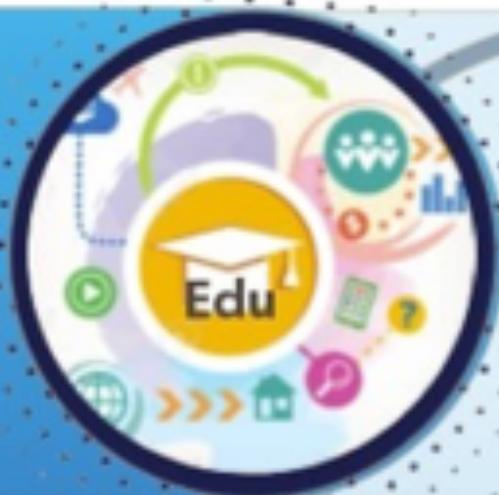




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# Differentiated Approaches to the Treatment of Surgical Infection of Soft Tissues Complicated by Sepsis in the Background of Diabetes Mellitus

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## ABSTRACT

**Background.** Over the past fifty years, there has been a steady increase in the prevalence of diabetes mellitus all over the world. This trend remains very characteristic of industrialized countries, where, along with coronary heart disease, obesity and metabolic syndrome, diabetes mellitus is registered from 5% to 10%. The problem of treating purulent diseases of soft tissues, remaining relevant throughout the history of mankind, under conditions of a high incidence of diabetes mellitus, is becoming more and more important both clinically and socially.

**Material and methods.** The object of the study was the data of a comprehensive examination and treatment of 123 patients with wound infection complicated by sepsis against the background of diabetes mellitus from 2011 to 2022. The subject of the study was: general and local clinical status of patients, laboratory blood parameters, including cytokine profile, predictors of inflammatory response, morphometric impressions of the wound, biopsionic material of the wound, wound exudate. In the dissertation, clinical, immunological, hematological, biochemical, morphological, microbiological, planimetric and statistical research methods were used.

**Results.** It has been proved that the use of the method developed by us for diagnosing the phase of the wound process complicated by sepsis in patients with diabetes mellitus makes it possible to increase the probability of diagnosing the development of generalization of the inflammatory process and to determine the option of using the method of treating wound infection.

**Conclusion.** The introduction of a new therapeutic and diagnostic algorithm for the local treatment of wound infection complicated by sepsis in patients with diabetes mellitus, developed by us, made it possible to increase the number of good and satisfactory treatment results, reduce the number of cases with unsatisfactory treatment results and avoid cases with fatal outcomes in the main group of patients.

**Keywords:** surgical infection of soft tissues, surgical sepsis, diabetes mellitus

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## INTRODUCTION

Scientists have long studied the pathogenetic factors affecting the course of the wound process in patients with diabetes mellitus. It has been proven that diabetes mellitus creates favorable conditions for the development of a wound infectious process. At the same time, the infectious process itself adversely affects the course of diabetes mellitus, through depression, insulin deficiency and, accordingly, provoking the development of metabolic acidosis. Thus, a close relationship is formed, which strengthens the aggressive aspects of the disease [1, 8].

Along with this, the course of the purulent-inflammatory process in conditions of progressive metabolic acidosis is often complicated by accelerated generalization of infection. A systemic inflammatory response syndrome develops, which "randomly" activates the body's immune system [2, 10].

The study of pathogenetic factors in the development of the wound process complicated by the syndrome of systemic inflammatory reaction in patients with diabetes mellitus becomes paramount, determining the high relevance of this problem [3, 9].

The protracted course of regenerative processes of wound infection in patients with diabetes mellitus is the starting foundation for the development of sepsis, which often does not reduce the duration of the inpatient period of treatment. Constant monitoring of both the course of the wound process and the general manifestations of possible generalization of infection is required. This, in turn, leads to an increase in bed-days and a high risk of developing a nosocomial infection. This problem can be solved by optimizing the methods of local wound treatment, based on objective methods for assessing the phases of the inflammatory process [4, 10].

Objective. Improving the results of treatment of wound infection complicated by sepsis in patients with diabetes mellitus by optimizing approaches in the selection of pathogenetically substantiated methods of local impact on the wound process.

## MATERIAL AND METHODS

The object of the study was the data of a comprehensive examination and treatment of 123 patients with wound infection complicated by sepsis, who were in the multidisciplinary clinic of the Tashkent Medical Academy from 2011 to 2022.

