

Pathogenetic Approach in Complex Treatment of Diabetic Foot Syndrome with Critical Lower Limb Ischemia

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Abstract Comparative analysis of the results of complex treatment of 330 patients showed that when choosing tactics of treatment of diabetic foot syndrome with signs of critical ischemia of the lower extremities, preference should be given to a complex effect on all parts of the pathological process (infection, inflammatory reaction, critical reduction of hemopoiesis), which will contribute to a reliable advance in terms of cleansing the wound from infection, terms of resorption of infiltration around the wound, oxygen saturation of tissues, the appearance of granulation and epithelialization. For this purpose, it is advisable to simultaneously combine the use of intra-arterial injections of oxygenated perfluorocarbons (Perftoran) and local laser photodynamic therapy, which leads to a reduction in the duration of hospital treatment from 23.5 ± 3.5 to 14.5 ± 1.5 bed days and a significant reduction in the number of forced high amputations of the lower limbs from 36% to 6.25%, as well as the number of deaths from 14.11% to 2.5% of cases.

Keywords Diabetic foot syndrome, Critical ischemia, Perfluorocarbons, Laser photodynamic therapy

1. Introduction

In our opinion, when choosing the tactics of treatment of diabetic foot syndrome with signs of critical ischemia of the lower extremities, preference should be given to a complex effect on all parts of the pathological process (infection, inflammatory reaction, critical reduction of hemopoiesis), which can contribute to a reliable advance in terms of cleansing the wound from infection, terms of resorption of infiltration around the wound, oxygen saturation of tissues, the appearance of granulation and epithelialization. It is advisable to simultaneously combine the use of perfluorocarbons and local LFTT which leads to a reduction in the rehabilitation period and a significant reduction in the number of forced high amputations of the lower limbs, as well as the number of deaths.

2. Relevance of the Problem

Currently, much has been achieved in the world in the treatment of diabetic foot syndrome (DFS). Multidisciplinary approaches to treatment have been developed, the number of specialists engaged in foot care has

increased, modern antibiotics and topical treatments, therapeutic dressings, endovascular accommodation [4,5,8,12,14,20,25,30] are available. However, despite all the achievements, the number of amputations of legs in diabetes is growing. Every hour in the world 55 patients with diabetes lose their lower limb, and in economically developed countries varies from 13.7 to 32.3 per 100 thousand population, which in turn is accompanied by a high mortality rate, the cost of treatment and rehabilitation [4,5,21].

Purulent necrotic process against the background of diabetes mellitus is often accompanied by critical lower limb ischemia (CLLI), systemic inflammatory reaction syndrome (SIRS), deterioration of the patient's immune status and multiple organ failure, which in turn lead to an unfavorable outcome of both the course of the wound process and the disease itself [6,7,10,13,19,20,22].

Despite numerous attempts of complex treatment of patients with diabetic foot syndrome in critical lower limb ischemia, improvement of methods of surgical treatment, the outcome of the disease in most cases is gloomy, that is, patients lose a limb [23,24,26,27], in which postoperative purulent-necrotic complications and mortality are high, and the surviving patients are considered the success of surgeons [6,7,10,31].

The main concept of treatment of purulent wounds according to many researchers in recent years is the pathogenetic approach [15]. From the pathophysiology of wounds of various etiologies it is known that in the I phase of the wound process, one of the Central pathogenetic disorders

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is a violation of local microcirculation due to cellular and intercellular edema of tissues adjacent to the wound, which in turn leads to a decrease in oxygen transport in the lesion, and in the conditions of critical ischemia of the lower limb, metabolic processes proceed according to an anaerobic, energetically unfavorable type.

With the development of science and technology in the treatment of purulent inflammatory diseases (PID) in the pathogenesis of which is local tissue hypoxia on the background of critical ischemia began to be used combined methods of treatment with the use of perfluorocarbons (Perftoran) [1,2,31]. Perftoran is a submicron emulsion with gas transport properties containing 10% of perfluoroorganic compounds (PFOC). They are chemically inert compounds that do not undergo metabolic transformations in humans and animals [1,2]. The main gas components of the kidneys are Perpendicular and Performancecritterion. The influence of Perftoran on gas transportation is determined by the increase in oxygen capacity and gas exchange dynamics. The oxygen capacity of Perftoran is almost 3 times higher than that of all traditional non-gas-transport blood substitutes.

