Reviewer’s report

Title: Development of a TaqMan Array Card to Target 21 Purulent Meningitis-related pathogens

Version: 0 Date: 30 Nov 2018

Reviewer: Enitan Carrol

Reviewer’s report:

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General comments

This manuscript reports a TAC card array for bacterial meningitis (PM-TAC) in this study which can detect 21 PM-associated pathogens in 3 hours and shows a higher sensitivity than the CSF culture particularly for CSF samples collected after empiric antibiotic therapies. This is not novel, as there are now many commercial molecular assays for meningitis such as Biofire FilmArray (14 targets), FastTrack Diagnostics (4 bacterial, 5 viral)

Line 45/46 The disease is characterized by acute onset, high fever, severe headache, vomiting, stiff neck, and high disability and mortality rates

In infants and young children, these "classical " signs are often absent. They may be poor feeding, lethargy, disorientation or reduced conscious level.

Line 70: In the introduction, there is no mention of the Biofire FilmArray or FastTrack diagnostics panel as PCR platforms.

Line 81-84. Although TAC systems have been used successfully to identify pathogens, a comparison of the sensitivity of a TAC versus the CSF culture method to identify pathogens in CSF samples from patients receiving empiric antibiotic treatments is still lacking.


6: Graf EH, Farquharson MV, Cárdenas AM. Comparative evaluation of the FilmArray meningitis/encephalitis molecular panel in a pediatric population. Diagn Microbiol Infect Dis. 2017 Jan;87(1):92-94. doi:


Line 147-153 : total of 32 children with PM were selected with a representative cross-section of the patient population in the Department of Infectious Disease of Beijing Children's Hospital. Of the 32 patients, 13 showing positive CSF culture before receiving antibiotics but negative after receiving antibiotics, 2 showing positive CSF culture before antibiotic therapies and remaining positive after the antibiotic therapies, 17 showing negative CSF culture before and after antibiotic therapies.

Please can the authors explain how they got samples before and after antibiotics samples. Was the CSF repeated after receiving antibiotics? Is that ethical? Was there ethics approval to do 2 lumbar punctures?

Other comments

This study is let down by the small sample size. Only 7 samples subsequently had a Ct value which makes any meaningful interpretation difficult.

In the positive samples, it is encouraging to see concordance between sequencing and the PM-TAC. In the negative samples, also, all were negative by PM-TAC.

The cost of $126/sample is still prohibitively expensive for resource poor settings and is more than the Biofire FilmArray system, which takes 1 hour.
The finding of pathogen load correlation with severity is not new, and has been shown with pneumococcal meningitis. (Carrol ED, Pediatr Infect Dis J.2007)

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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