https://doi.org/10.46389/rjd-2021-1021
www.rjdnmd.org

Rom J Diabetes Nutr Metab Dis
2021; volume 28, issue 2, pages 131-136

Original Research

Complex treatment of patients with complicated syndrome of diabetic foot and sepsis

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Received: 6 January 2021 / Accepted: 18 February 2021

Abstract

Introduction: Efforts to improve survival in sepsis are based on a series of urgent medical interventions. The article presents the data obtained in the process of complex treatment of patients, in which sepsis was caused by complicated diabetic foot syndrome. **Materials and Methods:** The article presents materials on the retrospective study of treatment results of 1678 patients with complicated diabetic foot syndrome. In 146 patients (8.7%) the disease was burdened with sepsis. **Results:** A common feature of the treatment strategy for patients in both groups was surgical intervention, the administration of antibiotic therapy (ABT) and infusion-transfusion therapy. With the help of developed algorithms, it was managed to improve the results of septic patients' treatment. **Conclusions:** The applied tactics of treating patients with sepsis has allowed to reduce the frequency of execution of high amputations and postoperative complications, increase the number of "small" amputations, which led to a reduction in mortality, shortening the length of patients' stay in the hospital.

Keywords: amputation, antibiotic therapy, diabetic foot syndrome, sepsis

Introduction

At the beginning of the new century, purulent-inflammatory processes in patients with diabetes and sepsis remain one of the most pressing and unresolved problems of modern medical science. With the development of sanitary and hygienic measures, development and implementation of new antibacterial drugs, the incidence curve has come gone down. On the contrary, there is a tendency to the increase of sepsis incidence [1, 5, 10].

Surgical complications of diabetes mellitus, namely purulent-necrotic lesions of the tissues of the foot are among the most common pathologies in the clinics of purulent-septic surgery. Since about 8–12% of patients with sepsis are with impaired carbohydrate metabolism. The features of diagnosis and treatment of sepsis in patients with complicated DFS (diabetic foot syndrome) is a significant medical problem. Unsatisfactory results of treatment of complicated DFS require a comprehensive multidisciplinary approach to solving this problem [8, 9, 19, 20].

It is known that without elimination of the center of a purulent infection in patients with sepsis the most powerful intensive care is doomed. An equally important component

that ensures the success of treatment is a full infusion-transfusion and inotropic support [4, 15, 17]. The latter statement is embodied in the "Sepsis-3" guidelines [2, 3, 6, 7, 11–14, 16, 18].

The aim of the work

The article is aimed to improve the treatment results of patients with purulent-necrotic lesions of the tissues of the foot and sepsis on the background of complicated DFS.

Materials and Methods

Under our examination and treatment from 2010 to 2020 there were 1678 patients with complicated DFS, who were in a purulent-septic center with beds of diabetic foot in the nonprofit municipal enterprise "City Hospital № 3" in Zaporizhzhia (Institute of Sepsis of SI "Zaporizhzhia Medical Academy of Postgraduate Education of the Ministry of Healthcare of Ukraine") (Department of outpatient, purulent-septic surgery and ultrasound). In 146 patients (8.7%) the disease was aggravated by sepsis.

The definition of "complicated DFS" combines purulent-necrotic lesions of the foot-ulcers, abscesses, phlegmon, purulent tendovaginitis, purulent arthritis, gangrene, as well as diabetic osteoarthropathy.

The patients were divided into two clinical groups:

1. The first group (comparison group) included 724 patients with complicated DFS who received treatment for the period from 2010 to 2016 (beginning). In 71 patients the disease was aggravated by sepsis – they formed the 1 subgroup.
2. The second (main) group consisted of 954 patients (with 75 cases of sepsis included into the 2 subgroup) who were treated during 2016–2020.

Patients in both groups had type 2 diabetes, the average duration of which was (12.4 ± 2.3) years.

Criteria for inclusion in the study: type 2 diabetes, the presence of complicated DFS with purulent-necrotic processes of the tissues of the foot.

Exclusion criteria: type 1 diabetes, DFS with intact skin (stage 0 according to the Wagner classification), patients on hemodialysis.

Certain difficulties arose in the gradation of patients with sepsis, as according to the "Sepsis-3" guidelines the concept of "severe sepsis" is excluded. All cases of sepsis were carefully analyzed according to the new bedside clinical indicator of gSOFA, which is characterized by a respiratory rate of more than 22 per 1 min., impaired consciousness (Glasgow coma scale) and an average blood pressure of 100 mmHg or less. With the help of above said indicators, patients of subgroups 1 and 2 were randomized.

