Editorial comment

Waheedullah Karzai and Konrad Reinhart

Address: Department of Anesthesiology and Intensive Care Medicine, University Hospital, Friedrich-Schiller-University Jena, 07740 Jena, Germany.

Correspondence: Prof. Dr. med. Konrad Reinhart, Department of Anesthesiology and Intensive Care Medicine, University Hospital, Friedrich-Schiller-University Jena, 07740 Jena, Germany.
Tel: +49 3641 933041; fax: +49 3641 933256;
e-mail: reinhart@anae1.med.uni-jena.de

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In this issue of the journal, Steinwald *et al* [1] extend limited clinical studies and report an animal experiment showing that calcitonin precursors (predominantly procalcitonin) are elevated in proportion to the severity of bacterial sepsis. They conclude that procalcitonin, the major calcitonin precursor, is a good indicator of the activity and severity of the inflammatory response and may be used for monitoring bacterial infections.

In recent years, a variety of laboratory and immunologic parameters have been proposed as possible indicators of severe inflammatory response to infections. One such parameter is procalcitonin, which has emerged as a possible marker of severe generalized infections [2]. The exact role of procalcitonin during infection is unclear. The elevated amount found during sepsis does not lead to increased levels of calcitonin and there is, as yet, no evidence that it may be involved in calcium metabolism. Also, its exact site of production during sepsis is unclear; however, recent research suggests that the monocytes may be one possible source during sepsis. Despite the unknown (and potentially very important) pathophysiology of procalcitonin during sepsis, much clinical research has focused on using procalcitonin as a marker of the inflammatory response to severe generalized infections.

Why is it important to have markers of infection? Although a recent concensus conference has set up new definitions and diagnostic criteria of sepsis, two major problems remain. First, uncontrolled infections are not the only cause of systemic inflammation and other stimuli such as pancreatitis, major trauma, and thermal injury can also trigger a systemic inflammatory response. In the clinic, therefore, it is frequently difficult to decide on the aetiology of an inflammatory response syndrome and direct appropriate therapy. Second, the disappointing results of immunomodulatory trials in septic patients have raised doubts as to whether conventional clinical and laboratory criteria used for recruiting septic patients may suffice in identifying groups of patients who would most likely benefit from such therapies [3]. Because of these problems, parameters that could provide early information on the aetiology and severity of an inflammatory response would be of interest. Such (a) marker(s) could also help target the populations of septic patients who would benefit from immunomodulatory trials.

Clinical data suggest that, whereas non-infectious inflammatory stimuli and viral infections produce only minor increases in procalcitonin levels, generalized bacterial infections produce large increases that seem to reflect the severity of the infection [2,4]. Procalcitonin has been used to differentiate infectious from non-infectious pancreatitis, infectious from non-infectious aetiology of acute lung injury, and in differentiating transplant rejection from infectious complications after organ transplantation.

However, although procalcitonin offers considerable advantages in comparison to conventionally used laboratory monitoring parameters, it does not fulfil all the criteria of an ideal marker of severe microbial infections. Procalcitonin may not or may only slightly increase when infection remains confined to a tissue or organ with no systemic manifestations. This may be one of the reasons why calcitonin precursor levels in Steinwald's study are very similar in controls and less severe septic animals. Therefore, very low levels of procalcitonin after the treatment of infection do not always indicate complete eradication of the infection, and continuation of antibiotic therapy or surgical measure may be necessary until all clinical signs of infection have disappeared. Furthermore, procalcitonin levels may also be elevated after major trauma or surgery, after cardiopulmonary bypass, and in patients with C-cell carcinoma of the thyroid gland and small-cell carcinoma of the lung [4].

Other important questions pertaining to procalcitonin remain unanswered. Is procalcitonin release related to bacterial products (alone) or do cytokines also play a role? Which cells produce procalcitonin during severe infection? What specific endocrinologic or immunologic (dys)function does procalcitonin serve during severe infections? Because of these unanswered questions and limitations, more clinical and laboratory studies are needed to uncover the nature of this parameter in inflammatory states.

References

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