

DIABETIC NEUROPATHY: ETIOLOGY, PATHOGENESIS, CLINICAL FEATURES AND TREATMENT APPROACHES

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The urgency of the problem

Diabetic symmetrical polyneuropathy is one of the most common chronic complications of diabetes. The presence of diabetic neuropathy determines a high risk of death, development of pain symptoms, foot ulcers and amputation of the lower limbs.

Data on peripheral nervous system damage in diabetes vary from 15 to 90% (4,236), depending on the diagnostic methods used to confirm the diagnosis of DPN and the patient population examined. In clinical practice, DPN can be diagnosed using special examination methods that assess the condition of the peripheral nervous system at the patient's bedside. It is important to consider the symptoms (nature, severity, intensity, duration) when making a diagnosis of DPN. At the same time, many patients have subjective symptoms that are not always related to DPN, which leads to overestimation of the symptomatic form, unreasonable and ineffective prescription of drug treatment. In this regard, the study of the frequency and severity of neurological symptoms in patients with type 1 and type 2 diabetes using specially developed neurological examination methods, including scales of neurological symptoms and disorders, is considered an urgent issue.

During the OSCT and iCROB studies, reliable information was obtained about the role of the state of carbohydrate metabolism in the course of microvascular complications of diabetes. However, the number of studies evaluating the effect of glycemic control on the clinical manifestations of diabetic neuropathy is very small. Also, there is insufficient information on the comparative effectiveness of thiosic acid preparations depending on the level of glycosylated hemoglobin and the severity of neurological symptoms. The lack of a systematic approach to the treatment of patients with neuropathic pain leads to a lack of effectiveness in the treatment of this category of patients.

Peripheral neuropathy is the main cause of diabetic foot syndrome. The study of vibration sensitivity, temperature and pain sensitivity at one level or another allows to predict the formation of wound defects and amputation of the lower limbs. Motor function of peripheral nerves research using neuropsychological methods is often used for their dynamic evaluation, the prognostic role of neuropsychological parameters in relation to the development of diabetic foot syndrome and lower leg amputation has been little studied.

Foot ulcers in diabetic patients are a major medical and socioeconomic problem due to lower limb amputations, mortality, and high financial costs of managing this category of patients. The

existence of a relationship between the early manifestations of microcirculatory disorders represented by sympathetic adrenergic nerve fibers in arterioles and arteriolar-venular shunts and damage to the autonomic nervous system is valuable for early signs of damaging disease by measuring the partial pressure of oxygen in soft tissues. allows you to get data. Decreased sensitivity and microcirculation are accompanied by biomechanical disturbances on the plantar surface of the foot, which determine the typical localization of wound defects in the neuropathic form of diabetic foot syndrome. Measuring the highest pressure on the sole of the foot has become an integral part of the comprehensive examination of patients with diabetes. However, most studies provide threshold values for pressure on the metatarsophalangeal joints, although it has been shown that as neuropathy progresses, the load on the heel decreases and increases at the metatarsophalangeal joints. This raises the question of the feasibility of using the index of the ratio of the threshold values of the forefoot and hindfoot to identify patients with a high risk of developing leg ulcers and to search for possible ways to correct these disorders.

The study of pathophysiological mechanisms affecting the formation and course of reparative processes in the neuropathic form of diabetic foot syndrome gave rise to the concept of chronicity of the wound process in diabetes mellitus.

The importance of the role in amino acid metabolism is the fact that L- arginine has been found during the normal treatment of skin lesions in people with impaired carbohydrate metabolism. However, the contribution of impaired metabolism of the amino acid L-arginine and its regulation by cytokines to delayed healing in diabetic patients is a poorly understood problem.

Over the last 10 years, the number of patients suffering from the neuro-ischemic form of diabetic foot syndrome has been steadily increasing. In addition, this form of injury is the most in terms of the risk of amputation of the upper limbs is dangerous. The number of surgical interventions aimed at restoring blood flow in patients with diabetes has increased from 2% to 10%.

The increase in the number of revascularizations was mainly due to a significant increase in the frequency of angioplasty operations, which ranged from 0 to 8%. Restoration of blood flow affects the condition of soft tissues, which allows to restore their vitality. At the same time, the possibility of saving the limb is mainly determined by the condition of the peripheral nervous system. The dynamics of the functional state of the nervous structures of the lower limbs in response to the restoration of blood flow through the main arteries requires careful consideration, taking into account the important contribution of neuropathy in the pathogenesis of diabetic foot syndrome.

The relative risk of amputations associated with peripheral nervous system dysfunction is comparable to the risk associated with critical limb ischemia. Evaluation of the short-term and long-term results of blood flow restoration in patients with neuroischemic forms of damage is of interest from the point of view of developing a comprehensive approach combining angiosurgery and conservative treatment methods. This can significantly reduce the number of amputations in patients with the neuroischemic form of diabetic foot syndrome.

The purpose of the study

Study of clinical, metabolic and neurophysiological characteristics of distal polyneuropathy in patients with diabetes; development of an algorithm for the treatment of painful forms of diabetic neuropathy and evaluation of the effectiveness of drug treatment; to determine the relationship

between distal polyneuropathy, diabetic macroangiopathy and microangiopathy.

