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Changes in Local and Systemic Immune Factors in Patients with Purulent Wounds

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Abstract **The aim of the study was** to study changes in pro-inflammatory and anti-inflammatory interleukins, as well as protease inhibitors, as local and systemic immune factors in patients with purulent wounds. The following results were obtained: the indicators of pro-inflammatory interleukins TNF-α and IL-1, both in patients in the washings of purulent wounds, as well as in the same patients in the blood serum, were significantly higher than similar results in patients with postoperative wounds. At the same time, the results of changes in anti-inflammatory interleukin IL-10 and TGF-β in patients in the washings of purulent wounds, as well as in the same patients in the blood serum, had the opposite direction and were significantly lower than similar results in patients with postoperative wounds. Similar changes as in anti-inflammatory intelukins were observed in the study of protease inhibitors α-1-anti-trypsin and α-2-macroglobulin in patients in washings of purulent wounds, as well as in the same patients in the blood serum, which were significantly lower than the same data of patients with postoperative wounds.

Keywords Pro-inflammatory interleukins, Anti-inflammatory interleukins, Protease inhibitors, Purulent wounds, Postoperative wounds, Wound healing

1. Introduction

The influence of pro-inflammatory and anti-inflammatory interleukins on local and systemic immunity is well known. However, inhibitors of proteases, in addition to their anti-protease activity, also have the ability to influence local and systemic immunity. They can also contribute to the termination of inflammatory processes, including the modulation of cytokine expression, signal transduction, and tissue remodeling [8,9].

It has been established that the endogenous release of interleukin-10 is increased after the application of protease inhibitors. This research demonstrates the unique anti-inflammatory activity of protease inhibitors, which may have clinical significance [1]. Additionally, it has been shown that low doses of protease inhibitors, such as apronin, administered to humans, reduce systemic TNF release and subsequent activation of CD11b neutrophils. The effect of apronin is similar to that found in a comparison group of patients receiving only glucocorticoids (methylprednisolone). These data demonstrate that protease inhibitors have an anti-inflammatory effect in humans [1].

Protease inhibitors can increase the biological activity of TGF-β by releasing it from its complex with α-2-macroglobulin [3]. Moreover, protease inhibitors inhibit markers of inflammation, as well as the production of FN-α and interleukins 1, 8, and 6. They also inhibit the secretion of IL-1, IL-6, IL-8, IL-10, IL-11, TNF, NO, and PAF [5,7].

The data presented demonstrate the significant involvement of protease inhibitors in the regulation of local and systemic immune factors. It was also discovered that certain bacterial proteases can degrade cytokines and their receptors [2]. Proteases can also prevent the activity of some cytokines and cause their degradation [4].

Moreover, protease inhibitors and their inhibitors contribute to the balance between degradation and retention of the extracellular matrix (ECM), creating a balance necessary for timely and coordinated wound healing. However, when this balance is disrupted, wounds transition to a chronic state, characterized by elevated protease levels and reduced protease inhibitor levels [4].

In summary, these data highlight the complex interplay and regulation of cytokines, proteases, and inhibitors of proteases, both locally and systemically in the immune system. This emphasizes the need for continued research to better understand this interaction and its potential therapeutic correction.

The aim of the study was to investigate the changes in pro-inflammatory and anti-inflammatory interleukins, as well as protease inhibitors, in patients with chronic purulent wounds.

2. Materials and Methods

In the first group, 26 patients with postoperative wounds

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(control) and, in the second group, 29 patients with purulent wounds were examined. All patients in the study had no history of heart disease, diabetes, or metabolic disorders. The material for the study was obtained by collecting samples from the surface of postoperative and purulent wounds using sterile physiological solution [6].

In the composition of postoperative and purulent wounds, as well as in blood serum, cytokines were studied, including pro-inflammatory ones such as interleukin-1 beta (IL-1β), tumor necrosis factor-α (TNF-α), and anti-inflammatory ones such as interleukin-10 (IL-10) using the enzyme-linked immunosorbent assay (ELISA) method with "Vector-Best" LTD test systems. Additionally, inhibitors of proteases α-1-antitrypsin and α-2-macroglobulin were determined using the "Sentinel" test systems from Italy.

