CRITICAL CARE

COMMENTARY

PSP/reg: a new stone in sepsis biomarkers?

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See related research by Que *et al.*, http://ccforum.com/content/16/4/R114

Abstract

Rapid diagnosis, appropriate management, and time are the key factors for improving survival rate in many emergency clinical scenarios such as acute myocardial infarction, pulmonary embolism, cerebral stroke, and severe sepsis. Clinical signs and electrocardiographic, radiological, and echographic investigations associated with biomarkers usually allow a quick diagnosis in all of the above situations, except severe sepsis, in which the diagnosis in the early phases is often only presumptive. In sepsis, microbiological cultures are still considered the 'gold standard' for diagnosis, whereas the numerous biomarkers investigated are actually valuable only for patient stratification and evaluation of clinical course. In this issue of *Critical Care*, Que and colleagues describe the prognostic value of pancreatic stone protein/regenerating protein (PSP/reg) concentration in patients with severe infections. The data reported are interesting, but several questions about this biomarker arise, and further studies are needed to understand its role in sepsis and clinical practice.

In recent years, several biomarkers, such as procalcitonin (PCT), interleukin-6 (IL-6), soluble triggering receptor expressed on myeloid cells-1, and soluble urokinase-type plasminogen activator receptor, have been investigated to discriminate non-infectious diseases from sepsis. In this issue of *Critical Care*, Que and colleagues [1] describe the prognostic value of pancreatic stone protein/regenerating protein (PSP/reg) concentration in patients with severe infections.

PSP/reg functions historically have been reported mainly in regard to the pancreas, and, indeed, pancreatic acinar cells are considered the main source of this protein. PSP/reg was initially described as inhibiting pancreatic stone formation, but later this role was revised [2]. Its serum elevation seemed to be correlated strongly with severe acute pancreatitis and less tightly with chronic pancreatitis and pancreatic cancer [3]. In the '90s, preclinical studies demonstrated that PSP/reg appeared to stimulate islet B-cell growth and regeneration [4] and recently this function was hypothesized to play a role in a therapeutic approach to diabetes mellitus [5]. In recent years, PSP/reg investigations bypassed pancreatic diseases and focused on infection and inflammation [6]. Recent data from Keel and colleagues [7] showed that 83 patients with severe trauma but not pancreatic trauma had PSP/reg upregulation and that the number of patients with post-traumatic septic complications increased significantly. The authors postulated that PSP/reg binds and activates neutrophils behaving as an acute-phase protein that responds to injury during the early phase of infection. Boeck and colleagues [8] demonstrated predictive properties of PSP/reg regarding survival in patients with ventilator-associated pneumonia with two cutoff values for predicting survival and death with high specificity.

The study by Que and colleagues [1] enrolled 107 patients admitted to the intensive care unit (ICU) with severe infections. Within 24 hours after ICU admission, the authors measured the concentrations of PSP/reg, C-reactive protein, PCT, inflammatory cytokines, leukocyte count, and severity scores – Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score (SAPS) II and III, and Sequential Organ Failure Assessment (SOFA) – and correlated all of these parameters with in-hospital mortality. The authors demonstrated that PSP/reg and SAPS III were the only two variables associated with mortality and thus concluded that PSP/reg is the only bedside biomarker useful in predicting the outcome of patients with sepsis. The data presented in the article are sound, but several questions arise: Is PSP/reg related to infection or to tissue hypoperfusion? Do comorbidities affect PSP/reg values in patients with sepsis? Is a single PSP/reg measurement helpful in clinical practice?

Tumor necrosis factor-alpha, interferon-gamma, and IL-6 are known to induce PSP/reg expression and thus PSP/reg can be assumed as a potential sepsis marker [9]. Nevertheless, to our knowledge, no studies on PSP/reg

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concentrations in other types of shock (that is, hemorrhagic or cardiogenic) have been performed. So the high values observed in patients with septic shock may not necessarily be related to the infection pathway but may be due to tissue hypoperfusion or systemic inflammatory response or both. PSP/reg is increased in patients with chronic renal failure, gastric cancer, peptic ulcer, liver cirrhosis, or diabetes mellitus [2]. Que and colleagues [1] reported that 'most patients had at least one comorbid condition', but unfortunately the authors did not analyze how these comorbidities affected the initial levels of PSP/reg. A useful biomarker ought to fulfill different clinical needs such as early diagnosis and accurate evaluation of clinical course. A single PSP/reg measurement correlated with the severity of the disease, but we do not know whether this biomarker is reliable in the early diagnosis of bacterial infection or, for instance, in monitoring the therapy response. Que and colleagues added new and interesting findings on the relationships between PSP/reg and patients with severe sepsis. However, there is a long way to go before PSP/reg, along with other biomarkers, can be implemented in clinical practice.

Abbreviations

ICU, intensive care unit; IL-6, interleukin-6; PCT, procalcitonin; PSP/reg, pancreatic stone protein/regenerating protein; SAPS, Simplified Acute Physiology Score.

Competing interests

The authors declare that they have no competing interests.

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