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EXPERIMENTAL DEVELOPMENT OF DIAGNOSTIC CRITERIA FOR WOUND PROCESS PHASES IN EXPERIMENTAL ANIMALS WITH DIABETES MELLITUS

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Annotation: The optimal model was selected for the diagnosis of the stage of the wound process course complicated by systemic inflammatory response syndrome against the background of diabetes. It makes it possible to diagnose the stage of the wound process, predict the probability of generalization of the pathological process, and can be used as a criterion for choosing the optimal method of local treatment of wound infection.

Key words: Diabetes, depression, metabolic acidosis, insulin.

The last fifty years have seen a steady increase in the prevalence of diabetes mellitus worldwide (11,19). The problem of treating purulent diseases of soft tissues, while remaining relevant throughout the history of mankind, with a high incidence of diabetes mellitus, is becoming increasingly important both clinically and socially (3, 4, 20-24, 36).

Scientists have long studied the pathogenetic factors that influence the course of the wound process in patients with diabetes mellitus (16). It has been proven that diabetes mellitus creates favorable conditions for the development of wound infection. At the same time, the infectious process itself negatively affects the course of diabetes mellitus, by depressing insulin deficiency and, accordingly, provoking the development metabolic acidosis. In this way, a close relationship is formed that enhances the aggressive aspects of the disease (1.5, 26, 30).

Along with this, the course of the purulent-inflammatory process in conditions of progressive metabolic acidosis is often complicated by the accelerated generalization of the infection. A systemic inflammatory response syndrome develops, which “indiscriminately” involves the body’s immune system (2,7, 8, 20, 25, 27, 30, 31).

And today, the study of pathogenetic factors in the development of a wound process complicated by the systemic inflammatory response syndrome in patients with diabetes mellitus becomes paramount, determining the high relevance of this problem (10,18,19).

The protracted course of regenerative processes of wound infection in patients with diabetes mellitus is the starting foundation for the development of systemic inflammatory response syndrome and sepsis, which often does not allow reducing the duration of the inpatient treatment period (13,14,17). Constant monitoring is required both over the course of the wound process and over the general manifestations of possible generalization of infection. This in turn leads to an increase in bed days and a high risk of developing hospital-

acquired infections (2,6,9,12,15). The solution to this problem is possible by optimizing methods of local wound treatment, based on objective methods for assessing the phases of the inflammatory process.

The presented data indicate the feasibility of conducting research devoted to a more in-depth and detailed study of the effect of various methods of local complex treatment of wound infection in patients with diabetes mellitus complicated by systemic inflammatory response syndrome, which would reduce the number of adverse and fatal outcomes of the disease and reduce the length of hospital treatment.

Purpose of the study: development and experimental substantiation of the effectiveness of diagnostic criteria for the phases of the wound process in experimental animals with diabetes mellitus and systemic inflammatory response syndrome.

Material and methods. Experimental studies were carried out on 280 white mature Wistar rats weighing 180-280 g, of both sexes, without external signs of disease, who underwent a 10-day quarantine in a vivarium. All animals were divided into 3 large groups and 3 subgroups, consisting of standard series of experiments. Accordingly, each series of experiments corresponded to a specific model of the pathological process and was numbered by us in Roman numerals. I a series of experiments - control, consisted of animals with a wound process without the introduction of an infectious agent. In this series of experiments, the skin, subcutaneous tissue and superficial fascia were opened in the back area of animals under superficial inhalation anesthesia, followed by removal of a flap of soft tissue measuring 1.5x1.5 cm. We recorded this manipulation as a stage of surgical treatment. The wound was left open using as a therapeutic agent, the appropriate drug according to the established objectives of the study. The second series of experiments - comparative-1, consisted of animals with the course of a wound process with the introduction of an infectious agent into the soft tissues. In this series of experiments, animals under superficial inhalation anesthesia were injected subcutaneously at 5 points on the animal's back with 3-4 ml of a 30% suspension of animal auto-feces, diluted with a 10% solution of calcium chloride. After the manifestation of the inflammatory process, which occurred 3-5 days after the administration of the autoscal suspension, CHO was performed with complete necrectomy. The wound was left open with the use of an appropriate drug as a therapeutic agent in accordance with the established objectives of the study. III series of experiments - comparative-2, consisted of animals with a wound process with the introduction of an infectious agent into the soft tissues with the subsequent development of SIRS. Modeling was carried out according to the method developed by A.O. Okhunov. According to the conditions of this development, animals on an empty stomach under ether anesthesia were intraperitoneally injected with antilympholine - Kr at a dose of 0.03 mg per 100 g of animal weight for 2 days. On the 3rd day, 3-4 ml of a 30% suspension of the animal's auto- feces, diluted with a 10% solution of calcium chloride, was injected subcutaneously into 5 points on the animal's back. After the manifestation of the inflammatory process, which occurred 5-7 days after the administration of the autoscal suspension, CHO was performed with complete necrectomy. The wound was left open with the use of an appropriate drug as a therapeutic agent in accordance with the established objectives of the study.

