoughts, images, impulses, and desires. (32-34). Compulsions, on the other hand, include behaviors done to relieve anxiety arising from obsessions. Common compulsions include; washing, sorting, checking, counting, and repeating actions or words (34). The lifetime prevalence of OCD is reported to be 1.6% (35). It is supported by studies that PD is frequently diagnosed with neuronal degeneration in the substantia nigra pars compacta and the presence of Lewy bodies in the remaining neurons, and that it affects the frontostriatal circuits, which are involved in the pathogenesis of many psychiatric disorders, especially OCD (36). According to the results of a study, it was found that patients with PD show more obsessive features than the healthy control group, and the severity of obsessive-compulsive symptoms was related to the severity and duration of PD (37). In a study examining the relationship between obsessive-compulsive symptoms and motor asymmetry in PD, a relationship was observed between the severity of motor symptoms in the left side of the brain and obsessive-compulsive symptoms related to cleanliness and repetition in PD, whereas obsessive-compulsive symptoms related to order/routine were associated with the right region of the brain (38).

IMPULSE CONTROL DISORDERS

Impulse control disorders (ICD) are defined as the inability of the person to prevent the urge to perform an action that harms himself or others (39,40). Recent research findings show that the prevalence of ICD in the PD population may be more than 25% (39). Studies indicate that pathological eating, pathological gambling, increased sexual desire (hypersexuality) and pathological shopping, which are among the ICD subgroups, may have a tendency to be seen in PD (39,40). While pathological gambling and hypersexuality are more common in male PD patients, excessive shopping is more common in female PD patients (40). Dysregulation in the mesolimbic pathway responsible for learning the reward mechanism and the mesocortical pathways responsible for decision making processes; are the dopaminergic systems that cause ICD. Mesocorticolimbic network functions as a bridge between the prefrontal cortex, amygdala, ventral striatum and ventral tegmental areas. After the actions included in the ICD, experience the pleasure of reward, this situation becomes uncontrollable over time. In the initial phase of reward pleasure, a strong emotional response occurs as a result of a sudden reaction in the ventral striatum, which causes an increase in the amount of dopamine in the ventral striatal. As this system repeats, the action that starts in the ventral striatum forms a habit and is reinforced by the dorsal striatum (41,42). According to the results of a detailed research; pathological shopping seen in 5.7% of PD patients, pathological eating in 4.3%, pathological gambling in 5%, and hypersexuality in 3.5%; and it was concluded that the rate of ICD was higher in PD patients (17.1%) treated with a dopamine agonist than in PD patients who were not treated with a dopamine agonist (6.9%), and treatment with a dopamine agonist increased the risk of developing ICD by 2 to 3.5 times. (43).

PSYCHOTIC DISORDER

Psychotic disorder is a severe mental disorder in which the individual loses his sense of reality, irregularities prevail in emotions, thoughts and actions, and seriously affect functionality. Studies have reported that the lifetime prevalence of psychotic disorders is 3.48%. Psychosis is a common non-motor symptom of PD and causes serious morbidity and increased mortality. The prevalence of psychosis in PD varies between 43-60%, and this rate can reach up to 75% in PD accompanied by dementia (44). Visual hallucinations are more common in PD rather than delusions, auditory and tactile hallucinations. Levodopa or dopamine agonists used in PD are dopaminergic treatments that are effective in improving motor symptoms; however, these treatments may cause psychosis to occur or increase the severity of existing psychosis. Also, antipsychotic drugs administered for the treatment of psychotic symptoms may cause motor symptoms or a more severe course of existing symptoms as a result of dopaminergic antagonism. In studies on the pathophysiology of psychotic

disorders, there are data showing that dopamine hyperactivity in the ventral striatum, which is a part of the mesolimbic dopamine pathway, contributes to the occurrence of positive symptoms, especially delusions and hallucinations (45).

In the serotonin theory, there is a hyperfunction of 5-hydroxytryptamine-2A (5HT2A) receptors in the cortex (46). With this hypothesis, a picture also emerges in intoxications of serotonergic agents such as Lysergic acid diethylamide (LSD) or psilocybin, which are triggered by neurodegenerative processes such as Parkinson's and respond better to 5HT2A receptor antagonists (47). In this picture, there is a relatively preserved insight together with more visual hallucinations and mystical beliefs (48,49).

Parkinson's disease is a neurological disease characterized by motor and non-motor symptoms resulting from degeneration of the central nervous system. Psychiatric comorbidities are frequently seen among non-motor symptoms. It has been reported in previous studies that the prevalence of psychiatric comorbidity is higher in this disease group than in the general population. Psychiatric comorbidities are often overlooked in the diagnosis and treatment methods of patients and this situation causes negative consequences on both the clinical course of the disease and the quality of life of the patients. It is important to prefer multidisciplinary methods in the diagnosis and treatment process and to follow up psychiatric symptoms that affect the quality of life in Parkinson's patients and to carry out remedial interventions.

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