



**RESULTS OF THE EFFECT OF POLYOXIDONIUM ON CD25 AND CD95
CONCENTRATIONS IN PATIENTS WITH SEVERE TRAUMA AND THEIR CORRECTION**

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Abstract

The purpose of the study: to evaluate the effect of polyoxidonium on the cd25 and cd95 content in the blood serum of patients with severe trauma.

Material and methods. The objects of clinical study were 48 patients with polytrauma, the age ranged from 18 to 47 years, men - 34, women – 14. The content of sAPO-1/FAS (cd95+) and the IL-2 receptor (cd25+) were determined by the enzyme immunoassay on the ELIZA apparatus using Bender Medsystems kits. The digital material was processed by the method of variation statistics.

Results. The victims with polytrauma showed a sharp decrease in the content of lymphocytes in the peripheral blood in the early stages. There was a significant increase in the level of sCD95 by 1.75 and 1.73 times on the 3rd day, by 1.42 and 1.22 times - on the 7th day after the injury. The analysis of the level showed an increase in sCD25 by 1.6 and 1.29 times on the 3rd day, by 1.35 and 1.22 times - on the 7th and by 1.22 and 1.16 - on the 14th day of the study. The greatest changes were characteristic of patients with combined trauma and the risk of developing post-traumatic infectious and inflammatory processes. In contrast to the values of the control group, the additional inclusion of polyoxidonium led to an earlier restoration of the content of lymphocytes in the peripheral blood of the victims, a decrease in high levels of sCD95 and sCD25.

Conclusion: polyoxidonium contributed not only to the restoration of the number of lymphocytes, but also to an increase in their functional activity, especially with the risk of septic complications.

Keywords: multiple injuries, treatment, polyoxidonium, sCD95 and sCD25 content.

Modern approaches to the treatment of the consequences of severe trauma require taking into account the functional activity of the immune system. According to the literature, patients with severe trauma have a decrease in the total number of lymphocytes, T- and B-lymphocytes, a violation of the ratio of T-helper and cytotoxic cells with a change in the immunoregulatory index [4, 8, 10]. Changes in the immune system are of a staged nature and depend on the duration of the injury, its severity and the risk of infection. Thus, severe trauma is characterized by two-phase priming of neutrophil granulocytes with a primary increase and subsequent suppression of their functional activity, and the development of septic complications is accompanied by a decrease in neutrophil apoptosis [2, 4, 9]. Inhibition of apoptosis in healthy individuals by the serum of patients with trauma has been shown.



Despite the continuous improvement of antibacterial therapy and surgical techniques, infectious complications, which are one of the main clinical manifestations of immune insufficiency, remain the main cause of death in patients with serious injuries [1, 3, 10]. In this regard, to prevent the risk of infectious and inflammatory processes in severe injuries, it is advisable to use polyoxidonium, which has a pronounced immunotropic effect [6, 7]. At the same time, its effect on the processes of apoptosis of immune cells in severe trauma has not been clarified.

The purpose of the study: to evaluate the effect of polyoxidonium on the cd25 and cd95 content in the blood serum of patients with severe trauma.

Material and methods of research. The objects of clinical study were 48 people who were admitted to the department of emergency traumatology of the Multidisciplinary Clinic of the Tashkent Medical Academy in a state of traumatic shock, aged 18 to 47 years, there were 34 men (70.8%) and 14 women (29.2%). According to the type of damage, the distribution was carried out according to the AO-ASIF classification as follows: A1-16; A2-8; A3-1; B1-3; B2-1; C1-7; C2-9; C3-3 [3, 10]. The victims were more often injured due to road accidents and on the street, less often at work and in everyday conditions (falling from a height).

Primary surgical treatment of wounds with osteosynthesis with a rod apparatus, compression-distraction osteosynthesis with an Ilizarov apparatus, periosteal, intramedullary and blocking intramedullary osteosynthesis was performed, with fractures of the pelvic bones, a spoke-rod apparatus was applied, and if the standing of bone fragments of long bones was satisfactory on the control radiography, conservative treatment was continued. Primary surgical treatment of wounds with osteosynthesis with a rod apparatus, compression-distraction osteosynthesis with an Ilizarov apparatus, periosteal, intramedullary and blocking intramedullary osteosynthesis was performed, with fractures of the pelvic bones, a spoke-rod apparatus was applied, and if the standing of bone fragments of long bones was satisfactory on the control radiography, conservative treatment was continued.

All patients included in the study received complex treatment: infusion-transfusion therapy; inotropic, vascular and respiratory support; enteral nutrition; antibacterial therapy, of which 27 patients continued to receive basic therapy (control group), and 21 patients additionally underwent immunological therapy with the inclusion of polyoxidonium for 10 days at a dose of 6 mg, intramuscularly, every other day, No. 5 (main group).

