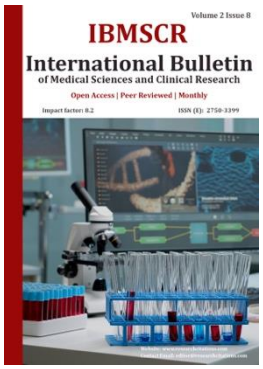

MODERN VIEWS ON NEUROTROPHIC FACTORS IN ENSURING NEUROPLASTICITY PROCESSES.

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Abstract. Distal symmetrical sensory motor diabetic polyneuropathy is one of the most common complications of diabetes and is one of the main causes of disability in patients with diabetes mellitus. According to epidemiological studies, depending on the verification methods used, the incidence of diabetic polyneuropathy in diabetes varies from 5% to 100%.

Keywords. Diabetes mellitus, immunological, cytogenetic, hematological methods, multisystems, hyperlipidemia, hypertension, hyperalgesia.

During epidemiological studies, despite severe metabolic disorders, DPN was found to develop in 5-50% of patients with Type 1 diabetes. On average, 25% of patients with diabetes suffer from peripheral neuropathy at the same time, the longer the duration of diabetes, the more percent of neuropathy is detected in patients. However, in some categories of patients, despite the long duration of the disease, there is evidence that there is no detection of signs of poor compensation of the underlying disease, damage to the peripheral nervous system, which suggests that the development of this complexity may indicate a hereditary predisposition.

Diabetic neuropathy significantly reduces the quality of life of patients and is one of the main risk factors for the development of foot ulcers, burns, frostbite and gangrene. It is found that between 40 and 70% of all undamaged amputations occur in patients with diabetes mellitus, so it is very important to diagnose neuropathy in a timely manner and take appropriate preventive and therapeutic measures.

In diabetes mellitus, damage to the nervous system is characterized by a variety of its forms, which is due to the involvement of both central and peripheral nerve structures in the process. Damage to the central nervous system (CNS) in diabetes is characterized by impaired neurotransmitter expression, primarily dysfunctional and later structural changes in neurons and conductors leading to cognitive deficits. The most common and typical sign of peripheral nervous system (Pat) injury in QD is diabetic polyneuropathy (DPN), characterized by symmetrical distal involvement of a particular type of nerve fiber. In addition to clinical signs, there are also differences in the rate of injury of different areas of the nervous system. Thus, Pat involvement in the process occurs during the 6 weeks after the onset of diabetes, at which time changes in MAT occur only from the 2nd month. Nevertheless, it has been accepted to speak of changes in MAT and PAT that occur during QD as the only disease defined by the term ⍰diabetic neuropathy⍰.

According to an epidemiological study, the prevalence of DPN among patients with diabetes varies in the range from 6.1% to 82.5%, depending on the diagnostic criteria used. The frequency of neuropathy among patients with QD is an average of 25%, but in a deepened clinical study this rate increases to 50%, compared to 90% when multi-informative

equipment electrophysiological research methods are used. At the time of the diagnosis of QD, polyneuropathy is diagnosed in 8% of cases, when the disease lasts for 20 years 40%, and in 25 years more than 50%. But a direct relationship between the duration and even weight of QD and the frequency of DPN is not always observed. Severe forms of polyneuropathy are also observed among patients with relatively mild QD and satisfactory glycemic control. In addition, when glucose tolerance is impaired (GTB), the frequency of detection of polyneuropathy varies from 8 to 32%.

Thus, in diabetes mellitus, damage to the nervous system occurs in the early stages, at the beginning it can go without symptoms, which makes it difficult to diagnose this complication in time. Despite the prevalence of diabetic polyneuropathy and the need to study it, research in this area is complicated by the fact that there is no single set of criteria for its identification. About 30 years ago, clinical trials, especially for routine physician practice, were developed by neurologists and endocrinologists gourhi, diagnostic criteria that were extremely severe and expensive. As a result, different criteria were used in each study group, which made it difficult for metataholic studies to be conducted. To address this problem, revised criteria were published by a Toronto team of experts in 2011, consisting of widely used structures for further testing.

According to these criteria, the following were distinguished: probable DPN, in which the symptoms or symptoms of polyneuropathy are identified; probable clinical DPN, which contains subjective and objective clinical data; confirmed clinical DPN, summarizes the presence of electrophysiological signs of clinical symptomatology and polyneuropathy; as well as subclinical DPN, in which clinical signs will not be present, but the equipment signs of polyneuropathy will be identified.

The group of patients with diabetes mellitus as well as healthy individuals evaluated in an electroneuromyographic study included 12 indicators of M-response amplitude, propagation speed of excitation (QTT), small calf, large calf, distal latency of elbow nerve motor fibers, C-response amplitude, SRV, posterior calf nerve sensory fibers F-wave latency. It was shown that patients with QD were diagnosed with no disorders using a 2.5/97.5 percentile threshold value: SRV reduction in the small calf 26.3% and in the large calf nerves 24.9%, posterior calf nerve C-wave amplitude in 2.4% patient; an increase in the small calf latency was reported in 16.9% and elbow nerves in 16.0% patients. Taking into account the possibility that the mentioned changes are detected even in healthy individuals, but at a low frequency, it was recommended to apply a different combination of the indicators of no to confirm DPN, as a result of which the criteria described above were developed. As the most impressive and specialized criteria, the rate of propagation of excitation on the small calf nerve and the amplitude of the impact potential of the spinal cord nerve, studied on two nerves at the limit point of 97.5 percentiles and more, were recognized. According to the results of the study of nerve conduction criteria, the authors came to the conclusion that more accurate diagnostics can be achieved in the general studies of no (criteria 7 and 8), while criteria 2 and 3 are also considered optimal for the diagnosis of DPN.

