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AFFECTIVE MODELS OF DEPRESSION AND ANXIETY IN PATIENTS WITH PARKINSON DISEASE AND MULTIPLE SCLEROSIS

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INTRODUCTION

Multiple sclerosis (MS) is a chronic, inflammatory, (auto) immune disease of the central nervous system (CNS) whose etiological background is not completely clear. The disease is characterized by decay of the myelin sheath, axons, as well as oligodendroglia. As a consequence, scars with a diverse spectrum of symptoms and signs of the disease remain at the site of decay, associated with significant consequences in behaviour and emotions [1, 2]. People with MS have to deal with a range of physical, cognitive and psychological symptoms on a daily basis, such as walking and limited mobility, pain, fatigue, depression, difficulty remembering and concentrating. MS affects all spheres of people's lives, including employment, contacts and social life, leisure and daily activities [3]. People with MS face significant unpredictability and uncertainty due to the changing nature of the disease course; for example, the risks of recurrence, hospital admission, and further development of disability. MS is usually diagnosed in the best years, people live with these challenging symptoms and changeable course of the disease for many years [4]. Parkinson's disease (PD) is the second most common neurodegenerative disorder. The main pathophysiological mechanism in Parkinson's disease (PD) consists of progressive degeneration of dopaminergic neurons in the central nervous system, with consequent lesions of nigrostrital projections and a lack of dopamine, and to lesser extent serotonin and norepinephrine, at the striatum level. In PB, spontaneous motor poverty as the most common clinical determinants of the disease is often associated with depression, anxiety, sleep disorders, hallucinations, delusions, apathy, impulsive and compulsive behaviour, and cognitive dysfunction [6]. Anxiety can be defined as diffuse, internal, free-floating tension, which has no real basis. Clinical expression of anxiety includes psychological and somatic symptoms. Risk factors include comorbidity with a diagnosis of depression and limited social support [7]. Depression is a complex disease and is thought to be etiologically caused by the interaction of genetic-biological and psychosocial factors. Symptoms of the depressive disorder include: typical symptoms (depressed mood, loss of interest and satisfaction, and decreased energy and increased fatigue) and other common symptoms (sleep disturbance, decreased appetite, decreased concentration and attention, decreased self-esteem and self-esteem, ideas of guilt and worthlessness, gloomy and pessimistic view of the future, ideas of self-harm or suicide). At least two type and two other symptoms lasting at least two weeks are required to diagnose the disease [8]. Anxiety and depression include emotional disorders, occurring in association with PB and MS can be an important sign of morbidity. Emotions are very rapid adaptive responses consisting of physiological, cognitive, and behavioural elements [9].

METHODS

The prospective study included 50 patients with relapse of remitting MS and Parkinson's disease. The analysis is based on the population of patients with PB and MS, with a disease duration of 1-5 years. Only patients with a definitive diagnosis of relapsing remitting MS were evaluated according to the 2010 McDonald criteria [10]. The paper also discusses patients with a diagnosis of PD that meets the clinical criteria for the diagnosis of possible Parkinson's disease [11]. Patients without cognitive impairment or with mild cognitive impairment were included in the study. The exclusion criterion was a score of 24 and a lower Mini-mental scale examination (MMSE) [12]. According to the duration of the disease, the subjects were divided into two groups, the first group where the disease lasts 1-3 years and the second group where the disease lasts 4-5 years. The Kurtzke Expanded Disability Status Scale (EDSS) was used as a method to quantify disability and the degree of clinical disability in participants with MS [13]. Clinical assessment of PB severity was performed with the Hoehn and Year

scale, which divides PB into five phases (from mild unilateral symptoms in the first phase, to the fifth phase when they are severe, bilateral, and when the patient's condition requires constant care of another person) [14]. Depression was measured by the Beck Depression Scale [15] and anxiety by the Hamilton Anxiety Rating Scale [16]. In the analysis of the obtained data, standard statistical parameters were used (mean value, standard T-test and X2 test, exact Fisher test, computer program SF-36.EXE, chance ratio). A p <0.05 value was considered significant.

