MODERN MEDICINE AND PRACTICE
http://innovatus.es/index.php/ejmmp
EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 03 No. 12 (Dec - 2023) EJMMP ISSN: 2795-921X

IMPROVING METHODS FOR COMPLEX SURGICAL TREATMENT OF DIABETIC FOOT SYNDROME

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Abstract. The use of long-term intra-arterial perfusions of L -arginine in complex treatment of patients with purulent-necrotic complications of diabetic foot syndrome with ischemia of the lower extremities led to a sharp decrease in the number of cases of progression of the pathological process and ischemia in the foot, which was observed in only 10.2 % patients at a time when they were an order of magnitude higher and amounted to 30.7% in patients without the use of this method of complex treatment. The mortality rate in treated patients was 4.54% and 13.18% respectively.
Key words: purulent-necrotic process, diabetic foot syndrome, lower limb ischemia.

Relevance. Despite advances in the treatment of patients with lower limb ischemia (LII), this problem remains relevant (3,16). In patients with diabetes mellitus (DM), INK occurs approximately five times more often, and diabetic foot syndrome develops in more than 10% of patients. Particularly severe are purulent-necrotic complications of diabetic foot syndrome (DFS) accompanied by INK (4,15). According to researchers, in patients with diabetes mellitus INC develops 40 times more often than in persons without diabetes (10,11,26,28,30,32,34,35).

A purulent-necrotic process against the background of diabetes mellitus, accompanied by ischemia of the lower limb (LI), leads to an unfavorable outcome of both the course of the wound process and the disease itself (9,12,13,14,17).

Endothelial dysfunction is a key link in the pathogenesis of lower limb ischemia (LI). The problem of endothelial dysfunction currently attracts many researchers, since it is one of the predictors of morphological changes in the vascular wall during atherosclerosis, arterial hypertension, diabetes mellitus, and lower limb ischemia (LI) (9). Endothelial dysfunction in this case, as a rule, is systemic in nature and is found not only in large vessels, but also in the microvasculature (8,27,29,31).

Despite numerous attempts at complex treatment of this category of patients, improvement of surgical treatment methods, the outcome of the disease in most cases is unfavorable, that is, patients lose a limb (16,23,33,35), in which postoperative purulent-necrotic complications and mortality are high, and surviving patients are considered a success for surgeons (5,8,15,20,21,22,24,25). With the development of science and technology in the treatment of purulent-inflammatory diseases (PID), the pathogenesis of which is local tissue hypoxia against the background of ischemia, combined treatment methods with the use of antihypoxic drugs (L-arginine) began to be used. As is known, L-arginine has antihypoxic, cytoprotective, antioxidant, detoxification, and membrane-stabilizing properties.

Researchers have proven that L-arginine plays an important role in the processes of neutralizing ammonia and stimulating its excretion from the body. As a donor of nitric oxide, L-arginine takes part in the processes of energy supply to the body, reduces the activation and adhesion of leukocytes and platelets to the vascular endothelium, preventing the formation and development of atherosclerotic plaques, and is included in the processes of fibrinogenolysis. The drug has a moderate anabolic effect, stimulates the activity of the thymus gland, promotes insulin synthesis and regulates blood glucose levels during exercise, and helps correct acid-base balance. Used in complex therapy of lower limb ischemia, atherosclerosis of peripheral vessels, diabetic angiopathy (1,5,35).

Available literature data on the positive results of the use of L-arginine in ischemia of the lower limb with pronounced signs of endothelial dysfunction of the vessels of the lower extremities with purulent-necrotic complications of diabetic foot syndrome do not fully reflect all the points associated with the study of the course of the wound process. However, there are no clear recommendations on the most optimal scheme for complex treatment of patients with this pathology accompanied by endothelial dysfunction. Solving the above problems would have an active impact in the treatment of this group of patients.

Purpose of the study: To develop an optimal method of using L-arginine in the treatment of purulent-necrotic complications of diabetic foot syndrome with vascular endothelial dysfunction accompanied by ischemia of the lower extremities.