As it is known, the dynamics of gas exchange in the body is influenced by three parameters: Change in blood flow rate (changes in blood viscosity and vascular bed); Change in the surface of gas exchange; Change in the rate of oxygen enrichment of blood in the lungs and the rate of its return from blood to tissue fluid.

Researchers have proven that perfluorocarbons, dissolving in the membrane of red blood cells, make them more elastic and easily deformable, which also reduces the viscosity of the blood. Increasing the elasticity and deformability of the erythrocyte membrane improves their passage through the capillaries, and hence the delivery of oxygen to tissues. Perfluorocarbons cause disaggregation of red blood cells, therefore, have antilogies effect. The particle size of the PFOC emulsion (0.07 microns) is 100 times smaller than the size of erythrocytes (7 microns). This allows PFOC emulsion particles to pass through spasmed, sclerosed, partially thrombosed, and slagged vessels. Having a disaggregational effect on platelets, perftoran destroys platelet aggregates, that is, also contributes to the recanalization of the vascular bed. By binding blood lipids, Perftoran prevents and eliminates fat embolism of the vascular bed. Since oxygen in PFOC dissolves 20 times better than in water / plasma, this condensed medium of particles around red blood cells increases the effective gas exchange surface several times [1,2].

Although there are numerous information about the positive results of perfluorocarbons in occlusive lesions of the arteries of the lower extremities accompanied by critical ischemia, however, it should be noted that there are few reports of the use of perfluorocarbons in the treatment of DFS with CLLI, not developed a single scheme and method of their use. At the same time, there are no studies aimed at studying the course of the wound process using perfluorocarbons.

Also, the local treatment of wound infection and resistance of pathogens to antibacterial therapy remains an unsolved problem. Every year there are many publications devoted to the treatment of purulent wounds. At the same time, neither experimental data nor numerous clinical and special studies have not allowed to find a method that would be closer to solving the problem of wound infection treatment.

Photodynamic therapy (PDT) is one of the most promising methods of treatment of patients with purulent necrotic diseases [3,17]. According to a number of authors – this direction is leading, which requires careful and further development. The essence of the method is that many biological objects (tumor cells, microbes) accumulate certain dyes-photosensitizers, as a result of which they become sensitive to the effects of light energy, as well as low-intensity laser radiation of the corresponding wavelength. In sensitized tissues and cells, a photochemical reaction develops with the release of singlet oxygen, free radicals and highly active biological objects, which have a detrimental effect, in particular, on tumor cells, microorganisms, etc. [9,29]. In recent years, there have been scientific publications on the use of PDT for the treatment of purulent wounds, which noted the advantages of PDT compared to conventional therapy, in particular, pronounced antibacterial and anti-inflammatory effect. It should be emphasized that the effectiveness of PDT does not depend on the spectrum of sensitivity of microorganisms to antibiotics, it is harmful even for antibiotic-resistant strains of microorganisms [3,9,17,28]. Pathogenic microorganisms do not develop resistance to PDT, while photodynamic damage is local in nature, and the bactericidal effect is limited by the zone of laser irradiation of sensitized tissues, which allows to avoid side effects observed in the application of traditional methods of treatment of surgical infection [16,18].

A number of authors have experimentally proved that the use of photodynamic therapy of purulent wounds of soft tissues is a promising development, which increases the success in the treatment of purulent processes of soft tissues, is pathogenetically and economically justified [9,16,28,29]. Another undeniable advantage of this method is the ease of use and the absence of significant material and physical effort.

It should be emphasized that the use of the above methods of treatment in isolation can not lead to the desired effect, and their combined application could significantly improve the results of treatment of patients with diabetic foot syndrome critical lower limb ischemia.

All of the above determines the relevance of the development of pathogenetically sound methods of treatment that acting on all parts of the pathological process (infection, inflammatory response, critical circulatory decline) could improve the results of treatment in patients with diabetic foot syndrome with signs of critical lower limb ischemia.

