Cognitive impairment in patients with Parkinson's disease and optimization of its treatment

Zokirov M.M.,
Fergana Medical Institute of Public Health
Department of Internal Diseases №1
Assistant of the department

Mukhammadjonov O
3rd year student of the Faculty of Medicine

ABSTRACT

Parkinson's disease is the most common neurodegenerative disease in the world, which requires a comprehensive study of this disease, as well as the prevention of its complications. The article discusses the impairment of the cognitive status of patients with Parkinson's disease using the MMSE and FAB test tests, as well as the effect of the drug memantine hydrochloride on the cognitive status.

Keywords: Parkinson's disease, Parkinson's syndrome, cognitive status, memantine hydrochloride, NMDA receptors.

Introduction. Parkinson's disease (PD) is one of the most common neurological diseases, which is very common in the elderly. According to epidemiological data, this disease develops in at least 1% of people over 65 years of age. 10 years after the onset of the disease, 65% of patients become severely disabled or die, after 15 years this figure reaches 80% [1]. The average life expectancy of patients with parkinsonism after the onset of disease 5 is 9 years, although individual fluctuations range from 1 to 33 years. The average age at which patients with parkinsonism die is 65-72 years. Currently, increasing the effectiveness of treatment and life expectancy of patients leads to an increase in disability in the population and, as a result, the prevalence of the disease. According to epidemiological studies, Parkinson's disease is observed in all ethnic groups of the world [1,2].

Based on the data obtained by assessing the localization of Lewy bodies, H. Braak (2002) put forward a hypothesis about the gradual development of a neurodegenerative process that successively goes through 6 stages, forming an ascending type of lesion. At stage 1, the dorsal motor nucleus of the vagus nerve and the olfactory bulbs are affected. In the clinical picture, anosmia and dysfunction of the gastrointestinal tract are observed. At stage 2, the raphe nuclei, the giant cell reticular nucleus, and the blue spot are affected. In the clinic, affective disorders and disturbances of the sensory system appear, in particular, pain manifestations. At stage 3, the compact part of the substantia nigra, the tonsils, the pedunculopontine nucleus, the oral raphe nucleus, the cholinergic magnocellular nucleus of the basal forebrain, and the tuberomammylar nucleus of the hypothalamus are involved. At this stage, sleep disorders develop and affective disorders intensify. Stage 4 is characterized by continued degeneration and a decrease in the number of substantia nigra neurons, involvement of the temporal mesocortex and hippocampus in the process. In the clinical picture, cognitive impairment appears, manifested by memory loss and frontal dysfunction. At stage 5, further degeneration of neurons of the substantia nigra occurs, damage

to the cortical zones (prefrontal, temporal and parietal). At the same time, cognitive impairment increases and mental disorders develop. At stage 6, changes in all the described structures increase, motor and sensory cortical centers are involved [2,3]. The hypothesis proposed by H. Braak is not generally accepted, but it allows to explain the early symptoms of parkinsonism, such as anosmia and affective disorders, as well as the later development of cognitive impairment [4,10]

The clinical picture of parkinsonism consists of a triad of main symptoms - tremor, muscle rigidity (the "gear wheel" phenomenon) and oligobradykinesia (or akinesia), which determine the main motor defect of Parkinson's syndrome. An additional symptom is postural instability ("aftereffect" instability). The varying severity of these symptoms determines the clinical form of the syndrome [5,9].

1) Akinetic-rigid form (the most pronounced hypokinesia and rigidity, including walking disorders and postural instability), occurs in 15-20% of cases.

2) Tremulous form (tremor hyperkinesia predominates in the form of a rest tremor or mixed tremor, including a postural kinetic component), occurs in 5-10% of cases.

3) Mixed form (includes the whole triad of symptoms, with varying degrees of their presentation), accounts for 60-70% of cases of Parkinson's disease [6]

The development of neuropsychological research methods in the second half of the 20th century made it possible to transfer the discussion about the presence or absence of cognitive impairment in PD to a more rigorous scientific basis. The problem of cognitive impairment in parkinsonism has been widely discussed in the literature over the past 15-20 years. However, despite the active study and a large number of publications, many questions of phenomenology, pathogenesis, diagnosis and treatment of disorders of higher mental functions in parkinsonism still remain open [7,8].

Materials and research methods. Under our supervision there were 50 patients with Parkinson's disease (PD), who received standard specific anti-Parkinsonian pharmacotherapy, in the department of neurology of the Ferghana city hospital number two. The age of the patients varied from 41 to 85 years, the average age was 66.4 ± 9.0 of the year. Cognitive status was analyzed using the Mini-Mental State Examination (MMSE) scale [Folstein M.F. et al., 1975]. Frontal Assessment Battery (FAB) was used [Dubois B. et al., 2000], Frontal Assessment Battery Test (FAB, B. Dubois et al., 1999)

Research results. We studied the effect of memantine hydrochloride (Alcheba) on the development of cognitive impairment in patients with PD. Being a non-competitive antagonist of N-Methyl-D-aspartate (NMDA) receptors, it has a modulating effect on the glutamatergic system. Regulates ion transport, blocks calcium channels, normalizes membrane potential, improves the process of nerve impulse transmission, improves cognitive processes, memory and ability to, increases daily activity. The drug was administered to patients with Parkinson's disease according to the following scheme:

I week	II week	III week	IV week
Morning	Morning + afternoon	Morning + afternoon	Morning + afternoon
½ tablet	½ tablet + ½ tablet	1 tablet + ½ tablet	1 tablet + 1 tablet

Inside, during meals. The dosing regimen is set individually. Treatment began with the appointment of the minimum effective dose. The approximate value of the maintenance dose is 20 mg / day. The last dose was recommended to be taken before dinner. The drug was taken for 3 months.