Material and methods: The work is based on data based on a study of the results of surgical treatment of 272 patients with purulent-necrotic lesions of the lower extremities against the background of diabetes mellitus with pronounced signs of vascular endothelial dysfunction, which was accompanied by ischemia of the extremities, treated in the department of purulent surgery of the Bukhara Multidisciplinary Medical Center during the period from 2017 to 2022. We used the method of stratified randomization of patients. In accordance with the objectives of the study, all patients were conditionally divided into 3 groups: (I – control and II a, II b - main). Among the patients, there was a predominance of men (69.5%). Most patients were aged from 38 to 83 years. The first control group consisted of 91 (33.4%) patients with purulent-necrotic lesions of the lower extremities, who underwent a complex of treatment measures, including surgical placement, antibacterial therapy, infusion, detoxification therapy, drugs that improve microcirculation - angioprotectors, correction of glycemic levels, and also symptomatic treatment of concomitant diseases. Local treatment was carried out in the traditional way (ointments on a water-soluble polyethylene glycol (PEG) base - oflomelid). In o Group II included 93 (34.2%) patients who, in addition to traditional measures (antibacterial therapy, anticoagulants, local treatment (water-soluble PEG-based ointments - oflomelide), received intravenous infusions of L-arginine once a day in order to improve microcirculation, reducing endothelial dysfunction of the vessels of the lower extremities, given that this drug has antihypoxic and antioxidant properties.

In o Group II included 88 (32.4%) patients who, in addition to traditional measures (antibacterial therapy, anticoagulants, local treatment (ointments on a water-soluble PEG basis - oflomelid), catheterization of the femoral artery was performed for long-term intra-arterial infusions of L-arginine during and 24 -48 hours using the “aitecs® 2016” dispenser.

In the 272 patients examined, the identified changes in the foot were represented by the following forms: focal tissue necrosis - 35; purulent-necrotic ulcers of the toes – 39; purulent-necrotic phlegmon of the foot – 51; gangrene of the toes (dry and wet) – 46; ganren of the distal parts of the foot (dry and wet) – 73. Proliferating putrefactive phlegmons of the foot, supra-calcaneal space and shin-28.

The surgical stage, whenever possible, was performed against the background of a complete examination of the patient in combination with adequate conservative treatment and unloading of the affected limb. Our surgical treatment was based on the principle of maximum preservation of the tissues and functions of the foot. During surgical treatment (CS) of a purulent-necrotic lesion, wide access to the purulent-necrotic lesion was provided, its adequate drainage was carried out, necrotic tissues supporting the infection were removed, combined with the use of water-soluble ointment dressings on a multicomponent water-soluble polyethylene glycol (PEG) base.

For deep phlegmons of the supracalcaneal space, we performed excision of all connective tissue structures, fascia, thickened perimysium, infected tendons, up to the Achilles tendon. Atypical, guillotine amputations of the foot and leg within healthy tissue were also performed.

The examination of patients included general clinical methods, laboratory methods, instrumental methods for studying the arterial bed of the lower extremities (Dopplerography, angiography), as well as assessment of endothelial dysfunction by studying immunological parameters - endothelin 1 (ET-1), NO -nitric oxide, VEGF A (Vascular endothelial growth factor - Vascular endothelial growth factor), TGFβ (transforming growth factor beta - Transforming growth factor beta). All examined patients underwent bacteriological examination of wound exudate.

The dynamics of general and local manifestations of the wound process were assessed according to subjective criteria (nature of wound discharge, resorption of infiltrate, features of the development of granulation tissue and epithelization) and objective indicators (body temperature, general clinical blood test, leukocyte index of intoxication, procalcitonin (PCT) and C- levels reactive protein - CRP).

Results and discussion: 91 patients included in control group I, after following the basic principles of surgical treatment and antibiotic therapy taking into account the sensitivity of the flora, received local dressings with a water-soluble ointment based on polyethylene glycol (PEG) (oflomelid).

The general condition of the patients in most cases upon admission was moderate or severe. All of them complained of general weakness, malaise, pain in the area of the pathological process of the lower extremities, increased body temperature to 37.8 - °40.2 °C, dry mouth, sleep disturbance and lack of appetite. Local symptoms included moderate or severe hyperemia of the skin around the pathological process on the foot and swelling of the tissues. Painful infiltration was determined by palpation, the foot was hypothermic to the touch in all cases without exception, the pulsation in the arteries of the foot was sharply weakened or not detected at all. Most patients were admitted to us within a period of 3 to 21 days after the onset of the disease and the first phase of the wound course.