3. The Purpose of Research

Creation of pathogenetically substantiated treatment scheme for diabetic foot syndrome with critical lower limb ischemia.

4. Material and Research Methods

The work is based on the data based on the study of the results of surgical treatment of 330 patients with purulent-necrotic lesions of the lower extremities on the basis of diabetes mellitus and critical ischemia, patients were treated, in the Department of purulent surgery of Bukhara state multidisciplinary medical center, during the period from 2011 to 2019. We used the method of stratified randomization of patients. In accordance with the objectives of the study, all patients are divided into 4 groups: (I – control and main II-III-IV). The prevalence of men (71.5%) was noted among the patients. The majority of patients were aged from 42 to 78 years. The first control group consisted of 85 patients with purulent-necrotic lesions of the lower extremities, who underwent a complex of therapeutic measures, including surgical accommodation, antibacterial therapy, infusion, detoxification therapy, drugs that improve microcirculation - angioprotectors, correction of glycemic levels and symptomatic treatment of comorbidities. Local treatment was carried out in the traditional way (ointments on water-soluble polyethylene glycol (PEG) basis-oflomelid). Group II included 82 (49.5%) patients who, in addition to traditional measures (antibacterial, therapy, anticoagulants, local treatment (ointments based on water - soluble PEG-oflomelid), underwent femoral artery catheterization for long-term intraarterial injections of perftoran (registration number B-250-9502414, date of registration RUz 17.01.2014 year) to improve oxygen saturation of tissues of the damaged limb. Group **III consisted** of 83 patients who, in addition to the above complex therapeutic measures, after surgical treatment of a purulent focus, local treatment was supplemented by laser photodynamic therapy (LPT). Local laser PDT was performed as follows: a photosensitizer – 0.05% solution of Mytilene blue belonging to the phenothiazine group (cationic azines) with a maximum absorption λ_{\max} (nm) – 620-670 nm was applied to the wound after washing with antiseptic solutions and drying. with an exposure of 10 minutes. Then, after washing off the wound surface of the photosensitizer, the wound surface was illuminated by laser radiation using the ALT-Vostok mode 03 apparatus. The distance from the end of the fiber to the wound surface was 1.5-5.0 cm in the absence of thermal discomfort in the patient. The total time of irradiation depended on the area of the wound surface and ranged from 10 to 15 minutes. With a large area of the wound, polypositional irradiation of wound surfaces was used (Innovation grant no. I-2014-6-13). **Group IV included 80 patients** who, in addition to the above complex therapeutic measures, underwent femoral artery catheterization for

long-term intra-arterial injections of oxygenated perftoran (registration number B-250-9502414, date of registration RUz 17.01.2014 year) and local treatment was supplemented by laser photodynamic therapy (LPT), that is, both methods of treatment of the studied groups II and III were combined.

In all groups of patients was performed the following interventions: an Autopsy phlegmon of the back and the plantar surface of the foot, the creeping autopsy phlegmon of the leg, amputation of toes, amputation of the foot at Sopara, Sharp, Lisfranc, necrectomy. During surgical treatment of the purulent-necrotic focus, wide access to the purulent-necrotic focus was provided, its adequate drainage, removal of necrotic tissues supporting the infection was performed. Examination of patients included General clinical methods, laboratory methods, instrumental methods of investigation of the arterial bed of the lower extremities (dopplerography, angiography), microbiological studies of wound exudate. Efficacy of tissue oxygen saturation was assessed by tcpo2 determination of wound tissue using transcutaneous oxyhemometer SCI 2. The sensor of the device was installed in the boundary zone between visually determined healthy and pathologically altered soft tissues. Normal values were 45.5 ± 0.50 mmHg.art. All examined patients underwent bacteriological examination of wound exudates. Patients before determining the species composition and sensitivity of the micro flora underwent empirical antibacterial therapy, as well as symptomatic, detoxification therapy.

The dynamics of General and local manifestations of the wound process was assessed by subjective criteria (nature of wound discharge, infiltration resorption, peculiarities of granulation tissue development and epithelialization) and objective indicators (body temperature, General clinical blood analysis, leukocyte intoxication index).