To conduct a comparative analysis of the effectiveness of local treatment methods, all patients were divided into 2 groups: control, 59 (48%) patients who were treat-

ed and examined in our clinic from 2011 to 2016 inclusive; the main group, 64 (52%) patients who were treated and examined in our clinic from 2017 to 2022 inclusive. The control and main groups differed in that in the control group of patients, the options for local treatment methods were reduced to the use of hyperosmolar water-soluble ointment (Levomecol), and in the main group – to a differentiated approach to the use of groups of drugs (Oflovelid, Sulfargin and Altrazael), based on objective diagnostics of the phase of the wound process according to the method developed by us and according to the therapeutic and diagnostic algorithm developed by us. The main contingent of patients (52.8%) were patients in the age range from 41 to 60 years, that is, in the most able-bodied age. Male patients prevailed (54.5%). Wound infection was mainly localized on the extremities (45.5%). All patients, both in the control and study groups, had signs of systemic inflammatory reaction syndrome upon admission to the clinic. The main proportion of patients were patients with three signs of systemic inflammatory response syndrome (59 patients – 48.0%).

The depth of tissue damage by the purulent-inflammatory process was estimated according to the classification of D.N. Ahrenholz, and the prevalence was estimated according to the classification of S.V. Goryunov. After surgical debridement of the purulent focus, the course of the wound process was carried out by determining the wound area according to the method of L.N. Popova: the wound area, the percentage of reduction in the wound area and the rate of wound healing. The presence of septic complications was identified on the basis of criteria proposed by the Chicago Conciliation Conference. The concentration of cytokines (IL-1b, IL-6, TNF- $\alpha$ ) in the blood serum was determined by the solid-phase enzyme immunoassay method using a set of reagents of the test system manufactured by Cytokines LLC.

The data obtained during the study were subjected to statistical processing on a Pentium-IV personal computer using the Microsoft Office Excel-2016 software package, including the use of built-in statistical processing functions and BioStat for Windows (version 2007). Methods of variational parametric and nonparametric statistics were used with the calculation of the arithmetic mean of the studied indicator, standard deviation, standard error of the mean, relative values, the statistical significance of the measurements obtained when comparing average quantitative values was determined by the parametric Student's criterion with the calculation of the probability of error when checking the normality of the distribution and equality of general variances. The effectiveness of

the developed prognostic and diagnostic criteria was determined by the indicators of their sensitivity and specificity. The results of the research were carried out in stages, based on the principles of translational medicine.

## RESULTS AND DISCUSSION

In the process of using traditional methods of treating wound infection complicated by sepsis in patients with diabetes mellitus, in 47.2% of cases, wound healing was achieved only after repeated repeated necrectomy followed by plastic surgery, and in 15.1% of cases, even after repeated repeated surgical debridements of the purulent focus, the inflammatory process in the wound persisted during the comparative period.

The ability to work was restored only in 32.1% of patients, and in 13.2% of patients it was restored only partially. At the same time, in 2 (3.8%) patients, unfortunately, the ability to work was completely lost, however, as well as self-care.

The mortality rate in the control group of patients was 10.2%. The main reasons for the onset of lethal outcomes in the control group of patients were: the advanced age of patients ( $67.8 \pm 12.3$  years), more than 10 years of diabetes mellitus and its complications, a large area and level of depth of soft tissue damage by purulent-inflammatory process ( $1329.5 \pm 184.7$  cm<sup>2</sup> and III-IV degrees) and a high incidence of complications of wound infection in the form of septic shock and severe sepsis with multiple organ dysfunction or insufficiency.

The traditional approach to the treatment of wound infection complicated by the syndrome of systemic inflammatory reaction in patients with diabetes mellitus has a number of factors that, in our opinion, determine the entire proportion of unsatisfactory treatment results. Unfortunately, such cases in the control group of patients turned out to be in the majority of cases. The standard approach used as a topical treatment of wound infection complicated by a systemic inflammatory reaction syndrome in patients with diabetes mellitus requires revision taking into account a number of fundamental key positions.