An analysis of the study of the species composition of the microflora of the wound contents in patients of the study group showed that in most cases, representatives of the aerobic microflora in the wound exudate were staphylococci, Escherichia coli and Proteus, and among the sown anaerobes, Pr.melaninogenica and Bacteroidesspp were more common. At the same time, the initial level of microbial contamination of wounds in patients of group I showed that it averaged 10 10-11 mt/g. After surgical treatment of the wound with the application of an ointment dressing, the microbial contamination was 10 6 mt/g, the next day it increased to 10 7-8 mt /g, 6-7 days of complex treatment in these patients the degree of microbial contamination began to significantly decrease and amounted to an average 10 5-6 mt/g, and only by 10-12 days of treatment it became below the critical level and amounted to 10 3 microbial bodies per 1 g. fabrics.

A study of body intoxication indicators showed that on the first day of treatment, the body temperature in patients was on average 38.6 □1.1 □C. The content of leukocytes in the blood averaged 13.6 □2.5x10 9 /l.

There was an increase in the leukocyte intoxication index (LII) and erythrocyte sedimentation rate (ESR) to 4.7 1.30 □and 40.2 □1.6, respectively, the PCT and CRB indicators were 1.2 □0.2 ng /ml and 16. 5 □2.1 mg/l respectively. On the third day of treatment, there was a slight decrease in body temperature (from 38.6 □1.1 □C to 37.9 □0.5 □C), the content of leukocytes in the blood decreased to an average of 11.0 □0.5 10 9 /l. Changes in LII indicators on the third day of treatment tended to decrease from 4.7 □1.30 to 3.4 □0.18 units, while ESR decreased to an average of 34.7 ± 2.2 mm/h. Indicators _ _ PCT and CRB on these days were 0.8–0.1 □ng / ml and □12.1–1.4 mg/l, respectively. By 7-9 days of treatment, the examined patients in the control group remained slightly subfebrile (37.0 □0.4 °C). At the same time, there was a further decrease in body intoxication indicators: L, LII, ESR, P CT and C RB in the blood, that is, there was a tendency towards normalization. So, by 12-14 days of treatment, all analyzed indicators of intoxication except ESR were normalized.

Dynamics research results endothelin a 1, NO and growth factors VEGF -A and TGF-β in blood serum showed that in patients in the control group on the day of admission, the initial level of endothelin 1 and NO was 9.22 ± 0.64 pg /ml and 16.32 ± 1.12 μmol /l, VEGF-A was 1042.25 ± 5 pg /ml, TGF-β 187.74 ± 2.5 pg /ml. Against the background of traditional therapy, by day 3 endothelin 1 was equal to 7.82 ± 0.57 pg /ml, NO 18.64 ± 1.44 μmol /l, and VEGF-A indicators were equal to 1154.27 ± 5 pg / ml, TGF-β 192.78 ± 2.5 pg /ml, by days 7-9 they (endothelin 1, NO, VEGF-A and TGF-β) were 6.94 ± 0.44 pg / ml, 20.62 ± 1.24 μmol /l, 1019.5 ± 5 pg /ml and 192.78 ± 2.5 pg /ml, respectively. Even by 12-14 days of treatment, endothelin 1, NO, VEGF-A and TGF-β values were still above normal values and amounted to 5.62 ± 0.25 pg /ml and 21.48 ± 1.31 μmol/l, 609.5±5 pg /ml and 172.54±2.5 pg /ml, respectively (Table 1).

Table 1.

Dynamics of endothelin 1, NO, VEGF-A and TGF-β indices in blood serum in the examined patients of the control group (I)

Indicators	Since the start of treatment			
	1 (day of admission)	3rd	7-9th	12-14th
ET-1, pg /ml	8.22 ± 0.64	7.82 ± 0.57 _	6.94 ± 0.44	5.62 ± 0.25
NO, μmol /l	16.32 ± 1.12	18.64 ± 1.44 _	20.62 ± 1.24	21.48 ± 1.31
VEGF-A, pg /ml				
1042.25±5				
1154.27±5				
1019.5±5				
609.5±5				
TGF-β, pg /ml				
192.78±2.5				
192.78 ± 2.5				
192.78±2.5				
172.54±2.5				

Note where * P <0.05 – reliability indicator in relation to the previous day of treatment.

At the same time, in patients in the control group, wound cleansing from infection occurred on average by 12.0 to □1.5 days. By 7-9 days, resorption of the infiltrate around the wound was noted. The beginning of the

appearance of granulations was noted at 12-14 days, and the beginning of epithelization only at 17-19 days of treatment. At the same time, the duration of inpatient treatment was 21.5±2.5 bed days.

