



## FEATURES OF THE INFLAMMATORY RESPONSE IN PATIENTS WITH ACUTE AND LONG-LASTING NON-HEALING BURN WOUNDS

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**Annotation:** *The problem of treating chronic wounds remains relevant, but the topic of research on the inflammatory process in patients with long-term non-healing burn wounds has not been sufficiently covered in the literature. The article is devoted to the study of the peculiarities of changes in the content of inflammatory markers in patients during the acute period of burn disease and with a duration of the wound process of more than 35 days. The conducted studies indicate the severity of inflammation, which persists despite the age of the process and undoubtedly has an effect on wound healing. Everyone has patients showed a significant increase in the level of C-reactive protein, and  $\alpha_1$  - antitrypsin. When assessing the content of  $\alpha_2$ -macroglobulin ( $\alpha_2$  -MG) and haptoglobin (GG), individual variability of these indicators was established. In patients with long-term non-healing wounds, a greater frequency of a decrease in the concentration of  $\alpha_2$ -MG and an increase in GH was found compared with similar indicators in patients during the acute period of burn disease. The level of ceruloplasmin turned out to be a more stable indicator than other acute-phase proteins and exceeded the limits of Normal values are found in only one patient during the acute period of burn disease, as well as in one patient with long-term non-healing wounds. There was no correlation between changes in the concentrations of the studied acute-phase proteins, except for the found relationship between the level of GH and  $\alpha_2$ -MG, which indicates compensatory rearrangements leading to increased synthesis of GH neutralizing lysosomal enzymes against the background of reduced  $\alpha_2$ -MG activity. Analysis of changes in the content of acute-phase blood proteins ( $\alpha_1$ -antitrypsin,  $\alpha_2$ -MG, GG) can it can be important in assessing*



*the severity of the course and prognosis of the disease, which will make it possible to outline tactics for regulating the inflammatory process and thereby increase the effectiveness of treatment of chronic wounds in burned patients.*

**Keywords:** *burn wounds; C-reactive protein;  $\alpha_1$ -antitrypsin;  $\alpha_2$ -macroglobulin; haptoglobin; ceruloplasmin*

**Introduction.** In response to severe thermal injury, infection, which can join and complicate the course of the underlying disease, physiological reactions develop in the body of the burned patient aimed at localizing the lesion and restoring impaired functions. The resulting inflammatory reaction is accompanied by changes in the immune system, intensification of catabolic reactions, increased energy consumption, and impaired microcirculation and blood coagulation [1-4]. The classic acute phase lasts for several days, but this The process can be prolonged if the damaging factors continue to act or if the control and regulation mechanisms are disrupted, as a result of which the acute phase response can be converted into a chronic phase of inflammation [5-8]. During the development of the inflammatory reaction, an increase in the content of acute phase proteins (OFBS), which occupy an important place in the system of immunoregulation and nonspecific resistance, is noted in the blood serum and damaged tissues. The dependence of the course of the wound process is known It depends on the level of acute-phase proteins with antiproteolytic activity [9-12]. On the one hand, a decrease in the activity of proteolytic enzymes of wound secretions slows down the cleansing of wounds from necrotic tissues, but on the other hand, a significant increase in proteolytic activity can contribute to deep tissue alteration with increased invasion of microorganisms. Such changes, depending on the course of the wound process, must be taken into account in the treatment of wounds using bandages containing immobilized enzyme preparations [13-14].

Among the victims of thermal trauma, there are patients with long-term wounds, the treatment of which is quite lengthy. The healing time of chronic burn wounds is influenced by many factors, including infection, inflammation, and microcirculation disorders [15-16]. The topic of studying the features of the





inflammatory process in this category of patients has not been sufficiently covered in the literature and needs further study.

**The purpose of this work** is to study changes in inflammatory process reactants in patients with acute period of burn disease and with long-term non-healing burn wounds.

**Material and methods.** 17 patients with a burn area of more than 20% of the body surface and a duration of the wound process of more than 35 days were examined (group 2). The comparison group (group 1) included 16 patients with a similar lesion area who were examined during the first 12 days after injury. The control group consisted of 20 practically healthy people. The groups were comparable in gender and age. The severity of the systemic inflammatory response was assessed by the content of acute phase proteins in the blood. Levels of haptoglobin (Hp), ceruloplasmin (CP),  $\alpha_1$ -antitrypsin ( $\alpha_1$ -AT),  $\alpha_2$ -macroglobulin ( $\alpha_2$ -MG) was studied using ptec kits (Belgium) on a semi-automatic biochemical analyzer "lima-15" (Spain). C-reactive protein levels (CRP) was determined using the diagnostic system "ycoard®" (xisc-hield, Norway). The concentration of total protein and albumin was studied using an ab-650 biochemical analyzer (Italy, USA, Japan).

