SOP: Blinding of cranial ultrasound readings and data entry

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Content

1.0 Why blinding of cranial ultrasound readings?

Several observational studies have shown, that inadequate blinding of participants, personnel, and outcome assessors in randomised clinical trials tends to introduce bias, by overestimating the beneficial treatment-effect of an intervention for all outcome types, including subjective outcomes such as radiologic image interpretations and even mortality (1–4). The variability of treatment effect seems higher in unblinded trials with subjective outcomes, compared to other outcome types, suggesting that in trials with subjective outcomes, the heterogenicity and overestimation of benefits are larger (1).

Due to the nature of the experimental intervention of the SafeBoosC III randomised clinical trial, it is difficult to blind the clinical staff and the parents. In order to minimise bias in cranial ultrasound reading, diagnosis of brain injury and filling the eCRF on severe brain injury outcomes at 36 weeks postmenstrual, must be coducted by a person that is as well blinded to the infants' group allocation as possible. This Standard Operating Procedure contains examples on how this blinding may be obtained.

2.0 Reporting of blinding method and data entry into eCRF

In order to maximise the likelihood of effective blinding in all participating clinical sites, principal investigators must develop a local procedure, describing how blinding will be achieved. Furthermore, the procedure description of blinding must be reported to Copenhagen at mathias.safeboosc@gmail.com for central approval, before enrollment of infants.

3.0 Suggestions for blinding methods

1)

In some sites, radiologists perform the cUS and diagnose the cerebral affections of the infants. In these sites, blinding of intervention during diagnosis of brain injury would be fulfilled if the principal investigator could ask a colleague unaware of group allocation to read the radiologists image description and fill in the eCRF data field on severe brain injury and the question regarding achievement of blinding.

2)

In some sites, the neonatologists themselves perform the cUS. In this situation, the PI could ask a colleague unaware of group allocation, to review all images until 36 weeks postmenstrual age and fill-in the eCRF data fields on severe brain injury and the question regarding achievement of blinding.

4.0 References

1. Savović J, Turner RM, Mawdsley D, Jones HE, Beynon R, Higgins JPT, et al. Association Between Risk-of-Bias Assessments and Results of Randomized Trials in Cochrane Reviews: The ROBES Meta-Epidemiologic Study. Am J Epidemiol. 2018;187:1113–22.

2. Hrobjartsson A, Thomsen ASS, Emanuelsson F, Tendal B, Hilden J, Boutron I, et al. Observer bias in randomized clinical trials with measurement scale outcomes: a systematic review of trials with both blinded and nonblinded assessors. Can Med Assoc J. 2013;185:E201–11.

3. Hróbjartsson A, Thomsen ASS, Emanuelsson F, Tendal B, Rasmussen JV, Hilden J, et al. Observer bias in randomized clinical trials with time-to-event outcomes: Systematic review of trials with both blinded and non-blinded outcome assessors. Int J Epidemiol. 2014;43:937–48.

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