CRITICAL CARE

COMMENTARY

Leptin in sepsis: a well-suited biomarker in critically ill patients?

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See related research by Yousef *et al.*, http://ccforum.com/content/14/2/R33

Abstract

The value of monitoring serum leptin in critically ill patients is important for early diagnosis and differentiation between sepsis and non-infectious systemic inflammatory response syndrome (SIRS). The early diagnosis of sepsis, the identification of its origin, and an adequate therapeutic management are crucial to overcome sepsis-associated mortality. Cytokine levels are an obvious choice as sepsis markers, since cytokines are key mediators of the inflammatory response to sepsis. Leptin, a hormone mainly generated by adipocytes, acts centrally in the hypothalamus to regulate body weight and energy expenditure. There is, however, strong evidence that leptin is also involved in cell-mediated immunity and cytokine crosstalk. The finding that a serum leptin threshold of 38 μg/l can distinguish between sepsis and non-infectious SIRS (sensitivity 91.2%, specificity 85%) is the major finding in the article by Yousef and colleagues (in this issue). Much remains to be learned about the precise mechanisms by which leptin signaling participates in sepsis and non-infectious SIRS. This knowledge will potentially contribute to new therapeutic approaches.

Yousef and colleagues' article discussing the value of monitoring serum leptin in critically ill patients touches on the important matter of early diagnosis and differentiation between sepsis and non-infectious systemic inflammatory response syndrome (SIRS) [1]. The early diagnosis of sepsis, the identification of its origin, and an adequate therapeutic management are crucial to overcome sepsis-associated mortality [2].

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Cytokine levels are the obvious choice as sepsis markers since cytokines are key mediators of the inflammatory response to sepsis. Among the cytokines, TNFα, IL-1, IL-6, IFNγ, IL-10, and IL-13 best characterize the immune dysregulation during sepsis [3].

In 1998 Bornstein and colleagues reported an increase in leptin levels and the loss of the diurnal rhythm of this adipokine in survivors of acute sepsis [4]. They also observed that low leptin and high IL-6 levels indicated an unfavorable prognosis in patients with sepsis syndrome. Owing to contradictory findings in latter reports [5-9], however, the interest in leptin as a sepsis marker waned.

Leptin, a hormone mainly generated by adipocytes, acts centrally in the hypothalamus to regulate body weight and energy expenditure. There is, however, strong evidence that leptin is also involved in cell-mediated immunity and cytokine crosstalk [10].

Yousef and colleagues confirmed a positive correlation between leptin and IL-6 and TNFα in patients with sepsis [11]. The finding that a serum leptin threshold of 38 μg/l can distinguish between sepsis and non-infectious SIRS (sensitivity 91.2%, specificity 85%) is the major finding in the article by Yousef and colleagues (in this issue).

The matter at heart in the early differentiation between sepsis and non-infectious SIRS is the impact on outcome. In patients with surgically confirmed secondary peritonitis, our group found that a serum level of leptin <10 ng/ml was accompanied by a 4.25-fold increase in the risk of death. Our results were limited to moderate to severe peritonitis where the measurement was made 24 hours into the postoperative period (±2 hours) [12]. Since leptin apparently inhibits an excessive or harmful lipopolysaccharide-induced inflammatory reaction to or prevents TNFα-induced lethality in sepsis [13], it would have been interesting if Yousef and colleagues had reported the results of the 11 patients that died in their study group [1]. Our findings [12] concur with those reported by Bornstein and colleagues: an increase is found in leptin serum levels in septic patients, while a low leptin level is associated with a negative outcome [4] – possibly due to the lack of the protective effect of leptin [13].

Yousef and colleagues' report contributes to our understanding of the regulation of the inflammatory cascade in sepsis [1]. Much remains to be learned about the precise mechanisms by which leptin signaling participates in sepsis and non-infectious SIRS. This knowledge will potentially contribute to new therapeutic approaches.

Abbreviations

IFN, interferon; IL, interleukin; SIRS, systemic inflammatory response syndrome; TNF, tumor necrosis factor.

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Competing interests

The authors declare that they have no competing interests.

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