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NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE

68 patients with PD with a disease duration of 4 (2-6) years without dementia. It was established that patients with parkinsonism have emotional disorders in the form of anxiety and depressive disorders, fatigue, suprasegmental autonomic and dissominal disorders, the severity of which is independent from the age and gender of patients, as well as from the main motor manifestations of the disease. The relationship between the investigated non-motor symptoms of PD was established.

Keywords: Parkinson's disease, non-motor manifestations, fatigue

Introduction

In the end of the XIX - XX centuries it was believed that Parkinson's disease is a disease mainly of the motor sphere, while in our days the concept of the clinical picture of Parkinson's disease has expanded significantly. Today it is generally recognized that this disease is characterized by a wide range of non-motor disorders [1]. As the disease progresses, some of them acquire dominant clinical significance, adversely affecting to increase the quality of life patients' lives, leading to their disability and reducing life expectancy. Non-motor symptoms of PD include autonomic, mental, dissomic, sensory and some other disorders. Most non-motor symptoms of manifestations appear and increase as the disease develops in parallel with the aggravation of motor disorders, but some non-motor symptoms, such as impaired sense of smell, constipation, depression, sleep disorder with fast eye movements, pain syndromes occur before the development of classic motor symptoms of PD. In this regard, they talk about the "premotor stage" of BP. The absence of specific symptoms makes clinical diagnosis BP at the "premotor" stage almost impossible. Nevertheless, examination of patients with such disorders using functional methods of neuroimaging and some other instrumental methods, especially if they have relatives suffering from PD, is a promising way to identify PD as early as possible.

Clinical diversity, high frequency, a significant impact on the quality of life of patients and their families make this problem significantly urgent. Objective: to establish the presence, severity and relationship of non-motor symptoms of PD and their dependence on the main characteristics of the disease. Methods 68 patients (41 women and 27 men) with Parkinson's disease without dementia were examined. Verification of the diagnosis was carried out in accordance with ICD-10, a special rubric code for BP - G20. The diagnosis was formulated according to the recommendations of the Center for Extrapyrimal Diseases of the Ministry of Health of the Russian Federation, indicating the clinical form, the presence of postural instability and impaired walking, the distribution of identified symptoms in the extremities, the severity of cognitive impairment, depression and autonomic insufficiency, clarifying the stage of the disease according to Hen and Yar (1967) and the rate of progression.

The average age of the patients was 64 (55-72) years, the duration of the disease was 3.5 (1-7) years, the severity of disease on the Hen - Yara scale - 2.5 (2.0 - 3.0). According to the severity of the disease, patients were divided into the following groups: 25 patients - with a mild degree of severity (first group), 36 with an average (second group), 7 with a severe (third group). The control group consisted of 15 healthy individuals, comparable in gender and age to the main group. Clinical examination was carried out according to the scheme: assessment of objective somatic, neurological status, professional history, past and related diseases, taking into account the age of manifestation of PD, the rate of progression and duration of the disease. The severity of motor disorders was assessed using the USOPS — the Unified Parkinson's Disease Rating Scale. The stage of the disease was established on the Hen-Yara scale. To assess fatigue, the MFIS scale was used. Assessment of affective disorders was administered by using the HADS Hospital Anxiety and Depression Scale, and daytime sleepiness using the Epworth Drowsiness Scale (ESS). To assess autonomic disorders, a questionnaire was used to identify signs of autonomic changes (A. Wayne, M., 1998). Statistical data processing was performed using the Statistica 6.0 software package and nonparametric methods. Quantitative traits are characterized by the median, upper and lower quartiles. To compare two independent features Mann-Whitney test was used.

Correlation analysis performed according to Spearman. The critical level of significance in testing statistical hypotheses was assumed to be 0.05.