Research tasks

1. To study the prevalence of peripheral polyneuropathy among adults with diabetes.
2. To determine the frequency, severity and structure of neurological symptoms in the population of patients with type 1 and type 2 diabetes.
3. Determination of indications for the treatment of the painful form of diabetic neuropathy with drugs and evaluation of the comparative effectiveness of treatment with auxiliary analgesics and lipoic acid preparations.
4. To study the relationship between the biomechanical properties of the foot and the pedobarography data reflecting the severity of diabetic neuropathy.
5. To study the state of microcirculation and tissue oxygenation in patients with a high risk of developing diabetic foot syndrome.
6. Evaluation of the prognostic value of various methods for the study of the peripheral nervous and vascular systems in the development of diabetic foot syndrome and lower leg amputation in patients with diabetes.
7. To study the effect of L-arginine, nitric oxide, transforming growth factor B 1 metabolism on the development of the neuropathic form of diabetic foot syndrome.
8. Study of the dynamic state of the peripheral nervous system against the background of critical ischemia caused by diabetic macroangiopathy before and after revascularization operations in the arteries of the lower limbs.
9. Quantification of the severity and localization of obliteration and stenosis lesions of the arteries of the lower limbs in patients with diabetes compared to individuals with impaired carbohydrate metabolism.
10. To study the influence of distal diabetic polyneuropathy on the clinical course, localization and results of obliterating lesions of the arteries of the lower limbs in patients with diabetes.
11. Prospective study of the results of conservative and surgical treatment of patients with neuro-ischemic form of diabetic foot syndrome.

Scientific news

For the first time, a study was conducted to determine the incidence of diabetic neuropathy according to the severity of neurological manifestations. Clinical descriptions of different variants of the course of the painful form of DPN are given with an assessment of the severity of pain symptoms. Factors affecting the intensity and frequency of pain in patients with diabetes were determined.

For the first time, based on many years of experience, the effectiveness of drug therapy for the painful form of DPN was evaluated. An analysis of the structure of treatment of patients with painful neuropathy in general medical practice was carried out. A diagnostic algorithm was

developed and drug therapy recommendations for diabetic polyneuropathy were structured taking into account the availability of several drugs.

For the first time, during a 5-year follow-up period, peripheral blood in the formation of foot ulcers, lower limb amputations and death in patients with diabetes the prognostic role of various parameters reflecting the state of the nervous and vascular system was shown. The most reliable indicators predicting the formation of a new alternative defect are indicators of the speed of propagation of the excitation along the motor nerve fiber; An important predictor of lower limb amputations is mediocalcinosis of lower limb vessels.

For the first time, peak pressure ratios of the metatarsophalangeal and heel segments of the foot were obtained, reflecting significant biomechanical disturbances caused by diabetic polyneuropathy.

For the first time, the metabolism of the amino acid L-arginine was studied in diabetic patients with long-term untreated leg ulcers. The important role of transforming growth factor P1 (TGF- β 1), which is involved in the regulation of L-arginine metabolism, has been proven in the chronicity of reparative processes in patients with the neuropathic form of diabetic foot syndrome.

The functional status of peripheral nerve fibers was studied in patients with critical ischemia. Nerve dysfunction has been shown to be more significant on the side with a higher degree of ischemia compared to the contralateral limb. It is known that the restoration of blood flow is not accompanied by a significant improvement in nerve function, regardless of the type of vascular repair, the severity of ischemia and neuropathy.

For the first time, the immediate (after 4 weeks) and long-term results (up to 12 months) of balloon angioplasty and stenting were observed in patients with diabetes and critical limb ischemia compared with complex conservative treatment. Algorithm and criteria for the selection of treatment using balloon angioplasty were developed and clinical effectiveness of the elimination of critical ischemia in patients with diabetes was proven.

Practical significance

A system for early diagnosis of diabetic polyneuropathy was proposed based on the study of clinical, metabolic and neurophysiological criteria. Criteria for evaluating the effectiveness and safety of drug treatment have been developed.

In the treatment of patients with neuropathic pain associated with DPN, it is necessary to differentiate the tactics of drug selection depending on the initial state of carbohydrate metabolism and the severity of pain symptoms according to the visual scale of neurological symptoms.

The results obtained based on the analysis of computer pedobarrography data are one of the factors determining the high risk of the development of a gastric ulcer defect.

Suggests using the ratio of plantar pressure at the top of the metatarsophalangeal portion and heel. This indicator can also be used to evaluate the effectiveness of orthopedic correction, as well as an objective indicator for lengthening the Achilles tendon to correct the pressure distribution on the plantar surface of the foot.

Information obtained on the role of transforming growth factor P1 and L-arginine in the regulation of reparative processes allows to optimize the treatment of patients with the neuropathic form of diabetic foot syndrome and predict the duration of treatment.

The lack of dynamics of neurophysiological indicators and deterioration of the functional state of the peripheral nervous system in patients with critical limb ischemia after reconstructive surgery necessitates the need to strengthen the dynamic control of this category of patients.

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