NOVATEUR PUBLICATIONS
JournalNX- A Multidisciplinary Peer Reviewed Journal
ISSN No: 2581 - 4230
VOLUME 8, ISSUE 10, Oct. -2022

A NEW APPROACH TO THE TREATMENT OF SEPSIS IN PURULENT-NECROTIC COMPLICATIONS OF DIABETES MELLITUS

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ABSTRACT
The article analyzes the work carried out to create a new algorithm for the diagnosis and complex treatment of sepsis in patients with purulent-necrotic complications of diabetes mellitus. In the departments of purulent surgery of the ASMI clinic and the regional adult health center of Andijan region, 180 patients with purulent-necrotic complications of diabetes mellitus underwent a study where tasks were set to create a new step-by-step algorithm for the diagnosis and complex treatment of sepsis in patients with purulent-necrotic complications of diabetes mellitus.

Keywords: Sepsis, diabetes mellitus, purulent-necrotic process.

НОВЫЙ ПОДХОД К ЛЕЧЕНИЮ СЕПСИСА ПРИ ГНОЙНО-НЕКРОТИЧЕСКИХ ОСЛОЖНЕНИЯХ САХАРНОГО ДИАБЕТА

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Аннотация:
В статье анализируется работа проведенная с целью создания нового алгоритма диагностики и комплексного лечения сепсиса у пациентов с гнойно-некротическими осложнениями сахарного диабета. В отделениях гнойной хирургии клиники АГМИ и областного центра

здоровья взрослых Андижанской области 180 пациентов с гнойно-некротическими осложнениями сахарного диабета прошли исследование, где были поставлены задачи по созданию нового пошагового алгоритма диагностики и комплексного лечения сепсиса у пациентов с гнойно-некротических осложнений сахарного диабета.

Ключевые слова: Сепсис, сахарный диабет, гнойно-некротический процесс.

The term "sepsis" was introduced into medicine by Aristotle and is characterized by severe blood poisoning by the products of putrefaction of the body's own tissues, Currently sepsis means that sepsis is an organ dysfunction induced by infection. The course of septic infection is localized infection (primary locus) + systemic inflammatory reaction syndrome (SIRS) (T >38°C or 12 x109/L or 20/min; heart rate >90/min)+Sepsis + PON* (SOFA scale) (ODN, OPN, OPecN, impaired consciousness, OSN, thrombocytopenia) + Septic shock: refractory hypotension – ADsr. < 65 mmHg, despite the infusion of catecholamines, and violation of tissue perfusion – lactate > 2 mmol /l, despite the replenishment of BCC this is the concept of sepsis according to Sepsis-3 [13,14]. The disease is characterized by progressive spread of bacterial, viral or fungal microflora in the body, or poisoning of the body with their toxins [1,3,6,11].

Sepsis can occur acutely, sometimes almost instantly (when, in the absence of proper treatment, death occurs within a few hours or days), or chronically. Currently, the nature of the course of sepsis is largely changing as a result of early antibacterial therapy. Despite the high development of methods of antibacterial therapy, the incidence of sepsis tends to increase, and mortality from this pathology averages 45-50%[2,5,6]. In the USA, up to one million people get sepsis every year and 28-42% of these patients die, this figure also corresponds to the CIS countries – in Russia, Uzbekistan, Belarus, mortality is up to 34-40%, and up to 90% of patients die from septic shock [13,14]. The revision of the opinion on the frequency of sepsis, which arose thanks to the efforts of the French scientist R.Bone in 1991-1992 of the conciliatory conferences of sepsis specialists of the world led to a rapid increase in these indicators, in addition, it gave us the opportunity to look at in addition, it gave us the opportunity to look at this problem more broadly and use all possible methods of treatment in our arsenal [3,6]. New methods and comprehensive programs have been developed for the diagnosis and treatment of sepsis, especially in patients with purulent-septic complications in diabetes mellitus, which in our opinion are considered manifestations of sepsis [4,5,6,11]. Sepsis is a disease characterized by the progressive spread of bacterial, viral or fungal flora in the body and poisoning of the body with their toxins. Especially the role of toxins in the development of sepsis has been important recently, when the cytokine theory in the pathogenesis of sepsis development, proposed by J.Ertel in 1982, is developing. According to this author, under the action of bacterial exo- and endotoxins of the body, biologically active substances are produced. Endotoxin is a polymer whose biological activity is largely dependent on its lipid component (lipid A) and the concentration of one of the serum proteins, the so-called lipopolysaccharide binding protein. Only in the form of a complex with this protein, endotoxin is able to interact with a specific receptor located on the surface of macrophages [5,6,9,12,13]. The interaction of the complex with the receptor apparatus of macrophages is accompanied by the activation of macrophages and the synthesis of a group of proteins, the so-called anti-inflammatory cytokines (TNF - tumor necrosis factor - alpha, interleukin-1, interleukin-6, interleukin-8, some growth and cell differentiation factors - colony-stimulating factors, etc. .). These cytokines have a wide range