It is known that the purulent-inflammatory process of soft tissues in patients with diabetes mellitus proceeds in a more severe form, often complicating the process with generalization of infection. But in this case, this postulate should be considered in the key of the "vicious circle", which, in our opinion, creates conditions that complicate the achievement of positive results of treatment. And here we would like to focus not on the presence of diabetes mellitus itself, but on its complication in the

form of diabetic angiopathy, which, in our opinion, is the main factor in the "protracted" nature of the wound process [5].

It is necessary to study the nature of changes in the morphological picture of the wound process, especially if there are signs of generalized infection. Along with this, the attention of scientists in recent years has increasingly been drawn to the value of information regarding changes in the level of a number of pro-inflammatory blood cytokines that characterize the intensity of the development of the systemic inflammatory response syndrome [6].

In our opinion, of course, in the presence of diabetic angiopathy and a severe form of purulent-inflammatory soft tissue disease, the study of this issue will make it possible to determine specific "points of contact" between clinical and pathomorphological changes in the dynamics of the wound process [7].

The first stage of treatment and diagnostic care is reduced to surgical treatment of the purulent focus with the removal of all non-viable tissues, with the opening and emptying of all leaks and full adequate drainage of the wound. The next stage of the algorithm is diagnostic and is reduced to the diagnosis of the phase of the wound process. In the diagnosis of phase I of the wound process, the use of Oflomelid ointment is indicated as a local treatment of wound infection, as a remedy with high hyperosmolar efficacy, exceeding 10% sodium chloride solution by 20 times. Oflomelid is also a broad-spectrum antimicrobial agent from the group of fluoroquinolones. In dynamics, the phase of the wound process is diagnosed. In the diagnosis of phase II of the wound process, the use of Sulfargin ointment is indicated as a local treatment of wound infection, which has a bactericidal property due to the presence of active silver ions, which, as a result of getting into the wound, gradually, but for a long time, provide an antimicrobial effect. Due to the presence of only insignificant osmotic activity and the absence of necrolytic properties, this drug apparently did not show such high efficacy in the first phase of the wound process. In the diagnosis of phase III of the wound process, the use of Altrazeal is indicated as a local treatment of wound infection, which has been distinguished by its effectiveness at this time.

During the dynamic examination of the patients of the main group, the following data on the reliability of the diagnostic criteria for the phases of the wound process were obtained. The average percentage of reliability of values prevailed for true positive test results (74.8%).

The highest significant value for true positive results was observed in cases with four signs of systemic inflammatory response syndrome (95.3%), three signs of systemic inflammatory response syndrome (87.5%), and IL-6 (81.3%).

TNF- $\alpha$  (76.6%), with two signs of systemic inflammatory response syndrome (68.8%) and IL-1b (64.1%) were above average. Only a single indicator of systemic inflammatory response syndrome accounted for a very doubtful true positive result (50/50).

Comparison of the sensitivity and specificity of diagnostic tests for determining the phase of the wound process in patients with wound infection complicated by the syndrome of systemic inflammatory reaction against the background of diabetes mellitus showed greater functionality according to the proposed program. The close correlation between changes in the level of pro-inflammatory cytokines and the form of the systemic inflammatory response syndrome in the main group of patients was ambiguous. In 75% of cases, IL-6 was the leader in the pathogenetic chain, and, accordingly, TNF- $\alpha$  was less active. Nevertheless, the nature of the direct correlation between cytokines and the form of the systemic inflammatory response syndrome indicates the importance of these laboratory parameters in assessing the course of the wound process.

Having carried out a comparative assessment of the forms of sepsis between the control and the main group of patients with wound infection complicated by the syndrome of systemic inflammatory reaction against the background of diabetes mellitus, it should be noted that out of 123 patients admitted to the clinic, 56.9% of patients had severe sepsis, and 33.3% of patients had sepsis syndrome. It should be noted that in the control group of patients, patients with sepsis syndrome prevailed (by 4.1%) than in the main group of patients. Whereas in the case of severe sepsis and especially septic shock, the number of patients was higher in the main group of patients (by 6.5% and 1.6%, respectively).

In the subsequent periods, although there is a tendency to reduce the number of patients with sepsis, the numerical superiority in severe sepsis remains with the patients of the main group (an excess of almost 5%). And starting from the 5th day of treatment of the main group of patients using the therapeutic and diagnostic algorithm developed by us, it was possible to significantly reduce the number of patients with sepsis in general.

