The strategies of sepsis treatment and new marker searching for sepsis monitoring and preventing

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Abstract. This article describes the problem of sepsis and sepsis-like diseases (e.g. severe sepsis, septic shock) as a result of the systematic inflammatory reaction syndrome appearance, which are the major cause of the high morbidity and mortality, particularly in the intensive care units. Otherwise, sepsis and sepsis-like diseases are still one of the dangerous medical problems which are not well and fully understood. The advanced biomedical research under the searching universal biochemical markers in the SIRS, sepsis, severe sepsis and septic shock conditions are still performed. Previously the most important and useful protein markers in recognition, treatment and monitoring processes are procalcitonin (PCT), C-reactive protein (CRP) and serum amyloid A proteins (SAA) and also interleukins, e.g. IL-1, IL-6, TNF-alpha. These parameters are not specific for the inflammatory reaction as well as for infections caused by the different pathogens, particularly for Gram-negative infections which are responsible for the SIRS-related disorders. The Gram-negative bacteria infections are dominating pathogens during microbiological cultures test and were recognized as the main etiological factors of the severe sepsis (48%). For these reasons, the new and highly specific parameters are necessary to search in order to minimize the social and economic negative effects of the SIRS pathogenesis. These new biochemical markers for monitoring and preventing of interested diseases may be based on specific antibodies, recognizing specific molecules participated in the cascade of the inflammatory reaction (e.g. antibodies against TNF-alpha or PCT proteins) or antibodies against specific molecules, recognizing the Gram-negative bacterial specific molecules structures, participating in the sepsis and sepsis-like disorders (e.g. antibodies against LPS specific fragments).

Keywords: sepsis, sepsis-like disorders, protein markers, specific antibodies

Introduction

Sepsis and sepsis-like diseases as pathological conditions are still one of the dangerous medical problems which are not well and fully understood. Despite of the progress in the biomedical research, the sepsis syndrome as well sepsis-like disorders characterize by the high mortality rate, particularly in intensive care units. The main reasons for sepsis and sepsis-like disorders are the population aging, the increasing resistance to antibiotics, or application the invasive medical treatments. These pathological conditions have also very significant economical and social consequences despite of the progress in application of many diagnostic and therapeutic procedures. Standard procedures for sepsis, severe sepsis and septic shock recognition and monitoring are used in many countries around the world [1-2].

The advanced biomedical studies under the searching universal biochemical markers in the SIRS, sepsis, severe sepsis and septic shock conditions are performed. Until now, during the clinical treatment of sepsis and sepsis-like disorders, the most important and useful protein markers are procalcitonin (PCT), C-reactive protein (CRP) and serum amyloid A proteins (SAA) and interleukins level (IL-1, IL-6, TNF-alpha). Unfortunately, these parameters are not specific for the inflammatory reaction as well as for infections caused by the different pathogens, particularly by Gram-negative bacteria. These parameters may be clinically useless also for the SIRS and sepsis differentiation processes. Although, the laboratory parameters of systematic inflammatory reaction are slightly helpful only for the sepsis recognition, they are rather used to monitor the course of disease. They may be used also for the assessment of the therapy effectiveness [3-5].

Thus, many attempts are being made in order to find new and highly specific parameters which would facilitate both the detection of sepsis as also bacterial infection causes sepsis or sepsis-like disorders. In consequence, a new differential marker is urgently awaited for SIRS syndrome and for sepsis differentiation. This parameter should fulfill many clinical and also analytical demands. These new biochemical markers for sepsis and sepsis-like diseases monitoring and preventing may be based on specific antibodies, recognizing the specific molecules participated in the cascade of the inflammatory reaction (e.g. antibodies against TNF-alpha or PCT proteins) or antibodies against specific molecules, recognizing the Gram-negative bacterial specific molecules structures (e.g. antibodies against LPS specific fragments). These antibodies may be promising and new diagnostic markers during monitoring and treatment of sepsis and sepsis-like diseases.

Standard procedures for sepsis, severe sepsis and septic shock recognition and monitoring

Currently, the sepsis term refers to the systemic inflammatory response to infection and is defined as the group of clinical symptoms which cause the changes in the haemodynamic, hematological and also in biochemical parameters. Although sepsis is a common clinical syndrome recognized after any infection, it must be remembered that the infection does not disclose in any case. The confirmation of the infection etiology in sepsis requires precisely adherence of sepsis and sepsis-like diseases definitions as well as establishes the diagnostic criteria of the blood infections according to guidelines proposed by e.g. the Centres Disease Control (CDC), or by the WHO and also by ACCP/SCCM [3-6].

According to ACCP/SCCM guidelines, a sepsis should be always suspected in all patients staying in the intensive care units after recognizing such symptoms as: fever or hypothermia, unexplained tachycardia or tachypnea, arterial hypoxemia, shock of unknown cause, confusion, hypotension, leukocytosis or leukopenia, parameters changes of renal function and liver function of unknown etiology, thrombocytopenia and/or DIC syndrome. In this sense, the suspicion of the SIRS syndrome is always alarming and prescribes the implementation of procedures for the confirmation or exclusion of the SIRS infectious etiology. Consequently, these procedures may improve the process efficiency during identification and selection of patients with the developing and spreading sepsis [3-5].

It is worth to noting that during the clinical treatment of sepsis and sepsis-like disorders, the most important and useful protein markers are procalcitonin (PCT), C-reactive protein (CRP) and serum amyloid A proteins (SAA). Moreover, there are many different mediators of the inflammatory reaction which are biologically active during these reactions. The inflammatory properties are characteristic features also for catecholamines, endogenic opioids, histamine, cortisol as well as reactive oxygen species (ROS), adrenocorticotropic hormone (ACTH), and also for the degradation fibrinogen products [6-9].

The advanced biomedical studies under the searching universal biochemical markers in the SIRS, sepsis, severe sepsis and septic shock conditions

In order to minimize the social and economic negative effects of the sepsis and sepsis-like diseases problem, the implementation of more precise and faster sepsis diagnostics methods is required as well as the verification the specific systems for making the faster and reliable qualifications of patients into different groups depending on the disease severity and also depending on the increased a death risk degree.

Many attempts are being made in order to find new and highly specific parameters which would facilitate both the detection of sepsis as also bacterial infection causes sepsis or sepsis-like disorders. In consequence, a new differential marker is urgently awaited for SIRS syndrome and for sepsis differentiation. This parameter should fulfill many clinical and also analytical demands e.g. 1. the high (absolute) specificity against bacterial infections factors and the insensitivity against the other pro-inflammatory stimulants; 2. the high sensitivity as a result of the lack of this marker in the sera of healthy volunteers or in patients without bacterial infections (high diagnostic sensitivity during bacterial infection identification process); 3. the large dynamics of the rises or drops of this parameter in the blood of infectious patients (serum or plasma) and the half-life sets at 1-3 days what providing the possibility to use this parameter to both the early diagnosis and for the monitoring treatment progress during bacterial infections; 4. the significant correlation against systematic inflammatory reaction level what may lead to the severe condition assessment (differentiation) and also for the prognosis of the disease course or death risk identification; 5. the high stability of designed marker in patients sera storing under the appropriate conditions and the possibility of using it in the easy, faster and economical identification methods of this marker. This marker would improve the effectiveness of the therapeutic process and, consequently, it would bring the measurable economic and social benefits.

BIBLIOGRAPHY


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