5. Results and Discussion

85 patients included in the I control group, after performing the basic principles of surgical treatment and antibiotic therapy, taking into account the sensitivity of the flora, local application of bandages with water-soluble ointment (oflomelid) was carried out.

The General condition of patients in most cases at admission was moderate or severe. All of them complained of General weakness malaise, pain in the pathological process of the lower limbs, fever to 37.5° - 40° C, dry mouth, sleep disturbance and lack of appetite. Of the local symptoms, moderate or severe hyperemia of the skin around the pathological process on the foot and swelling of the tissues were noted. Palpation was determined painful infiltration, the foot to the touch in all cases without exception was hypothermic, pulsation on the arteries of the foot was sharply weakened or not determined at all. Most patients were admitted to us within 7 to 20 days after the onset of the disease and the first phase of wound flow.

Patients I control group willernie changes of the foot was

presented in the following forms: focal tissue necrosis – 7; necrotic ulcers of the toes – 11; necrotic cellulitis of the foot – 19; Osteoarthropathy in combination with destructive osteomyelitis of foot bones – 4; gangrene of the toes (dry and wet) – 25; Gangrene distal portions of the foot (dry and wet) – 18;. 97.5% of patients had one or more comorbidities, coronary heart disease CHD -21, Postinfarction cardiosclerosis PICS - 17, hypertension - 19, 7 (%) of them had a history of acute cerebrovascular accident. Diabetic retinopathy and nephropathy were detected in 25.5% of patients. All patients before surgical treatment and during treatment were determined partial oxygen tension of tissues around the wound surface.

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 micro flora in the wound exudate were staphylococci, *E. coli* and *Protea*, and among the seeded anaerobes, *Pr* was more common. *melaninogenica* and *Bacteroides* spp. At the same time, the initial level of microbial contamination of wounds in group I patients showed that it averaged 109-10 MT/g. After surgical treatment of the wound with the application of ointment dressing microbial contamination was 105 MT / g, the next day it increased to 107-8 MT/g, 6-7 days of complex treatment in these patients, the degree of microbial contamination was significantly reduced and averaged 105-6 MT / g, and only 12-14 days of treatment, it was below the critical level and amounted to 103 microbial bodies per 1G.tissue.

The studied indicators of intoxication showed that the day of admission body temperature for patients in average was equal to $38.7 \pm 1.1^\circ\text{C}$. the Content of leukocytes in the blood was averaged $12.5 \pm 2.7 \times 10^9 / \text{L}$. the Volume of middle molecules (VMM) were on average equal to 0.185 ± 0.015 units, there was an increase of indicators leukocyte index of intoxication (LII) and erythrocyte sedimentation rate (ESR) to 4.2 ± 1.30 and 42.4 ± 2.1 respectively. On the third day of treatment showed a slight decrease in body temperature (from 38.7 ± 1.1 to $37.8 \pm 0.5^\circ\text{C}$), leucocytes (L) in the blood decreased to an average of $8.0 \pm 0.5 \times 10^9 / \text{L}$. the VMM Level in the blood decreased to an average of 0.165 ± 0.018 units Changes in indicators LII on the third day of treatment, there was a downward trend from 4.2 ± 1.30 to 2.9 ± 0.16 ed, while ESR decreased on average to 38.6 ± 2.2 mm/h To the fifth day of treatment in patients of the control group remained insignificant low-grade fever ($37.5 \pm 0.4^\circ\text{C}$). At the same time, there was a further decrease in the indicators of intoxication: L, VMM, LII and ESR, that is, there was a tendency to normalization.