RESULTS

By consecutive selection of patients with Parkinson's disease (PD), out of a total of 50 patients, 54% (27) and men 46% (23). The average life expectancy was 63.18 +/- 10.42 years. In the group of consecutively selected patients with multiple sclerosis (MS), women were 80% (40) and men 20% (10) (Table 1).The average age was 37.4 +/- 8.65 years (Table 2).Participants were divided into two groups according to the duration of the disease in patients with PB and MS, the first group where the disease lasts 1-3 years and the second group where the disease lasts 4-5 years. In patients with PB in the first group there were 34 participants (68%) and in the second group 16 participants (32%). Participants with MS were represented in the first group in 64% of cases (32 participants) and in the second group in 36% of cases (18 participants). According to the degree of disability, the participants with PB were divided into two groups: the first group (disease stages I and II) in which there were 29 participants (58%) and the second group (stage III-V) included 21 participants (42%) . Participants with MS were also classified according to the degree of disability in two groups: the first group were those with EDSS 0-5.0 and there were 44 participants (88%), and in the second group of participants with EDSS 5.5-10 there were 6 participants).

Tabe 1. Distribution of participants by gender

Disease	Gender			
	Men		Women	
	N	%	N	%
Parkinson's disease	23	46	27	54
Multiple sclerosis	10	20	40	80

Table 2. Distribution of participants by age

Disease	Age	
	Middle age (in years)	SD
Parkinson's disease	63.77	12.57
Multiple sclerosis	35.7	5.83

SD- standard deviation

According to the degree of anxiety, the participants were divided into two groups: the first group of participants with moderate anxiety (Hamilton score up to 17), the second group of participants with moderate and severe anxiety (Hamilton score 18-30). All participants with PB showed some degree of anxiety. Moderate anxiety was shown by 36% and moderate and severe anxiety by 64% of participants. The most represented age group of participants aged 60-69 (44% of participants) had the most pronounced anxiety (68.2%). The Chi-square test (P = 0.75) and the exact Fisher test (P = 0.74) show that there is no correlation between the frequency of moderate to moderate and severe anxiety on the one hand and the duration of the disease on the other. Anxiety is present regardless of the duration of the disease, and the frequency of moderate and severe anxiety is more pronounced in stage III and IV of the disease (P = 0.04). The ratio of the chances of developing moderate and severe anxiety is 3.97 times higher in the group with advanced phase of the disease (phase III-V) (Figure 1).

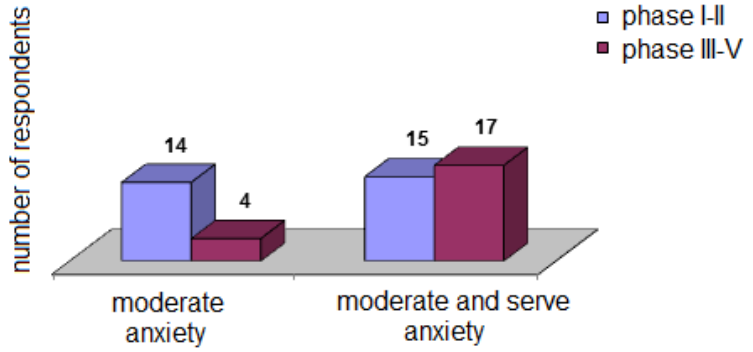

Figure 1. Distribution of anxiety by disease stages in subjects with Parkinson's disease

Figure 1. Distribution of anxiety by disease stages in subjects with Parkinson's disease Depression is present in 82% of participants with PB. The occurrence of depression is present regardless of the duration of the disease. A more severe form of depression was experienced by participants in advanced stages (III and IV phases) (P = 0.01). The chance ratio determined that the possibility of more severe forms of depression is 6.92 times higher in the group with phase III-IV disease (Figure 2).

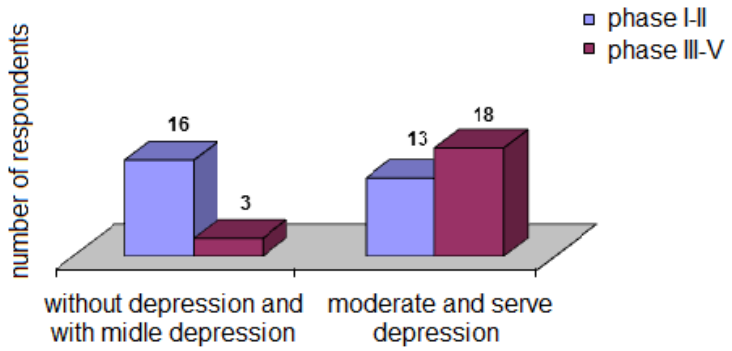

Figure 2. Distribution of depression by disease stages in subjects with Parkinson's disease In participants with MS, moderate anxiety occurs in 32% and moderate and severe anxiety in 68% of cases. In MS patients, there is no correlation between the frequency of anxiety and the duration of the disease (P = 0.87) or the degree of clinical disability (EDSS) (P = 1.0). Depression in people with MS occurs in a large percentage of participants (86% of participants showed some form of depression), and only 14% of them were not depressed at the time of testing. It was found that the chance of developing more severe forms of depression (moderate, severe and severe) is 5.48 times higher in the group with EDSS 5.5-10 but without a statistically significant difference between the groups. The frequency of depression does not depend on the duration of the disease (Figure 3) or the degree of clinical disability (Figure 4).

