Author’s response to reviews

Title: Neutrophil CD64 index in cerebrospinal fluid as a marker of bacterial ventriculitis in children with external ventricular drainage

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Cover letter for revision of manuscript: Neutrophil CD64 index in cerebrospinal fluid as a marker of bacterial ventriculitis in children with external ventricular drainage (BPED-D-17-00653R1)

English editing is indicated by using track changes, all other changes are in red.

Technical Comments:

1. In abstract section of the manuscript the style of heading and keywords were changed according to BMC Pediatrics style.

2. Tables were placed in the main manuscript file after the figure legends and references (and removed from additional files).

3. Figure legends were included in the main manuscript.

Editor comments:

1. Gramatical and spelling errors were eliminated by native speaker.

2. Individual consent was required – the word individual was added in the manuscript
3. PCR: the discussion about PCR methods is in discussion; PCR of course can be used in children with EVD with some limitations; it is difficult to differentiate between infection, ventricular drain colonization, sample contamination and nonviable organisms due to antibiotic treatment or previous infection [38]. Phrase or previous infection was added to the discussion. In children with prolonged EVD infections are very often as well as drain colonization. The gold standard for ventriculitis in our study therefore based on culture of CSF which detects only viable organisms and not some nonviable organisms from past infections.

4. In all our patients CSF samples were obtained prior to antibiotics which is now clearly stated in the manuscript: “which were all obtained before antibiotic treatment started” was added.

5. The initiation of diagnostic work up was based on clinical suspicion of ventriculitis – criteria are well written in the manuscript. In all children in our study the initiation of a diagnostic workup for ventriculitis and the prescription of empirical antibiotic therapy was done.

6. At least one week was chosen as in our previous study (18). This is the time, when CSF culturing is usually completed.

7. Yes, probably CD64 varies in hours, but not many studies about postoperative rise of CD64 in hours are available. In study of Daryapeyma et al, in adult vascular surgery we can notice slightly increased values of CD64 obtained immediately after surgery in comparison to preoperative one (Daryapeyema A. et al. Neutrophil CD64 as a marker for postoperative infection: a pilot study. Eur J Vasc Endovasc Surg 2009; 38: 100-103.)

8. That is true, there was no variation by age in our previous study (25), but that was not what we discuss. We discussed different diagnostic accuracies in our study and neonates and children in previous study. Cut-off levels were different, but in recent study we measure CD64 in CSF, while in previous one blood CD64 was studied.

9. Other possible influences on CD64 and other markers are added to the limitations of the study.

10. Yes, the data are the same when CD64 level are analysed and used to compare.

11. CD64 index ratio method was clarified in Method section.

12. Ref 22: the reason could be different study design, they collected CSF every second day and therefore were maybe late for diagnosis in some cases, we obtained markers immediately after clinical suspicion and this could explain also low PCT and CRP values. The second reason could be premature newborns included into the study with different PCT dynamics.

13. Tables 1 and 2 were combined. Instead the symbol / number 0 was used.

14. Serum glucose data were unfortunately not obtained from our patients at the same time.
15. CSF protein could be elevated post-haemorrhage and this was included into the limitations of the study.

14. In result section the main results were described. Figure 1 and 2 were added with scatter diagram for CD64 and LCCSF.

15. Data were presented as medians with IQR.

Reviewer 1

Result section: key findings in each table/figure were highlighting.

Figure 1 (simple Scatter/Dot Graph) was added for CD64 in and leukocyte count in CSF. Data were presented as medians with IQR.

Reviewer 2

Technique for analysis and processing time was explained in Method section in more details and cost of CD64 test was added.