IV series of experiments - the main one, consisted of animals with the course of a wound process with the introduction of an infectious agent into soft tissues with the subsequent development of SIRS against the background of diabetes mellitus with diabetic microangiopathy. Modeling was carried out according to the method developed by A.O. Okhunov. According to the conditions of this development, animals on an empty stomach under ether anesthesia were intravenously injected with 100-110 mg/kg of the drug doxorubicin in a 0.9% sodium chloride solution, and 48 hours after the administration of doxorubicin, 0.2 was injected retroperitoneally once daily for 3 days. -0.4 ml per 100 grams of animal weight of 70% sorbitol solution. After clinical ¬and laboratory confirmation of the development of diabetes mellitus (hyperglycemia, glycosuria), antilympholin-Kr was administered intraperitoneally for 2 days under ether anesthesia at a dose of 0.03 mg per 100 g of animal weight. On the 3rd day, 3-4 ml of a 30% suspension of the animal's auto-feces, diluted with a 10% solution of calcium chloride, was injected subcutaneously into 5 points on the

animal's back. After the manifestation of the inflammatory process, which occurred 3-5 days after the administration of the autoscal suspension, CHO was performed with complete necrectomy. The wound was left open with the use of an appropriate drug as a therapeutic agent in accordance with the established objectives of the study.

Subgroups of animals were formed and named according to the type of local treatment of wound infection used. Experimental animals were exposed comprehensive clinical examination using modern clinical, biochemical and instrumental research methods.

Express methods for local assessment of the state of the wound process and signs of inflammation intensity were: hyperemia, edema and tissue infiltration in the wound area, the amount and nature of wound discharge, the intensity of necrolysis, the timing and degree of epithelization of the wound and the formation of scar tissue. Important research methods included assessing the area and level of depth of spread of the purulent-inflammatory process of soft tissues. Depth was assessed according to classification D. H. Ahrenholz, and prevalence - according to the classification of S.V. Goryunova. After CHO, the course of the wound process was determined by the method of L.N. Popova: wound area, percentage reduction in wound area and wound healing rate.

The presence of septic complications was identified based on the criteria proposed by the Chicago Consensus Conference. For differentiation, we adhered to the following specific clinical concepts: systemic inflammatory response syndrome, sepsis syndrome, severe sepsis, and septic shock. In experimental animals to identify clinical signs of SIRS Respiratory movements were visually counted per minute. Pulse rate was determined by the number of heartbeats in 1 minute. Rectal temperature was measured and the number of leukocytes in the blood was counted to determine the number of neutrophils.

Special laboratory research methods went beyond the general approved standards and were carried out initially for scientific research. The concentration of cytokines (IL -1 b, IL -6, TNF - a) in blood serum was determined by enzyme-linked immunosorbent assay using a set of test system reagents produced by Cytokines LLC (Russia).

The material for microbiological studies was purulent exudate taken from the deep parts of the wound immediately after opening the pathological focus and during the course of treatment.

Morphological studies were carried out in experimental animals and included histological and morphometric studies. Morphometric indicators were: the area of stromal edema, dermal vessels and granulation vessels; diameter of dermal and granulation vessels; the number of wound fibroblasts, granulocytes, lymphocytes and macrophages. Studies of laboratory animals were carried out according to the general design. Moreover, in group No. 1 of experimental animals

it was planned to investigate the clinical laboratory and morphofunctional dynamics of the course of the wound process on days 1, 3, 7, 14 and 28 after CHO. As a therapeutic agent in all four series of experiments, a bandage soaked with a 3% solution of hydrogen peroxide was used.