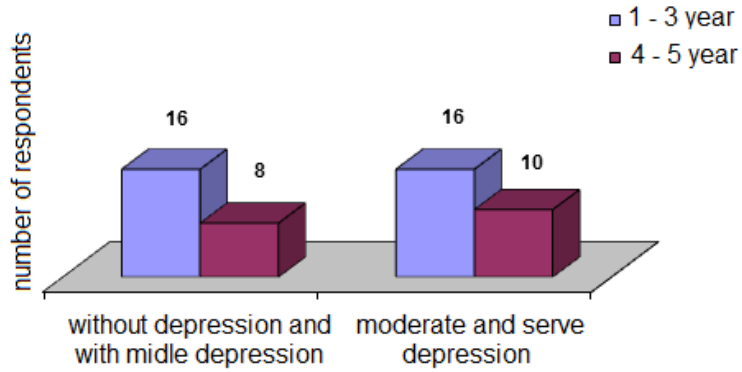

Figure 3. Distribution of depression according to the duration of the disease in patients with multiple sclerosis

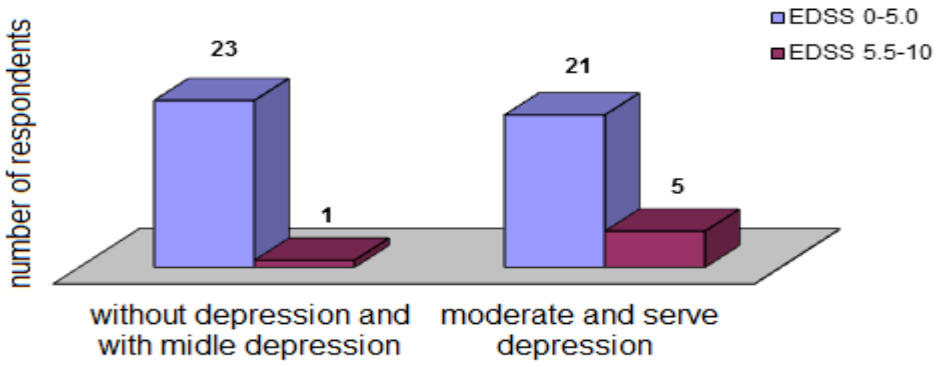

Figure 4. Distribution of depression according to the degree of disability in patients with multiple sclerosis

DISCUSSION

Neurodegenerative diseases such as multiple sclerosis and Parkinson's disease, depending on the localization of the pathomorphological substrate and the manner and extent of involvement of individual neurotransmitter systems, or functional circuit in the brain, in different ways and to different extent affect the occurrence and course of emotional disorders. Anxiety and depression are felt by the individual in terms of positive or negative emotions [6]. Affective models outline common and unique components of depression and anxiety. In particular, negative affect is widely associated with these symptoms, while a low positive affect is relatively specific to depression and social anxiety. However, it is unknown how affects relate

