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PARKINSON'S DISEASE (CLINIC, DIAGNOSIS, PRINCIPLES OF MODERN TREATMENT)

N.Y. Eshankulova
R.B. Azizova
D.T. Akramova
Department of Neurology and Medical Psychology
Tashkent Medical Academy

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Abstract:

PC is the second most prevalent among neurodegenerative diseases. 1% of the population over the age of 65 suffers from this disease. We can observe a rejuvenation of the disease in the coming decades. The role of several factors in the pathogenesis of the disease is being studied, including hereditary, sexual, age-related factors, metabolic factors and environmental factors affecting the organism. Parkinson's disease has long been considered an "extrapyramidal" disease of the musculoskeletal system. However, at present, much attention is paid to its symptoms. Parkinson's disease begins slowly, unnoticed and progresses to the level of severe disability. The main symptoms of movement are tremor at rest, slowing and slowing of movements, stiffness and loss of postural reflexes. Nonmator symptoms include autonomic symptoms, sleep disturbances, loss of sense of smell, depression and pain. The effective treatments currently offered are pharmacological (dopaminergic drugs, MAO inhibitors, dopamine agonists and amantadine sulfate), operative (apomorphine-pump, duodopa and deep brain stimulation (DBS)) and physical (a set of exercises used for Parkinson's patients). In the surgical treatment of DBS, great attention is paid and good prospects are expected.

Keywords: Parkinson's disease, motor symptoms, nonmator symptoms, levodopa, Deep brain stimulation.

INTRODUCTION. The symptoms of Parkinson's disease (PD) were first described in detail in 1817 by James Parkinson in his essay "Vibrating Paralysis", which he called Agitans' paralysis.

PD is the second most common neurodegenerative disease. 1% of the population over the age of 65 suffers from this disease. In the coming decades, we can see the rejuvenation of the disease. Early onset / Young onset Parkinson's Parkinson's currently accounts for 5-10% of all Parkinson's patients in Europe [17]. The disease is more common in men. Although PD disease is usually sporadic, 10% of patients have a family history or are associated with certain genetic factors[7,22].

Epidemiology

Numerous studies show that the incidence of Parkinson's disease varies from 4.5% to 26%, depending on the country of residence and methods of diagnosis. Because the onset of the disease is imperceptible and based on the patient's retrospective memory, it is difficult to determine exactly when the disease began. The role of race in the development of the disease is also important. The highest rate is among Latin Americans - 16.6 per 100,000 populations. The lowest morbidity rates are among Asians and blacks at -11.3 and 10.2, respectively.

Geographical differences in morbidity suggest that there is a link between the onset of Parkinson's disease and the environment. The role of several other factors (heavy metals, agricultural minerals, etc.) in the pathogenesis of the disease is also being studied. Caffeine and cigarettes are currently considered to reduce the risk of Parkinson's disease. However, the investigations did not reach the end. A few years ago, it was suggested that the term "atherosclerotic parkinsonism" be used to suggest that cerebrovascular disease could cause these symptoms. However, this nosological form was not approved, but returned in the form of vascular Parkinson's disease. The lethargic encephalitis pandemic of the 1920s led to the development of post-encephalitic Parkinsonism, but the nosological form of the disease disappeared due to the absence of new encephalitis over the decades, but was recently re-reported as a neurological complication of West Nile encephalitis.

Diagnose.

Parkinson's disease has long been considered a disease of the "extrapyramidal" musculoskeletal

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system. However, at present, much attention is paid to its symptoms. Parkinson's disease begins slowly, unnoticed, and progresses to the level of severe disability. The main symptoms of motor are tremor at rest, slowing down and slowing down, stiffness and loss of postural reflexes.

The various nonmator symptoms observed in Parkinson's disease are not always specific. These symptoms include autonomic symptoms, sleep disturbances (rapid sleep movements), loss of sense of smell, depression, pain, and all other motor symptoms. Therefore, the concept of "prodromal Parkinson's disease" was proposed. None of the four symptoms are specific to Parkinson's disease, so the clinical diagnosis is only tentative. The slow progression of the disease and the absence of other symptoms (pyramidal, sensory, and autonomic disturbances) are signs of Parkinson's disease, but in most cases constipation may occur and may be the first symptom [3,4]. The clinical diagnosis is confirmed by a positive response to Levadopa or dopaminergic drugs.

Pathogenesis:

The pathophysiology of Parkinson's disease is still unclear. Dopaminergic denervation of the basal ganglia (mainly striatum) remains central. Describes the interconnectedness of the motor ganglion, the basal ganglia, the subthalamic nucleus, the thalamus, and the cortex[7,20]. However, their function has not been adequately studied. It is not fully understood how dopamine deficiency leads to peaceful tremor, increased tone, brady- and hypokinesia. The reason for the disappearance of postural reflexes is less.