The purpose of the studies conducted in experimental animals in the second group was aimed at assessing the effectiveness of the effect various methods of local treatment on the dynamics of the wound process. At the same time, the group, consisting of 3 subgroups, included conducting studies to assess the effectiveness of Oflomelid, Sulfargin and Altrazeal in all series of experiments on days 1, 3, 7, 14 and 28 after CHO.

To develop a diagnostic and treatment algorithm for the optimal method of local treatment of wound infection, group No. 3 was created, in which studies were also conducted based on a modified method for assessing the phase of the wound process. The studies, as in other groups, were carried out on days 1, 3, 7, 14 and 28 after CHO.

To evaluate the results of treatment of wound infection complicated by systemic inflammatory response syndrome in patients with diabetes mellitus, we used a modified technique proposed by the Republican Center for Purulent Surgery and Surgical Complications of Diabetes Mellitus of the Ministry of Health of the Republic of Uzbekistan. The following criteria were distinguished in the assessment structure: 1. The wound healed completely by self-scarring, the anatomical structure of the tissues and ability to work were completely restored; 2. The wound healed after plastic surgery, the anatomical structure of the tissues is restored within the limits of cosmetic defects and partial restoration of working capacity; 3. Wound healing occurred after repeated necrectomy followed by plastic surgery, there is a rough deforming scar, activity has been restored only within the limits of self-care; 4. Preservation of the inflammatory process in the wound even after repeated CHO, the integrity of the wound is not restored, the ability to work is completely lost; 5. Death of the experimental animal.

The correlation significance and prognostic value of the obtained data were determined using the R. Fletcher method.

Results and its discussion. During a local examination, we established the following indicators: the time frame for the disappearance of edema in

peripheral part of the wound; the timing when the wound was cleared of necrotic tissue; the time frame when it was possible to visualize the presence of granulation tissue; the timing when signs of epithelization of the wound edges appeared. The minimum time for wound transformation was noted by us in I series of experiments, while the maximum is in III and IV.

Since I a series of experiments was characterized by the absence of infectious provocation; the wound remained macroscopically clean throughout the study. Granulation already appeared on days 2.7±0.6, and marginal etithelization - on days 3.4±0.8 of the postoperative period. In the main series of experiments, peripheral tissue edema persisted until 9.8±1.3 days of the postoperative period ($p< 0.05$). Cleansing of the wound from necrotic tissue (including secondary formed ones) occurred only on the 13.8±4.3 day of observation ($p< 0.05$), which of course is not comparable with the control series of experiments. Granulation in the wound appeared 16±2.6 days later than in the control ($p< 0.05$). Accordingly, the beginning of marginal epithelization of the wound was registered by us only on day 25.9±3.7 of the postoperative period ($p< 0.05$). We deliberately do not dwell on the indicators in II and in III series of experiments, since they were intermediate in nature between the control and main groups, which, in fact, was expected. Of the total number of animals in this block of experiments, the frequency of occurrence of SIRS manifestations was 56% of cases.

Such a high value of this indicator is due to the totality in the analysis of all studied groups. However, the number of animals with signs of SIRS 2 or more was 47.5%. Number of animals, with targeted SIRS modeling (III and IV series of experiments) amounted to 43.7%.

Among animals IV series of signs of SIRS were registered by us in 98% of cases. Moreover, out of 36 animals with SIRS 4, in 75% of cases there were animals IV series of experiments.

Thus, analysis of the frequency distribution of SIRS registration showed that the selected various experimental models of wound infection are reliable in terms of clinical and laboratory signs of the course and can be used in further studies.

A microbiological study of the wounds of all animals in the dynamics of the development of wound infection showed that on average, on the 1st day of experimental experiments, the number of microorganisms was the highest - 68.6 x 10 7 ± 15.8 CFU/g. In the dynamics of the experiments, already on the 14th day of the study, a more than 2-fold decrease in this indicator was noted, both in the number of microorganisms and their colonies. Among the series of experiments, on day 1 of the experiments, the highest contamination of the

wound was recorded among animals III and IV series (92.4 x 107 ± 25.8 CFU/g ($p< 0.05$) and 89.9 × 108 ±17.6 CFU/g ($p<0.05$), respectively).