By 7-9 days of treatment, these indicators, although they tended to further decrease, were higher than normal. So to 12-14 days of treatment all analyzed indicators of intoxication except ESR, normalized. The results of studies of the dynamics of oxygen saturation of TcPO₂ tissues showed that in patients of the control group on the day of admission the initial level of TcPO₂ was 12.5 ± 3.5 mm Hg. against the background of conventional therapy TcPO₂

increased to 17.5 ± 2.5 mm Hg by 3 days. St, by 5 days it was 21.5 ± 3.5 mm Hg. by 7-9 days of treatment TcPO₂ reached values equal to 24.5 ± 2.5 mmHg.art. By 10 days oxygen saturation of wound tissues was 25.5 ± 2.2 mm Hg. even by 12-14 days of treatment, TcPO₂ of wound tissue was still below normal values and was 27.5 ± 1.5 mmHg.CT, that is, the cellular saturation of TcPO₂ was significantly low from normal values. At the same time, in patients of the control group, wound cleansing from infection occurred on average by 12.0 ± 1.5 days. By 7-9 m days there was a resorption of infiltration around the wound. The beginning of the appearance of granulation was noted by 12-14 days, and the beginning of epithelialization only by 19-22 days of treatment. The duration of inpatient treatment was 23.5 ± 3.5 bed days.

Against the background of the complex of measures in 21 (36.0%) patients of the control group, there was a progression of the pathological process and signs of CLLI, in which according to vital indications in 17 (20.0%) patients, amputation of the lower limb at the level of the upper third of the tibia was performed, and 9 (10.5%) cases due to involvement in the pathological process of the tibia and occlusion of the arterial bed in the femoral and iliac segments were forced to resort to high amputations at the level of the middle and upper thirds of the thigh. In 7 (8.23%) patients who underwent minor surgical interventions at the foot level, there was a progression of comorbidities which could not be corrected, and therefore came: acute violation of cardiovascular activity in 3 patients, systemic inflammatory reaction syndrome with the development of septic shock in 2 patients and renal failure on the background of diabetic nephropathy in 2 patients with fatal outcome. Postoperative mortality in patients of the control group who underwent high amputations at the level of the thigh and lower leg was observed in 5 (19.23%) patients. The analysis of the structure of postoperative mortality showed that against the background of anesthesia in 2 patients there was uncontrollable hypotension with profound violations of vital functions of the body, in 2 patients there was pulmonary embolism and in 1 patient there was a progression of signs of multiple organ failure with a fatal outcome. Total mortality in this group was 12 (14.11%) cases.

As it was noted above, the II main group consisted of 82 patients who, in addition to traditional measures, underwent femoral artery catheterization for long-term intra-arterial injections of oxygenated perfitoran to improve oxygen saturation of tissues of the damaged limb. In patients of the main group were performed comparable in volume and nature of surgery as in patients of the control group.

A mandatory procedure in the treatment process was to determine the partial stress of oxygen in the tissues around the wound surface.

The study of the nature of the species composition of wounds of the affected limb showed that the number of species occurrence of aerobic microorganisms in the examined patients of the main group in relation to the number of patients was 140% of observations, and anaerobic

– 87.0%, which was explained, as in patients of the control group by frequent sowing of microbial flora in associations. The study of microbial contamination of wound tissues 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 109-10 MT/g. After surgical treatment of the wound and the beginning of intra-arterial perfusion of oxygenated Perftoran, there was a significant decrease in microbial contamination of wounds and by the 3rd day of treatment it averaged 105-6MT / g, and by 4-5 days of treatment microbial contamination in the wound on average decreased to 103 microbial bodies per 1G of tissue and below.

The analysis of the degree of endotoxemia in patients of the main group in the treatment process, showed that by the third day of treatment was a decrease in body temperature (from $39.0 \pm 1.2^\circ\text{C}$ to $37.5 \pm 0.5^\circ\text{C}$), leucocytes in blood decreased on average to $9.0 \pm 1.5 \times 10^9 / \text{L}$. the VMM Level in the blood decreased to an average 0.155 ± 0.018 units. Changes in indicators LII on the third day of treatment, there was a downward trend from 4.5 ± 1.50 to 2.5 ± 0.15 units, while ESR declined to an average of 27.5 ± 2.5 mm/h. By the fifth day of treatment in the examined patients of the main group normalization of the temperature curve ($36.8 \pm 0.4^\circ\text{C}$) was noted. At the same time, there was a further decrease in the indicators of intoxication: L, VMM, LII and ESR, that is, there was an earlier trend towards normalization than in patients of the control group. The study of tissue oxygen saturation showed approximate identity, that is, on the day of admission to the hospital TcPO₂ of wound tissue was 12.5 ± 1.7 mmHg.art. After the beginning of long-term intra-arterial perfusion of perftoran, there was a rapid improvement in tissue oxygen saturation, which increased to 25.5 ± 3.5 mmHg on the first day on the background of complex treatment with perfusion of perftoran by 3 days TcPO₂ increased to 34.5 ± 3.5 mmHg.St and by the 5th day of treatment there was a restoration of oxygen tension in the wound tissues, which was 40.5 ± 1.4 mmHg.art. In patients of the analyzed group, wound cleansing from infection occurred on average by 5.0 ± 1.0 days, in parallel, there was a resorption of infiltration around the wound. The onset of granulation was noted to 8-9 m days, and the beginning of epithelialization to 12-14 days of treatment. The duration of inpatient treatment was 14.5 ± 1.5 bed days.

