Reviewer's report

Title: Serum procalcitonin for the early recognition of nosocomial sepsis in the critically ill patients: a preliminary report

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Reviewer: Charles-Edouard Luyt

Reviewer's report:

In the present study, Dr Charles and colleagues evaluated the usefulness of procalcitonin (PCT) for the diagnosis of nosocomial infections (namely ventilator-associated pneumonia and bloodstream infection). The authors included 70 patients with suspected sepsis and showed that PCT serum levels were higher in patients with microbiologically proven infection than in patients without. Moreover, they showed that an increase in PCT serum level the day the infection was suspected (in comparison to a dosage obtained the day before) was a good predictor of nosocomial infection.

The results are interesting, but I have the following reservations regarding the manuscript:

Major compulsory revisions:

1- Methods section. The authors stated that VAP was defined as the combination of a new lung infiltrate, a positive quantitative endotracheal aspirate culture and a CPIS of 6 or more. Did the authors calculate the CPIS proposed by Pugin (reference 12 of the paper), or a “modified” CPIS, as proposed by Singh et al. (AJRCCM 2000; 162:505-511). As the authors know, the CPIS proposed by Pugin et al. is not easy to calculate at the bedside, in particular for the tracheal secretion item. Moreover, in the CPIS proposed by Pugin and in the modified CPIS proposed by Singh, both used semi quantitative cultures of endotracheal aspirate, which was not done in the present study. Because this is a key issue in the present study, the authors should be more precise and explain how they calculated CPIS in their patients.

2- Another limitation of the study is the use of CPIS to diagnose VAP. As the authors know, its sensitivity, although reliable, was estimated at 80-90% in 2 different studies (Schurink et al., Intensive Care Med 2004;30:217-224 and Luyt et al, Intensive Care Med 2004; 30:844-852). How many patients had a CPIS below 6 but a positive tracheal aspirate culture (> 106 CFU/ml)? Are the results different if these patients are included in the “infection” group? This limitation should be addressed more strongly in the manuscript.

3- Methods section. Which variables were included in the logistical regression model? Was CPIS included in that model?

4- I am concerned by the study population, which is very particular, with
prolonged durations of mechanical ventilation and ICU length of stay. Those are not usual ICU patients. The authors should give more information in table 1, in particular admission categories, reason for admission, reason for mechanical ventilation, duration of mechanical ventilation before VAP (or sepsis) suspicion, comorbidity score, immunosuppression…

5- I am very surprised by the prolonged time elapsed from ICU admission to infection suspicion (Table 2). Did the authors take into account the first episode of infection suspicion? (In my experience, first suspicion of nosocomial infection occurs sooner than 15 days after ICU admission) Or did the patients experience previous episodes of infection suspicion that were not retained because of lack of data? Could the authors precise this particular point and, if necessary, add this as a limitation?

6- I disagree with the authors’ interpretation of their results. The authors give sensitivity and specificity of PCT on D0 for diagnosing sepsis. I suggest them to add (table 4) positive and negative likelihood (LR) ratios; this is a better way to present the results for a diagnostic test. If I am correct, positive LR is 2.08 and negative LR is 0.42. As an example, for a pre-test probability of 64% (the study population), post-test probability increase to roughly 73%. To my mind, combined to the poor value of sensitivity given by the authors, PCT (crude value) is not a good marker of nosocomial infection.

7- Discussion section, page 8. The authors stated that their study population differed from that of another study, which was constituted of patients with sepsis on admission and patients who had undergone surgery prior to VAP. Once again, what was the study population of the present study? They did not have patients with sepsis or septic shock, patients with previous surgery, or with previous conditions known to increase PCT serum level, such as multiorgan failure?

8- In a real life, it is probably not realistic to propose a PCT dosage each day of ICU stay for every patient, mainly (but not only) because of economical concern. As a matter of fact, only a few patients with bacteraemia could be included, and only 2/3 of the 70 patients included in the study had a PCT dosage the day before (D-1). Then, although interesting, one of the main message of the study, i.e. accuracy of PCT variation the day infection is suspected (as compared to the day before), is not applicable in a day to day practice. However, a more liberal strategy, i.e. PCT dosage 2 times a week, could be more realistic. How many patients had a PCT dosage in the 3 days preceding the day infection was suspected? What were the results if delta PCT was calculated with a “previous” PCT dosage comprised between day - 1 and day -3 (as done in reference 13)?

9- Discussion section, page 8, line 5 (sentence “Our findings also suggest….. ICU-acquired sepsis”). Because of the poor diagnostic value of PCT serum level the day infection is suspected (see comment 6), I suggest the authors to be more prudent with such an assumption and replace “should” with “could” or “might be”, and add “in this particular setting” at the end of the sentence. Or to delete this sentence.
Minor essential revisions:
1- Figure 1. The authors should add the number of patients in each group and for each day.
2- Table 3 duplicates data that are already in the body of the manuscript, and should therefore be deleted.
3- Economical concern (performing daily monitoring of PCT) should be address as a limitation.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I received payments from Brahms (3400 Euros in the past five years) and Biomerieux (700 euros last years), both manufacturers of PCT assays, for lectures on PCT.