It is noteworthy that even on the 28th day of observation, microbial contamination of animal wounds was IV series of experiments still remained high, both above the average value (3.5 times) and above all other comparative values (27.8 times compared to II and 10.4 times compared to III group, respectively) and control (compared to 14 days of experiments) groups ($p<0.05$). You should also focus on the number of degrees of microbial contamination of the wound. The maximum degree at the level of 10 7 -10 8 was noted by us in III and in IV series of experiments, that is, in animals with a model of the septic course of the inflammatory process.

Dynamics of cytokine levels in the blood of animals I a series of experiments did not reveal any significant changes. All cytokine indicators, including their average value, were within normal values and any increase or decrease in the digital value did not have a fundamental deviation.

Maximum value in relation to IL -1 b and IL -6 was noted on the 28th day of observation. We recorded the same kind of changes in TNF - a on the 3rd day after COGO. Average value of all cytokines over time after CHO in animals I series of experiments varied from 3.0±0.4 pg /ml to 4.3±0.8 pg /ml. In II series of experiments, the average concentration of pro-inflammatory cytokines was high during 1-7 days of the process dynamics. The peak value occurred on day 1 of the study with a gradual decrease on day 7, that is, the dynamics of changes corresponded to the dynamics of the process.

Among the proinflammatory cytokines, TNF - a stood out, the level of which ranged from 9.3±0.5 pg /ml ($p< 0.05$) to 22.4±1.6 pg /ml ($p<0.05$) over 1 year -14 days postoperative period. IL -1 decreased already from the 3rd day of the study by 2.7±0.2 pg /ml ($p<0.05$), and IL -6 - from the 7th day by 12.6±1.2 pg /ml ($p <0.05$).

III a series of experiments where the complication of a wound infection in the form of SIRS was purposefully modeled, the average value of all pro-inflammatory cytokines studied was higher than the values of the control series of experiments. Already on the 1st day of the study, their level exceeded the indicators of the control series by 11.3 times ($p < 0.05$), and the indicators of II series of experiments - 2.6 times ($p<0.05$). It should be noted that the 3rd day of the postoperative period also had a significant difference between III a series of experiments and I - II in series. The difference was manifested in an increase in the average value by 15.4 ($p< 0.05$) and 3.6 times ($p<0.05$). This confirms the existence of a connection between the development of cytokinemia and the presence, in this case, of a bacteriological presence in the inflammatory process.

Even on the 28th day of the postoperative period in III We did not find any hint of normalization of cytokine levels in a series of experiments. IL -1 was 1.6 times higher than control values ($p<0.05$), IL -6 - 9.1 times ($p<0.05$), and TNF - a - 1.4 times ($p<0.05$).

In animals IV series of experiments, the level of cytokines was increased for all cytokines studied throughout the experiment. The average value of cytokinemia on day 1 of the postoperative period exceeded the control values by 25.5 times ($p < 0.05$). On the 3rd day of observation, no significant changes in dynamics were noted. Only starting from the 7th day of the postoperative period, on average, a decrease of 1.6 times ($p < 0.05$) was noted compared to the previously studied period. Meanwhile, in relation to I series of experiments, in IV this indicator exceeded its values by 16.3 times ($p < 0.05$). Throughout the research in IV series of experiments, the leading level among pro-inflammatory cytokines was IL -6, and its dispersion compared to other pro-inflammatory cytokines was paramount, exceeding IL -1 by 2.5 times ($p<0.05$) and TNF - a - 2.9 times ($p<0.05$). On day 1 of the study, the dispersion of pro-inflammatory cytokines was distributed in descending order according to the IL -6/ IL -1/ TNF - a scheme. Starting from the 3rd day of the postoperative period, the pattern changed, acquiring the pattern IL -6 / TNF - a / IL -1. And although the order of their

dispersion changed, nevertheless, in numerical value, all the studied proinflammatory cytokines exceeded both the control values and the values of the comparative experimental groups. Compared to the control series of experiments, on the 28th day of observation, the increase in pro-inflammatory cytokine IL -1 was 6.8 times ($p < 0.05$), IL -6 - 18.7 times ($p < 0.05$), TNF - a - 6.9 times ($p<0.05$).

Thus, a comparative assessment of the dynamics of changes in the level of pro-inflammatory cytokines in animals with various experimental models of wound infection made it possible to determine the important role of these indicators as criteria for differentiating the type and duration of the inflammatory process. Modeling of wound infection against the background of diabetes mellitus and complications in the form of SIRS influenced not only the change in the numerical change of these indicators, but also the nature of their dispersion redistribution. This indicates the reliability of both the selected options for modeling the pathological process and the possibility of using these indicators in predicting purulent-septic complications of the wound process.

