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Letter to the Editor

Reply to: Procalcitonin is effective to stop antibiotics only in patients with less severely critical sepsis

We appreciate the comments of Nadeem R and colleagues on our meta-analysis, which concluded that PCT-guided antibiotic therapy would not suit severely critically ill patients, although it revealed the benefit of PCT-guided cessation of antibiotics on the short-term mortality in patients with an average SOFA score of <8 (Peng et al., 2019a).

Heterogeneity plays a vital role in the quality of meta-analysis (Higgins and Thompson, 2002). There is no significant heterogeneity in meta-analysis of short-term mortality ($p = 0.88$; $I^2 = 0\%$), which was persistent in the result of the influence analysis. Thus, we believed that the enrolled patients in included trials were homogeneous. Actually, high heterogeneity ($p < 0.0001$; $I^2 = 90\%$) was observed in the meta-analysis of secondary outcome antibiotic duration. Several factors contributed to that heterogeneity; firstly, the cut-off of PCT value for the algorithm was different ranging from 0.1 ng/l to 0.5 μg/l or 10% to 35% of its peak value in the included trials. Secondly, the adherence of PCT algorithm was rung from 47% to 97%. Finally, antibiotic duration as the secondary outcome assayed in the included trials led to bias. Therefore, it suggested methodological diversity, but not different patient populations.

The positive microbiological result is crucial for sepsis diagnosis, but not necessary (Singer et al., 2016). Furthermore, our meta-analysis performed aims to determine the efficacy of PCT-guided antibiotic therapy in critically ill patients, including suspected sepsis and confirmed sepsis. The subgroups meta-analysis revealed that both PCT-guided antibiotic therapy and cessation failed to decrease the short-term mortality of patients in the subgroup of confirmed sepsis, compared to the standard care. The necessity to assess the efficacy of PCT-guided antibiotic therapy in patients with positive microbiological sepsis needs more discussion.

Our meta-analysis analyses the short-term mortality and other mortality, the results were consistent. In addition, the post discharge mortality was lacking in the included studies. Therefore, the post discharge mortality was not focused on in our meta-analysis. Moreover, we agree with Nadeem R that greater organ failure, renal failure or fungal infection make PCT level less reliable, but the effect of PCT-guided antibiotic therapy in patients with different severities of illness needs further validation (Peng et al., 2019b). Based on our results, we insist that antibiotics should be initiated or withheld according to symptoms, signs, and positive laboratory examinations, but not be based on PCT alone.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Competing interests

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