Against the background of a complex of measures, 28 (30.7%) patients in the control group showed progression of the pathological process and signs of INC, in which, for health reasons, 19 (20.8%) patients underwent amputation of the lower limb at the level of the upper third of the leg, and in 10 (11%) cases, due to the involvement of the lower leg in the pathological process and occlusion of the arterial bed in the femoral and iliac segments, they were forced to resort to high amputations at the level of the middle and upper thirds of the thigh. In 7 (7.69%) patients who underwent minor surgical interventions at the foot level, there was a progression of concomitant diseases which could not be corrected, and therefore there occurred: acute impairment of cardiovascular activity in 3 patients, systemic inflammatory response syndrome with the development septic shock in 2 patients and renal failure due to diabetic nephropathy in 2 patients with a fatal outcome. Postoperative mortality in patients in the control group who underwent high amputations at the level of the femur and tibia was observed in 5 (5.5%) patients. An analysis of the structure of postoperative mortality showed that, against the background of anesthesia, 2 patients had uncontrollable hypotension with profound impairment of the vital functions of the body, 2 patients had pulmonary embolism, and 1 patient had progression of signs of multiple organ failure with a fatal outcome. Overall mortality in this group was 12 (13.18%) cases.

As noted above, main group II was divided into 2 subgroups (II a and II b). Group II consisted of 93 patients who, in addition to traditional measures, received intravenous infusions of L-arginine once a day, and II b group a consisting of 88 patients who underwent catheterization of the femoral artery for long-term intra-arterial infusions of L-arginine. Patients in the main group underwent surgical interventions comparable in scope and nature to those in the control group. A mandatory procedure during treatment, in addition to standard examination, was the study of ET-1, NO, VEGF-A and TGF-β in blood serum to determine endothelial dysfunction.

The study of microbial contamination of wound tissue in wound exudate in patients of the main group showed that the initial level of microbial contamination of wounds, as in patients of the control group, was 10 9-10 mt/g. After surgical treatment of the wound and the start of intravenous infusion of L arginine, a relatively lower microbial contamination of the wounds was observed than in the control group. In group IIb, which underwent intra-arterial perfusion of L arginine, there was a significant decrease in microbial contamination of wounds and by the 3rd day of treatment it averaged 10 5-6 mt/g, and by 7-9 days of treatment microbial contamination in the wound decreased on average to 10 3 microbial bodies per 1g. fabrics and below.

Analysis of the degree of endotoxicosis in patients of groups IIa and IIb showed that already by the third day of treatment there was a decrease in body temperature (in IIa from 38.8 □1.1 □C to 38.1 □0.7 □C, IIb from 39.2 □1.1 □C to 37.4 □0.3 □C), the content of leukocytes in the blood decreased on average in group IIa to 12.5 □1.0 10 9 /l, and in IIb 8.7 □1.0 10 9 /l. Changes in LII indicators on the third day were in IIa from 4.8 1.30 □to 4.4 □0.22 units, in IIb from 4.9 □1.35 to 3.2 □0.24 units, while the ESR decreased on average in both groups up to 31.5 □1.8 mm/h and 22.2 □1.5 mm/h, respectively. And PCT and CRP indicators decreased in group □II from 1.25 0.24 ng / ml to 1.02 □0.2 ng / ml and from 15.9 □2.1 mg/l to 13.2 □1.1 mg/ l, in group II b from 1.26 □0.23 ng / ml to 0.52 □0.2 ng / ml and from 15.4 □2.2 mg/l to 9.4 □1.1 mg/l, respectively. By 7-9 days of treatment, the examined patients of group II a had higher than normal indicators of body intoxication: T- body, L, LII, ESR, PCT and blood CRP; in group II b there was an earlier tendency to normalization than in patients I and II a group.

The results of studies of the dynamics of ET-1, NO and growth factors VEGF-A and TGF-β in blood serum showed that in patients of group IIa on the day of admission the initial level of ET-1 was 8.94 ± 0.44 pg /ml, NO 16.32 ± 1.12 μmol /l, VEGF-A was 1054.27±5 pg /ml, TGF-β 190.56±2.5 pg /ml. After the start of intravenous infusion of L -arginine, there was a slight improvement in ET-1, NO, VEGF-A and TGF-β compared to the control group. Against the background of complex treatment with intravenous L -arginine, by day 3, ET-1 was 7.82 ± 0.38 pg/ml, NO 18.64 ± 1.44 μmol /l, VEGF-A 922.20 ± 5 pg / l ml, TGF-β 165.44 ± 2.5 pg /ml, by days 7-9 they were 5.80 ± 0.42 pg/ml, 21.66 ± 1.22 μmol/l, 504.5 ± 5 pg / ml and 130.57±2.5 pg /ml, respectively. And by 12-14 days of treatment, the indicators of these markers were almost within normal limits (Table 2).