In general, summing up the analyzed clinical and laboratory manifestations of wound infection, we can state that the level of proinflammatory cytokines, the number of signs of SIRS and microbial contamination of the wound should be taken into account when developing diagnostic criteria for the phases of the wound process. To assess the effectiveness of these criteria, a more in-depth morphological and morphometric study of the wound process in dynamics after CHO is required.

Morphological and morphometric characteristics of the course of the wound process in various types of wound infection on the 1st day after modeling in II, III and IV series of experiments looked like this. There are overlays along the entire wound surface, which were due to fibrin. The entire area of connective tissue that was examined at the bottom of the wound was loosened, and the tissue itself was filled with macrophages and leukocytes according to the type of infiltration. It was in this area that pronounced tissue swelling was determined. The blood vessels were dilated. Areas of hemorrhage may be seen around dilated vessels, most likely due to diapedesis. When examining the deeper areas of tissue along the periphery of the wound surface, we identified the presence of edema. On the 3rd day of research, differences in the morphological structure of tissues appeared in the series of experiments. In particular, in I In a series of experiments, the wound was infiltrated with neutrophils, but under the infiltration one can see edematous granulation tissue, which was of a developing nature. In II In a series of experiments, fibrin completely covered the wound surface.

The deeper lying tissues were represented by early granulation, which, unlike the previous series of experiments, had a pronounced infiltration of leukocyte cells. The nuclei of these cells were polymorphic. The fatty tissue around the wound was distinguished by the presence of pronounced edema. B III A series of experiments revealed that the dermis was stratified. At the same time, a pronounced infiltrate is noted between its layers. The infiltrate contains a large number of leukocytes with different morphological patterns of nuclei. Tissue swelling occurs due to obstruction of lymph outflow, which is manifested by the expansion of lymphatic capillaries. The deep layers of tissue are also edematous and also have stratification due to edematous infiltration. B IV series of experiments, in fact, all layers of tissue are filled with a pronounced infiltrate, which was worn inflammatory in nature and was richly saturated with neutrophils. The inflammatory process was destructive in nature, so a similar transformation was noted throughout the entire depth of the tissues with a transition to the muscles. On days 7-14 in I series of experiments, the process of epithelization is actively developing, the wound is without areas of necrotic tissue.

In II In a series of experiments, collagen appears around the wound surface. Over the entire surface of the wound covering, there is activation of the growth of granulation tissue. However, in some areas the fibrin is still superimposed on the germ tissue. Moderate swelling is noted under the layers of epithelialized areas of the wound.

B III We have not identified any special dynamics of the morphological picture in a series of experiments. The granulation tissue is also edematous. In this case, the swelling also spreads into the layers of fatty tissue around the wound.

B IV A series of experiments in the wound determines tissue necrosis. The vessels are filled with blood clots. Their diameter is sharply reduced. The tissue around the wound is sharply swollen and infiltrated. Swelling and infiltration reaches the muscles. The latter with areas of necrotic change

The average value of indicators characterizing the morphological picture of the course of the wound and wound infection, with the cumulation of indicators between the control, comparative and main groups, revealed the ambiguity of changes. However, when assessing the cellular composition of wound prints in the dynamics of the postoperative period (Table 4), already on the 1st day of the postoperative period, one can note the predominant number of granulocytes, accounting for more than half of the total volume studied at this time.

A targeted study of the dynamics of this indicator reflected a decrease in its quantity, already starting from the 3rd day of the postoperative period, and from the 7th day this change began to acquire significant significance.

The level of lymphocytes was characterized by an unreliable change in the total value. And only on the 28th day of the postoperative period it reached a significant value, decreasing compared to the 1st day of the study by 1.4 times ($p < 0.05$).

In general, the dynamics of changes in the pattern of cellular composition of the wound infiltrate in the postoperative period, even assuming their average value, was characterized by a well-known pattern. However, when assessing changes in these indicators in the dynamics of the postoperative period in various studied groups of experimental animals, a very differentiated picture was revealed. The peak value in the control series of experiments in relation to fibroblasts occurred on the 14th day of the postoperative period, while for granulocytes - on the 3rd day. Against this background, there was a progressive decrease in the number of lymphocytes and macrophages during all periods of the experiments in animals of this series.

