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LABORATORY INDICATORS OF DIABETIC POLYNEUROPATHY

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ЛАБОРАТОРНЫЕ ПОКАЗАТЕЛИ ДИАБЕТИЧЕСКОЙ ПОЛИНЕЙРОПАТИИ

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This study is devoted to diabetic polyneuropathy (DPN) — one of the common complications of diabetes mellitus (DM). The possibilities of laboratory diagnosis of this condition are shown. ***The purpose*** of this study was to examine the pathogenetic and diagnostic significance of certain neurospecific proteins and cytokines in DPN. The analysis of the literature data on the possibility of using neurospecific proteins and some cytokines in patients with diabetes as markers of neural tissue damage has been carried out.

Keywords: diabetic polyneuropathy; neurospecific proteins; cytokines.

Работа посвящена диабетической полинейропатии (ДПН) — одному из распространенных осложнений сахарного диабета (СД). Показаны возможности лабораторной диагностики данного состояния. ***Целью*** настоящей работы являлось рассмотрение патогенетической и диагностической значимости некоторых нейроспецифических белков и цитокинов при ДПН. Проведен анализ литературных данных о возможности использования у пациентов с СД в качестве маркеров повреждения невной ткани нейроспецифических белков и некоторых цитокинов.

Ключевые слова: диабетическая полинейропатия; нейроспецифические белки; цитокины.

Introduction. DPN is a specific complication of diabetes type I and II. It is heterogeneous in clinical manifestations and the nature of the lesion of the peripheral nervous system. DPN arises and develops against the background of chronic hyperglycemia and is associated with pathological metabolic changes. Normalization of glucose leads to stabilization of the flow of DPN. Microcirculatory disorders also play an important role in the development of DPN. However, despite the widespread use of DPN, its pathogenetic mechanisms are not fully understood, and the mechanisms underlying neuropathy in DM type I and DM type II are overlapping, but different [1].

The purpose of this study was to examine the pathogenetic and diagnostic significance of certain neurospecific proteins and cytokines in DPN.

Currently, the following metabolic and vascular factors underlie the development of DPN: activation under conditions of hypoxia in diabetes alternative, polyol, glucose oxidation pathway with the formation of sorbitol and fructose, reduced levels of myo-inositol and increased activity of protein kinase C, which leads to disruption membrane Na^+/K^+-ATPases and accumulation of sodium inside the cell, which causes an increase in intracellular osmolarity; violation of the synthesis of fatty acids contributes to inhibition of prostaglandin production by endothelium and impaired endoneural blood flow, which leads to the development of ischemia, hypoxia and damage to the membrane structures of the nerve, microvascular and hemorheological disorders; oxidative stress; deficiency of neurotrophic factors (nerve growth factor (NGF), insulin-like growth factor, neurospecific enolase (NSE), etc.) and disruption of axonal transport; accumulation of the end products of excess glycation in nerve and/or vascular wall proteins; immunological processes with an increase in systemic inflammation and the formation of autoantibodies [1–3].

Some authors believe that NGF may be an early marker of DPN [4]. It was previously believed that NGF is involved only in the development of the nervous system in the fetus. Recent studies have shown that it plays an important role in the functioning of the nervous system and in the regeneration of damaged neuronal structures in adult organisms. Thus, NGF affects the expression of neuropeptides. The decrease in the level of NGF leads to a decrease in the release of neuropeptides in the nervous system of adults, which, causes disruption of the synthesis of components of axoplasm, axonal degeneration, and ultimately leads to apoptosis. Currently, NGF is considered as an important neurotrophic factor, without maintaining the basal level of which the existence of sensory neurons is impossible. Experimental data from animals showed a decrease in the level of NGF and some other neuropeptides in animals with experimental diabetes. Similar results were obtained in patients with diabetes. Thus, it was shown that a decrease in neutrophin production and sensitivity to them plays an important role in the development of sensory impairments in diabetes [1, 4].

The involvement of immune mechanisms in the onset and development of DPN has been suggested for many years. Thus, it was found that the serum of patients with DM type II contains an autoimmune immunoglobulin that causes complement-independent, calcium-dependent neuronal apoptosis. The content in the blood of this factor is associated with the degree of damage to the neurons. Thus, it is shown that autoimmune immunoglobulin, along with hyperglycemia, is involved in the development of DPN, causing neuronal damage [5, 6].

NSE is a cytoplasmic enzyme of neurons and neuroendocrine cells and is involved in the glycolytic conversion of 2-phospho-D-glyceric acid into phosphoenolpyruvate. It is known that the emergence and development of various pathological processes, accompanied by the death of neurons, causes it to enter the bloodstream and circulate in the blood for a long time. It is shown that the level of NSE in the blood of patients with DPN is elevated and correlates with the progression of neuropathy. The content of NSE in healthy individuals and patients with mild neurodestructive and neurodegenerative diseases remains within the normal range or slightly increased [2].

Another neurospecific indicator is the protein S-100, which is a marker of astrocyte death. A number of researchers have shown that the simultaneous determination of NSE and S-100 allows detecting cerebral lesions at an early stage, when successful treatment is still possible [1, 2].

Brain neurotrophic factor (BDNF) can serve as a marker indicating brain damage in diabetes. Its functional activity is great. Thus, during the development of the nervous system, it participates in the differentiation, maturation of neurons and the formation of synapses. In the adult organism, it performs the function of a neuroprotector, protecting nerve cells from ischemia, and also ensures the normal functioning of neurons and their interaction with each other. A decrease in the concentration of BDNF in the blood indicates damage to the nervous tissue [7].

Thus, with DPN, the study of the level of neurospecific proteins provides valuable information on the presence and severity of neuronal damage.

Recent studies suggest that adipose tissue plays an important role in the occurrence and progression of the inflammatory process, stimulating the synthesis of pro-inflammatory cytokines, such as IL-1, IL-2, IL-6, tumor necrosis factor alpha (α-TNF), etc., which contribute to the development of insulin resistance. Thus, a number of researchers have shown that in patients with DM type I, the content of IL-1 during the clinical manifestation of the disease is significantly increased compared with healthy donors. When compensation for carbohydrate metabolism is achieved, a certain decrease in its level is observed [5].

An important role in the development of DPN is played by α-TNF, the content of which increases with the progression of this complication of diabetes. It was experimentally shown that α-TNF acts in conjunction with proinflammatory interleukins such as IL-1 and IL-6 secreted by adipocytes. α-TNF has pro-inflammatory properties, participates in carbohydrate and fat metabolism, affects the secretion of leptin, regulates the functional activity of mitochondria, causes insulin resistance in adipose tissue and muscles and inhibits insulin secretion by α-cells of the pancreas, which ultimately leads to demyelination of the nerve fiber and the development of polyneuropathy clinic [5].

Thus, the participation of cytokines in the development of diabetes and its complications is important and indisputable, however, it is not fully understood and requires further clarification.

To date, a large amount of experimental and clinical data on DPN has been accumulated. At the same time, it is necessary to take into account the leading role of hyperglycemia in the onset and development of DPN, which indicates the need to achieve and maintain an adequate glycemic level throughout the course of the disease. There is a wide variety of markers of damage to the nervous tissue, however, their role in the development and progression of DPN in DM is not fully understood. In this regard, further research is needed to create algorithms for complex diagnostics of this state.

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