of biological effects, manifested in various changes in metabolism, leukopoiesis and hematopoiesis, properties of the endothelium of the vascular wall, the function of regulatory humoral systems, and primarily the central nervous system [13,14,15]. In the last decade, close attention has been paid to the cytokine system as the basis of the pathophysiological mechanism of sepsis, the principles of functioning of this system and the possibility of its regulation have been studied [5,6,7].

It should be noted that, according to many scientists, damage to the vascular endothelium is the main cause of the development of multiple organ failure of the body, which leads to an increase in deaths in patients with sepsis. The mechanism of endothelial lesions of the vascular wall is complex: the appearance of microbial cells in the blood stream activates the blood coagulation system. The complement system, blood cells, primarily macrophages and neutrophils, are activated, which is accompanied by the synthesis and release of a wide range of biologically active substances. Activation of neutrophils and platelets, an increase in their adhesive properties, degranulation and release of oxygen radicals lead to profound toxic changes and the appearance of their own toxic proteases. The strongest irritation of the body under the action of large doses of microbial toxins and endotoxins leads to the activation of the macrophages themselves and is accompanied by the release of biologically active compounds: cytokines, platelet activating factor, colony stimulating factors, TNF - tumor necrosis factor - alpha, metabolites of the arachidonic acid cycle, tramboxane A2, prostaglandins, leukotrienes. There is an activation of T-lymphocytes with the release of interleukin-2, gamma-interferon. These factors cause disturbances in humoral regulation or direct damage to the endothelium. The clinical manifestation of all these processes is a generalized inflammatory reaction and sepsis [5,6,7,13,14,15].

It should be noted that gram-negative microorganisms are very common causes of the development of a common surgical infection of a severe course and the frequent development of fulminant, septic shock types of sepsis, and multiple organ disorders occur with particular speed in sepsis, which is caused by a significantly higher (more than 2 times) mortality in population studies. [6,9,12].

Sepsis caused by gram-positive flora begins slowly, proceeds classically, from the very beginning is accompanied by the development of a pronounced inflammatory component, is prone to abscess formation and permanent long-term course with the gradual development of multiple organ failure. In order to create a new algorithm in the diagnosis and complex treatment of sepsis in patients with purulent-necrotic complications of diabetes mellitus, we conducted the present study.

We were tasked to create a new algorithm in the diagnosis and complex treatment of sepsis in patients with purulent-necrotic complications of diabetes mellitus, to determine the steps of the algorithm for the application of complex treatment of sepsis and to determine changes in the indicators of cellular and humoral protection of the body in patients with diabetes mellitus.

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Material and methods. In the departments of purulent surgery of the clinic of the ASMI and the regional adult health center of the Andijan region, 180 patients with purulent-necrotic complications of diabetes mellitus were examined. These patients were - diabetic foot - 120 patients, necrotic phlegmon of soft tissues - 40 patients, Fournier's disease - purulent-necrotic fusion of the tissues of the