The group of the main series of experiments was characterized by a depressed value of the number of fibroblasts, lymphocytes and especially macrophages, as in in general, and in the early stages of the postoperative period. The level of fibroblasts on the 1st day of the postoperative period in the main series of experiments was 1.5 ± 0.2 times lower than the control values ($p < 0.05$). Moreover, on the 14th day (the deadline for observations for the control series of experiments) in the main series of experiments, the level of fibroblasts in the wound infiltrate was 1.7 ± 0.3 times lower ($p < 0.05$).

When assessing changes in the level of granulocytes, one should note the same dynamics in the decrease in the number of indicators. When comparing the corresponding periods of a series of experiments, the decrease was noted in almost the same proportion ($1.1 \pm 0.3\%$; $p < 0.05$). However, as a percentage, the number of granulocytes in the main series of experiments on the 14th day of the study was higher than the control values by $25.3 \pm 2.5\%$ ($p < 0.05$). Since in the control series of experiments the wound was practically closed by the 28th day of the study, a comparison of the main group was carried out with II and III series of experiments. At the same time, the level of granulocytes on the 28th day of the experiments was higher by $38.9 \pm 7.8\%$ ($p < 0.05$) and by $11.9 \pm 0.95\%$ ($p<0.05$), respectively. In general, in the main series of experiments the level of granulocytes was close to II series. The difference was not significant, which indicates the similarity of pathological processes between these groups.

Another characteristic dynamics for the main series of experiments was the relative stability of the level of lymphocytes and macrophages in the prints of the wound infiltrate. However, in contrast to the control series of experiments, even on the first day of the experiments, there was a low value of macrophages in the wound

by 12.1±1.8% (p< 0.05). At the height of wound infection on the 7th day of the postoperative period, the level of macrophages in the infiltrate in the main series of experiments was 3.6 ± 0.8% than in the control group (p < 0.05).

In general, the minimum value of macrophages in the wound infiltrate of animals was noted on the 28th day of the postoperative period in III series of experiments (1.1±0.08%; p< 0.05). At the same time, the minimum value of lymphocytes in the wound infiltrate occurred in the main series of experiments (4.1±1.0%; p< 0.05).

A morphometric study of wound biopsies in animals of various series, on average, showed the following: stromal edema decreased the most, starting from the early stages of the postoperative period, reaching its minimum value on day 28 (from 20.2 ± 3.8% to 9. 6±1.7%, respectively; p< 0.05). At the same time, a decrease in this indicator was noted by 2.1±0.4 times (p< 0.05).

The area of dermal vessels (as well as their diameter in other respects) decreased on the 28th day of experimental studies (almost 2.5 times). The area of granulation vessels and their diameter increased significantly (11.8±2.4 times (p< 0.05) and 3.3±0.8 times, respectively; p<0.05). It should be noted that these indicators changed significantly starting from the 3rd day of the study, whereas in the previous case such changes were noted only on the 28th day of the postoperative period.

In the main series of experiments, within the subgroup itself, significant changes were noted only in relation to the volume of vessel area dermis. A progressive decrease in this indicator was noted on the 28th day of the postoperative period (2.5 times) compared to the 1st day of observation. In other indicators of the morphometric picture, compared with the intra-group picture, no significant changes were noted. The pathological process seems to have stopped in dynamics, without leading to any significant dynamic changes. Meanwhile, in a comparative analysis between the control and main series of experiments, changes of a mirror opposite nature should be highlighted. In the control series of experiments, stromal tissue edema increased, reaching its maximum value already on the 7th day of the postoperative period. In the main group, in the presence of an initially high value of this indicator, there was a smooth, non-significant decrease over the 7-14 days of the postoperative period. However, in relation to the control series of experiments, this was quite noticeable. It should be noted that, unlike the control series of experiments, in the main series, we did not find indicators characterizing the nature of granulation on days 1-3. This process began to form only from the 7th day of the postoperative period. B III In a series of experiments, we noted this trend on the 1st day of the postoperative period.

A morphometric study confirmed the role of the experimental model of diabetes mellitus in the protracted nature of the course of wound infection. An important role in this process should be attributed to the presence of diabetic angiopathy and, of course, the initial decrease in the protective properties of the body against the background of SIRS.

