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# CLINICAL RESULTS AND INDICATORS OF CYTOKINES IN THE TREATMENT OF PURULENT WOUNDS IN PATIENTS WITH DIABETES MELLITUS

Vladimir Melnikov<sup>✉</sup> , Aleksandr Gololobov 

Astrakhan State Medical University, Astrakhan, Russia

✉ [mvastr@mail.ru](mailto:mvastr@mail.ru)

**ABSTRACT** — The authors provide a comparative assessment of the results of a clinical study of purulent wound healing and the profile of pro- and anti-inflammatory cytokines in 71 patients with type 2 diabetes mellitus. In group 1 (44), Biointegra ointment, lymphatic and NO-therapy were used. In 27 patients (group 2), comparable by sex and age, treatment was carried out by ultrasonic cavitation of wounds, dressings with Levomekol ointment and traditional intramuscular administration of a similar antibiotic and immune preparation. In the group 1, the general condition normalized on the 5–7<sup>th</sup> day, the level of glycemia decreased, the purulent process was localized within the damaged tissues and the imbalance in the cytokine profile was eliminated. In the group 2, positive dynamics was observed 4–5 days later than in the first group. The terms of treatment in the main group were 14.6±1.2, in the comparison group — 19.8±1.8 inpatient days.

**KEYWORDS** — Purulent wound, diabetes mellitus, wound healing, cytokines.

## INTRODUCTION

In the XXI century, there has been a steady increase in the number of patients with diabetes mellitus with purulent surgical infection. This is due to the annual increase in the registration of cases of diabetes and their doubling every 10 years [1].

In patients with diabetes, the healing of purulent wounds is characterized by a mild course of the phases of the wound process, which is associated with a violation of all types of metabolism. Surgical infection aggravates the clinical course of diabetes mellitus, insulin deficiency increases, followed by impaired function of the organs of the effector and regulatory systems. In diabetes mellitus, there is a deficiency of endogenous NO-universal messenger regulator [2].

The healing of purulent wounds depends largely on the effectiveness of local drug treatment [3, 4].

In the fight against purulent infections, the technique of lymphatic (direct and indirect) administration of antibiotics and immune preparations has not yet been properly evaluated.

However, exogenous NO and Biointegra ointment in combination with lymphatic therapy have not been used in the complex treatment of purulent wounds in patients with diabetes mellitus.

### *The aim of the study*

is to argue the feasibility of using exogenous NO, Biointegra ointment, and conducting indirect lymphotropic antibiotic and immunotherapy in the treatment of purulent wounds in patients with diabetes mellitus of the second type.

## MATERIALS AND METHODS

In the studied group of patients (24 people) with type 2 diabetes mellitus with purulent wounds of various origins, regional lymphatic therapy was carried out: 1 time per day with 48 hour intervals, departing 1cm from the edges of the wound on both sides from 4 points, in half the daily dose, ceftriaxone 1.0 was introduced diluted in 8ml of a 2% solution of lidocaine + 32 units of lidase, and after 5 minutes, in the same place, imunofan (0.05 g) was injected subcutaneously. Every day, after wound cleaning, its surface was treated for 5 minutes with exogenous NO produced by the apparatus SKSV/NO-01 *Plazon* in the *stimulator* functioning mode. The wounds were treated with Biointegra ointment — (the patent name of the drug), which is *NanoZnHApAM-Antibiotic-PEG*, with the inclusion of a water-soluble antioxidant — ethylene polyglucol with a molecular weight of 400 to 1500 cu.

In the comparison group — 21 patients with a similar pathology, comparable by sex and age, the antibiotic and imunofan were administered in the traditional intramuscular manner, and local wound treatment was carried out with dressings with Levomekol ointment. All patients underwent correction of hyperglycemia in accordance with the prescription of an endocrinologist. The effectiveness of the treatment was evaluated clinically by examining laboratory and by biochemical blood parameters, qualitative and quantitative studies of microflora, cytograms of touch smear, pH-metry of wound exudate. Studies were performed at the beginning of treatment, on 3–5<sup>th</sup>, 7–9<sup>th</sup> and 10–14<sup>th</sup> days. The concentration of cytokines was determined using immunoenzymometric test systems (LLC *Cytokine*, St. Petersburg).

The assessment of the reliability of the average data obtained and the difference between them, the correlation coefficients were assessed by the Student criterion. Indicators were considered reliable at  $p < 0.005$  and  $p < 0.001$ .

## RESULTS AND THEIR DISCUSSION

On admission, the general purulent infection prevailed in all patients, the blood glucose exceeded the norm by 2–3 times. The concentration of pro-inflammatory cytokines was: IL-1b —  $399.16 \pm 16.7$  pg/ml; IL-6 —  $158.22 \pm 15.6$  pg/ml; IL-8 —  $147.12 \pm 12.8$  pg/ml; FNO —  $265.14 \pm 10.14$  pg/ml; anti-inflammatory: IL-4 —  $88.8 \pm 6.72$  pg/ml; IL-10 —  $194.6 \pm 12.2$  pg/ml (N — for the listed cytokines — 0–50). In the study group, by the end of 5–7 days, the general condition normalized, the purulent process was localized within the damaged tissues, the activity of the wound microbiota was suppressed, the walls of the wounds were cleaned from necrotic plaque, islands of granulation tissue appeared, and a regenerative type of cell reaction was recorded in smears. By this time, there was a significant decrease in systemic production of IL-1b by 1.52 times ( $p < 0.005$ ), IL-6 by 1.6 times ( $p < 0.005$ ), IL-8 by 8.2 times ( $p < 0.005$ ), IL-10 6.2 times ( $p < 0.005$ ). The FNO content was significantly reduced ( $1.65 \pm 0.14$  pg/ml, ( $p < 0.005$ ).

By the end of 10–14 days, the clinical picture of the regeneration phase of the wound healing process prevailed in the wounds, the microbial colonization of the wound wall decreased by 3–4 orders of magnitude, and the concentration of pro- and anti-inflammatory cytokines in the blood serum, except for FNO, did not exceed the reference values.

In the comparison group, on 10–14<sup>th</sup> days from the start of treatment, such a significant clinical effect was not noted, the decrease in cytokine profile indicators exceeded the highest normal range from 10.2 to 23.4%. FNO of the study group amounted to  $62.24 \pm 8.18$  pg/ml ( $p < 0.001$ ), in the comparison group —  $88.64 \pm 9.16$  pg/ml ( $p < 0.005$ ).

## DISCUSSION

In the study group, it was much faster to eliminate the detrimental effect of the etiological factor, to optimize the components that contribute to the transition of the purulent wound process into the regeneration phase, which ultimately led to the elimination of the causes of the imbalance of some pro- and anti-inflammatory cytokines. The remaining concentration of the proinflammatory cytokine FNO in both groups of patients is a consequence of the systemic, specific immunobiological reaction characteristic of patients with diabetes mellitus [5].

## CONCLUSION

1. In the complex treatment of patients with diabetes mellitus and purulent wounds, regional antibiotic and immune therapy in combination with local wound treatment with Biointegra ointment and treatment with exogenous nitric oxide allow targeted, pathogenetically substantiated therapy of purulent wounds.
2. In the study group of patients, the quality of treatment improved, which ultimately led to a reduction in treatment time by an average of 5 days: in the study group,  $14.6 \pm 1.2$ , in the comparison group —  $19.8 \pm 1.8$  inpatient days.

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