Assessment of innate antimicrobial response disorders in critically ill patients with severe infections and malnutrition

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SUMMARY

Severe infections, malnutrition and the accompanying immune disorders remain among current diagnostic and therapeutic problems in the critically ill group. Patients treated in Intensive Care Units (ICUs), primarily septic patients or patients with severe trauma, or who have undergone extensive surgery, are at high risk of malnutrition and the resulting homeostatic, metabolic, histological and immunological disorders leading to organ failure and increased susceptibility to infection. Little-known mechanisms of immune response in sepsis and still insufficiently effective diagnostic tools remain the key reasons for high mortality in patients with severe infections treated in ICUs. On the other hand, nutrition disorders, found even in 100% of patients treated in ICU, are an independent factor significantly affecting prognosis. It seems that only early diagnosis of immune and nutritional disorders, anticipating irreversible metabolic, immunological disorders and organ damage, as well as monitoring of malnutrition and selected immunity parameters may result in improvement of treatment results.

The aim of the study was to investigate disorders of innate antibacterial response in critically ill patients with infections and malnutrition treated in the intensive care units. The subject of the detailed study was an attempt to determine the practical usefulness of determining the concentration of selected proteins of pro-, anti-inflammatory and antibacterial response in peripheral blood, first of all: as potential indicators that may be of significant importance in early diagnosis of severe infections that increase mortality, with special attention to their prognostic value; secondly, as potential indicators for early detection of malnutrition/malnutrition degree and the associated changes in immunity. The impact of nutritional status on prognosis (mortality) was also assessed in patients treated in ICUs.

Changes in the concentration of selected proteins associated with the TLR4 signaling pathway, including its effectors – pro and anti-inflammatory cytokines and selected proteins of antibacterial response (IL-1Ra, TNF-α, sTNFR1, IL-6, IL-10, sTLR4, MyD88, A20, HSP70, HMGB1-by ELISA) were assessed in 163 patients treated in the ICU. On the first day of treatment, beside immunological tests, the severity of the condition (scale APACHE II), severity of infection according to the criteria of ACCP / SCCM, and nutritional status (NRS

2002) of the patients were assessed. The course of the disease and mortality of every patient were monitored. The control group consisted 48 healthy people.

As a result of the study, significant innate immunity disorders were found in the group of patients treated in the ICU. It has been shown that severe infections and malnutrition have a significant impact on selected immune parameters. The changes in concentrations of selected proteins may have significant diagnostic and prognostic significance in assessing the risk of serious complications and death. In the analysis of differences in the course of the immune response in severely infected and non-infected patients, significantly higher sTNFR1 levels were found in patients with infections. In the group of patients who died, significantly higher concentrations of sTNFR1, IL-6, IL-10, HSP70 were observed compared to the group of survivors. In assessing the prognostic value of the studied proteins, they were compared with the assessment of patients on the APACHE II scale (AUC = 0.726). The study of ROC curves found that the determination of the concentration of sTNFR1 protein (AUC = 0.686) is a particularly effective prognostic tool in patients with infections, while in other patients treated in the ICU the effectiveness of IL-6 determination (AUC = 0.736) was confirmed, while excluding the efficacy of this cytokine in predicting death from infections.

In assessing the impact of malnutrition on immune disorders, it was found that compared to healthy people with good nutritional status, there are significant deviations from the norm in most immunological parameters in malnourished patients. In the whole group of malnourished patients, median values of sTNFR1, TNF-α, IL-6, TLR4, IL-1Ra were significantly increased, while the levels of MyD88 and A20 proteins were significantly reduced. Only in the case of sTNFR1 protein, a significant difference between mild and moderate, moderate and severe malnutrition was detected alongside increased concentrations as the severity of malnutrition worsens. In the correlation study centred on the sTNFR1 protein, it was found that as the degree of malnutrition increased, the protein concentrations grew as well ($r = 0.5442$; $p = 0.0000$). Regardless of the reason for hospitalization in the ICU, both in patients with infections ($r = 0.3914$; $p=0.0018$), as well as without infections ($r = 0.4124$; $p = 0.0003$), sTNFR1 protein correlated with the degree of malnutrition. In assessing the prognostic value of malnutrition, it was observed that death was significantly more frequent in the group of patients who on the first day of hospitalization in the ICU received 5 or more points on the NRS2002 scale (severe malnutrition) ($p = 0.0004$). A correlation was noted between the malnutrition status (NRS2002) and the APACHE II scale score assessing the severity of a patient's condition ($r = 0.3382$; $p = 0.0000$).

The results of the presented studies are encouraging and indicate the relevance of undertaking further clinical trials, including the routine monitoring of sTNFR1 and nutritional status in various groups of patients treated in intensive care units. This protein may be useful in the early diagnosis of immune disorders, severe infections, malnutrition, and assessment of malnutrition already in the first hours after admission to the ICU.