Planimetric studies showed that the average value of the area, in the dynamics of the studies, significantly decreased from 333.0 ± 1.5 mm 2 to 131.9 ± 0.9 mm 2 (p < 0.05). We registered progress in reducing the wound area on the 14th day of observation (1.7 times compared to day 1). It is noteworthy that the decrease in the percentage of wound surface area, which was only 0.8±0.09% on day 1, increased to 68.9±1.1% on day 28 of the experiments (p< 0.05). The wound healing rate averaged 2±0.1% per day. Moreover, the peak value of this indicator occurred on the 14th day of experimental studies (5.2±1.2% per day; p< 0.05). And although the rate of wound healing on the 28th day of experimental studies was 1.5±0.5% per day, nevertheless it was slower than on the 3rd day of the wound process (1.7±0.4% per day; p< 0.05).

When randomizing the studies, a very differentiated picture of the wound healing process was revealed (Table 8). It should be noted that in group I a series of experiments where the wound was without infection, the healing process was completed before the last period of the experiments. At the same time, it should be emphasized that when assessing the rate of wound healing, analysis was possible only starting from the 3rd

day of the experiment. We marked the 0th day of dynamics as the period after completion of CHO in order to ascertain the differentiated scope of surgical intervention.

The results showed that the volume of COGO in animals of the main series of experiments significantly exceeded that value than in the control series of experiments. Wound surface area of animals with diabetic angiopathy against the background of signs of SIRS was more by 160±5.9 mm 2 compared to II ($p< 0.05$) and by 89.8±4.1 mm 2 compared to III series of experiments ($p<0.05$). This indicates that the inflammatory process is more widespread in the main group and the need for more extensive necrectomy.

The control and comparative groups of experiments were characterized by an acceleration in the rate of wound healing starting from the 14th day of experimental studies (from 5.4±1.1% per day to 7.6±0.9% per day; $p< 0.05$). Moreover, this indicator in the main series of experiments during all periods of the studies did not exceed 0.6 ± 0.03% per day. Percentage reduction in wound area in IV series of experiments increased by 31.7±1.3 times, while the area of the wound surface itself decreased by only 57.3±1.2 mm2, which amounted to 12.7±0.8% of the initial area of the wound surface ($p < 0.05$).

For the analysis and practical application of such a massive information block, the development of a software model is required, which can then be easily implemented in practical healthcare.

Based on the set goal and objectives, we present the results of developing objective criteria for diagnosing the phase of wound infection, which will serve as the basis for creating a diagnostic and treatment algorithm for the local treatment of purulent wounds in patients with diabetes mellitus due to SIRS.

The first step in completing this task, due to the impossibility of conducting studies of this kind on patients, was the study of morphological, morphometric, cytological and microbiological parameters of experimental animals.

The correlation assessment of the indicators of the conducted studies was carried out depending on the series of experimental models of the pathological process. However, it had certain distinctive aspects.

In all series of experiments, the correlation values of the dynamics of the course of the wound process indicated an increase in their significance in one direction or another (direct or reverse). In particular, the rate of wound healing had a direct correlation with the number of fibroblasts on the wound surface ($R = 0.732 ± 0.012$; $p < 0.05$) and a weak

inverse correlation with the number of granulocytes ($R = -0.469±0.009$; $p < 0.05$), lymphocytes ($R = -0.364±0.006$; $p <0.05$) and macrophages ($R = -0.298±0.007$; $p <0. 05$) wound. At the same time, the main series of experiments had the most pronounced picture ($R = -0.965 ± 0.01$; $p < 0.05$), exceeding those of the control series by 68.7% ($p < 0.05$).