Against the background of the complex of measures carried out due to the depth of purulent necrotic limb lesions in 9 (10.9%) patients of group II, there was a progression of the pathological process and signs of CLLI, in which, according to vital indications, 5 (6.1%) patients underwent amputation of the lower limb at the level of the upper third of the Shin, and 4 (4.87%) cases were forced to resort to high amputations at the level of the middle and upper thirds of the thigh. In 3 (3.7%) patients who underwent minor surgical placement at the level of the foot, there was a progression of multiple organ failure ended with a fatal outcome. Postoperative mortality in patients of the main group who underwent high amputations at the level of the thigh and

lower leg was 2 (2.43%), the cause of which in one case was pulmonary embolism, and in the other acute cardiovascular insufficiency. Total mortality in this group was 6.13% of cases.

Comparative analysis of the complex treatment of patients of the control and II groups showed that if the patients of the control group microbial contamination of wounds persisted for quite a long period of time and only by the 10th day of treatment, this indicator fell below the critical level, while in patients receiving intraarterial infusions of oxygenated Perftoran by 3-4 days of treatment, microbial contamination in the wound on average decreased to 103-4 microbial bodies per 1G of tissue and below. In patients of the control group, even by 12-14 days of treatment, there was no significant recovery Of tcpo₂ oxygen saturation of wound tissues (27.5 ± 1.5 mm Hg.art.), while in patients of the main group normalization of oxygen saturation TcPO₂ of wound tissues was noted already by 5 days of treatment amounting to 40.5 ± 1.4 mmHg.art. the Use of intra-arterial injections of Perftoran in complex treatment of patients with purulent-necrotic lesions of lower extremities in diabetes mellitus and CLLI helped complete cleansing wounds from infection already on day 5 of treatment. By this time, there was an active resorption of infiltration around the wound, granulation began to appear to 8-9 m days of treatment, and epithelialization began to 12-14 m days. Studies have revealed a significant advance of these indicators in group II for 3-5 days, compared with group I. The average duration of treatment decreased from 23.5 ± 3.5 to 14.5 ± 1.5 bed days. Application in the complex treatment of perfusion of perftoran in patients of the main group led to a sharp decrease in the number of cases of progression of the pathological process and critical ischemia, which was observed only in 9 (10.9%) patients while in the control group they were much higher and amounted to 21 (36.0%), in which a high amputation of the lower limb at the level of the upper third of the Shin and thigh was performed. Despite the complex of therapeutic measures mortality in patients of the control group was 14.11% while in patients of the main group there was a sharp decrease in the number of deaths that amounted to 6.13% of the total number of treated patients.

The study of the results of group III studies (83 patients), which after surgical treatment of purulent foci, local treatment was supplemented by LFTT showed that upon admission to the hospital in all patients, as in the previous groups, there were signs of intoxication of varying severity, as evidenced by changes in the leukocyte formula and an increase in the leukocyte index of intoxication (LII) to 5.2 ± 0.5 .ed. Bacteriological studies revealed that the main microorganisms that made up the microbial landscape of wounds were: *S. aureus*, *S. epidermidis*, *Ps.aeruginosa*, and representatives of the family Enterobacteriaceae-Klebsiella, *Proteus*, *Enterobacter cloacae* and the family Bacillaceae. It should be noted that in most cases the flora of purulent wounds were represented by microbial associations. The study of antibiotic sensitivity of isolated strains revealed that they all had polyvalent resistance to many antibacterial drugs.

