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PATHOPHYSIOLOGICALLY AND CLINICALLY SUBSTANTIATE CHANGES IN INTERLEUKIN DYNAMICS IN DIABETIC MACRO - AND MICROANGIOPATHIC WITH PATIENTS

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The purpose of the work. Determination of the effectiveness of ozone therapy and its pathomorphological properties with new pharmacological drugs for the treatment of purulent necrotic process of the foot. By studying the dynamics of anti-inflammatory cytokine levels: analysis of the need and possibility of immunoprotection by studying cytokine status in IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, TNF-α, INF-γ patients on the development and recurrence of purulent-necrotic processes of DFS.

Materials and methods. The concentration of cytokines in the blood plasma was determined using the StatFax 2100 immunological complex (manufactured by Cytokin LLC, St. Petersburg) by enzyme immunoassay (IFA). The obtained results are carried out using descriptive and non-parametric statistical methods on a personal computer with mathematical processing using Statistica 6.0 software. Control parameters of the manufacturer's cytokine norms were used - the normative parameters obtained as a result of testing the donors were obtained from the manufacturer Cytokin LLC, St. Petersburg, Russian Federation. Plasma collection and cytokine level testing were performed on day 1 before surgery and on days 3, 5, 7, and 10 after surgery. The study was conducted in three phases and, accordingly, the patients were divided into 3 research groups: Group I (control group) - blood serum of patients with purulent-necrotic lesions of diabetes for the study of the cytokine system; II group (comparison group) - blood serum obtained during the treatment of patients with purulent-necrotic lesions of diabetes with ozone therapy and "Reosorbylact" - 200.0 ml (YURIYA-FARM LLC, Ukraine); Group III (main group) - blood sera obtained during the treatment of patients with purulent-necrotic lesions of diabetes with ozone therapy and Reomannisol - 200.0 ml (REKA-MED FARM LLC, Uzbekistan). To determine the imbalance of cytokines, consists of taking the blood plasma of 60 patients with purulent-necrotic lesions of diabetes and

determining the amount of cytokines in it. 60 patients were treated at various levels in the Purulent surgical department of the Yakkasaroy District Medical Association between 2021 and 2023. The age range of the patients was between 48-60 years. Neuropathic form of DFS - 25 people (type 1 DM - 2 patients, type 2 DM - 23): 12 were men and 13 women, and neuroischemic form of DFS - 35 patients (all with type 2 DM): 15 men and consisted of 20 women. Most often, amputations were performed at the thigh level - 33.3%, heel area - 20%, finger level - 18.3%, necrotomy - 6.7%, and sequestrectomy - 11.7%. Upper amputations were also performed as the main option, as a result of the failure of the approach to save vital organs: at the thigh level - in 33.3% of cases, and at the heel level - in 20%.

Results. The procedures performed in patients of group III. Operations performed to save the leg: necroctomies - 42.9%, sequestrectomy - up to 31.3%, amputations at the level of toes - 42.8%, amputations at the level of the heel - 34.3%. In addition, the number of high amputations: at the hip level - 28.6%, and at the heel level - 2.9%. Compared to the second group, the number of upper amputations decreased from 65.7% to 28.6%. In addition, the antioxidant effect of Reomannisol manifested in the induction of inflammatory and anti-inflammatory cytokines, was determined. IL-1β: high level of cytokine up to 64.59±3.3 pg/ml on the first postoperative day, increased to 95.27±2.2 pg/ml on the fifth day and decreased to 20 ± 1.8 pg/ml. IL-1b promotes the proliferation of monocytes, macrophages, neutrophils, endothelium, smooth muscle cells, fibroblasts, keratinocytes, T- and B-lymphocytes, along with other cytokines; increases the stimulation of receptors for IL-2; activates endothelial cells; induces an acute phasic response. IL-2: increases to 1.2±0.3 pg/ml on the first postoperative day, to 1.7±0.13 pg/ml on the third day, and 0 at discharge. After an increase in IL-2, the active implementation of the immune response and the activation of T cells show. IL-4: fluctuations were noted within normal limits and an increase was observed in only one case, that is, 76 pg/ml in a patient with an allergic background, which increased due to the development of postoperative traumatic dermatitis on the limbs after surgery. Reomannisol may stimulate the production of this cytokine by mononuclear cells in the peripheral blood of allergic patients. However, as a result of antioxidant activity, there are fluctuations in the group of cytokines with pro-inflammatory effects, but only within normal limits. IL-6: a high level of cytokine up to 228.92±5.1 pg/ml was recorded on the first postoperative day. Then it gradually returned to normal, and by the time

of discharge from the hospital, it was back to normal. IL-6 is produced by T-lymphocytes, monocytes, macrophages, and fibroblasts. Hematopoiesis causes the differentiation of progenitor cells, stimulates the development and production of megakaryocytes, promotes the growth and differentiation of platelets, T- and B-lymphocytes, and stimulates the production. IL-8: peak cytokine levels increased to 181.14 ± 4.1 pg/ml on the first postoperative day, 245.47 ± 5.9 pg/ml on the fifth day, and 53 ± 1.1 pg/ml at hospital discharge. decreased to ml. As revealed in the study of the previous two groups, the growth of this cytokine characterizes the transition of the process to a chronic form. IL-10: An anti-inflammatory cytokine produced by T-lymphocytes, macrophages, keratinocytes, and B-lymphocytes. It blocks the functional activity of macrophages and the production of anti-inflammatory cytokines by monocytes and macrophages. It increases the proliferation of B-lymphocytes and the secretion of immunoglobulins IgE. However, IL-10 can stimulate the synthesis of IL-4 in a balanced state. By preventing the systemic response to the inflammatory process, IL-10 ensures a balanced level of inflammatory and anti-inflammatory cytokines and controls the immune response, which has a positive effect on the prevention of purulent-necrotic recurrence. TNF-α: produced by macrophages, monocytes, keratinocytes, T-lymphocytes, B-lymphocytes, neutrophils, and endothelial cells. TNF-α has a variety of effects, occurs due to the modulation of the expression of genes for cell growth factors, cytokines, transcription factors, cell surface receptors, and acute phase proteins, and plays an important role in protection against them. The increase of this cytokine on the third day up to 150.6±5.3 pg/ml after the operation is included in the high activity and the cytokine itself. INF-γ: on the first day, a high level was recorded to 194±3.4 pg/ml, on the third day it increased to 205.9±6.5 pg/ml and decreased to 5.39±0.3 pg/ml, this indicates its immunomodulatory value and involvement in the regulation of the anti-inflammatory response.

Conclusion. In the case of purulent-necrotic processes in DFS, the adequate introduction of the cytokine system is characterized by the slowing down of the local process, corresponding to acute inflammation, but increases the tendency of the process to go into a chronic state. With the recurrence of purulent necrotic inflammation, there is a synchronization of the process and a secondary immune deficiency, which does not allow the cytokine system to adequately join the anti-inflammatory system. Reomannisol allows us to consider it a physiologically active

compound with clear antioxidant activity. Reomannisol has an antioxidant effect on the cytokine system, correcting the cytokine balance. It can decrease the function of pro-inflammatory and anti-inflammatory cytokines, and interferons. Reomannisol is effective in preventing the recurrence of purulent-necrotic lesions of DFS in conditions of secondary immunodeficiency, so it is a necessary drug in the main therapy complex.

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