The most plausible hypothesis today is that the nigrostriar pathway leads to the activation of dopaminergic receptors in the striatum. To date, 5 subtypes of dopaminergic receptors have been identified, the most important of which is the D2 receptor. The role of D1 receptor activity in the development of dyskinesia is being studied. The subthalamic nucleus and globus pallidum are rich in iron, and its concentration increases with age, especially in Parkinson's disease. This may be due to peroxidation of lipids, indicating that the metal has neurotoxic properties. Recently, the prion hypothesis has been proposed in Parkinson's disease, focusing on the role of microbes in Parkinson's disease. This opens up new perspectives in the study and treatment of Parkinson's disease.

Treatment:

Parkinson's disease treatment can now be divided into three major groups. These include drug treatment, surgical treatment, and physical therapy. Each method of treatment has its own advantages and disadvantages, and experts do not agree on a single alternative treatment.

In the treatment of Parkinson's disease, the first priority is to supplement the dopamine deficiency. And levodopa is always the drug of choice. Levodopa is well absorbed from the gastrointestinal tract and, through amino acids, passes through the Blood-Brain Barrier (BBB) and affects the brain. In the brain and periphery, levodopa is converted to dopamine by the L-amino acid decarboxylase enzyme. This enzyme can be blocked by benserazide or carbidopa, which is used for dopamine synthesis by increasing levodopa concentrations in the brain and increasing levodopa uptake at dopaminergic terminals. Therefore, today levodopa is produced in combination with one of two enzymes. Inhibition of peripheral dopamine conversion minimizes various side effects, such as orthostatic hypotension and nausea. The second enzyme involved in levodopa metabolism, catechol-O-methyltransferase (COMT), is used in combination with levodopa in clinical practice with tolcapon and entacapon. COMT inhibitors reverse the effects of dopamine. Dopaminergic therapy works very well in Parkinson's disease, rigidity, hypokinesia, and tremor, but has little effect on postural instability [8].

Given that the decrease in dopaminergic receptors does not stop despite treatment with levodopa, the symptoms of the disease continue to develop. As a result, the dose of the drug can be increased. As a result of increasing the dose, peak dose dyskinesia occurs.

The introduction of levodopa in the treatment of Parkinson's disease has been so highly valued that no substitute drug has been recommended to date. Levodopa has no effect on the development of the disease, and neurons in the brain continue to die. Levodopa masks the symptoms of Parkinson's disease and remains the only symptomatic treatment. Therefore, there are different views on levodopa treatment, with some researchers recommending that it be started at an early stage of the disease, while others suggest that it should be used in the later stages[9,21].

Monoamine oxidase (MAO), an enzyme involved in the metabolism of catecholamines and indolamines, has two variants: MAO-A and MAO-B. MAO-B is important in the pathogenesis of Parkinson's disease and is an enzyme involved in the formation of the neurotoxin MFP + from MFTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). Therefore, selegiline and razagilin, MAO-B inhibitors, are used in the treatment of Parkinson's disease. In newly diagnosed patients, treatment with MAO-B inhibitors can be continued for a long time [10,11,13]. However, its effectiveness in long-term Parkinson's disease is low and the cause has not been fully elucidated.

There are clear complications of Parkinson's disease with long-term dopaminergic therapy,

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including fluctuations in the symptoms of Parkinson's disease and dyskinesia. As a result of these complications, the patient's lifestyle becomes much more difficult. In the pathogenesis of these complications lies the hyperactivity of glutamate NMDA-receptors in the striatum, and antiglutamatergic drugs are used to combat dyskinesia. An example of this drug is amantadine sulfate[12,15]. Dopamine receptor agonists are pramipexole, piribedil, ropinirol (proof level A). When used in the early stages of the disease, it slows the development of motor symptoms, and its use in young people gives good results. Lack of treatment can exacerbate dementia and hallucinations in older patients and lead to behavioral disorders [16,22]. Surgical methods in the treatment of Parkinson's disease include apomorphine-pump, duodopa, and deep brain stimulation (DBS). At present, the first two surgical treatments are almost non-existent due to their many complications. In modern medicine, DBS has received a great deal of attention in the surgical treatment of Parkinson's disease, and good prospects are expected. Deep brain stimulation, or DBS, involves the surgical implantation of electrodes into a specific part of the brain, usually the subtalamic nucleus or globus pallidus. A pulse generator (battery block) placed under the chest of a pacemaker-like device sends electrical signals controlled by wires under the skin to electrodes placed inside the brain. Once activated, this remote-controlled device painlessly blocks signals that cause multiple symptoms of Parkinson's disease by stimulating them in 21 different ways[16,17]. Deep stimulation of the subthalamic nucleus (STN) is the most effective surgical procedure used in the movement complications of dopaminergic therapy in developing Parkinson's disease [19]. Placing electrodes on or near the dorsolateral part of the STN increases the effectiveness of the treatment and minimizes side effects [7,18].

CONCLUSIONS: The use of DBS in Parkinson's disease is still a new method, and there are still differences of opinion among neurologists and neurosurgeons. Some argue that the use of this method of treatment should be postponed as late as possible, while others argue that the implementation of the disease in the early stages has a positive effect on the course and progression of the disease. In addition, work on preoperative and postoperative patient control and optimization of the type and dose of drugs is ongoing. Many questions remain open when patients choose the most postoperative treatment.

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