Procalcitonin and C-reactive protein in SIRS and sepsis

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Use of CRP and PCT is effective during the diagnoses of SIRS and sepsis. The obvious advantage of their use is clearly visible during the early stage of sepsis. In this regards, marking of the procalcitonin may have preference, which is indicator of infectious process more than inflammation, in contrast to C-reactive protein.

Key words: Sepsis, Prolcalcitonin.

Introduction:

Infections are common in critically ill patients. Rapid diagnosis of sepsis is of importance in order to administrate the prompt appropriate antimicrobial agents. This decreases morbidity and mortality in patients with sepsis. However, diagnosis of sepsis has no “gold standard” in critically ill patients. Microbiological culture lacks sensitivity and specificity and takes 24-48h to provide definitive quantitative results. Since a high proportion of critically ill patients have the systemic inflammatory response syndrome (SIRS), we have to distinguish sepsis from SIRS. Therefore, we need reliable sepsis markers to facilitate early, accurate diagnosis. An ideal marker of infection would be highly specific, highly sensitive, easy to measure, rapid, inexpensive, and correlated with the severity and prognosis of infection. Therefore, this review evaluates the accuracy of procalcitonin (PCT) and C-reactive protein (CRP) in the differential diagnosis of SIRS and sepsis and the role of PCT in antibiotic therapy.

1. Procalcitonin (PCT)

PCT, a precursor of calcitonin, is a 116 amino acid protein with a molecular mass of 13 kDa that has proposed as a marker of bacterial infection. PCT is synthesized physiologically by thyroid C cells. In normal conditions, serum PCT levels are low (<0.1 ng/ml). In bacterial infection, PCT is synthesized in extrathyroidal neuroendocrine tissues. After infection, PCT levels increase from 3 to 4 h, peak at about 6 h and then plateau for up to 24 h. It is degraded by specific protease and has a half-life of between 25 and 30 h. PCT undergoes successive cleavages in the neroendocrine cells of the thyroid, lung and pancreas to form three distinct molecules; calcitonin (32 amino acids),

katacalcin (21 amino acids) and an N-terminal fragment called aminoprocalcitonin (57 amino acids). A merit of PCT is that PCT levels are not significantly affected by steroids.

PCT is useful as a marker in the diagnosis of severe bacterial infection. Localized infections or infections without systemic inflammation may induce no or only small increase in PCT levels. PCT levels were significantly higher in patients with severe sepsis and septic shock compared those with localized infection. PCT rises in proportion to the severity of sepsis and reaches its highest levels in patients with septic shock. PCT levels decreased after resolution of the infection, but increased when infections worsened.

On the other hand, PCT remains low in viral infections. Thus, PCT is the best marker for differentiating between bacterial and viral infection. In addition, PCT levels were less elevated in patients with candidemia than in those with bacteremia. A PCT cut-off value of 2ng/ml separated candida sepsis from bacterial sepsis. Therefore, a low PCT value in a critically ill septic patient is more likely to be related to candidemia than to bacteremia.

PCT levels are also increased in trauma and surgery. Trauma causes elevated PCT levels dependent on the severity of the injury. PCT levels peak on day 1-3 and fall thereafter. A secondary rise in PCT appears to indicate superadded bacterial sepsis. After surgery, PCT levels transiently increase and peak at 24-48 h, rarely exceed 5 ng/ml, and then fall back to normal levels. In patients with SIRS and multiple organ dysfunction syndrome (MODS), PCT is induced to very high serum levels during advanced stages of MODS and severe SIRS. PCT is elevated in renal impairment in the absence of infection. Therefore, we have to be careful of these situations. Recently.the role of PCT in antibiotic therapy has been reported. PCT-guided algorithms of antibiotic therapy has been shown to decrease the duration of antibiotic therapy for critically ill, septic patients without compromising clinical outcome.

2. C-reactive protein (CRP)

CRP was first discovered in 1930. CRP was named for its capacity to precipitate the somatic C-polysaccharide of Streptococcus pneumoniae. CRP is a 115,-dalton cyclic pentamic protein made of five promotors, each consisting of 206 amino acids. CRP is an acute phase protein and a sensitive systemic marker of inflammation and tissue damage. CRP levels rise between 12 and 18 h and peaks 36 h after bacterial challenge. CRP levels are determined by the synthetic rate of its production in the liver regulated predominantly by interleukin-6. CRP has a half-life of 19 h and is relatively slow in onset and offset in response to an acute inflammatory process when compared to PCT.

CRP levels are increased in sepsis. While the optimal cut-off value of CRP for the diagnosis of sepsis has yet to be established, some studies suggest that 5-10 mg/dl may be reasonable. A high CRP levels may include infections such as bacterial infections, fungal infections and severe viral infections including severe acute respiratory syndrome. Thus, the absolute CRP levels cannot be used to differentiate between bacterial, fungal and severe viral infections. In critically ill patients, CRP levels are elevated by various etiologies without sepsis such as surgery, trauma, burns, acute pancreatitis, inflammatory disease, and myocardial infarction. In patients with SIRS and MODS, CRP is often already in the upper concentration range even in patients with low severity scores. Since CRP is a quite unspecific parameter, a single CRP measurement may not be important for the diagnosis of sepsis. A failure of the CRP levels to reduce after 48 h of initiation of antimicrobial therapy may signify inadequate therapy and needs to be revised. A persistently elevated CRP levels during the recovery phase of a critical illness may signify the presence of persistent inflammation or new nosocomial sepsis.

Hemodialysis does not affect the CRP level. However, some drugs affect CRP levels. Corticosteroids may reduce CRP response to infection. Interleukin-2 treatment and donor granulocyte transfusion can induce a significant rise in CRP (>15mg/dl) in the absence of infection.

3.Comparison between PCT and CRP

Several studies have shown that PCT demonstrated the higher sensitivity, specificity, positive predictive value, and negative predictive value compared with CRP as a marker of sepsis. However, other studies have shown that PCT is no better than CRP in diagnosing infectious diseases. Taken together, PCT and CRP are not perfect, but equally effective in differentiating between SIRS and sepsis. On the other hand, PCT levels reflect the severity of sepsis and outcome, while CRP levels do not always reflect them because of ceiling effect.

Conclusions:

CRP and PCT are effective, not perfect, in differentiating sepsis and SIRS. PCT can now be used as a quick and early diagnostic test of sepsis in critically ill patients. PCT seems to be a more reliable marker of the severity and prognosis of sepsis than CRP due to the close correlation between the PCT levels and the severity of sepsis and outcome. The sensitivity for differentiating bacterial from viral infections was also higher for PCT markers than CRP; the specificities were comparable.

Taken together, the combined evaluation of PCT and CRP responses better predicted the causative microorganism in sepsis. In addition, PCT is used as a tool to reduce antibiotic course length.

C – რეაქტიული ცილის და პროკალციტონინის დიაგნოსტიკური მნიშვნელობა SIRS-ის და სეფსისის დროს

ჩ.მიტაკა (ტოკიო, იაპონია)

CRP და PCT გამოყენება ეფექტურია SIRS-ის და სეფსისის დიაგნოსტიკის დროს. მათი გამოყენების უდაო უპირატესობა მკვეთრად არის შესამჩნევი სეფსისის ადრეულ სტადიაზე. ამ თვალსაზრისით ერთგვარი უპირატესობა შესაძლოა ჰქონდეს პროკალციტონინის მარკირებას, რომელიც უფრო ინფექციური პროცესის მაჩვენებელია ვიდრე ანთების, განსხვავებით C - რეაქტიული ცილისაგან.

გასაღები სიტყვები: სეფსისი, პროკალციტონინი.