Damage to each type of nerve fiber has individual electroneuromiographic specificities. thus, a decrease in the amplitude of the M-response at the regulatory rate of impulse transfer to axonopathy is characteristic. In the demyelinating process, an increase in latency in ENMG as well as a decrease in the rate of excitation spread are noted. In sensory fibers, the momentum transfer rate (but not the amplitude of the nerve action potential) is

more impressive to temperature than in motion fibers. Optimal data can be achieved by heating the limbs, if heating is impossible, then correction coefficients are obtained to obtain suboptimal records, but this has a lower Information Value. traditional electrodiagnostic methods are not impressive for the protected neuropathy of thin fibers, ENMG data remains at the norm level, since thin fibers are not involved in muscle innervation, while studying the rate of conduction along the nerve surface does not provide enough information to assess permeability on thin fibers, since the response to excitation is low-amplitude and diffuse. Thus, ENMG only assesses the condition of the colon myelinated fibers in high accuracy, this method is not effective for damage to thin myelinated pain fibers.

Sensory signs of polyneuropathy can be manifested by both ⍰positive⍰ and ⍰negative⍰ symptoms, which in many ways are associated with the rate of morbidity. Due to the earlier damage to the longer fibers, sensitivity disorders occur earlier in the distal sections of the legs, then spread more and more proximally and appear on the toes of the forearm when reaching knee level. Symptoms of ⍰miscarriage⍰ in DPN are associated with decreased sensitivity and are mainly manifested by hypesthesia. That being said, the sensor system has a large ⍰stock of consistency⍰, hypesthesia occurs when at least more than 60% of fibers are destroyed, which leads to subclinical stages of DPN and, accordingly, to difficulties in diagnostics.

In most cases, the main reason for the patient's appeal for medical help is the occurrence of positive sensory symptomatology, which is manifested by neuropathic pain in harmony with other phenomena of sensitivity (dysesthesia, hyperpathy, allodynia). The pathophysiological aspects of neuropathic pain occurrence include a number of Ionic, biochemical and anatomical modifications of the peripheral and central structures of the sensory system responsible for the perception, conduction and processing of the pain impulse. At the level of the peripheral apparatus, primary afferent excitation activation occurs due to increased sodium channel density in the nerve fiber, the appearance of ectopic excitation foci, neurokinins, R substation, myelinized C-fiber activation secreting calcitonin-gene-family peptide. The expression of these biogenic amines leads to the development of ⍰neurogenic inflammation⍰, an increase in vascular permeability, the separation of prostaglandin, cytokinin, histamines from the main cells, which affect the membrane of the nerve tip, increasing the excitability of C-afferents and completing the pathological range of primary hyperalgesia.

The consequence of this is a decrease in the excitation limit of the sensation of pain, as well as a high sensitivity of nerve fibers. In addition to functional disorders, fibers undergo structural changes, on the surface of which receptors are formed that cannot exist under normal conditions, expanding the range of triggers capable of activating nociceptors. In particular, A2-adrenoreceptors appear on the surface of the C-fiber axons, which provide sensitivity to catecholamines, confirming that neuropathic pain depends on the emotional state.

In addition, myelin shell degradation and subsequent regeneration leads to the formation of new atypical directional tumors, the creation of a pathological synaptic relationship between fibers with different sensory modality, increased neuroplastic processes with the ephaptic administration of momentum between adjacent fibers, which is manifested clinically by the phenomena of allodynia, dysesthesia and hyperpathy.

In addition to the fact that the activation of insulin receptors performs specialized functions (activation of glucose transport, strengthening glycolysis, gluconeogenesis and reduction of lipolysis), growth factors are able to trigger intracellular signaling pathways responsible, which leads to an increase in cell survival and growth gene trancryption, blockage of apoptosis genes. In addition to the central nervous system, the expression of insulin receptors has been detected in several types of peripheral nerve fibers that contain thin sensory C-type, vegetative fibers, Schwann cells. Experimental data from the last decade suggest that dysregulation of insulin may lead to sensory fiber damage.

Despite the unsatisfactory results in the use of recombinant neurotrophins in human diabetic polyneuropathy, research in this area is not stopped. Subsequent research has focused on modulating the activity of specialized receptors by not being influenced by growth factors by creating specialized agonists based on neuropeptides. Currently, promising results have been achieved in the use of TrkB agonists in the treatment of Alzheimer's, Gentington, Parkinson's disease, injury to the brain and even physiological aging. There is also much hope for VEGF genetic therapy trials in the treatment of diabetic foot palms. But such studies are limited, firstly, to the possibility of the development of mitogenic effects of VEGF as well as proliferative processes, and secondly, to the impossibility of treating one vascular complication without aggravating another. Thus, increased antogenesis is necessary for peripheral angiopathy as well as polyneuropathy, but the issue remains open as to whether systemic treatment can aggravate proliferative retinopathy, or vice versa.

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