CRITICAL CARE

COMMENTARY

Predicting treatment failure in severe sepsis and septic shock: looking for the Holy Grail

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See related research by Schuetz *et al.*, http://ccforum.com/content/17/3/R115

Abstract

Procalcitonin has been proposed as a specific biomarker of bacterial infections and has been related to the severity of sepsis. The prognostic ability of the initial concentrations of procalcitonin in sepsis is controversial. Some studies find higher initial concentrations in non-survivors but others find no differences. Prognostic assessment based on follow-up of procalcitonin levels may be better than evaluation of the initial levels of procalcitonin. The persistence of elevated procalcitonin levels is indicative of poor prognosis and is associated with mortality.
Procalcitonin kinetics could be a tool for assessing the evolution of severe sepsis and sepsis shock.
Procalcitonin should find its place as a biomarker for predicting treatment failure of severe sepsis and septic shock.

In the previous issue of *Critical Care*, Schuetz and colleagues [1] present further evidence about the usefulness of procalcitonin (PCT) for prognostic prediction in septic patients. The hypothesis of their study was that PCT plasma kinetics over the first 72 hours of critical care improved mortality prediction of septic patients. The conclusion was that PCT kinetics over the first 72 hours of critical care provided prognostic information about ICU mortality and in-hospital mortality in patients with confirmed or likely sepsis.

One of the problems in the ICU is the need to differentiate patients with an inflammatory response from those with an infecting reaction. This is very prominent in respiratory tract infections [2]. Moreover, in lung transplant, it is necessary to differentiate sepsis from acute humoral or cellular rejection when respiratory failure is developing. Assessment of early resolution is a secondary problem, associated with management decisions such as the need for an additional source control, a change of antibiotics, initiating adjunctive therapy or searching for complications. In these scenarios, PCT, C-reactive protein and other biomarkers are objective variables to add to clinical assessment, becoming areas of active research, whereas genomics may provide additional clues in the future.

In medical practice, it is important to have evidence to assess the prognosis or to predict patient outcome. This is especially relevant in severe sepsis. PCT has been proposed as a specific biomarker of bacterial infections [3,4] and has been related to the severity of sepsis [5]. The initial absolute peak of PCT in the inflammatory process induced by sepsis is early; it reaches plateau values at 6 to 24 hours and has a half-life around 24 to 36 hours [6].

The prognostic ability of initial concentrations of PCT in sepsis is controversial and while some studies [7,8] find higher initial concentrations in non-survivors, others find no differences [9-12]. Significant changes induced by the therapeutic measures taken can occur even in patients with very high initial concentrations of PCT, so it is not always associated with poor prognosis. However, prognostic assessment based on follow-up of PCT levels may be better than evaluation of the initial levels of PCT.

In their study, Schuetz and colleagues [1] concluded that, in septic patients, PCT kinetics over the first 72 hours of critical care provided prognostic information beyond that from clinical risk scores and might assist physician decision-making regarding care intensification or early transfer from the ICU to the floor. For ICU and in-hospital mortality, a 72-hour PCT decrease >80% had a negative predictive value of 91%, and no decrease or an increase in PCT over 72 hours had a positive predictive value of 48%. This prognostic information was independent of initial

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severity scores (Acute Physiology and Chronic Health Evaluation Score IV and Simplified Acute Physiology Score II). As addressed by the authors, some limitations are relevant. It is a non-interventional study, including two independent cohorts of adults (with some imbalances) admitted to critical care units of different hospitals based on International Classification of Diseases edition 9 (ICD-9) and retrospective medical record reviews. Indeed, ICD-9 codes do not adequately identify cases of infection and sepsis, may underestimate certain infections and may overestimate severe sepsis due to the introduction of patients with organ dysfunction already present at the time of infection. Furthermore, it has been suggested that important differences in diagnostic coding strategies may be associated with each hospital [13].

The persistence of elevated PCT levels is indicative of poor prognosis. PCT kinetics could be a tool for assessing the evolution of severe sepsis and septic shock. Several papers have been published emphasizing the importance of measuring PCT kinetics. In patients with septic shock, Suberviola and colleagues [14] showed that a decrease in PCT levels at 72 hours was an independent marker of hospital survival. Karlsson and colleagues [11] showed that mortality in patients with severe sepsis was lower in those in whom PCT concentrations at 72 hours fell by more than 50% with respect to initial values. Assessment of PCT levels at an earlier time could also provide prognostic information. In this regard, Ruiz-Rodríguez and colleagues found that a decrease of PCT levels at 48 hours was a predictor of survival in patients with septic shock and multiorgan failure [15].

In summary, the study of Schuetz and colleagues [1] is welcome because it provides additional information on the potential contribution of biomarkers for the early identification of patients with poor prognosis. Predicting treatment failure depends on three issues: the antimicrobial therapy, the host and the bug. Therefore, further information is required regarding the interaction of these elements. Initial bacterial load in pneumococcal pneumonia has proven to anticipate the need for mechanical ventilation and vasopressor requirement [16]. Further research introducing newer molecular techniques of diagnosis plus biomarkers might serve to identify patients with sepsis candidates for pre-emptive adjuvant therapy.

Abbreviations

ICD-9: International classification of diseases edition 9; PCT: Procalcitonin.

Competing interests

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