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Plasma Neutrophil Gelatinase- Associated Lipocalin (NGAL) in Combination with Procalcitonin (PCT) and MR-Proadrenomedullin (MR-proADM) in the Diagnosis and Prognosis of Sepsis and Sepsis Associated Acute Kidney Injury

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Abstract:

Early recognition of sepsis is important to prevent progression to severe sepsis and septic shock conditions that may lead to Acute Kidney Injury (AKI).

Sepsis is a systemic syndrome characterized by a Systemic Inflammatory Response Syndrome (SIRS) in the presence of a definite or suspected infection. Sepsis is defined "severe" when cooperate with hypo perfusion or dysfunction of at least one organ system and can progress to septic shock when severe sepsis is accompanied by persistent hypotension or need for vasopressors. Severe sepsis and septic shock will problem a multiple organ dysfunction syndrome, which induces high morbidity and mortality in critically ill patients. Organ dysfunctions and failures in sepsis patients can be evaluated though the sepsis-related organ failure assessment (SOFA) scores.

Sepsis and septic shock are important contributing factors of sepsis associated (SA)-acute kidney injury (AKI) accounting for patients access in the intensive care unit (ICU) and may be an independent risk factor of mortality. Sepsis associated AKI usually is accompanied by hyper dynamic circulation. When showing with AKI of nonpeptic origin, septic AKI is characterized by a distinct pathophysiology and therefore requires a different approach. The pathophysiology, diagnostic procedures, and appropriate therapeutic interventions in sepsis are still more debatable. Numerous immune modulatory agents showing promise in preclinical studies fail to reduce the overwhelmingly high mortality rate of sepsis. Different markers have been proposed to improve sepsis diagnosis and prognosis.

Sepsis was defined using the International Guidelines for management of severe sepsis and septic shock: surviving sepsis campaign 2012 based on the presence of a recognized site of infection and evidence of a systemic inflammatory response.

Blood samples for blood culture were collected before antibiotic therapy start. Every blood culture comprised three sets (time 0, time 30 and time 60) of one aerobic and one anaerobic broth bottles (Bactec Plus Aerobic/F, Bactec Plus Anaerobic/F, Beckton Dickinson, Franklin Lakes, NJ USA) per patient drawn during 1-h period from cases of clinically suspected bloodstream infection. Blood culture vials were incubated in the Bactec 9240 automated system (Beckton Dickinson, Franklin Lakes, NJ USA). From positive broths, subcultures were showed and, according to the appearance of colonies on subculture plates, the isolates were identified, and the antimicrobial susceptibility test performed by Vitek 2.0 compact instrument (Bio- Merieux, Mercy L'Etoile, France).

PCT, MR-proADM, NGAL and creatinine were shown at admission (time T=0), at 12-24 hours (time T=1) and in the third or fifth day of antibiotic therapy (time T=3-5) in septic patients, whereas in patients with localized infection or SIRS and in healthy controls as a single determination coinciding with the enrollment time (T=0). PCT and MR-proADM were measured by an automated analyzer using a time-resolved amplified emission method (Kryptor; Brahms AG, Hennigsdorf, Germany), with commercially available assays (Brahms, Germany), as previously described.

The Mann-Whitney for individual samples was used to compare at T=0 NGAL, creatinine, PCT and MR-proADM found in the different categories of patients (sepsis, SIRS and patients with localized infection) and in healthy donors. A p-value < 0.05 was considered statistically significant.

Plasma NGAL values were significantly more in septic patients than patients with SIRS and patients with bacterial localized infections. These data help the hypothesis that plasma NGAL could distinguish sepsis from other inflammatory conditions as supported by ROC curve analysis. At the cut-off value of 300 ng/mL NGAL distinguish septic patients from SIRS and localized infections with high sensitivity and specificity. Plasma NGAL is increased in septic patients and significantly correlated with PCT and MR-proADM markers that rise in case of sepsis, as previously described. This strict correlation could be useful to further confirm the presence of a sepsis and to improve the management of critically ill patients.

Keywords: NGAL; Sepsis; Multi-marker approach; MR-proADM; Bacterial infection