Results

The following data characterizing the emotional disorders in patients with parkinsonism. The average level of depression was 7 (5-9) points. The normal value of this indicator (0–7 points) was observed in 33 patients, subclinically expressed depression (8–10 points) was observed in 17 patients, clinically pronounced depression (11 and higher points), there were 6 patients. The average depression score in patients with a mild disease severity was –7.5 (4–9), moderate –7 (5–8), severe –8 (8–11) points, ($p_{1-2} = 0.784$; $p_{13} = 0.261$; $p_{2-3} = 0.097$). By the method of correlation analysis, it was not possible to identify a reliable relationship between the total indicator of the depression scale and age ($R = 0.12$, $p = 0.36$), the duration of Parkinson's disease ($R = 0.06$, $p = 0.651$), and the stage on the Hen - Yar scale ($R = 0.13$, $p = 0.330$), severity motor symptoms on the USHOP scale ($R = 0.12$, $p = 0.370$). The average anxiety level was 8 (4-9) points. The normal value of the indicator (0 - 7 points) was observed in 35 patients, subclinically expressed anxiety (8 - 10 points) was observed in 22 patients, clinically expressed (11 and higher points) - in 11. The average anxiety score in patients with mild disease severity Parkinson's score was –7 (3-10), medium - 8 (4-9), severe - 8 (8-9) points, ($p_{1-2} = 0.597$; $p_{13} = 0.563$; $p_{2-3} = 0.235$). A reliable connection between the total indicator of the alarm scale and age ($R = 0.05$, $p = 0.671$), the duration of Parkinson's disease ($R = 0.25$, $p = 0.062$), stage (according to the Hen - Yara scale) ($R = 0.18$, $p = 0.161$) and the severity of motor no symptoms ($R = 0.06$, $p = 0.640$) were detected. The analysis of relationship between the total fatigue index and manifestations of emotional disorders showed a statistically significant correlation of this symptom with the presence of depression ($R = 0.27$, $p = 0.047$) and anxiety ($R = 0.43$, $p = 0.001$). Marked also the relationship of the anxiety index and individual subscales of MFIS: with "psychosocial" fatigue ($R = 0.29$, $p = 0.034$), "cognitive" ($R = 0.27$, $p = 0.043$), "physical" ($R = 0.60$, $p = 0.000$). The correlation between the total score of depression and individual MFIS subscales is close to reliable: with "psychosocial" fatigue ($R = 0.23$, $p = 0.080$), "cognitive" ($R = 0.26$, $p = 0.057$), "physical" ($R = 0.20$, $p = 0.070$). Fatigue in the main and control groups was evaluated. The average fatigue score was 33

(25-42) points, which was significantly ($p = 0,000$) higher than in the control group (15; 9 - 19 points). The average fatigue score in patients with mild Parkinson's disease severity was 28 (19-38) points, average 31.5 (26-42), severe 46.5 (39.5 - 50.5), ($p_{1-2} = 0.340$; $p_{1-3} = 0.046$; $p_{2-3} = 0.046$). Fatigue (more than 36 points according to MFIS) was noted in 34 (50%) patients. The total indicator of the fatigue scale did not correlate with the age of patients ($R = 0.12$, $p = 0.343$), duration ($R = 0.25$, $p = 0.060$) and the severity of the disease ($R = 0.22$, $p = 0.090$), severity motor disorders ($R = 0.16$, $p = 0.210$). The indicator of "cognitive" fatigue did not correlate with the age of patients ($R = 0,23$, $p = 0,301$), continued severity ($R = 0.34$, $p = 0.122$) and the severity of the disease ($R = 0.26$, $p = 0.242$), the severity of motor disorders ($R = 0.04$, $p = 0.831$). The indicator of "physical" fatigue was not associated with the age of patients ($R = 0.20$, $p = 0.360$), duration ($R = 0.05$, $p = 0.811$) and the severity of the disease ($R = 0.32$, $p = 0.140$), severity of motor disorders ($R = 0.12$, $p = 0.591$). The indicator of "psychosocial" fatigue did not depend on the age of the patients ($R = 0.21$, $p = 0.342$), duration ($R = 0.03$, $p = 0.873$) and the severity of the disease ($R = 0.13$, $p = 0.562$), the severity of motor disorders ($R = 0.15$, $p = 0.501$).

The correlation analysis between the individual points of the USHPP scale and fatigue indices revealed a reliable correlation between the degree of tremor of the right hand and "psychosocial" fatigue ($R = 0.28$, $p = 0.031$), "cognitive" ($R = 0.33$, $p = 0.010$) and the total MFIS score ($R = 0.30$, $p = 0.011$), the degree of tremor of the right leg and "psychosocial" fatigue ($R = 0.34$, $p = 0.001$), "cognitive" ($R = 0.40$, $p = 0.012$) and the total MFIS score ($R = 0.38$, $p = 0.001$). The total value of USBP did not correlate with the severity fatigue syndrome. When assessing sleep disorders, increased daytime sleepiness was detected in 9 patients (13.2%). The average ESS score was 6.9 (5-9) with a normal value of 9 points. 17 patients noted the difficulty of falling asleep, 23 - a shallow, shallow sleep, 13 - frequent awakenings, 9 - a feeling of lack of sleep, tiredness in the morning. There was not found a reliable correlation between the degree of daytime sleepiness and the age of patients ($R = 0.06$, $p = 0.626$), duration of the disease ($R = 0.19$, $p = 0.175$), severity of the disease ($R = 0.02$, $p = 0.849$) the severity of motor disorders ($R = 0.02$, $p = 0.850$), the level of anxiety ($R = 0.17$, $p = 0.212$) and depression ($R = 0.23$, $p = 0.103$). Reliable correlation between the daytime sleepiness indicator and the "cognitive" subscale indicators were identified ($R = 0.39$, $p = 0.004$) and "physical" fatigue ($R = 0.41$, $p = 0.003$), the total fatigue score on a scale MFIS ($R = 0.41$, $p = 0.002$). An analysis of autonomic disorders revealed a significant ($p = 0.048$) increase in the average value of the A.M. Wayne questionnaire in patients with parkinsonism, which was 22 (15-27) points with a control value of 18 (13-25) points. The indicator in patients with mild severity was 22 (15-28), moderate severity was 21.5 (14.5-27), severe severity was 23 (20-26) points without significant differences between the groups. No reliable correlation was found between the degree of autonomic disorders and the age of patients ($R = 0.01$, $p = 0.886$), the duration of the disease ($R = 0.06$, $p = 0.614$), and the severity of the disease ($R = 0.01$, $p = 0.917$), the severity of motor disorders ($R = -0.01$, $p = 0.908$), an indicator of depression ($R = 0.16$, $p = 0.222$). Reliable correlation between the indicator of autonomic disorders and anxiety ($R = 0.40$, $p = 0.002$), indicators the subscale "cognitive" ($R = 0.34$, $p = 0.010$), "physical" ($R = 0.38$, $p = 0.003$), and "mental" fatigue ($R = 0.32$, $p = 0.010$), the total fatigue score for MFIS scale ($R = 0.40$, $p = 0.001$).

