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IM - COMMENTARY

Could hypoglycemia and hypoalbuminemia allow the identification of septic patients at high mortality risk in addition of clinical scores?

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Sepsis and severe sepsis are an important public health problems because of elevated mortality (as high as 28.6%) and expensive treatment (about $18,600 USD per hospital stay in the US) [1, 2]. Sepsis incidence and septicemia-related deaths are reported to be growing [3]. Despite the case-fatality rate has declined due to advances in supportive care for the critically ill patients [4], this trend is expected to continue because of aging of the population, increasing of chronic health conditions, and increased use of immunosuppressive therapy, transplantation, chemotherapy, and invasive procedures.

Since 1991, the diagnosis of sepsis has undergone a metamorphosis because of the use of a standardized definition [5]. Sepsis-3 introduced new observations on the biopathology of sepsis, on the lack of sensitivity and specificity of the SIRS criteria and on the excessive attention to inflammation as a part of the alterations [6].

The updated definitions in Sepsis-3 focus on organ failure in the case of infection, which can be evaluated using the sequential (sepsis-related) organ failure assessment (SOFA) score [6]. Studies performed in the setting of Intensive Care Unit (ICU) have proposes SOFA as a score to identify septic patients at higher mortality rate.

In the attempt to make the therapeutic approach more immediate and effective, even in conditions of limited availability of resources and in the early stages of rescue, the concept of quick SOFA (qSOFA) was introduced. In recent years, several studies have compared the SIRS criteria with qSOFA in trying to identify high-risk septic patients as early as possible [7–11]. These studies clearly show the difficulty to identify a valid criterion for the early recognition of septic patient in Emergency Department.

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The lack of a "perfect" biomarker of sepsis has led to the production of numerous scoring systems, none of which presents the characteristics of an ideal test. Nevertheless, once the sepsis is diagnosed, it is important to start therapy as soon as possible, because this is demonstrated to reduce mortality [12–14].

The study of Furukawa et al. [15] is a contribution to international debate in looking for indicators that can help us to identify in a short time the septic patient at high risk of death. The authors have shown that hypoglycemia and hypoalbuminemia are independent factors to identify high-risk patients in the first approach in the emergency room. The study also highlights how these indicators correlate with the SOFA and APACHE scores that are instruments used in Intensive Care Units and still require a longer time in the evaluation of the various parameters.

The main characteristic of this study is certainly that the considered values of blood glucose and albuminemia were performed at the arrival in the Emergency Department. The study shows that the values of glycemia and albuminemia could have an added meaning to the patient's clinical condition [15].

However, both for glucose levels control and albumin administration there is still debate about optimal management in septic patients.

Several studies have been carried out to evaluate the effects of an aggressive control of blood sugar levels. It was described that septic patients with blood glucose between 80 and 110 mg/dl could have an advantage in terms of survival [16]. However, a successive large randomized international study demonstrated that in patients treated to intensive glycemic control (81–108 mg/dl), compared to maintaining of glucose values $\leq$ 180 mg/dl, the absolute risk of death was increased by 2.6% at 90 days [17]. Therefore, excessive and more intensive glycemic monitoring cannot be recommended in critical adults, being superior in terms of mortality, probably due to the adverse effects on the cardiovascular system of both hypoglycemia and insulin excess [17].

For as regard hypoalbuminemia, some data can be extrapolated from large randomized trials comparing crystalloids and albumin in the general population. In a subgroup of 1218 patients with severe sepsis enrolled in the SAFE study, multivariate analysis revealed that those treated with albumin had a lower risk of 28-day death than saline-treated patients [18]. Furthermore, a meta-analysis that compared albumin and crystalloids in septic patients has shown a beneficial effect of albumin on survival [19]. However, these positive result has been questioned by the results of a large randomized trial (ALBIOS study). In this study, albumin administration did not improve survival at 28 and 90 days. However, based on post hoc analysis, a benefit of albumin in the subset of patients with septic shock has been shown [20]. A specific benefit of albumin could also derive from the non-oncotic properties of the molecule as they can antagonize some of the pathophysiological mechanisms related to septic shock [21].

As the authors point out, the study presents some limits that need certainly to be considered in future studies, but the results presented are certainly interesting for their implications in clinical practice.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights This article does not contain any studies with human and animals performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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