High levels of bacterial contamination of wounds 109-10 CFU/ml were detected in the study group of patients prior to treatment.

Comparative analysis of the results carried out in patients first and control and III groups showed that if the initial level of microbial contamination of wounds and patients in the control group were 109-10 MT/y, after the debridement and the beginning of the local LVDT indicators of microbial contamination of the wounds was as follows: on the 3rd day of treatment of microbial contamination of the wounds averaged 103 -104 CFU/ml, 5 –days 102 -103 CFU/ml, at 6-7-day treatment crops of wound exudate for microbial growth is not allowed. The analysis of the degree of endotoxemia in patients of the main group in the treatment process, showed that by the third day of treatment was a decrease in body temperature (from $39.0 \pm 1.2^\circ\text{C}$ to $37.5 \pm 0.5^\circ\text{C}$), leucocytes in blood decreased on average to 8.0 ± 1.5 109 /L. the VMM Level in the blood decreased to an average of 0.160 ± 0.017 units Changes in indicators LII on the third day of treatment, there was a downward trend from 5.2 ± 0.5 to 2.0 ± 0.25 units, while ESR declined to an average of 23.5 ± 2.5 mm/h. By the fourth day of treatment, the examined patients of the main group III showed normalization of the temperature curve ($36.8 \pm 0.4^\circ\text{C}$). At the same time, there was a further decrease in indicators of intoxication: L, VMM, LII and ESR of blood, that is, there was an early tendency to normalization than in patients of the control group.

The study of tissue oxygen saturation showed approximate identity, that is, on the day of admission to the hospital TcPO₂ of wound tissue was 12.5 ± 1.5 mmHg.art. the start of LFTT, some improvement in tissue oxygen saturation was noted, which increased to 18.5 ± 2.5 mmHg on the first day. on the background of complex treatment with the use of TcPO₂ increased To 24.5 ± 3.5 mm Hg by 3 days to 5 days of treatment oxygen tension in wound tissues was 27.5 ± 1.4 mmHg.art. In patients of the analyzed group, wound cleansing from infection occurred on average to 2.5 ± 1.0 days, in parallel, there was a resorption of infiltration around the wound. The onset of granulation was noted by 7 days, and the beginning of epithelialization by 10 days of treatment. The duration of inpatient treatment was 15.5 ± 1.5 bed days.

On the background of laser photodynamic therapy in patients III main group only 7 (8.43%) patients experienced progression of the pathological process of the foot, the cause of progression served as a critical ischemia of the lower limbs in connection with multilevel atherosclerotic lesions of the arteries of the limb. High amputations were performed in all patients for life indications, including 4 (4.81%) patients with myoplastic amputation at the level of the upper third of the Shin and 3 (3.61%) patients with amputation at the level of the upper third of the thigh. In 3 (3.61%) patients with progressive signs of multiple organ failure, cardiac arrest was observed leading to a fatal outcome.

Comparative analysis of the results of complex treatment of pyo-necrotic lesions of the foot in diabetes mellitus

showed that the use of laser photodynamic therapy helps to reduce the time of wound cleansing from infection by 1.5-2 times, accelerate the normalization of signs of intoxication and rapid relief of local edema, infiltration in the region of wound edges.

It should be emphasized that the use of the above methods of treatment of the examined groups in an isolated form could not lead to the desired effect, and therefore we have decided to use complex perfluorocarbons and LFTT.

As mentioned above, the IV –main group consisted of 80 patients who, in addition to the above complex therapeutic measures, catheterization of the femoral artery for long-term intra-arterial injections of oxygenated perfuran was performed, as well as local treatment was supplemented by laser photodynamic therapy (LFTT), that is, both methods of treatment of the studied II and III groups were mixed. All patients on severity of a condition, prevalence of the pathological center were comparable to the previous groups.