Table number 1. The effect of memantine hydrochloride on the cognitive sphere in patients with Parkinson's disease before and after treatment, depending on the form of the disease (in points)

Scales	Trembling	Akinetic-rigid-trembling	Akinetic-rigid	Trembling-akinetic

	before	after	before	after	before	after	before	after
MMSE	26,0	27,0	25,0	26,0	24,0	25,0	23,0	25,0
FAB	16,0	16,0	15,0	16,0	13,0	14,0	13,0	14,0
CDT	10,0	11,0	8,0	9,0	7,0	8,5	7,0	8,0

The results of the study showed the effectiveness of the drug in all forms of Parkinson's disease, especially the improvement in the cognitive sphere with significant differences was observed in the tremor-akinetic form on the MMSE scale - 23.0 points to; and 25.0 points after treatment, there were also improvements in the cognitive sphere on the FAB and CDT scales. The greatest improvement was observed in terms of orientation in place, time and speech.

Analysis of intellectual-mnestic disorders in patients with PD depending on the rate of progression of the disease revealed that the onset of the disease in patients with a rapid rate of progression was recorded at a later age (64.6±5.6 years, $p<0.0001$) . The results of neuropsychological testing on the MMSE scale were lower with a rapid course of the disease (21.5 points), and the highest rates were observed with a moderate rate of progression (24.0 points) (Table 9). We analyzed the efficacy of alcheba and found that in patients with a moderate rate of disease progression, the efficacy of the drug was greater (MMSE-26.0 points, FAB - 17.2 points, CDT - 10.0) compared with other rates of disease .

Analysis of frontal-type cognitive impairment on the FAB scale after treatment revealed statistically significant differences between groups with different rates of progression, in which the lowest rates were observed with a fast rate of progression of 11.0 points, while with a slow rate of progression 13.5 points and with a moderate rate of 17 .2 points

The use of a unified rating scale for assessing the manifestations of parkinsonism (URSHOPP) showed the following. According to the section URSHOPP 2, which characterizes the daily activity of patients, the total indicator was 12.4±0.7 for women and 12.8±0.5 for men. According to the section URSHOPPP 3, which assesses motor disorders, the total score for females was 23.2±1.0, for males - 24.7±1.4 ($p>0.05$), on average - 23 .7±0.8. When examining patients with PD using the cumulative index scale (CIRS), which characterizes the level of comorbidity, this indicator averaged 2.5±0.2. It was significantly higher in males than in females (3.05±0.33 versus 2.2±0.2, $p<0.02$); mainly, diseases of the respiratory organs, pathology of the genitourinary system were detected. The level of education also did not differ significantly in women and men, 12.6±0.42 years and 12.4±0.6, respectively, $p>0.05$. At the same time, according to the results of the examination of patients using the Brief Mental Status Assessment Scale (MSSS), the total score for females was 24.3 ± 0.8, for men - 22.9 ± 1.2.

When examining patients with PD, there were no significant differences in age, onset time, duration, severity of the disease, in daily activity and severity of motor disorders, the level of education of patients depending on gender. The data obtained made it possible to consider together the results of examinations of women and men in the analysis of factors affecting cognitive functions in patients with PD. All patients with PD underwent neuroimaging studies (CT or MRI of the brain), which did not reveal changes indicative of the vascular genesis of parkinsonism syndrome. According to the EEG data, diffuse changes were detected in patients with PD, mainly by the type of desynchronization with the presence of slow theta waves, single or in the form of synchronous discharges, which corresponds to changes in the bioelectrical activity of the brain detected in this disease. In patients with cognitive disorders, slow-wave activity was more pronounced, which is consistent with the data of other researchers.

It was found that in 21 patients with PD, the total score for KSHOPS fluctuated in the

range of 28–30 points, which indicates the absence of cognitive impairment. The value of the total score for KShOPS from 24 to 27 points was found in 20 patients, on average - 25.3 + 0.2 points. This indicated that they had moderate cognitive impairment, which met the criteria for moderate cognitive impairment according to ICD-10 and the modified diagnostic criteria of S.Guatheir, J.Tnuchjn, R.Petersen [2004],

In 25 patients with PD, the total score for KSHOPS ranged from 23 to 11, which indicated the presence of dementia. The cognitive defect in these patients corresponded to the diagnostic criteria for dementia according to the ICD - 10 and DSM - 4. At the same time, 13 patients had mild dementia (total score according to KShOPS 20 - 23, according to the clinical rating scale of dementia - I point), in 12 - dementia of moderate severity (total score according to KSHOPS 11-19, according to the clinical rating scale of dementia - 2 points). The dependence of the value of the total score on KSHOPS on the form of PD was revealed: this indicator significantly decreased in the series of tremor-rigid, rigid-trembling and akinetic form.

Conclusions: 1. The results of the study showed the effectiveness of the drug in all forms of Parkinson's disease, especially the improvement in the cognitive sphere with significant differences was observed in the tremor-akinetic form according to the MMSE scale.

2. Thus, the examination of patients with PD using KSHOPS revealed cognitive disorders in 68.2% of patients, among them 30.3% had moderate cognitive impairments, and 37.9% had dementia. Correlation analysis was used to study the factors influencing the development of cognitive impairment in patients with Parkinson's disease. It was shown that the severity of cognitive impairment did not depend on the sex of patients with PD. A significant relationship between the age of patients with PD and the severity of cognitive impairment has also not been established.

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