Author's response to reviews

Title: Cognitive deficits following exposure to Pneumococcal Meningitis: An Event-Related Potential study

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Version: 3 Date: 20 March 2012

Author's response to reviews: see over
19th March 2012

Dear Editor,

REF: MS: 4475451785222504 - Cognitive deficits following exposure to Pneumococcal Meningitis: An Event-Related Potential study

Thank you for your offer to expedite the publication of this paper. We were clearly very disappointed by the delay.

As a matter of interest, we have taken into consideration the review provided by Dr van Furth

Reviewer: A.M. M van Furth

Although the authors has made some revisions it is not acceptable to publish in BMC Infectious Diseases:
- the main conclusion that cognitive deficits are present due to pneumococcal meningitis has not been studied with this study and is incorrect as such
- it is a very technical paper (with methods used which are not widely used in this field) which could be better published in an audiological or ENT journal
- the discussion is still to lengthy and to technical
- references are still out-dated

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.”

To answer the main criticism that “the main conclusion that cognitive deficits are present due to pneumococcal meningitis has not been studied with this study and is incorrect as such”, we would disagree. Cognition usually refers to an information processing view of an individual’s psychological functions and includes but is not limited to attention, memory, producing and understanding language, solving problems, and making decisions, and includes conscious and sub-conscious processes. Event related potentials are a measure of information processing, and can be used to measure one aspect of cognition, namely attention. We would suggest that this reviewer does not have the expertise to review a paper on neuro-cognitive outcomes of meningitis. However we have tried to emphasize this point and added further references to justify our argument.
Correction has been done in the Abstract on Page 2, under conclusion (3rd last line) and also under the study conclusions on page 12, 2nd paragraph (last line). Furthermore we have simplified the language to make it more understandable and updated the references.

In addition we have responded to the few queries raised by the Editorial board and some that had been mentioned by the reviewer. We have carefully responded to these in a point by point fashion below.

Many thanks,

Michael Kihara

Advice from our Editorial Board:

1. Please clarify how the patients were chosen. You indicate that 92 cases were randomly chosen based on sample size calculations of a neuro-developmental study. I need clarification on exactly what that means.

The selection of the study participants has been made more clear by adding a sentence on the selection criteria and subject exclusion criteria:

“A sample size of 80 children was required to detect a difference between cases and controls with 90% power and 95% confidence interval [31]. To account for potential 15% failure-rate in recruitment, we generated a random list of 92 children who had been admitted to Kilifi District Hospital with PM from 1994 to 2004”.

This information is present in the updated manuscript on Page 4, last paragraph.

2. There needs to be better definition of the control group.

The control group has also been defined more clearly in the updated manuscript on Page 4, 2nd paragraph under the “subjects” heading:

“controls were matched for sex and age (within 3 months), were residents in the Kilifi DSS for more than one year and had informed consent from parent/guardians. Those with a history of severe birth asphyxia, pre-existing neurological conditions and a history of neonatal jaundice were excluded.”

The only demographics listed are age and sex. What about other co-morbidities, including developmental delay, baseline intelligence, birth defects, HIV infection, malnutrition, lab data, etc. Since you are looking to examine findings between a disease and control group, it is critical to know if there are significant differences between the groups. Perhaps a table of all of these comparisons would also be useful.

The baseline data of the groups in the present study is limited. We do not yet have acceptable intelligence tests for our population and HIV status was not measured for this group (this is mentioned in the manuscript under limitations of the study on page 14, last
paragraph). However, children with developmental delays, pre-existing conditions, birth defects were excluded from the study.

3. In figures 2 and 7, I think it would be more illustrative to examine the control and PM groups in individual groups based on age.

We felt think that Figures 3 to 6 present the data as suggested by the reviewer and hence it would be repetition to change Figures 2 and 7 to show individual groups based on age.