Table 2.

Dynamics of endothelin 1, NO, VEGF-A and TGF-β indices in blood serum in examined patients of group IIa

Indicators	Day			
	Day of admission			
leniya	3	7-9	12-14	
ET-1, pg /ml	8.94 ± 0.44	7.82 ± 0.38 _	5.80 ± 0.42	4.24 ± 0.25
NO, μmol /l	16.32 ± 1.12	18.64 ± 1.44 _	21.66 ± 1.22	25.84 ± 1.33
VEGF-A, pg /ml	1054.27±5	922.20±5	504.5±5	340.45±5
TGF-β, pg /ml	190.56±2.5	165.44±2.5	130.57±2.5	118.78±2.5

Note where * P <0.05 – reliability indicator in relation to the previous day of treatment.

And the results of studies of group II b of patients who had an intra-arterial catheter installed for long-term perfusion of L -arginine showed a rapid improvement in ET-1, NO, VEGF-A and TGF-β. Against the background of complex treatment using intra-arterial perfusion of L -arginine, by day 3 ET-1, NO was equal to 7.04 +0.36 pg /ml, 19.62 ± 1.44 μmol /l, and VEGF-A was equal to 842.24±5 pg/ml, TGF-β 160.44±2.5 pg/ml, by days 7-9 they were 4.87 ± 0.48 pg/ml, 24.88 ± 1.28 μmol /l, 524.5±5pg/ml and 124.72±2.5pg/ml, respectively. And by 12-14 days of treatment, the indicators of ET-1, NO, VEGF-A and TGF-β were normal (Table 3).

Table 3.

Dynamics of endothelin 1, NO, VEGF-A and TGF-β in blood serum in examined patients of group II b

Indicators	Day			
	Day of admission			
leniya	3	7-9	12-14	
ET-1, pg /ml	9.24 ± 0.35	7.04 ± 0.36 _	4.87 ± 0.48	3.22 ± 0.22
NO, μmol /l	16.33 ± 1.10	19.62 ± 1.44 _	24.88 ± 1.28	27.94 ± 1.66
VEGF-A, pg /ml	1066.27±5	842.24±5	524.5±5	240.45±5
TGF-β, pg /ml	194.23±2.5	160.44±2.5	124.72±2.5	98.78±2.5

Note where * P <0.05 – reliability indicator in relation to the previous day of treatment.

In patients of the analyzed groups (II a and II b), wound cleansing from infection occurred on average by 9.0 □1.0 and 5.0 □1.0 days, respectively, and in parallel with this, resorption of the infiltrate around the wound was noted. The beginning of the appearance of granulations was noted in group II a by the 10-11th day, and in group II b by the 7-8th day. The beginning of epithelization is 14-15 in group II a, 10-11 days in group II b of

treatment. At the same time, the duration of inpatient treatment was 16.5±1.5 and 11.5±1.5 bed days, respectively.

Against the background of a complex of measures, due to the depth of purulent-necrotic lesions of the limb, in 16 (17.2%) patients of group II, progression of the pathological process and signs of INC was noted, in which, for health reasons, 9 (9.67%) patients underwent the operation was amputation of the lower limb at the level of the upper third of the leg, and in 7 (7.53%) cases, they were forced to resort to high amputations at the level of the middle and upper third of the thigh. In 5 (5.37%) patients who underwent minor surgical interventions at the foot level, progression of multiple organ failure was observed, resulting in death. Postoperative mortality in patients of group II who underwent high amputations at the level of the femur and lower leg was 4 (4.3%), the cause of which in two cases was pulmonary embolism, and in the other acute cardiovascular failure. Overall mortality in this group was 9 (9.67%) cases.

