



## Methods of Improving the Treatment and Prevention of Patients with Diabetic Foot Syndrome

1. Kurbanova Nazima  
Sobirzhonovna

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<sup>1</sup> Assistant of the department. Samarkand  
State Medical University, Samarkand,  
Uzbekistan

**Abstract:** Lesions of the lower extremities in diabetic patients concern doctors of various specialties. This is due to the fact that a violation of carbohydrate metabolism leads to changes in peripheral blood flow, innervation, the development of trophic ulcers, and in some cases, the need for limb amputation. Chronic hyperglycemia aggravates the course and complicates the treatment of ulcerative defects of other genesis (postthrombo-phlebotic syndrome, lipid necrobiosis, eczema, etc.). All this determines the need for accurate diagnosis, differentiation and selection of adequate treatment in each case of the development of trophic disorders of the skin of the lower extremities.

**Key words:** diabetes, carbohydrate metabolism, diabetic heel syndrome, hyperglycemia.

Diabetic foot syndrome combines pathological changes in the peripheral nervous system, arterial and microcirculatory bed, osteoarticular apparatus, which pose a direct threat to the development of ulcerative necrotic processes and foot gangrene. (1 .5 )

Despite a sufficient amount of information on the pathogenesis, diagnosis, methods of treatment and prevention of complications of DM, data on the incidence and outcome of lesions of the lower extremities are still disappointing. The results of epidemiological studies conducted in various - countries indicate that in the structure of all amputations of the lower extremities of a non-traumatic nature, patients with DM account for 50-75%.

The frequency of amputations depends on the age of the patients, the duration of the disease, and the type of diabetes. Elderly people have a higher incidence of diabetic foot syndrome with a tendency to generalization of the inflammatory process and the development of gangrene, resulting in a greater number of large-volume amputations. The frequency of development of diabetic foot syndrome correlates with the duration of the course of the underlying disease. It should be noted that with type 2 diabetes at the time of diagnosis, up to 30% of patients have changes in peripheral sensitivity or atherosclerotic lesions of peripheral arteries of varying severity. The incidence of foot ulcers is the same regardless of the type of diabetes. (3)

A comparative analysis of the frequency of amputations showed that such operations on the lower extremities in patients with DM are performed 17-45 times more often than in the general population, although the incidence of obstructive lesions of peripheral arteries in DM is 4 times higher than that in

people without diabetes. The number of amputations in patients with DM is determined not only by the high frequency of obliterating atherosclerosis of peripheral arteries, but also by other factors. The most important among them can be considered the underestimation of the role of neuropathy in the genesis of ulcerative lesions of the lower extremities, untimely and inadequate treatment, and the lack of proper foot care skills in patients. (7)

The Diabetic Foot Syndrome (DFS) is defined by the International Working Group as “an infection, ulcer and/or destruction of deep tissues associated with neurological disorders and a decrease in the main blood flow in the arteries of the lower extremities of varying severity.” This formulation was based on the WHO definition. Thus, SDS is represented mainly by purulent-destructive lesions of the lower extremities. A significant proportion of patients with diabetes mellitus (DM) have other lesions of the lower extremities - diabetic neuropathy (DN), diabetic angiopathy, etc., which are not formally related to DMS, but also require active detection and treatment.

The prevalence of DFS in most populations is estimated by experts to be 4-10% of all patients with diabetes (International Working Group on the Diabetic Foot, 2000). The prevalence of DN is more than 50% of all cases of DM (one of the most common complications of diabetes), diabetic macroangiopathy of the lower extremities (according to ultrasound screening) is about 10-20%. (1,4,8)

About 85% of SDS are trophic foot ulcers, the rest are abscesses, phlegmona, osteomyelitis, tendovaginitis, purulent arthritis and other processes that develop either as a complication of a trophic ulcer, or initially, without a previous ulcer. In addition, a rare (<1% of patients) **nonpurulent destructive** lesion of the limb skeleton, diabetic osteoarthropathy, which is one of the complications of DN, also belongs to DFS. SDS also includes the consequences of amputations within the lower extremities.



**Rice. 1. Diabetic osteoarthropathy:** *a* - typical foot deformity caused by this complication; *b, c* - destruction of the bones of the foot (left) on the x-ray

In screening studies conducted in Uzbekistan, the prevalence of trophic ulcers in patients with diabetes was 2-3.8%, which is significantly lower than foreign expert estimates. Perhaps further research will show whether these figures reflect the true picture or are associated with the "falling out" of the screening of some patients.

### Pathogenesis of lesions of the lower extremities in DM

Previously, it was believed that all foot lesions in DM are the result of vascular damage. Since the mid-1970s - 1980s, more and more evidence has been accumulating that, with completely intact blood flow, DN can be the cause of trophic ulcers and other necrotic lesions of the feet. Today, DN, macro- and microangiopathy are considered as the main mechanisms of late complications of DM.