Mathematical data processing was performed using descriptive statistics, sample comparison (Mann-Whitney U-test), and correlation analysis based on the calculation of Spearman's nonparametric correlation coefficient. The critical value of the significance level was assumed to be 0.05. The data was provided in the form of Me (P25; P75), where Me is the median, P25 and P75 are the first and third quartiles. Statistical data processing was performed using the statistical 6.0 program.

**Results and discussion.** In both groups of patients examined, pronounced changes in inflammatory markers were found. In all patients of the examined groups, a high level of the "golden marker" of inflammation, CRP, was detected, the average content of which changed slightly with the duration of the disease. This acute-phase reactant has proinflammatory and procoagulant properties by inducing the release of inflammatory cytokines, activating monocyte differentiation into macrophages, and stimulating thrombosis by suppressing tissue plasminogen activator [9].



Investigation of the content of the main antiprotease of blood plasma- $\alpha_1$ -AT- revealed her increased. The level is high both in the acute period of burn disease and in patients with long-term non-healing wounds. The increase in the content of this enzyme has a protective mechanism and is due to the activation of its synthesis, aimed at interacting in damaged tissues with proteases, primarily with neutrophil elastase and collagenase [10]. When assessing the content of the universal protease inhibitor  $\alpha_2$ -MG, the individual variability of this indicator was established. In the first group of patients, the frequency of decrease in  $\alpha_2$  content-MG was 18%, in 9% of cases it exceeded the values of healthy people and in 63% of cases it did not exceed the normal values. A different pattern was observed in patients with long-term non-healing wounds: the frequency of occurrence of normal  $\alpha_2$ -MG values was 53%, a decrease was detected in 47% of cases. When comparing the values of this protease, a statistically significant difference was found between the patient groups ( $p=0.005$ ). Apparently, the overall decrease in the level of  $\alpha_2$ -MG is associated with its expenditure on inhibition of endopeptidases and removal from the vascular bed. It can be assumed that another reason for the decrease in the level of  $\alpha_2$ -MG is a violation of the protein-synthesizing function of the liver in patients at all follow-up periods, manifested by a decrease in the concentration of total protein, as well as albumin – a negative reactant of the acute phase of inflammation. A decrease in macroglobulin production contributes to the predominance of blood coagulation processes over fibrinolysis, which allows for the creation of a pathological barrier to the spread of tissue destruction [11]. At the same time, there is an excess of proteinases, metabolic disorders in the focus of inflammation and, as a result, the accumulation of under-oxidized metabolic products and a decrease in the pH of the medium cause damage to  $\alpha_2$ -MG. The resulting complex of damaged  $\alpha_2$ -MG with enzymes such as plasmin preserves the catalytic properties of the latter, but protects hydrolases from inhibition by serpins, which allows it to freely destroy specific substrates and contribute to the further development of necrosis. It is possible that the inhibition of  $\alpha_2$ -MG synthesis by in the later stages of inflammation, it minimizes the formation of such autoaggressive complexes [12].

In patients of the second group, the incidence of values exceeding those of healthy people was 88.2%, while in other patients the indicator was within the normal range. The pathogenetic significance of increasing the level of this acute-phase protein lies in the fact that, in addition to binding free hemoglobin, it inhibits lysosomal hydrolases, modulates the activity and proliferation of leukocytes in the inflammatory site, and, being a peroxidase, provides protection against reactive oxygen species [13]. The CP level turned out to be a more stable indicator than the rest of the AFB, and exceeded the normal values in only one patient during the acute period of burn disease (66.4 mg/dl at a norm of 20-61 mg/dl) and in one patient with long-term non-healing wounds (79.8 mg/dl). It should be noted that there was no correlation between the changes in the concentrations of the studied OFBS, with the exception of the detected relationship between the level of GH and  $\alpha_2$ -MG ( $r = -0.62$ ,  $p = 0.007$ ), which may indicate compensatory changes leading to reduced  $\alpha_2$  activity.

**Conclusion.** The conducted studies in patients both in the acute period of burn disease and in patients with long-term non-healing burn wounds indicate the severity of inflammation, which persists despite the prescription of the process and undoubtedly affects wound healing. Analysis of changes in blood OFB content, namely  $\alpha_1$ -antitrypsin, Hp and  $\alpha_2$ -MG, may be important in assessing the severity of the course and prognosis of the disease, which will allow us to outline the tactics of regulation the inflammatory process and thereby increase the effectiveness of treatment of chronic wounds in burned patients.

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