to symptoms because they occur naturally in everyday life or as a dynamic process within a person [17]. Anxiety in people with MS may be the most prominent symptom at the onset of the disease. It represents a psychological and social disorder as a reflection of a young person's coping with a severe chronic illness, and the occurrence of depression as a very common psychological comorbidity is associated with a neurobiological process. Depression is associated with sexual dysfunction and impaired mobility. In the further course of the disease, sleep problems, sexual and depressive disorders are common in people with MS. Depression is the most common psychological comorbidity in MS patients, with a prevalence of 20-50%, and depressive symptoms are recognized in approximately 80% of all MS patients. Gay et al. pointed out that anxiety is a strong predictor of depression and that its impact on depression is exacerbated by the presence of alexithymia and lack of social support [18]. Risk factors include female gender, comorbidity with a diagnosis of depression, and limited social support. Korostil and Feinstein. (2007) state in their study that anxiety disorder in a patient with MS is often unnoticed and unrecognized. In conclusion, they state that clinicians should test all patients with MS for anxiety and depression because they represent areas that can be treated in an MS patient [7]. In the study of Legera et al. (2002) found that lower levels of disability acceptance were associated with higher levels of anxiety and depression, higher anxiety, higher levels of intolerance and insecurity [19]. Anxiety disorders have been reported in the literature that is present between 36 - 54% of the MS population, and about 30% of people with MS have symptoms consistent with generalized anxiety disorder [20,21,22]. All participants with MS showed some degree of anxiety in this study. However, no association was found between the incidence of moderate, moderate and severe anxiety on the one hand and the duration of the disease on the other. There is no significant difference in the occurrence of higher anxiety compared to the clinical stage of the disease (EDSS). 86% of participants showed some form of depression, and only 14% of them were not depressed at the time of testing, which is correlated with other studies [23,24]. The incidence of moderate, severe and severe depression does not depend on the duration of the disease or the clinical stage of the disease (EDSS) (p> 0.05). Although it was found that the chance of developing more severe forms of depression (moderate, severe and severe) is 5.48 times higher in the group with EDSS 5.5-10, there is no statistically significant difference compared to the participants and EDSS up to 5.0. In a study by Mendes et al. (2003) in a group of patients with MS, the relationship between depression, disability, gender, age, and disease duration was analyzed. It was found that there is a correlation between depression and functional disability, and no correlation was found between depression and gender, age and duration of the disease [25]. In a study by Chwastiak et al. (2002) analyzed 1374 participants with MS and found that 41.8% showed moderate symptoms of depression and 29.1% had severe depression. Severe forms of MS are highly associated with severe depressive symptoms as an accompanying sign of the disease. More than half of people with MS experience depression at some point during their illness [26]. The current prevalence of anxiety in PB is uncertain, but it is estimated that 40% of patients with PB experience some anxiety. Although most patients with motor fluctuations experience greater anxiety during the "OF" phase this is not a universal phenomenon. Anxiety sometimes develops before motor symptoms, suggesting that anxiety is not a psychological and social disorder in adapting to the disease but is related to a neurobiological process occurring in PB [27]. In this study, anxiety was present in all participants with PB regardless of the duration of the disease, and the chance of developing more severe forms of anxiety was 1.58 times higher in the group where the disease lasted longer. The frequency of moderate and severe anxiety is more pronounced in the advanced stages of the disease and there is a significant difference (P = 0.04). The ratio of the chances of moderate to severe anxiety is 3.97 times higher in the group with an advanced phase of the disease (phase III-V). This finding correlates with a study by Richard (2005) that found that anxiety disorders associated with PB can be an important cause of morbidity [27]. Estimates related to the prevalence of depression in PB differ considerably primarily due to methodological differences in the causes of the methods themselves and the specific case. A study by Menza et al. (1993) found that participants with PD had high levels of anxiety that did not resemble the primary psychological response or the effects of levodopa treatment, and that most patients with an anxiety disorder had comorbidity with a diagnosis of depressive disorder. This study ultimately suggests that anxiety and depression are associated with manifestations of concomitant neurochemical changes in PB itself. The biological hypothesis shows neurochemical deficits in PB (mainly norepinephrine and serotonin deficiency, lack of ability to reduce dopaminergic stimuli) as causes of depression [28]. The study of depression in PB is complicated due to diagnostic difficulties because the diagnosis of depression in patients with PB is difficult due to the overlap of depressive symptoms and PB symptoms [29]. In summary, judges show a prevalence of depression in PB between 20-45%. A small percentage of patients (only about 1%) reported symptoms of depression, while 50% of participants were depressed after objective testing (Beck Depression Scale > 10) [27]. Depressive symptoms occur frequently in patients with PB (82% of respondents). This finding is correlated with the aforementioned comparative study by Menza et al. (1993) who found that 92% of participants with anxiety disorder have comorbidity with a diagnosis of depressive disorder [28]. In this study, the occurrence of moderate, severe and severe depression in patients with PB is present regardless of the duration of the disease, and there is a significant difference in the occurrence of these forms of depression and the clinical stage of the disease, ie a higher degree of depression shows participants in advanced clinical stage (P = 0.01). It was determined that the chance of developing more severe forms of depression is 6.92 times higher in the group with phase III-V disease. This result can be explained by the fact that participants who have been affected by the disease for a long time suffer more due to limitations in everyday life on the one hand, but also because the accompanying neurochemical changes in PB lead to depressive manifestations of these events.

CONCLUSION

Emotional difficulties resulting from coping with severe chronic illness, with the interaction of genetic-biological and psychosocial factors, result in the development of affective disorders such as depression and anxiety in patients with PB and MS. Patients with Parkinson's disease and multiple sclerosis have a high rate of emotional disturbances. As a rule, comorbidity consists more of subjective suffering, reduced psychological coping and negative interference especially depression change the course of these diseases. Therefore, the pharmacological and non-pharmacological treatment of depression and anxiety in PB and MS can change the course of the disease in a positive direction.

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