Author's response to reviews

Title: Early Blood Glucose Profile and Neurodevelopmental Outcome at Two Years in Neonatal Hypoxic-Ischaemic Encephalopathy

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Author’s response to reviews:

To the Editor:

Thank you most sincerely for giving us the opportunity to respond to the recommendations of the referees. We have addressed each of the comments as follow. We hope they are to your satisfaction and that of the reviewers.

Referee 3: Reviewer's report Title: Early Blood Glucose Profile and Neurodevelopmental Outcome at Two Years in Neonatal Hypoxic-Ischaemic Encephalopathy Version: 4 Date: 7 January 2011 Reviewer: Rosemary D Higgins

Reviewer's report:

Comment: It would be ideal to have information related to the incidence of seizures in this population.

Response: We are extremely grateful for the reviewer’s comments. Out of the 52 infants, 12 had seizures. We have added this information to table 1.

Referee 2

Reviewer’s report Title: Early Blood Glucose Profile and Neurodevelopmental Outcome at Two Years in Neonatal Hypoxic-Ischaemic Encephalopathy Version: 4 Date: 4 January 2011 Reviewer: Alistair Gunn

Reviewer’s report:

The authors have appropriately revised this manuscript. Critically they have added a multivariate analysis which confirms that early hypoglycaemia was strongly associated with severity of encephalopathy. The MS it is now suitable for publication. I have some very trivial suggestions that the authors may wish to correct for completeness.

Comment: results, page 7. "The median timing of initial blood glucose sampling was 25 minutes after birth (range 9-30 minutes)." The range is incorrect, since we are next told that the latest outborn glucose level was 10 min. either this statement refers only to the inborn infants --- and should be specifically described as such, or the range should be 9-100 min, and ? the median may need to be recalculated.
Response: We have amended this information.

Comment: Page8. "The occurrence of early hypoglycaemi_a_ correlated 
Response: Thank you, this sentences has been amended.

Comment: discussion. page 11. "In infant rat_s_, it has"
Response: We have amended this sentence.

Comment:
Ibid. "However, in newborn piglets, fetal sheep and adult ratsanimal models, hyperglycaemia following hypoxia-ischaemia insult was shown to be harmful (21-23)." this statement misquotes the study in fetal sheep, which examined hyperglycaemia _during_ asphyxia only. Further, the paper by Park et al, only examined the immediate reperfusion period, and only examined metabolic changes; it is unclear whether there was any persistent deleterious effect, or not. that is to say: a slightly more nuanced description of these data would give the reader a better feel for the relatively limited implications of these experimental data.
Response: Thank you for all these information. We have adjusted our text to provide this information to the reader.

Comment: discussion: "Initial blood glucose samples were collected within 30 minutes". this statement is incorrect based on the results, since some initial glucose data were not available until 100 min.
Response: We have amended this information.

Comment: Figure legend 2. "The whiskers represent the minimum and maximum of the data." are the authors sure that this is correct? I ask because there are some symbols outside the whiskers. many graphics programmes show the 90% or 95 CI and use symbols to show the full range. If the whiskers are indeed the full range, then the symbols need to be explained. There are additional symbols that may be asterixes above or below at least 4 infants. What do these represent?
Response: Thank you, the legend has been amended.

Comment: Figure 1. The authors have not spread the symbols horizontally as requested, but rather made the data in to thin lines. This is (just) acceptable but much less visually easy to interpret.
Response: Thank you, we agree that the figure much less visually easy to interpret, so the figure has been amended and we spread the symbols horizontally as requested.

Comment: Table 1. a. Please add the denominators to the data on mortality for severity of HIE. These data are in the MS of course, but it is much easier for the reader not to have search to find it.
b. I recommend adding a formal subheading for mortality for each level of HIE, again for easy of reading the table: ie,
Mortality Mild HIE: 2/25 Moderate HIE:etc Severe HIE:etc
Response: We added this information to table 1.

Editorial request: Please ensure that the Abstract you have provided in our online submission system matches the one in your manuscript.
Response: Thank you very much, we have amended this information.

Comment: Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals ). It is important that your files are correctly formatted.
Response: Thank you, we have amended this information.