Due to the depth of the purulent-necrotic lesion of the limb in group II b, 9 (10.2%) patients experienced progression of the pathological process and signs of INC, in which, for health reasons, 5 (5.68%) patients underwent amputation of the lower limb at the level of the upper third of the leg, and in 4 (4.54%) cases they were forced to perform high amputation at the level of the middle and upper third of the thigh. In 2 (2.27%) patients who underwent minor surgical interventions at the foot level, progression of multiple organ failure was observed, resulting in death. Postoperative mortality in patients of group II b who underwent high amputations at the level of the femur and lower leg was 2 (2.27%), the cause in both cases being pulmonary embolism. Overall mortality in this group was 4 (4.54%) cases.

A comparative analysis of the complex treatment of patients in the control, II a and II b groups showed that if in patients of the control and II a groups microbial contamination of wounds persisted for a rather long period of time and only by the 10th and 9th days of treatment, respectively, this indicator dropped below the critical level, while in patients who received intra-arterial infusions of L -arginine as part of the treatment complex, by the 7-9th day of treatment, microbial contamination in the wound decreased on average to 10 3 microbial bodies per 1 g. fabrics and below. In patients in the control group, even by 12-14 days of treatment, no significant normalization of ET-1, NO (nitric oxide), VEGF-A and TGF-β was observed (5.62 ± 0.25 pg/ml and 21.48 ± 1, 31 μmol/l, 609.5 ± 5 pg /ml and 172.54 ± 2.5 pg /ml, respectively), while in patients of the main group II b the normalization of indicators is higher than the specified factors.

The use of intra-arterial infusions of L -arginine in the complex treatment of patients with purulent-necrotic lesions of the lower extremities against the background of diabetes mellitus and INC contributed to the complete cleansing of the wound from infection already on days 4-5 of treatment. By this time, active resorption of the infiltrate around the wound was observed, granulation began to appear by the 7-8th day of treatment, and epithelization began by the 10-11th day. Research has revealed a significant advance of these indicators in group IIb by 4-5 days, compared to groups I and IIa. At the same time, the average duration of treatment decreased from 21.5±2.5 to 11.5±1.5 bed days. The use of intra-arterial infusions of L -arginine in complex treatment in patients of the main group II b led to a sharp decrease in the number of cases of progression of the pathological process and ischemia, which was observed only in 9 (10.2%) patients while in the control group I and II a group they were an order of magnitude higher and amounted to 28 (30.7%), 16 (17.2%), respectively, in which a high amputation of the lower limb was performed at the level of the upper third of the leg and thigh. Despite the implementation of a complex of treatment measures, mortality in patients in the control group was 13.18%, in group II and 9 (9.67%), while in patients of the main group there was a sharp decrease in the number of deaths, which amounted to 4 (4.54%)) of the total number of patients treated.

The data obtained allow us to propose the optimal method of using L -arginine in the treatment of ischemia in patients with diabetic foot syndrome. The proposed method of complex treatment using long-term intra-arterial infusions of L -arginine makes it possible to quickly eliminate signs of ischemia of the lower extremities, helps reduce the progression of the pathological process in the foot, reduces forced amputations and deaths from this pathology. All of the above indicates an improvement in treatment results with an increase in the quality of life, as well as a return to normal work activities for these patients.

Conclusions.

1. With traditional methods of treating diabetic foot syndrome with ischemia of the lower extremities, cleansing the wound from infection, healing processes and restoration of normal levels of ET-1, NO (nitric oxide), VEGF-A and TGF-β isn't happening fast enough. The duration of inpatient treatment is 21.5±2.5 bed days.
2. Complex treatment should include targeted measures that correct severe endothelial dysfunction of the vessels of the lower extremities, accompanied by hypoxia and ischemia of the affected lower extremity.
3. The use of long-term intra-arterial therapy with L -arginine perfusion within 24-48 hours in the complex treatment of diabetic foot syndrome with limb ischemia helps resolve vascular endothelial dysfunction with improved reparative processes in the tissues of the affected lower extremities
4. Perfusion of L -arginine helps to accelerate the time it takes to cleanse wounds from infection by 4-5 days, reduce the progression of purulent-necrotic processes of the lower extremities, which in turn leads to a reduction in the number of forced high amputations from 11% to 4.54% and mortality with 13.18% to 4.54 % of cases.
5. Indications for the use of L -arginine are the presence of pronounced signs of ischemia of the lower extremities, while reliable criteria for assessing the severity of vascular endothelial dysfunction are ET-1, NO (nitric oxide), VEGF-A and TGF-β.
6. Suggested method of using L -arginine in the treatment of diabetic foot syndrome has a high social significance, which consists in improving treatment results, improving the quality of life and early restoration of working capacity of this category of patients.

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