Reviewer's report

Title: Serum procalcitonin elevation in the critically ill patients at the onset of bacteremia caused by either gram negative or gram positive bacteria

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Reviewer: Vandack Nobre

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General comments

In this retrospective study involving septic patients with bacteremia hospitalized in the Intensive Care Unit (ICU), Charles et al tested if the baseline procalcitonin (PCT) levels can help in the distinction between blood stream infections due to gram positive (GP) and gram negative (GN) bacteria. Authors warn that circulating PCT levels elevation starts as early as two hours following a bacterial challenging. Furthermore, PCT measurement takes only few minutes and is therefore available before the results of conventional blood cultures.

Procalcitonin has been shown to be helpful in guiding antibiotic therapy, mostly in patients with suspected or confirmed respiratory tract infections. Moreover, observational studies have demonstrated that high baseline or persistently elevated procalcitonin correlates with a poor prognosis in critically ill patients. The present study, conducted by Charles comes out to ad interesting information on this field. Nevertheless, some important concerns arise when the study’s design and presentation are considered

Title: I suggest a more straightforward title, such as Baseline plasma procalcitonin levels help to distinguish between gram positive and gram negative bacteremia in septic patients.

Major compulsory revisions:

1- Although the results presented by authors suggest that procalcitonin is helpful in distinguishing between GP and GN bacteremia, and even if all patients presented BSI, the significant differences in the sources of infection observed among the studied patients limit the conclusions of PCT usefulness. We know that skin and soft tissues infections are usually caused by GP agents. Conversely, urinary tract infection and intra-abdominal infectious conditions have GN and aerobic flora as the most prevalent bacterial aetiologies. These differences along with the knowledge about local nosocomial flora usually help clinicians in their decisions about the spectrum of the initial empirical antibiotic therapy. Moreover, the sensitivity (76.9%) and specificity (82.2%) found by authors are not sufficiently good to safely change the clinicians’ mind. For instance, in a post coronary artery by-pass graft patient who develops a septic shock, the spectrum of antibiotic therapy should ideally include skin gram positive
flora even if the procalcitonin levels are higher than 16 ng/ml.

2- Skin and soft tissues infections are easier to identify than other deep localized infections, which might lead to earlier therapies. Moreover, these infections are usually suitable to be managed with concomitant surgical procedures, i.e. source control. These characteristics can, at least partially explain the large differences in plasma PCT levels observed in the group with gram positive infections, as well the higher mortality in the patients infected by GN bacteria. Did authors test the difference in PCT levels between GP and GN bacteraemia originated from the same source (e.g., lungs, abdomen)? Conversely, recent studies suggest that surgical patients with sepsis present higher procalcitonin levels than their medical counterparts. Which kind of surgical procedures were performed in the 11 episodes of the GN bacteremia classified as surgical? Did intra-abdominal procedures predominate? Also, how close to the date of procalcitonin tests were these procedures performed?

3- The levels of procalcitonin were highly variable among studied patients. In the GP bacteremia group, levels as low as 0.07 ng/ml were found. Which kind of infection had this or these patient(s)? Were there other patients with procalcitonin levels below 0.5 ng/ml? If so, could authors describe their clinical findings?

Minor Essential Revisions

In the last sentence p. 8, authors wrote “Conversely, there was no difference when the rate of appropriate antibiotics administration within the 24 hours preceding bacteraemia onset was considered (2 out of 45 vs. 3 out of 52 patients with either GP or GN bacteremia, respectively).” Would not it be “inappropriate”?

Additional statements:

- I agree with the electronic publication of my report along with the article in case of acceptance.
- I consider that I am unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.
- The written English is acceptable.
- I declare that I have no conflict of interest.