The comparative correlation of changes in the incidence of septic complications of wound infection in patients with diabetes mellitus showed that in the preopera-

tive period, the intermediate value of the correlation was expressed among patients with severe sepsis and septic shock, and they had a direct value of changes ( $R=0.612\pm 0.012$  and  $R=0.485\pm 0.03$ , respectively). Patients with sepsis syndrome ( $R=-0.521\pm 0.041$ ) were inversely correlated.

On the 1st day after surgical debridement of the purulent focus, the nature of the change in the correlation dependence changes in patients with septic shock. It acquires an inverse value in the study group of patients compared to the control group ( $R=-0.512\pm 0.035$ ;  $p<0.05$  compared to the preoperative period). A decrease in values, but stability of character, was noted among patients with severe sepsis and sepsis syndrome (1.2 and 2.1 times, respectively). Starting from this period, there is an increase in the correlation value among patients without septic disease (from  $R=0.458\pm 0.021$ ;  $p<0.05$  on the 1st day of treatment and up to  $R=0.945\pm 0.022$ ;  $p<0.05$  on the 7th day, respectively) and the acquisition of the opposite value among patients with septic shock ( $R=-0.512\pm 0.15$ ;  $p<0.05$ ).

On the 3rd day of treatment, there was an inverse decrease in the number of patients in the study group with sepsis syndrome (1.6 times;  $p<0.05$ ) and a mirror pattern of changes in the frequency of severe sepsis ( $R=-0.515$ ;  $p<0.05$ ). In other words, starting from the 3rd day of treatment, the distinguishing parameters in the frequency of registration of cases of various forms of sepsis between the control and the main group of patients become diametrically opposed.

An increase in these values on the 5th day of treatment in patients with sepsis syndrome was noted almost 2-fold. The same trend persists for the subsequent terms of treatment, that is, a stable increase in the number of patients in the control group, accompanied by a maximum decrease in their number in the main group.

Thus, the comparative analysis of the effectiveness of the treatment and diagnostic algorithm developed by us in patients with wound infection complicated by the syndrome of systemic inflammatory reaction against the background of diabetes mellitus made it possible to confirm the importance of taking into account the phases of the inflammatory process in the wound and the timeliness of the treatment and diagnostic measures taken.

In 42.2% of patients, complete wound healing by self-scarring was achieved, which is 19.6% more than in patients in the control group. In 31 patients (48.4%) of the study group, the wound completely healed after autodermoplasty, including in 6 (9.4%) patients after repeated surgical debridements of the purulent focus,

which is 4% more than in the control group. There were no cases with a remaining inflammatory process in the wound in the study group of patients.

The anatomical structure of tissues in the patients of the study group was completely restored in 24 patients (37.5%), which is 13% more than in the control group of patients. In 60.9% of the patients of the main group, the anatomical structure of the tissues was restored within the limits of the cosmetic defect. This figure was 5.4 times higher than in the patients of the control group. Only in 1 patient of the main group the anatomical structure of the tissues was restored with a gross deformation of the scar.

In 63 patients (98.4%) of the main group, the ability to work was restored in full or in part, with temporary loss of ability to work, but under the conditions of full preservation of self-care.

### CONCLUSION

Thus, as a result of the application of the developed therapeutic and diagnostic algorithm of a complex of local methods of treatment of wound infection complicated by the syndrome of systemic inflammatory reaction, in general, against the background of the results of treatment in the main group of patients, we managed to avoid cases with lethal outcomes, the preservation of inflammatory processes in the wound even after repeated surgical treatments of the purulent focus, the unrestored anatomical structure of tissues and complete loss of both employment and patient self-service.

**Conflict of interest** – the author stated that there was no conflict of interest.

**Ethical aspects** – all ethical aspects were observed by the authors during this study.

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**DIABET FONIDA SEPSIS BILAN ASORAT-LANGAN YUMSHOQ TO'QIMALARNING JARROHLIK INFEKTSIYASINI DAVOLASHDA TABAQALASHTIRILGAN YONDASHUVLAR**

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**ABSTRAKT**

**Dolzarblik.** So'nggi ellik yil mobaynida butun dunyoda qandli diabet tarqalishining barqaror o'sishi kuzatilmoqda. Bu tendentsiya sanoat rivojlangan mamlakatlarga juda xos bo'lib qolmoqda, ularda yurak-qon tomir kasalligi, semizlik va metabolik sindrom bilan bir qatorda qandli diabet 5% dan 10% gacha qayd etilgan. Yumshoq to'qimalarning yiringli kasalliklarini davolash muammosi, insoniyat tarixi davomida dolzarb bo'lib qolib, qandli diabet bilan kasallanish darajasi yuqori bo'lgan sharoitda, klinik va ijtimoiy jihatdan tobora muhim ahamiyatga ega bo'lib bormoqda.

