MODERN ASPECTS OF DIAGNOSTICS REGARDING PARKINSON'S DISEASE (PD)

Azoidis I., Burnusus N.I., Yashenko I.A., Karpov S.M.

Stavropol State Medical University

Stavropol, Russia

Parkinson's disease (PD) is one of the most common neurodegenerative diseases of the central nervous system. Its prevalence is subject to significant fluctuations in different countries and an average of 0.3 percent, the incidence is about 12 in a population of 100,000 per year. Prevalence relates directly to age, reaching 1% in people older than 60 years [1].

According to available data, the main method of PD diagnosis is clinical criteria of the UK PD society. It includes six main symptoms that allowyou to make the correct diagnosis with any degree of certainty and begin treatment. These are:

1. Asymmetry and gradual onset of the disease;

2. Resting tremor;

3. Muscular cogwheel rigidity of the limbs;

4. Postural instability (antepulsion ,lateropulsion and retropulsion);

5. The presence of pain in the affected limb or back pain;

6. Positive response to levodopa.

These criteria are very objective, but postmortem studies suggest that the clinical diagnosis of idiopathic Parkinson's (genuine PD) made even by experienced neurologists are confirmed only in 10-30 % of cases [2]. Based on these unbiased statistics, it is necessary to develop new, more accurate and informative diagnostic methods of PD which will help accurately diagnose and effectively treat it in the early stages. This article focuses on reviewing the literature data of Russian and foreign researchers dealing with this issue, which will help understand the direction toward which science is moving in terms of more accurate of PD.

Of the many different methods that exist at the moment, two deserve special attention: the methods of functional neuroimaging and study of biochemical markers of PD.

Functional neuroimaging techniques.

These methods include positron emission tomography (PET), single photon emission computed tomography (SPECT) and proton magnetic resonance spectroscopy ((H1) -MPC) [3].

We will consider the principle of this method applied to PET. Pathogenesis of PDis known to be associated with the death of neurons in the substantianigra (SN). By means of PET using fluorodopa, defects in the presynaptic portion of the dopamine-sensitive neurons of SN are revealed. Even the number of neurons, themselves, in PD decreases noticeably. Characteristic of this method is the reduction of fluorodopa capture by putamen neurons on the opposite side of the motor symptoms [3], which explains the first clinical sign of the disease - the asymmetry of symptoms. Fluorodopa capture rate in the striatum reflects the process of its capturing by the cells of the basal ganglia and its subsequent transformation into the vesicles of these cells [4]. PD criterion in this case is the reduction of the fluorodopa capture by 30% or more [5]. Findings, encouraging this type of examination and prediction, demonstrate the likelihood of clinical onset of PD in different periods of life, in 34% of the examined. One year later, this prediction was confirmed in 36 % of cases [6].

Biochemical markers of PD.

As main biomarkers of PD, can appear substances produced in the body under the influence of oxidative stress (because it is considered that the pathogenesis of this disease are the mechanisms of mitochondrial injury), specific proteins accumulated in the nerve fibers (α- synuclein and others) and circulating components of the miRNA in plasma.

With regards to oxidative stress as a marker stands increasing amounts of enzyme superoxide dismutase in erythrocytes. As known, this enzyme belongs to the natural antioxidants, preventing the accumulation of free radicals in the blood. Naturally, when the amount of free radicals is increased, the amount of the enzyme increases several times [7]. According to other studies, there is an increase of another substance in the serum and urine deoxyguanosine, a product of oxidative damage of the cells' DNA [8].

When it comes to specific proteins, according to recent studies, specific proteins were identified such as α-synuclein accumulated in peripheral nerve tissue. As known, this protein accumulates primarily in the brain, is formed in the later stages of the disease and is visualized only postmortem. It is known that some symptoms of the autonomic nervous system disorders (excess sweating, blood pressure fluctuations), are precursors of motor disorders [9]. Described disorders in PD prompted some researchers, to do peripheral nerve biopsy. This study involved 20 patients with

a confirmed diagnosis of idiopathic pakrkinson's disease and 14 healthy patients. It turned out the increase in the concentration of α-synuclein in nerve fibers innervating sweat glands and pilomotor muscles, caused disturbance in nerve impulses reaching them, which led to the appearance of the very interesting symptoms described above [9]. This protein is a candidate, for one of the main criteria in diagnosis and now is being studied the emergence of such a protein in peripheral nerves in other neurodegenerative diseases of the central nervous system.

A study on the exploration of miRNA deserves a special interest. A team of scientists noted the importance ofmiRNA.Specifically miRNAcirculating in the plasma and accumulating in the tissues, has a number of unique properties, namely a large number per milliliter of plasma, high tissue specificity and stability. With the help of this biomarker some forms of cancer, Huntington's chorea, myelodysplastic syndrome and acute myocardial infarction are diagnosed [10]. The basis of the study was the extraction of miRNA from the plasma of patients with PD, by PCR, and loading it on microchips, which were placed in a special device that measured the level and type of miRNA in a particular patient. It is established that PD is characterized by specific miRNAs that are absent in healthy people. This miRNA is the miR-1826/miR-450b-3p type and some others. These biomarkers had a sensitivity of 91%, a specificity of 100%, the possibility of 100% accurate diagnosis and decrease in the possibility of misdiagnosis to 88% [10].

Thus, we conclude that there isinnovation of the scientific database and a broader study of PD, which allows new and unique diagnostic methods to be used in PD diagnosis. Since the advantage of this diagnostic method is low invasiveness, then surely the study of biomarkers, in particular miRNA in the blood and biological fluids would be the preferred method of diagnosis. In addition, if substances that appear exclusively in this pathology are detected, the new criteria will allow diagnosis of PD with absolute accuracy at an early stage of the disease and adequate therapy assignment before gross changes in the neurons of SN emerge.

References:

1. BayramukovaA.M., AjachmetovaA.K., KarpovS.M. «EpidimiologiabolezniParkinsonavrazlichnixstranachmira»/ Uspechisovremenogoestestvoznania/ 2013/ 9/ 20-21;
2. MumentalerM., BassetiK., DetvaylerK. «Diferencialnidiagnoz v nevrologie»/ 2012;

3. KatuninaE.A., TitovaN.V., AvakjanG.N. «Metodidiagnostikibolezniparkinsonanaranichstadiach»/ Jurnalnevrologii I psichiatriiim. Korsakova/ 2011/ 34;

4. Nahmias C., Garnett E.S., Firnau G. Striatal dopamine distribution in Parkinsonian patients during life./ Neuro Science 1985/ 69/ 223-230;

5. Brooks D.J. Morphological and functional imaging studies on the diagnosis and progression of Parkinson's desease./ Journal of neurology/ 2000;

6. Brooks D.J. Detection of preclinical Parkinson's desease with PET./ Neurology/ 1991/ 41: 24-27;

7. Younes-Mhenni S. Peripheral blood markers of oxidative stress in Parkinson's desease./ European neurology/ 2007/ 58: 2: 78-83;

8. Kikuchi A., Takeda A., Systemic increase of oxidative nucleic acid damage in Parkinson's desease and multiple system atrophy./ Neurobiology/ 2002/ 9/ 244-248;

9. Beth Israel Deakoness Medical Center (BIDMC)/ Jouranal of neurology/ 20134

10. SokKheanKhoo, D. Petillo Plasma-Based circulated microRNA biomarkers for Parkinson's desease./ Journal of Parkinson's desease/ 2012/ 321-331.