A direct relationship was also noted in relation to the percentage of the area of stromal edema of the wound (in I series $R =0.590±0.014$; $p <0.05$; in II series $R =0.612±0.014$; $p <0.05$; in III series $R =0.718±0.009$; $p <0.05$; and in IV series $R =0.962±0.027$; $p <0.05$) and to an increase in both the area of granulation vessels (in I series $R =0.485±0.01$; $p <0.05$; in II series $R =0.598±0.01$; $p <0.05$; in III series $R =0.628±0.01$; $p <0.05$; and in IV series $R =0.931±0.01$; $p <0.05$), and to the diameters of the granulation vessels themselves (in I series $R =0.320±0.01$; $p <0.05$; in II series $R =0.774±0.01$; $p <0.05$; in III series $R =0.918±0.01$; $p <0.05$; and in IV series $R =0.984±0.01$; $p <0.05$). An inverse correlation was noted for

change in the diameter of the vessels of the dermis (in I series $R = -0.618±0.01$; $p <0.05$; in II series $R = -0.832±0.01$; $p <0.05$; in III series $R = -0.932±0.01$; $p <0.05$; and in IV series $R = - 0.993±0.01$; $p < 0.05$), which was likely due to scar formation.

Microbial contamination of the wound, noted in an inverse correlation with the rate of wound healing (on average $R = -0.859 ± 0.01$; $p < 0.05$), had a direct relationship with the number of granulocytes (on average

R = 0.732 ± 0.01 ; p <0.05), lymphocytes (average R =0.649±0.02; p <0.05) and macrophages (on average R = 0.579 ± 0.05; p < 0.05) in the wound, and the reverse correlation with the number of fibroblasts in the wound surface (on average R = -0.598 ± 0.03; p < 0.05).

The area of stromal tissue edema was inversely correlated with the dynamics of microbial contamination of the wound (in I series R = -0.461±0.02; p <0.05; in II series R = -0.598±0.03; p <0.05; in III series R = -0.624±0.02; p <0.05; and in IV series R = -0.843±0.02; p <0.05). A weak correlation was noted in relation to other indicators of wound healing in the control series of experiments, since, apparently, this was due to the lack of targeted introduction of microorganisms into the wound in this series of experiments. The growth of granulation tissue vessels was inversely correlated with microbial contamination of the wound (on average R = -0.318 ± 0.02; p < 0.05).

Thus, the correlation analysis between the analyzed indicators of morphological, microbiological, cytological, morphometric and planimetric studies made it possible to identify a reliable pattern in changes in the course of wound infection and the objectivity of the presented data.

The analysis of static data allowed us to identify data that were similar in nature of significance and served as the foundation for the formation of the integration of indicators. These indicators can serve as data on the course of a wound process complicated by SIRS against the background of diabetes mellitus.

We used the least squares method as the basis for the formation of models that can differentiate the stages of the wound process in diabetes mellitus complicated by SIRS. The statistical basis was made up of model parameters that imposed the condition that their effectiveness should not be lower than p < 0.05 according to the t -test. This, in turn, allowed us to develop a model for diagnosing the phase of the wound process complicated with SIRS against the background of diabetes mellitus. Moreover, subject to the presence of a wound infection complicated by the syndrome of systemic inflammatory response against the background of diabetes mellitus diabetes has its own distinctive side, characterized by a more radical approach to the tactics of COGO. In this connection, it is logical to exclude the wound cleansing phase.

Morphological information, results of clinical and laboratory tests - all of them confirm the peculiarity of the course of the wound process in this experimental model and accordingly defines the phases as: 1) active inflammatory process, with the likelihood of developing SIRS in 75% of cases; 2) passive inflammatory process, with the likelihood of developing SIRS in 50% of cases; 3) active regeneration, with the likelihood of developing SIRS less than 25% of cases;

The characteristic changes were recognized as those closest in pathogenetic significance, primarily pro-inflammatory cytokines and the number of signs of SIRS. Subsequently, the construction included data on the microbial contamination of the wound and the rate of wound healing.

Thus, we have selected the optimal model for calculating the diagnosis of the phase of the wound process, complicated by the systemic inflammatory response syndrome against the background of diabetes mellitus. The developed mathematical model was the basis of the software module “Method for diagnosing the phase of a wound process complicated by systemic inflammatory response syndrome in patients with diabetes.” It allows you to diagnose the phase of a wound process, predict the likelihood of generalization of a given pathological process and can be used as a criterion in choosing the optimal method of local treatment of a wound infections.

Conclusions: The developed and experimentally substantiated model of diagnostic criteria for the phases of the wound process makes it possible to diagnose the phase of the wound process, which makes it possible to correctly assess the course of the pathological process and optimize local treatment. Based on the studies conducted, it has been proven that the use of diagnostic criteria for the phases of the wound process leads to

the correct approach to the choice of local treatment for wound infection, thereby reducing the average duration of the hospital stage of complex treatment.

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