Use of Procalcitonin to Guide Duration of Antimicrobial Therapy in Intensive Care Units: Proceed With Caution

To the Editor—I read with interest the recent systematic review of serum procalcitonin (PCT) in guiding duration of antimicrobial therapy in intensive care units (ICUs) [1] and wish to proffer several cautionary notes.

First, the authors’ claim of reviewing 6 “randomized controlled trials” (as stated in the abstract) may not be technically accurate because only 3 actually met the authors’ own criteria for appropriate randomization. Furthermore, by their own analysis, only 2 studies were investigator(s)-blinded, and only 1 was outcome assessor(s)-blinded, introducing potential bias in the conduction of these studies. These observations are particularly relevant because, in the absence of a meta-analysis, the authors’ conclusions regarding the favorable utility of PCT seem to be based on the results of “5 of the 6 studies” irrespective of their design flaws.

Second, the authors’ definition of the primary outcome included parameters varying from the number of antimicrobial days for the first infectious episode to the number of days of antimicrobial exposure/1000 patient-days to the number of days with antimicrobials. Although such an approach may allow for collective analysis of several heterogeneously designed studies, it may not be very useful to the reader who wishes to determine in advance which antimicrobial use parameter might be favorably impacted by the adoption of routine PCT measurement in his or her ICU. For example, of the 6 studies presented, 2 reported total duration of antimicrobial administration, of which 1 failed to show a significant reduction in the number of days of antimicrobial therapy, and 3 studies reported antimicrobial days/1000 patient-days, of which 1 failed to show a significant impact when PCT was utilized. What firm conclusions can one really draw from these disparate results?

Third, 2 of the 4 studies demonstrating a reduction in the duration of first antimicrobial course failed to report other relevant parameters such as total duration of use and number of antimicrobial days/1000 patient-days. This information is important because a shorter first antimicrobial course may be less desirable if it leads to increased antimicrobial use later during the patient’s ICU or hospital stay.

Last, the authors state that PCT is more sensitive and specific than C-reactive protein (CRP) and cite a review article published in 2004 [2]. However, since 2004, at least 2 studies have failed to show superiority of PCT to CRP in hospitalized patients with regard to its sensitivity or specificity in diagnosing infections [3, 4], and a recent meta-analysis of PCT in critically ill patients concluded that PCT could not reliably distinguish sepsis from other inflammatory conditions [5].

In summary, the authors’ conclusion that PCT guidance of antimicrobial duration “decreases antimicrobial use in the ICU safely and significantly” appears premature based on limitations of their methodology and the quality of the studies reviewed. Indeed, a recent multicentered, randomized trial of PCT-guided interventions against infections in ICUs demonstrated a significantly increased duration of use of several antimicrobials in the PCT-guided group, and demonstrated that PCT-guided intervention was associated with increased organ-related harm and prolonged admission to the ICU without improvement in patient survival [6]. The readers are advised to proceed with caution.

Note

Potential conflicts of interest. Author certifies no potential conflicts of interest.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References