However, although damage to the microvasculature (microangiopathy) can be detected in the microvessels of almost all tissues, the significance of these changes in different organs turned out to be different. It is generally accepted that diabetic microangiopathy leads to damage to the retina and renal glomeruli. Data from studies of the microvasculature of the extremities are less unambiguous. The assumption that changes in the capillary wall create obstacles for the diffusion of gases was not confirmed. In this regard, it is recognized that diabetic microangiopathy is not capable of causing tissue necrosis and trophic foot ulcers by itself (J. Bowker, 2001).

Morphologically, diabetic macroangiopathy is atherosclerosis, which has a number of features in patients with DM. DM is a powerful risk factor for atherosclerosis. This complication (as well as DN) can both bring suffering to the patient and lead to the development of SDS itself.

The main reason for the development of DN is the effect of chronically elevated blood glucose levels on nerve cells, mainly on the axons of peripheral neurons. DN itself is not capable of causing tissue necrosis, but it leads to the development of trophic ulcers in various ways. So, sensory distal polyneuropathy leads to a loss of sensitivity, which leads to unnoticed and often severe mechanical, chemical or thermal foot injuries, the patient wearing shoes that injure his feet.

For the slow healing of wounds in diabetes, as well as the mechanical load on the wound when walking, lead to a trophic ulcer. Motor distal polyneuropathy, contributing to the deformation of the fingers due to atrophy of the interosseous muscles of the foot, creates zones of increased pressure on the skin when walking. In these zones, areas of hyperkeratosis (corns) soon form, under them - hematomas, which quickly suppurate. Autonomic neuropathy in some patients leads to the development of diabetic osteoarthropathy (Charcot foot) with severe deformity of the feet and overload of areas of the foot unprepared for the support function (Fig. 1). In addition, autonomic neuropathy causes dry skin, sweating disorders, etc. Cracks quickly form on dry areas of the skin, which turn into trophic ulcers when an infection is attached, especially against the background of limb ischemia.

### Diagnosis and treatment of DN

DN is a heterogeneous condition in its manifestations (and, probably, in its nature). There are various classifications of it, one of them is the following (K.Shaw, 1996; J.Bowker, 2001).

- Damage to the cranial nerves (cranial mononeuropathy).
- diabetic radiculopathy.
- Diabetic plexopathies.
- Multiple (multifocal) mononeuropathy.
- Distal polyneuropathy:
  - ✓ acute,
  - ✓ chronic with a predominance of sensory and / or motor disorders:
  - ✓ with damage to large (thick myelin) fibers,
  - ✓ with damage to thin myelin fibers.
- Autonomic (vegetative) neuropathy.

The most frequent and most significant in the pathogenesis of DFS are distal polyneuropathy (DPN) and autonomic (vegetative) neuropathy (AVN).

There is a classification of DN by stages (P.Dyck, 2018): stage 0 - no neuropathy, 1 - asymptomatic - neuropathy, 2 - symptomatic neuropathy, 3 - severe (complicated) neuropathy.

Typical symptoms of DPN: pain in the distal parts of both feet, aggravated at night, at rest and

weakened by movement (walking, gymnastics, massage). Other sensory disturbances are also characteristic: numbness, burning or coldness of the feet, paresthesia. An increased reaction to a painful stimulus (hyperalgesia) or touch (hyperesthesia) is possible, as well as the perception of a non-painful stimulus as pain (allodynia), for example, pain when touching a blanket or sheet. Manifestations of motor neuropathy are less specific: it is weakness in the legs when walking (especially when walking up stairs), night cramps.

To verify the diagnosis, it is necessary to determine the sensitivity of the distal parts of the feet, primarily vibrational, as well as temperature and tactile. Vibration sensitivity is assessed using a graduated tuning fork or biothesiometer in the projection of bone protrusions. The examination technique and age norms for vibration, as well as the methodology for determining other types of sensitivity, are set out, in particular, in recently published manuals (I.I. Dedov et al., 2005; V.B. Bregovsky et al., 2004). The "gold standard" for assessing the function of nerve fibers is electroneuromyography. Diagnosis of DN is further complicated by the fact that minor deviations in 1 or even 2 instrumental tests are also found in healthy individuals (A. Bruno, 1994; K. Shaw, 2006). Therefore, several tests are required to make a diagnosis of DN. For the diagnosis of AVN DN, standardized exercise tests according to Ewing were adopted (Schkir, 2011).



Рис. 2. Рубеоз кожи стопы (левой) при критической



Рис. 3. Типичный вид некропатической язвы при СДС.



The treatment of DPN consists of 4 main components:

- achieving compensation of carbohydrate metabolism;
- proper foot care to avoid complications of DN - damage and trophic foot ulcers;
- the use of drugs;
- non-drug methods of treatment .

***Hyperglycemia is known to be the leading etiological factor in DN.*** In most patients with DN, there is a pronounced decompensation of carbohydrate metabolism. Normalization of glycemia not only prevents the progression of neuropathy, but also significantly reduces the manifestations of already existing DN. This is evidenced by

Numerous clinical observations: neuropathic pain often completely disappears upon recovery from decompensation of carbohydrate metabolism.