scrotum and perineum - 10 patients and putrefactive processes in the postoperative period - 10 patients. These patients were divided into three groups:
40 patients received traditional treatment;
40 patients received complex treatment;
100 patients received complex treatment with phased rehabilitation.
Patients underwent general clinical blood and urine tests, studies of biochemical parameters, the dynamics of daily changes in blood sugar, the identification of pathogens of purulent-necrotic processes by crops and wound discharge, as well as cellular indicators (leukocyte intoxication index (IL), phagocytic activity of leukocytes (FAN) , the indicator of phagocytosis completion - PZF) and humoral (determination of blood cytokine indicators) reactivity, which are indicators of the degree of inflammatory response, the body's immune response and the reaction to the introduction of foreign antigens.
Laboratory studies in patients with sepsis before treatment showed that, in all patients, secondary, toxic anemia of moderate to severe severity, hypoproteinemia, hypoalbuminemia, protein dysproteinemia due to hypergammaglobinemia, a significant decrease in the indicators of cellular reactivity of FAN, IL, PZF. The main indicators of the inflammatory response, changes in blood cytokines in the form of interleukins - IL-1α, IL-2, IL-4, IL-6, IL-8 and tissue damage factor TNF-α underwent corresponding changes.
Patients who received conventional treatment, who underwent standard short-term preoperative therapy, including intravenous and intramuscular administration of broad-spectrum antibiotics, at least two synergistic types of antibiotic, taking into account the determination of the sensitivity of microorganisms from the wound to the actions of the antibiotics used. When using antibiotics, we acted on the principle of rational antibiotic therapy, which characterizes the use of antibiotics in the appropriate dose and time interval of their use. Detoxification of the body was carried out using detoxification agents before hemosorption. Vitamin therapy was also used, the second group of 20 (52.6%) patients, along with antibiotic therapy, underwent complex conservative infusion ion therapy 5-8 days before surgery, including antiplatelet, protein, antioxidant, membranotropic, immunocorrective, detoxification, vitamin therapy. Membranotropic therapy consisted of tocopherol acetate (200-300 mg intramuscularly), Essentiale (10.0 ml per 200 ml of 5% glucose solution intravenously), rheosorbilate 250.0 each, ascorbic acid (10.0 ml each 250 ml 5% - th solution of glucose 2-3 times intravenously with insulin). Detoxification therapy included infusions of 5% glucose solution with insulin and saline solutions, additional forced diuresis. For disaggregate therapy, chimes (0.15 g/day), trental (0.5 g/day), reopoliglyukin intravenously drip (400 ml/day) were used in courses of 3-4 days. Correction of immunological disorders was carried out by the introduction of immunoglobulin, T-activin, specialy highly immunized gamma-globulins and antistaphylococcal plasma. Vitamin therapy was carried out with the introduction of vitamin C, vitamins A and B. In both groups (control and main), active surgical treatment of the primary purulent focus of sepsis, as well as some septicopyemic secondary foci, and external drainage of purulent cavities were performed. Subsequently, rehabilitation measures were taken in patients of both groups to restore the impaired functions of organs and systems.

Results and Discussion

As a result of the application of a complex of therapeutic measures for surgical sepsis in patients with diabetes mellitus, the stages of treatment algorithms developed by us resulted in the following results: clinical manifestations of sepsis in the form of signs of deep intoxication of the body proceeded more smoothly, no manifestations of encephalopathy were observed, consciousness was not lost, thermometry indicators were 39.3 ± 0.4°C, while in patients of the control group, septic manifestations of intoxication and signs of encephalopathy were more pronounced, consciousness was lost with all manifestations of septic shock and with the appearance of new septicopyemic foci, thermometry indicators were 40.3 ±0.4°C. Laboratory studies before treatment showed that, in all patients, secondary, toxic anemia from moderate to severe severity, hypoproteinemia, hypoalbuminemia, dysproteinemia due to an increase in the amount of the globular fraction of proteins due to hypergammaglobinemia, in the study of indicators of nonspecific cellular reactivity, significant changes in these indicators are noted in the form of a significant decrease in the indicators of FAN, IL, PZF and the corresponding reaction of the body with cytokines (Tables 1-4).

Table number 1. Comparative indicators of peripheral blood in patients with purulent-necrotic complications of diabetes mellitus

№	Study groups	Number of patients	Hemoglobin		Leukocytes b1mm3		Esr		Body temperature	
			before	after	before	after	before	after	before	after
1.	Patients have received emergency treatment.	40	63± 12	75± 8	13,4± 1,3	9,3± 0,9	43 ± 3,7	19 ± 2,1	40,3± 0,4	37,8 ± 0,7
3.	Patients who have received complex treatment with step-by-step rehabilitation.	100	63± 7	95± 4	12,9± 1,6	5,7± 0,9	37 ± 1,3	13 ± 1,2	39,8± 1,6	36,3± 0,3

When using traditional therapy for sepsis, hemoglobin increased by 16%, the number of leukocytes in peripheral blood decreased by 25%, the erythrocyte sedimentation rate decreased by half, and the body temperature became subfebrile. In patients who received complex treatment with the use of rational antibiotic therapy, these indicators were, respectively, an increase in hemoglobin by 30%, the number of leukocytes decreased by 38%, ESR decreased three times, the temperature returned to normal and when using the proposed step-by-step rehabilitation algorithm, these indicators were even better - hemoglobin increased by 45%, leukocytes decreased by half, ESR and body temperature returned to normal. These indicators were obtained in the period of 17±2.4 days after hospital treatment. Biochemical indicators also show that changes in the protein fraction are also noted hypoproteinemia, hypoalbuminemia, dysproteinemia due to an increase in the amount of the globular protein fraction due to hypergamma and bettaglobinemia.