Determination of the qualitative composition of the flora and the sensitivity of the selected cultures to antibiotics was performed automatically (Vitek 2 Compact – France). The technical capabilities of the method allowed to perform the identification of aerobic and facultative anaerobic microorganisms, in addition to non-spore-forming anaerobic microorganisms, as well as to detect the presence of the MRSA gene.

Thus, 57 (80.3%) patients with sepsis and 14 (19.7%) with septic shock (SS) were assigned to subgroup 1, and 53 (69.3%) patients with sepsis and 22 (30.7%) with septic shock – subgroup 2. Statistical data processing was performed taking into account the principles of evidence-based medicine, calculations were performed using a software package for statistical data analysis "STATISTICA 6.1".

Research Results

Common features of the treatment strategy for the patients of both groups were surgery, antibiotic therapy (ABT) and infusion-transfusion therapy.

Patients underwent various surgical interventions: necrectomy, necro- and sequestrectomy, dissection of abscesses and phlegmon,

https://doi.org/10.46389/rjd-2021-1021

amputation of fingers, feet and limbs. Extensive opening of the purulent center, excision within viable tissues and drainage during deep purulent-necrotic processes were performed. The amputation of the foot according to Shopar was preferred in common purulent-inflammatory lesions of the foot with the involvement of several toes. Further treatment of wounds was performed using modern dressings depending on the stage of the wound process. Criteria for assessing the effectiveness of treatment from the postoperative wound were: the speed of wound healing, maintaining the lower limb support ability, the number of repeated surgical interventions, the presence of certain complications. The average length of patients' stays in the hospital, general and postoperative mortality were also taken into account.

In the comparison group, wound cleansing and the appearance of the first granulations were recorded at (6.3 ± 0.23) days, in the main group, wound cleansing occurred at a faster rate – at (5.7 ± 0.21) days ($p < 0.05$).

In most cases, patients with sepsis had wet gangrene of the lower extremity. Therefore, they were performed high amputations at the level of the thigh on vital signs in an urgent manner. In patients with sepsis in middle age, amputations were performed at the level of the upper third of the tibia (according to Burgess). Successful implementation of this operation reduces postoperative mortality and creates opportunities for prosthetics and improvement of life quality. Burgess amputation at the level of the tibia (4 patients of subgroup 1 and 7 patients of subgroup 2) preserves the knee joint and increases the chances of successful prosthetics compared to amputation at the hip level. It is not advisable to perform amputations in this group of patients at a lower level of tibia.

The anterior and posterior skin and muscle flaps were excised. The length of the front was 2 cm, the back – up to 15 cm. The stump of the tibia was made 12–13 cm long, and the fibula was 5 cm longer than the level of the tibia. One of the main stages of the operation was considered the excision of the soleus muscle. Muscle removal was performed due to impaired blood flow and frequent complications in the form of necrosis of the latter. The superficial fascia of the calf muscles was sutured to the tibial bed and the medial periosteum of the tibia. The posterior flap was moved anteriorly to the rounded end of the tibial stump and sutured with a short anterior flap. The postoperative wound was drained by active aspiration.

High amputation was performed at the level of the middle or upper third of the thigh according to Pirogov or fascio-plastic method, with cutting of two skin-fascial flaps and active drainage of the postoperative wound.

These operations were effective because the septic process did not progress.

Verification of the etiological structure of the foci of infectious-inflammatory process in patients with purulent-inflammatory processes of the foot of diabetics and sepsis is a significant problem at the present stage, which is confirmed by numerous domestic and foreign scientific publications. Therefore, the microbiological characteristics of the bacterial flora of purulent-necrotic foci in patients with complicated DFS and sepsis are the basis for the formation of a program of rational ABT and assessment of the wound process.

ABT in patients with complicated DFS and the development of sepsis should provide the maximum therapeutic effect with minimal impact on the body of a patient suffering from severe comorbidities.

Technological features of antibacterial therapy:

- empirical ABT should be performed before obtaining the result of microbiological research, its effectiveness depends on the correct choice of drug and its effect on all potential pathogens;
- directed ABT can be assigned only after receiving the results of seeding. If necessary to re-correct ABT taking into account the selected microflora and its sensitivity to antibacterial drugs;
- targeted ABT was performed in a short course (10–12 days) to obtain a clear clinical result;
- in severe infection with sepsis, the duration of ABT is 2–4 weeks, and in the presence of osteomyelitis it can be increased to 6 weeks.

Infusion therapy (IT) in patients with DFS was started immediately in patients with hypotension or organ hypoperfusion. It was one of the primary measures to support hemodynamics and, above all, cardiac output.

In patients with sepsis and septic shock (SS), the approach to infusion therapy has slightly changed. Infusion therapy was regarded as a first-line intervention to restore systemic hemodynamics and increase oxygen delivery to meet the needs of septic patients.