The obtained data were subjected to statistical processing using standard programs of the MS Excel 2010 package, including the calculation of arithmetic means (M), their standard deviations (m), and the confidence coefficient of the difference in means (t) according to Student's t-distribution.

3. The Results and Discussion

The results and discussion showed that the concentration of pro-inflammatory TNF-α in postoperative wounds (control group) was on average 1.7±0.15 pg/ml, while in purulent wounds (experimental group) the result was 6.5±0.59 pg/ml ($p<0.001$). The data of this study demonstrate that the TNF-α levels in purulent wounds were significantly higher than in postoperative wounds. The pro-inflammatory IL-1 levels in postoperative wounds were 3.5±0.31 pg/ml, while in purulent wounds, this indicator was significantly higher and was at the level of 12.5±1.1 pg/ml ($p<0.001$).

TGF-β is a regulator of pro-inflammatory and anti-inflammatory interleukins, so the study of TGF-β in wound exudate has significant importance. It was found that in postoperative wounds, the TGF-β level was 36.8±3.2 ng/ml, while in purulent wounds, it was significantly lower and amounted to 25.5±2.3 ng/ml ($p<0.01$). The ratio of these indicators was similar to the results of anti-inflammatory IL-10 in postoperative and purulent wounds.

In the study of protease inhibitors, it was found that the α-1-antitrypsin level in postoperative wounds was 9.1±0.86 mg/dl, while in purulent wounds, the level of this indicator was significantly lower and amounted to 5.7±0.55 mg/dl ($p<0.001$). The results of the α-2-macroglobulin study in the composition of postoperative and purulent wounds showed a similar relationship to that of α-1-antitrypsin. In postoperative wounds, the α-2-macroglobulin level was 21.2±1.9 mg/dl, while in purulent wounds, it was 14.7±1.3 mg/dl ($p<0.01$). These data also demonstrate significantly lower levels of α-2-macroglobulin in purulent wounds compared to postoperative wounds.

The study of pro-inflammatory and anti-inflammatory interleukins, as well as inhibitors of proteases in serum, allowed us to establish that the level of pro-inflammatory interleukin TNF-α in the blood of patients with postoperative wounds was equal to 2.5±0.22 pg/ml. In patients with purulent wounds, the study demonstrated that the TNF-α levels were significantly higher and amounted to 8.2±0.75 pg/ml ($p<0.001$). The level of pro-inflammatory interleukin IL-1 in the blood of patients with postoperative wounds was 5.1±0.46 pg/ml, while in patients with purulent wounds, it was 15.5±1.4 pg/ml ($p<0.001$). According to these results, this indicator was significantly higher in relation to the results of patients with postoperative wounds. The ratio of these indicators was similar to the results of TNF-α in patients with postoperative and purulent wounds.

The study investigated the levels of various cytokines and protease inhibitors in the blood and wound exudate of patients with postoperative and purulent wounds. The results showed that the levels of the anti-inflammatory cytokine IL-10 were significantly lower in the blood of patients with purulent wounds compared to those with postoperative wounds. On the other hand, the levels of the pro-inflammatory cytokines TNF-α and IL-1 were significantly higher in the blood and wound exudate of patients with purulent wounds compared to those with postoperative wounds. The study also found that the levels of the protease inhibitors α-1-antitrypsin and α-2-macroglobulin were significantly lower in the blood and wound exudate of patients with purulent wounds compared to those with postoperative wounds. In contrast, the levels of TGF-β were significantly higher in the blood of patients with postoperative wounds compared to those with purulent wounds. The study suggests that the levels of these cytokines and protease inhibitors may be useful as biomarkers for wound healing and infection.

4. Conclusions

The levels of pro-inflammatory interleukins TNF-α and IL-1 in the washouts of purulent wounds of patients, as well as in the serum of these same patients, were significantly higher than the similar results of patients with postoperative wounds. At the same time, the results of the content of the anti-inflammatory interleukin IL-10 and TGF-β in the washouts of purulent wounds of patients, and in the serum of these same patients, had the opposite direction and were significantly lower than similar results of patients with postoperative wounds. Similar changes, as with anti-inflammatory interleukins, were observed when studying protease inhibitors α-1-antitrypsin and α-2-macroglobulin in the washouts of purulent wounds of patients and in the serum of these same patients, which were significantly lower than the same data of patients with postoperative wounds.

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