To assess the general condition of the patient's body, the peculiarities of the violation of his homeostatic functions, as well as the nature of the influence of the complex treatment method carried out in the clinic on the course of the wound process, clinical, radiation (X-ray, computed tomography, magnetic resonance imaging), electrophysiological, laboratory (general blood and urine analysis, blood biochemistry, etc.), pathomorphological research. The content of sAPO-1/FAS (cd95+) and IL-2 receptor (cd25+) were determined by enzyme immunoassay on an ALUMA apparatus (Germany) using Bender Medsystems kits. To obtain objective data on the spectrum of changes in sCD25 and sCD95 in patients with multiple and combined injuries, we determined their level in peripheral blood on the 3rd, 7th and 14th days of treatment.



The analysis of quantitative indicators was carried out on a Pentium IV personal computer running the Microsoft Windows 2000 Server operating system, using Microsoft Excel and Microsoft Access statistical programs, with the determination of average values (M), average error (m). The reliability of the difference in indicators was determined using the Student's t-test with confidence $p \leq 0.001$ and $p \leq 0.005$.

Results and their discussion

The conducted studies showed a sharp decrease in the content of lymphocytes in the peripheral blood of victims in the early post-traumatic period (Table 1). The severity of these shifts depended on the severity of the injury and the patient's condition, since we observed a wide variability in the level of lymphocytes. We did not find significant differences in the percentage of lymphocytes in patients with combined and multiple injuries. In subsequent periods, the content of lymphocytes continued to decrease, reaching minimum values on the 3rd-7th day of the post-traumatic period, especially in patients at risk of developing purulent-septic complications, which is associated with the migration of lymphocytes from the blood into the tissues to the foci of inflammation. The results obtained by us echo the data of other researchers and indicate the possibility of using this test in predicting complications [4, 9].

Table 1 Dynamics of changes in serum cytokine levels in patients with combined and multiple injuries,

M±m

Indicators	Practically healthy	Terms of the study, day		
		3	7	14
Number of lymphocytes, %	34,45±1,65	22,63±1,19 ^a	20,57±1,24 ^a	27,30±1,95 ^a
		21,16±1,27 ^a	20,29±2,01 ^a	30,42±1,67
Content sCD25, %	28,12±1,33	44,97±1,81 ^a	37,94±1,91 ^a	34,17±1,46 ^a
		36,23±1,79 ^a	34,18±2,17 ^a	32,59±2,12
Content sCD95, %	29,38±1,09	43,33±2,01 ^a	35,19±1,83 ^a	27,73±1,44
		42,88±2,14 ^a	30,25±1,73	26,37±1,62

Note: 1) the numerator represents the values of the group of patients with combined trauma, in the denominator – multiple trauma; 2) a - the differences between the indicators of practically healthy individuals and patients are significant ($P < 0.05$), b – the differences between the indicators of patients with combined and multiple injuries are significant ($P < 0.05$).

According to the literature, one of the causes of lymphopenia in the development of purulent-septic processes in the post-traumatic period is apoptosis, which at an early stage performs an adaptive function aimed at limiting the systemic inflammatory response, and at a later stage contributes to the development of lymphopenia and, consequently, an unfavorable outcome [4, 9]. Apoptosis is a regulator of adaptive immunity. Recently, apoptotic reactivity of lymphocytes, determined by the number of cells expressing membrane Fas receptors (CD95), has been considered as a marker for the prognosis of posttraumatic sepsis. Our studies conducted in this regard showed a significant increase in the level of sCD95 by 1.75 and 1.73 times on the 3rd day, by 1.42 and 1.22 times on the 7th day after



the injury, and later we observed a tendency to approach the normative values. More pronounced changes were typical for victims with combined trauma.

CD95, called Fas or APO-1, is a transmembrane glycoprotein, belongs to the family of tumor necrosis factor receptors. It is expressed in significant amounts on T-lymphocytes (CD4+ and CD8+) of peripheral blood and, to a lesser extent, on B-lymphocytes and NK cells, granulocytes, monocytes, tissue cells and neoplastic cells. Binding of CD95 to the Fas ligand (CD95L) induces apoptosis in cells. In the research of Samokhvalova I.M. et al. (2009) it was shown that the relative number of lymphocytes carrying CD95 in their membrane increased the upper limit of the norm in patients with subsequent sepsis by an average of 1.8 times, without sepsis – by 1.5 times [8, 9]. In non-bacterial multiple organ failure syndrome, the CD95 value was more than 2 times higher than normal. According to the authors, the CD95 count of more than 15% at a rate of 7% within 1-3 days after injury was observed mainly with subsequent severe sepsis, which can serve as its approximate prognosis.