Analysis of the results of complex treatment of patients with IV –basic groups showed that the initial level of microbial contamination of wounds and in patients with previous groups were 109-10 MT/yr After the debridement, the session LVDT and the start of intra-arterial perfusion of Perftoran there was a significant decrease in microbial contamination of wounds and by 2 days of treatment averaged 103-4 MT/y to 3 days of treatment of microbial contamination in the wound the average decreased to 103 microbial cells in 1g. tissue and below.

Analysis of the degree of endotoxemia in group IV patients during treatment showed that by the second day of treatment there was a decrease in body temperature (from $39.0 \pm 1.5^\circ\text{C}$ to $37.2 \pm 0.5^\circ\text{C}$), the content of leukocytes in the blood decreased to an average of 8.5 ± 1.5 109 /l. the level of VMM in the blood decreased to an average of 0.152 ± 0.018 units. Changes in LII indicators on the third day of treatment tended to decrease from 5.3 ± 1.50 to 2.4 ± 0.15 units, while ESR decreased to an average of 25.5 ± 2.5 mm/h. by 4-5 days of treatment in the examined patients of group IV normalization of the temperature curve ($36.8 \pm 0.4^\circ\text{C}$) was noted. At the same time, there was a further decrease and normalization of indicators of intoxication: L, VMM, LII and ESR of blood. The study of indicators of tissue oxygen saturation showed approximate identity with those of group II patients, that is, on the day of admission to the hospital TcPO₂ of wound tissue was 12.5 ± 1.5 mmHg. after the beginning of long-term intraarterial perfusion of perftoran, there was a rapid improvement in tissue oxygen saturation, which increased to 25.8 ± 3.7 mmHg on the first day.art. Against the background of the complex to 3 days TcPO₂ increased to 35.5 ± 3.5 mm Hg.art and by 5 days of treatment, oxygen tension was restored in the tissues around the wound, which was 41.5 ± 1.5 mmHg.art in patients of the analyzed group, as noted above, wound cleansing from infection occurred on average by 2.0 ± 0.5 days, in parallel, there was a resorption of infiltration around the wound. The onset of granulation was noted by 7 days, and the beginning of epithelialization by 9 days of treatment. The duration of

inpatient treatment was 12.5 ± 1.5 bed-days.

Against the background of the complex of therapeutic measures, only 5 (6.25%) patients of group IV noted the progression of the pathological process and signs of CLLI, in which, according to vital indications, 3 (3.75%) patients underwent amputation of the lower limb at the level of the upper third of the Shin, and 2 (2.5%) cases were forced to resort to high amputations at the level of the middle third of the thigh. Postoperative mortality was observed in 2 (2.5%) patients in one case the cause was pulmonary embolism, and in the other the progression of signs of organ failure with uncontrolled hypertension.

6. Conclusions

1. With traditional methods of treating diabetic foot syndrome with critical lower limb ischemia, cleansing the wound from infection, the healing processes and restoration of normal tissue oxygen saturation are not fast enough.
2. The use of prolonged intra-arterial therapy (PIAT) with oxygenating perfusion of perftoran in 24-48 hours in the complex treatment of DFS with CLLI stimulates reparative processes, restoring partial tension of oxygen in the tissues of the affected lower limb, pathogenetically creates favorable conditions for reducing the amount of progression of purulent-necrotic processes in the lower extremities related critical ischemia that turn to reduce the high numbers of forced amputations from 36% to 10.9% and mortality from 14.11% to 6.13% of cases, the average duration of treatment is reduced from 23.5 ± 3.5 to 14.5 ± 1.5 bed days.
3. The use of local photodynamic therapy in complex treatment of purulent-necrotic pathologies of the foot in diabetes helps to reduce the time of cleansing wounds from infection, as a pathogenetically justified and economically improves the success of treatment, however, the use of this technique in isolation, with concomitant critical ischemia of the lower limbs of necrotic lesions of the foot is poor.
4. The combined use of perfluorocarbons and local LPT contributes to the simultaneous impact on all parts of the pathological process, which leads to improved results of complex treatment, reducing the number of forced high amputations from 36% to 6.25% and mortality from 14.11% to 2.5% of cases compared to the control group, while the average duration of treatment is reduced from 23.5 ± 3.5 to 12.5 ± 1.5 bed days.

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