Septic patients with insufficient tissue perfusion, hypotension, or signs of hypovolemia received an initial fluid volume of 30 mL/kg body weight of crystalloid solutions during the first 3 hours of resuscitation, followed by infusion under systematic monitoring of the patient's hemodynamic status. One of the targets was mean arterial pressure (MAP)≥65 mmHg. Another target was the normalization of arterial lactate concentration.

Despite the conduct of IT in patients of both groups, inotropic support is important in the stabilization of hemodynamic parameters, which provides, along with limiting hemodynamic disorders, an adequate level of tissue perfusion. Drugs that provide inotropic support include epinephrine, norepinephrine, dopamine and dobutamine.

After the start of IT, the volume of subsequent infusion was determined depending on the patient's hemodynamic status.

After 72 hours (deescalation or "deresustation" phase), which usually occurs in 96 hours or after restoration of hemodynamic stability, attempts were made to achieve a negative fluid balance or to limit intravenous intensive care, or to increase fluid excretion through diuresis activation.

Thus, the monitoring of intensive care was as follows: blood pressure and heart rate (at normal values) – no indications for massive infusions; daily fluid balance (close to zero during admission to the intensive care unit); central venous pressure is no longer considered an informative indicator; determination of saturation of mixed venous blood with oxygen ($ScvO_2$) and lactate (at normal values) – no indications for massive infusions.

The most reliable test is to determine the reactivity of the organism to the introduction of fluid (organisms that respond and do not respond). A bolus of 500 mL of isotonic crystalloid is administered: if cardiac output and stroke volume increase by 13–15%, the infusion should be continued, if not vasopressors and cardiotonics are indicated.

Discussion

There are no unambiguous criteria for discontinuation of ABT (decision-making is based on the dynamics of local and systemic inflammatory response, wound condition, eradication of pathogens, the degree of contamination of the wound, normalization of leukocyte formula, C-reactive protein, decreased procalcitonin).

Here are the schemes of antibiotics: levofloxacin – intravenously, 0.5 g 2 times a day + metronidazole, intravenously, 0.5 g three times a day; piperacillin / tazobactam – intravenously, 4.5 g 3–4 times a day; cefaperazone / sulbactam – intravenously, 4.0 g 2 – 3 times a day; ceftaroline – intravenously, 0.6 g 2 times a day; ertapenem – intravenously, 1.0 g 1 time per day; imipenem / cilastatin - intravenously, 0.5 – 1.0 g three times a day; meropenem – intravenously, 1–2.0 g three times a day. Diagnosis of septic shock requires the appointment of imipine / cilastatin 1.0 g 4 times a day intravenously or meropenem 2.0 g 3–4 times a day intravenously + linezolid 0.6 g 2 times a day intravenously or vancomycin 15 mg / kg 2 times a day.

The administration of intensive infusion-transfusion therapy and inotropic support in patients with sepsis under the "Sepsis-3" guidelines helped to stabilize the condition of patients and prepare them for surgery. Out of 30 patients from the secondary comparison group, 8 (27.7%) patients who did not undergo surgery died. In the main group – 3 (18.8%) patients respectively. Thus, mortality in patients with SS, who were not operated, decreased by 8.9% (χ^2 = 5.63; $p < 0.0177$).

Introduction of optimized methods of purulent-necrotic processes treatment in patients with complicated DFS allowed to reduce

https://doi.org/10.46389/rjd-2021-1021

the number of repeated surgical interventions from 26.4 to 20.9% ($p < 0.05$), increase the number of organ-saving operations ($\chi^2 = 5.93$; $p < 0.0149$), to maintain the capacity of the lower extremity in 92.4% of cases in the main group against 82.3% in the comparison group ($\chi^2 = 5.70$; $p < 0.0169$), to reduce the average duration of treatment in the hospital by 4.7 ± 0.24 days ($t = 4.36$; $p < 0.05$).

Conclusions

1. The introduction of the proposed complex therapy, allowed to influence the final indicators of treatment: to reduce mortality in patients with sepsis from 36.1% (13 patients) in the comparison group to 8.3% (3 patients) in the main group ($p < 0.05$), and in septic shock from 72.7% (16 patients) to 56.3% (9 patients) accordingly.
2. Analysis of the obtained data shows that the application of the developed treatment algorithms allowed to significantly ($p < 0.05$) reduce the frequency of high amputations and postoperative complications, increase the number of "small" amputations, maintain the lower limb support ability, which led to reduced mortality and reduced duration of patients' stay in a hospital.

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Ethic Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of Interest

The authors declare no conflict of interest.

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https://doi.org/10.46389/rjd-2021-1021