Reviewer’s report

Title: Practice variation in anti-epileptic drug use for neonatal hypoxic-ischemic encephalopathy among regional NICUs

Version: 1 Date: 17 Jan 2019

Reviewer: Krisa Van Meurs

Reviewer's report:

Abstract

1. I'm surprised that one of your conclusions is not to harmonize use of neuromonitoring across centers since this definitely drives AED use and will discourage the treatment of clinical seizures without an electrographic correlate. I would suggest referencing the 2 articles about treating clinical versus electrographic seizures (van Rooij Pediatrics 2010 and Srinvasakumar Pediatrics 2015).

Introduction

1. I would suggest adding a sentence about the use of aEEG in the NICU as you mention that cEEG is resource intensive and not available in all centers.

2. You state that the field lacks randomized trials of AEDs, I would reference the trials that do exist (include Pressler Lancet 2015) and that have recently completed enrollment (NeoLev NCT 00461409).

3. The last paragraph of the Introduction belongs in the Methods section.

4. I would clearly state your objective for this study and mention the plan to identify opportunities for quality improvement as you do in the abstract.

5. You mention how head cooling precludes cEEG monitoring. I note that 20% of TH was head cooling. Since the Olympic device is not longer being sold in the US, has this rate significantly decreased in more recent years?
Methods

1. No further suggestions.

Results

1. I would mention that another reason for underestimation of seizures is that initiation of aEEG or cEEG is delayed (page 12).

2. I would give the range of incidences. You reference a single article which is not the best citation for this statement. It discusses the impact of seizures on outcome in HIE.

3. Did the incidence of seizures change as the rate of neuromonitoring increased?

4. On page 13 you state "Our data reinforce… as EEG seizures would indicate TH." I would change "would indicate" to "would indicate that the eligibility for TH had been met."

5. It would be interesting to report the variation by center in AED use at discharge in patients treated with AEDs during hospitalization.

6. I'm confused by the added sentences on page 15. You attribute the use of AED use in neonates without electrographic seizures to neuroprotection or seizure prophylaxis at referral sites and then suggest increased outreach education. Why wouldn't the receiving hospital discontinue the AED use if used for neuroprotection or even for seizures that did not recur? I suggest modifying this sentence.

Conclusions

1. Again, I suggest that focusing on not only AED utilization but also on use of "timely" neuromonitoring, optimally with cEEG but if not possible with aEEG.
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

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