Reviewer’s report

Title: Transcapillary fluid flux and inflammatory response during neonatal therapeutic hypothermia: an open, longitudinal, observational study

Version: 0 Date: 06 Apr 2016

Reviewer: Drude Merete Fugelseth

Reviewer’s report:

The study aim to explore the potential influence of therapeutic hypothermia (TH) on colloid osmotic pressure in plasma and interstitial fluid, and also the association between inflammatory markers and colloid osmotic pressure in asphyxiated newborn infants.

Overall comments:

The study is important in the view of adding some pieces to the challenging puzzle of understanding the physiological changes during TH and it is honorable that the group attempts to explore this difficult topic. However, the results must be interpreted with caution. The discussion of the results is some time a bit speculative and partly conflicting, and some of the references used are sometimes on the side of the current topic.

The first author has published studies with the same methods in healthy children and during topical anesthesia, and the methods seem well explored.

The main limitation of the study is the lack of a control group of non-cooled asphyxiated infants unfortunately influences the interpretation of the results. However, this is a problem all of us have to face today when TH has been the standard cares for moderate and severe HIE.

More specific comments:

Abstract:

Methods: line 40-41; "Biomarkers of inflammation and colloid osmotic pressure were measured in serum and interstitial fluid." The colloid osmotic pressure was measured in plasma.

Results: line 43-45; "A decline in mean arterial pressure was observed between 7 and 13 hours of life, with a concomitant decrease in fluid surplus during the first 7 hours." While in the Result p 9, line 200-201 is written; "The changes were significant for excess fluid accumulation during the first 7 hrs, with a significant reduction compared with the remaining treatment period." AND in Discussion p 12, line 280-284 "..dilution of plasma protein as a result of initial resuscitation...AND in Conclusion p 16, line 379; "The decrease in MAP and fluid surplus during the first 24 hours of TH… Please clarify this.
Background:

Page 4, line 77-78; please add reference.

Line 83; Ref 13; I cannot see that ref 13 cover any discussion about increased capillary permeability?

Methods:

Page 6, line 115; "(Criticool, Mtre, Pennsylvania, USA)" Is this right? I thought it was from Yavne, Israel?

Page 7, line 47; spelling - should be the arm or the leg

Results:

Page 9; were all 17 infants included in the final analyses in table 3 and 4? If not, what consequences?

Figure 2C; why is not IL-10 in serum included?

Both IL-1RA and IL-RA are used in the text, please be consequent.

Discussion:

Page 11, line 257-258; please add reference after the first sentence in reference

Page 12, line 261-262; "In the IF, the pro-inflammatory IL-1 showed increased levels during hypothermic treatment, which coincided with decreased total WBC count and no clinical or laboratory signs of edema (oedema) formation." What so? This is just repetition of results without any discussion.

Line 274-276; miss reference

Page 13, line 286; "a transient hypernatremia of 126 mmol/L", hyponatremia?

Page 13 and 14, line 308-317. Please define the abbreviations used in the text.

What about CRP? It is measured, but not discussed.

References:
This is a mess with use of different styles, so please clean up this part according to the journals recommendation

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.

Unable to assess

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

No

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