At the same time, for the diagnosis of immunodeficiency, information is also needed about the functional activity of immunocompetent cells. They are reduced to a single process – a change in their membrane receptor apparatus, i.e., a change in the density of receptors. CD25 is a single-stranded glycoprotein identified as a low-affinity receptor for IL-2 [12]. This receptor is expressed on activated T lymphocytes and, with a lower density, on activated B cells. Studies conducted in this regard showed an increase in sCD25 by 1.6 and 1.29 times on the 3rd day, by 1.35 and 1.22 times - on the 7th and by 1.22 and 1.16 - on the 14th day of the study, i.e. the greatest expression is observed in the acute period, and gradually decreases in subsequent periods. The greatest changes were characteristic of patients with combined trauma and the risk of developing post-traumatic infectious and inflammatory processes. The results obtained by us echo the data of other authors, which established the expression of peripheral blood lymphocytes of victims of thermal and mechanical trauma in the early stages of post-traumatic illness [5]. According to the researchers, activation processes in the immune system are the initial elements of the development of post-traumatic immune insufficiency, i.e. a part of the membrane receptors is discharged into the liquid phase. An increase in the content of cd25 antigen in serum is the initial stage of the development of posttraumatic immunosuppression.

In this regard, the additional inclusion of polyoxidonium, which is an immunomodulator, in the complex of therapeutic measures of polytrauma, was of interest. The conducted studies showed a gradual increase in the relative content of lymphocytes in the peripheral blood of the victims, especially by day 7, and an approximation of its values by day 14, while patients receiving basic treatment maintained a low level of lymphocytes (Table2). This was confirmed by a decrease in the high level of sCD95 and their approximation to the values of practically healthy individuals with the additional use of polyoxidonium. The same dynamics was noted in the study of the level of sCD25 in the blood serum of patients. Consequently, polyoxidonium contributed not only to the restoration of the number of lymphocytes, but also to an increase in their functional activity. The results obtained allow us to recommend the use of polyoxidonium in severe polytrauma, especially with the risk of septic complications. According to the literature, the target cells for polyoxidonium are natural resistance factors: macrophages, monocytes, neutrophils and NK cells [6,7]. Apparently, the acceleration of the



processes of differentiation and maturation of thymocytes under the influence of polyoxidonium leads to an increase in the number of T-lymphocytes, an increase in their functional activity in the conditions of an integral organism, which leads to the activation of both cellular and humoral immunity [11].

Table 2 Dynamics of changes in the level of cytokines in blood serum in patients with polytrauma, M ± m

Indicators	Practically healthy	Terms of the study, day		
		3	7	14
Number of lymphocytes,%	34,45±1,65	<u>21,95±1,04^a</u>	<u>20,46±1,72^a</u>	<u>28,97±1,45^a</u>
		26,30±1,41 ^a	29,62±1,81 ^b	32,86±2,17
Content sCD25,%	28,12±1,33	<u>40,60±2,16^a</u>	<u>36,06±1,98^a</u>	<u>33,38±2,16</u>
		36,85±2,14 ^a	35,06±0,76 ^a	29,21±1,82
Content sCD95,%	29,38±1,09	<u>43,06±2,18^a</u>	<u>32,70±2,12</u>	<u>27,55±1,76</u>
		31,32±2,15 ^b	30,03±0,72	27,77±1,23

Note: 1) the numerator represents the values of the control group of patients, the denominator represents the main group; 2) a – the differences between the indicators of practically healthy individuals and patients are significant (P<0.05), b – the differences between the indicators of the main and control groups of patients are significant (P<0.05).

Thus, it can be said that polyoxidonium has the ability to set in motion all factors of nonspecific and specific protection of the body affected by foreign antigens, and this movement spreads naturally, as it occurs during the development of an immune response in the body. In addition to immunomodulating, polyoxidonium has a pronounced detoxifying, antioxidant and membrane stabilizing effect, which apparently determines the earlier reparative regeneration of the damaged areas of the affected.

Conclusions:

1. With combined and multiple trauma, lymphopenia develops, an increase in the level of sCD95 and sCD25. Their greatest expression is observed in the acute period, in patients with combined trauma and the risk of developing post-traumatic infectious and inflammatory processes.
2. The additional inclusion of polyoxidonium in the complex of therapeutic measures increases the low level of lymphocytes, reduces the high values of sCD95 and sCD25, especially by the 7th day.

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