Discussion. Non-motor manifestations of PD are not limited to the studied syndromes. The choice suprasegmental autonomic disorders, emotional disturbances, and dysomnia among the many non-motor symptoms of PD were due to the initial object of study, which was fatigue syndrome. The clinical manifestations of this syndrome are similar to some symptoms of these disorders, therefore, affective, vegetative and dissominal disorders were monitored to exclude the secondary nature of fatigue syndrome. The conducted correlation analysis revealed the interconnection of the incidence of all the studied non-motor symptoms of BP with fatigue, which at this stage of the study does not allow us to reliably consider it an independent non-motor syndrome of PD. However, based on the literature on the primary fatigue in PD [3], it can be assumed that the established dependence is a consequence of the general pathogenetic mechanisms of non-motor symptoms of PD. In the literature, in particular, monoamine vava [4] and inflammatory [5] theories of the pathogenesis of non-motor syndromes of PD. The next step of our study will be to compare the severity of fatigue in patients with the presence and absence of affective, autonomic and dissominal disorders to confirm the independence of this syndrome and determine the concentration of pro- and inflammatory cytokines in the blood serum of patients to clarify some issues of pathogenesis of non-motor symptoms of PD. The literature discusses the possibility of a connection between non-motor symptoms of PD and natural aging processes. Analysis of the data showed the absence of dependence of the studied non-motor symptoms of PD on the age and gender of patients, which confirms the available information that non-motor symptoms are a consequence of the neurodegenerative process inherent in Parkinson's disease [6]. However, it was found that most of the studied non-motor disorders are independent of the main characteristics of the disease: the duration of the disease and the severity of motor disorders, and therefore have a different neurochemical and neurophysiological nature than motor symptoms of parkinsonism.

Conclusion

Anxiety and depression, fatigue, suprasegmental autonomic disorders, sleep disorders are naturally recorded in patients with parkinsonism. The severity of these syndromes does not depend on the age and gender of the patients, as well as on the main motor manifestations of the disease. The established conjugation of emotional, dissominative, autonomic disorders and fatigue indicates their comorbidity and common mechanisms of formation.

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ПАРКИНСОН АУРУЫНЫҢ МОТОРЛЫ ЕМЕС СИМПТОМДАРЫ

Түйін: ұзақтығы 4 жыл (2-6) деменциясыз Паркинсон ауруымен (ПА) 68 науқас зерттелген. Анықталғаны, ПА ауруымен науқастарда үрейлік және депрессия түріндегі эмоциональды бұзылыстар, шаршағыштық, сегментүстілік вегетативті және диссомниялық бұзылыстар анықталады, олардың айқындылығы науқастың жасы мен жынысына, сонымен қатар аурудың негізгі моторлы көріністеріне тәуелсіз.

Түйінді сөздер: Паркинсон ауруы, моторлы емес көріністер, эмоциональды бұзылыстар

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НЕМОТОРНЫЕ СИМПТОМЫ БОЛЕЗНИ ПАРКИНСОНА

Резюме: обследовано 68 пациентов с болезнью Паркинсона (БП) с длительностью болезни 4 (2-6) лет без деменции. Установлено, что у больных с БП имеются эмоциональные нарушения в виде тревожных и депрессивных расстройств, усталость, надсегментарные вегетативные и диссомнические расстройства, выраженность которых не зависит от возраста и пола больных, а также от основных моторных проявлений заболевания.

Ключевые слова: болезнь Паркинсона, немоторные проявления, эмоциональные нарушения