Editorial

Can we consider procalcitonin as a consolidated biomarker in sepsis management?

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Procalcitonin (PCT) belongs to the calcitonin superfamily of peptides and is encoded by the CALC 1 gene located on the short arm of the chromosome 11. In infective states, the release of bacterial endotoxin results in a ubiquitous expression of CALC 1 gene. It has been suggested that the presence of microbial infection-specific response elements within the CALC 1 gene promoter overrides tissue-specific selective expression pattern leading to an overwhelming response to infective stimuli. As a result, systematic proteolytic cleavage and enzymatic degradation result in the release of PCT into the circulation.[1]

Procalcitonin is one of the many biomarkers studied for sepsis (as sTREM1 and others) and appears to be one of the most promising markers of the presence and severity of a relevant bacterial infection.[2] With documented superiority to conventional markers such as white blood cell count or C-reactive protein, which lack diagnostic accuracy and are sometimes misleading, PCT has a significant role in facilitating early diagnosis and management of relevant bacterial infection thus lowering the associated morbidity and mortality. However, a single value of PCT done at the time of admission, cannot predict the prognosis of the critically ill septic patients and we must also remember that because PCT displays wide inter-individual variability, therefore, interpretation may require serial measurements. In this way is interesting, the study from De Azevedo *et al*.[3] referring that persistently high PCT concentrations in plasma, as well as reduced 24-h PCT clearance, were associated with a significant increase in mortality in patients with severe sepsis and septic shock.

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We must point out that there is no so much literature relating the prognostic value of the fall of PCT levels, and we enjoy the new scientific papers addressed to obtain this objective. In this sense is relevant, the elegant paper from Sudhir *et al*.[4] These authors studied different causes of sepsis-like severe generalized bacterial, parasitic or fungal infections with systemic manifestation and propose that although elevated serum PCT values during severe infections may decrease to very low levels with appropriate therapy, this does not always indicate complete eradication of the infection but only that generalization of the infection or the systemic response is under control. In this context is really interesting, the paper entitled "PCT kinetics as prognostic marker in severe sepsis/septic shock" published in these issue:[5] In this prospective paper the PCT value decreased by a median of 59.7% in the entire group; the median value in survivors and non survivors was 73.5% and 24.4%, and the difference was statistically significant ($P < 0.01$). The conclusion is that in critically ill patients with severe sepsis/septic shock, change (fall) in PCT is associated with good outcome.

On the other hand, the duration of antibiotic therapy in Intensive Care Unit (ICU) is often undefined, and clinical features are of limited help in guiding discontinuation of therapy. At the present time, we can consider PCT as the most extensively studied biomarker in the setting of both discontinuation and change of antibiotic therapy.

In the excellent systematic review from the Agency for Healthcare Research and Quality,[6] the authors found that PCT guidance reduces antibiotic use for adult patients in both medical and surgical ICUs. Studies included patients who had comorbidities that are common in ICU patients (e.g. cardiac disease, diabetes, chronic lung disease, cirrhosis, chronic renal failure, cancer), and thus, the evidence from these studies is applicable to the usual clinical practice in the ICU setting. They also refer that PCT guidance for initiation and discontinuation of antibiotic (AB) therapy significantly reduced antibiotic prescription rates and duration in patients with acute respiratory tract infections, including acute exacerbations of chronic obstructive pulmonary disease, community-acquired pneumonia, and acute bronchitis (high evidence). In the excellent and recent paper of our colleagues of the Department of Anesthesia of our hospital; the authors refer that in critically ill patients with secondary peritonitis PCT-guidance produced 50% reduction in AB duration ($P < 0.001$, log-rank test).[7]

The value of PCT-guided antibiotic therapy depends on the clinical benefits of reduced antibiotic use, which is difficult to quantify. Immediate consequences may include a decrease in allergic reactions, drug toxicities, and frequency of *Clostridium difficile* infection. A major downstream effect of reducing antibiotic use may be a lower probability of emergence of antibiotic–resistant strains. In contrast, PCT-guided intensification of antibiotics in adult ICU patients increases morbidity (moderate evidence).[8]

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