All patients with DM should follow the special Foot Care Rules (published as patient brochures). However, the "strictness" of these rules depends on the degree of sensitivity violations. For example, a patient with normal sensitivity may trim their nails with scissors (not too short and without cutting the corners). In case of impaired sensitivity (as well as with a decrease in visual acuity or cuts during the processing of nails in history), the nails should not be cut, but filed. If reduced sensitivity is detected, the previously given recommendations should be changed, and the special importance of their implementation should be explained to the patient.

Reduced sensitivity (especially in combination with deformity of the feet) significantly increases the risk of trophic ulcers and requires special selection or manufacture of shoes. Patients at risk also require regular check-ups in the Diabetic Foot Room, preventive Drug treatment of DN consists of two main components: pathogenetic and symptomatic therapy. Of the first group of methods, alpha-lipoic acid (ALA) has the greatest support for data from randomized trials. The drug has a multifaceted effect: it neutralizes free radicals, replenishes NADH deficiency, improves endoneural blood flow, etc. The effectiveness of ALA has been studied in a number of placebo-controlled studies: ALADIN, ALADIN II, ALADIN III (D. Ziegler, 1995, 2019; M. Reljanovic et al., 2009), SYDNEY I, SYDNEY II, as well as DEKAN, which has proven a therapeutic effect in autonomic neuropathy (D. Ziegler et al., 2017). Based on the results of these studies, the drug regimen was recommended: 600 mg/day intravenously drip for 3 weeks, then 600 mg/day orally for at least 2-3 months, but the duration of oral administration is not limited to this period: in the ALADIN study II it was 2 years. According to the results of these studies, the reduction in neuropathic symptoms after 3 weeks of intravenous administration of the drug was more pronounced than the long-term effect on the function of nerve fibers when taken orally.

However, in the ORPIL and SYDNEY II studies, short-term (3 and 5 weeks, respectively) oral administration of the drug was also effective, and in SYDNEY II, taking 600 mg had no less effect than 1200 or 1800 mg 1 time per day (D.Ziegler, 2006), and there were significantly fewer side effects.

In a placebo-controlled study in Russia (G.R. Galstyan, 2006), ALC was used for 1 year. A significant effect of the drug was detected only in patients with good compensation for diabetes -  $HbA_{1c} < 7.5\%$  - for indicators of neurological deficit (NISLL) and the speed of propagation of excitation along the nerves (NRV). At the same time, for the appearance of significant changes in SRV, continuous administration of the drug for at least 6 months was required. A decrease in pain symptoms was found already after 3 weeks of intravenous administration of the drug, but it was significant only in the group with  $HbA_{1c}$  from 7.5 to 9%.

It should be remembered that the negative effect of hyperglycemia, which causes further damage to neurons, significantly exceeds the restoring effect of "pathogenetic" drugs on them. Therefore, the appointment of these drugs against the background of decompensation of carbohydrate metabolism is a mistake. The optimal situation for treatment with these drugs is the persistent manifestations of DN, despite the stable compensation of DM (which occurs quite often due to the irreversibility of damage to nerve fibers).

In some cases, with a pronounced pain syndrome, symptomatic treatment is required. Standard analgesics (metamizole, paracetamol and other NSAIDs) are ineffective in DPN. The use of antidepressants (amitriptyline, imipramine, duloxetine), anticonvulsants (carbamazepine, gabapentin, pregabalin) and a number of other drugs (mexiletine, tramadol) is generally accepted.

Treatment of ulcerative-necrotic lesions of the feet

Based on the data on pathogenesis, a modern classification of DFS has been proposed. Allocate neuropathic form of the syndrome (50-70% of patients), neuroischemic (25-45%) and ischemic (5-10%). The criterion for the diagnosis of one form or another is, first of all, a verified diagnosis of diabetic polyneuropathy and macroangiopathy (see above). There are also a number of features of a trophic ulcer (Fig. 3, 4), which make it possible to attribute it to one or another type of lesion; they are set out in the relevant manuals (I.I. Dedov et al., 1998, 2005; V.B. Bregovskii, 2004). Neuroischemic and ischemic forms are often combined, since limb ischemia is the main factor determining the prognosis and choice of treatment.

**Conservative treatment of ulcerative defects.** The introduction of modern methods has ensured high efficiency in the treatment of SDS. In the neuropathic form, healing of a trophic ulcer (without any amputations) is achieved in 80-90% of cases. In ischemic and neuroischemic forms, healing occurs, according to the author, in approximately 30-40% of patients against the background of conservative treatment, however, the use of revascularization methods increases the likelihood of healing several times.

## CONCLUSION

Timely prevention significantly reduces the risk of diabetic ulcers. But even with the development of purulent-necrotic lesions of the feet, amputation is by no means an obligatory outcome. SDS today is - successfully treated, however, not quite as it seemed before. The introduction of such methods is realistic, but requires overcoming a number of difficulties. This requires the enthusiasm and concerted action of all specialists involved in the treatment of lesions of the lower extremities in DM.

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