Table number 2. Comparative indicators of protein metabolism in patients with purulent-necrotic complications of diabetes mellitus

№	Study groups	Number of patients	Albumins mg/ml	¥globulins in % β	β globulin
1.	Patients have received emergency treatment.	40	45,4±0,2	7,4±0,2	11,9±0,4
2.	Patients who have received complex treatment.	40	47,9±0,3	6,7±0,4	9,7±0,34
3.	Patients who have received complex treatment with step-by-step rehabilitation.	100	51,6±0,5	5,9±0,53	8,5±0,65

When studying the indicators of nonspecific cellular reactivity, it was noted that with purulent-necrotic complications of diabetes mellitus of septic genesis, these indicators of PHAN, IL and PF significantly decreased, which indicates a significant decrease in reactivity in the studied patients. The use of traditional treatment of the septic process using rational antibacterial therapy contributes to an increase in PHAN, IL and PF indicators, and when using the proposed algorithm of step-by-step rehabilitation in the form of complex treatment using rational antibacterial therapy, these indicators improved in statistically reliable figures than when using traditional sepsis treatment.

Table No. 3. Indicators of nonspecific cellular reactivity or phagocytosis in patients with purulent-necrotic complications of diabetes mellitus

№	Study groups	Number of patients	Phagocytic activity of leukocytes (%)	Leukocyte intoxication index (un)	Indicator of completion of phagocytosis (un)
1.	Patients have received emergency treatment.	40	67,8±0,36	6,13±0,4	0,58±0,05
2.	Patients who have received complex treatment.	40	76,8±0,54	6,29±0,34	0,65±0,08
3.	Patients who have received complex treatment with step-by-step rehabilitation.	100	83,4±0,65	6,39±0,53	0,73±0,12

The interaction of the complex with the receptor apparatus of macrophages is accompanied by the activation of macrophages and the synthesis of a group of proteins, the so-called anti-inflammatory cytokines (TNF–alpha - tumor necrosis factor - alpha, interleukin-1, interleukin 2, interleukin 4, interleukin-6, interleukin-8, some growth factors and cell differentiation – colony-stimulating factors, etc.). These cytokines have a wide range of biological effects, manifested in diverse changes in metabolism, hematopoiesis, properties of the vascular wall, the function of regulatory systems, primarily the central nervous system. In the last decade, the cytokine system has received close attention as the basis of the pathophysiology of sepsis, the principles of functioning of this system and the possibilities of its

regulation have been studied. In our studies, we also revealed, we can say, a significant irritation of the cytokine system, which respond to all the effects of antigens- foreign bodies. The performed algorithm of step-by-step, complex treatment using rational antibiotic therapy, immunomodulators, immunostimulators, desensitizing, detoxification, hormone therapy and a sufficient degree of surgical treatment at the focus of the purulent-necrotic process. Over time and under the influence of treatment, we noted a decrease in the indicators of irritation of the cytokine system.

Table No. 4. Indicators of cytokine activity of blood serum in patients with purulent-necrotic complications of diabetes mellitus

№	Study groups	Number of patients	IL-1β, pg/ml	IL -2, un./ml	IL -6, un/ml	FNO- α, pg/ml
1.	Patients have received emergency treatment.	40	456±7,5	311±5,2	564±8,3	233±3,5
2.	Patients who have received complex treatment.	40				
3.	Patients who have received complex treatment with step-by-step rehabilitation	100	245±4,3 134±2,4	144±4,3 11,6±0,14	453±6,7 145±2,6	164±4,4 15,2±0,87

The algorithm of step-by-step, complex treatment with the use of rational antibiotic therapy, immunomodulators, immunostimulators, desensitizing, detoxification, hormone therapy and a sufficient degree of surgical treatment at the focus of the purulent-necrotic process. Over time, we noted a decrease in the indicators of cytokine system irritation.

CONCLUSIONS

1. When studying clinical manifestations, laboratory changes in sepsis in patients with purulent-necrotic complications of diabetes mellitus, the manifestations of intoxication and signs of encephalopathy were more pronounced, consciousness was lost with all manifestations of septic shock and with the appearance of new septicopiemic foci, thermometry indicators were high 40.3 ± 0.4 ° C, secondary, toxic anemia, dysproteinemia, a significant decrease in the indicators of PHAN, IL, PF and toxic irritation of the cytokine system of the body was noted.
2. When using the proposed algorithm for the phased use of complex treatment using rational antibiotic therapy, these indicators improved in statistically reliable figures than when using traditional sepsis treatment.

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