**Materiallar va usullar.** Tadqiqot ob'ekti 2011 yildan 2022 yilgacha diabet fonida sepsis bilan murakkablashgan yara infeksiyasi bilan og'rikan 123 bemorning kompleks tekshiruvi va davolash ma'lumotlari edi. Tadqiqot mavzusi: bemorlarning umumiy va lokal klinik holati, laboratoriya qon ko'rsatkichlari, shu jumladan sitokin profili, yallig'lanish reaksiyasining prognotiklari, yaraning morfometrik taassurotlari, yaraning biopsionik materiallari, yara eksudatlari. Dissertatsiyada klinik, immunologik, gematologik, biokimyoviy, morfologik, mikrobiologik, planimetrik va statistik tadqiqot usullari qo'llanilgan.

**Natija.** Qandli diabet bilan og'rikan bemorlarda sepsis bilan murakkablashgan yara jarayonining fazasini tashxislash uchun ishlab chiqilgan usuldan foydalanish yallig'lanish jarayonining umumlashuvi rivojlanishini tashxis qo'yish ehtimolini oshirish va yara infeksiyasini davolash usulidan foydalanish imkoniyatini aniqlash imkonini beradi.

**Xulosa.** Qandli diabet bilan og'rikan bemorlarda sepsis bilan murakkablashgan yara infeksiyasini lokal davolashning yangi terapevtik-diaagnostika algoritmini joriy qilish yaxshi va qoniqarli davolash natijalarini ko'paytirish, davolash natijalari qoniqarsiz bo'lgan holatlar sonini kamaytirish va asosiy guruh bemorlarda o'limga olib keladigan holatlarning oldini olish imkoniyatini yaratdi.

**Kalit so'zlar:** yumshoq to'qimalarning jarrohlik infeksiyasi, jarrohlik sepsis, qandli diabet.

**ДИФФЕРЕНЦИРОВАННЫЕ ПОДХОДЫ К ЛЕЧЕНИЮ ХИРУРГИЧЕСКОЙ ИНФЕКЦИИ МЯГКИХ ТКАНЕЙ ОСЛОЖНЕННЫЕ СЕПСИСОМ НА ФОНЕ САХАРНОГО ДИАБЕТА**

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**АБСТРАКТ**

**Актуальность.** Последнее пятидесятилетие отмечается неуклонный рост распространенности сахарного диабета во всем мире. Данная тенденция остается весьма характерной для промышленно развитых стран, где наравне с ишемической болезнью сердца, ожирением и метаболическим синдромом, сахарный диабет регистрируется от 5% до 10%. Проблема лечения гнойных заболеваний мягких тканей, оставаясь актуальной во всей истории человечества, при условиях высокой частоты встречаемости сахарного диабета, приобретает все более важное как клиническое, так социальное значение.

**Материал и методы.** Объектом исследования послужили: данные комплексного обследования и лечения 123 больных с раневой инфекцией осложненной сепсисом на фоне сахарного диабета с 2011 по 2022 годы.

**Результат.** Доказано, что применение разработанного нами способа диагностики фазы течения раневого процесса, осложненного сепсисом у больных сахарным диабетом, позволяет повысить вероятность диагностики развития генерализации воспалительного процесса и определить вариант применения метода лечения раневой инфекции.

**Заключение.** Внедрение разработанного нами нового лечебно-диагностического алгоритма местного лечения раневой инфекции, осложненной сепсисом у больных сахарным диабетом, позволило увеличить количество хороших и удовлетворительных результатов лечения, уменьшить количество случаев с неудовлетворительными результатами лечения и избежать в основной группе больных случаев с летальными исходами.

**Ключевые слова:** хирургическая инфекция мягких тканей, хирургический сепсис, сахарный диабет.