Author's response to reviews

Title: Effects of propofol versus thiopental on Apgar scores in newborns and peri-operative outcomes of women undergoing emergency caesarean section: a randomized clinical trial

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Author's response to reviews: see over


Dear professor Ngan Kee Warwick,

Thank you for your critical analysis of our manuscript. The comments are very helpful.

We have attempted to make adjustments and correct the errors that you pointed out. Please see our responses below. Additionally we have indicated the line in which the correction stands.

General comments

1. The experimental question is indeed the effect of propofol versus thiopental on Apgar scores in emergency caesarean sections. We have rewritten the research objective to reflect this in line 34
2. The primary outcome was Apgar scores less than 7 and the conclusion has been edited to remove the bias towards propofol. Line 41-43 and 384-392
3. We have included the differences in the rate of neonatal admissions as an important clinical outcome. Additionally we included the admission criterion which was part of our protocol. This is in lines 153-157
4. We have improved our methodology section with regards to anaesthesia and statistical methods. lines 124-186

Specific comments

1. We have clarified the fact that this study was done in emergency cases, and we have clarified on the intended study outcome in the conclusion section.
2. We have revised and improved the statement regarding the pharmacology of propofol. We used the Korean article because it seemed to be the more recent of the literature exploring this question. We used google to translate it and we admit that we may have gotten some of the context wrong. Line 72-76
3. We did not study intraoperative awareness because that is a separate study being planned. We also wanted to keep things simple for the study team.
4. We have improved the methods section as advised. Lines 86-161
5. All mothers scheduled for emergency cesarean section and were scheduled to receive general anesthesia were approached for consent.
6. We have attempted to better describe what our randomization was. Lines 103-115

7. Our study setting like many low resource settings has prolonged surgical waiting times and in obstetrics, the long decision to delivery intervals. This gave the study teams ample time to approach mothers for informed written/or thumb print consent before recruitment into the study.

8. We calculated a sample size of 150 patients to achieve our desired power (90), alpha value (1.96) and effect size (20%), we then added a 8% loss to follow up, and that gave us the sample size of 162 that is shown in our trial registration form. During the study recruitment period, we arrived at our goal of 150 patients without any loss to follow up and therefore stopped the study on advice of our DSMB/Study monitor.

9. Zero minute was determined as the time at which the cord was clamped. Apgar score at 0 minutes therefore reflects score at that time. These scores were assessed for by the attending midwife and delivering obstetrician.

10. We have improved the detail of our statistical methods. Lines 164-186

11. We are now reporting the number of neonates with an Apgar score of less than 7 at each of the time intervals. This is line 230-234

12. Neonatal intervention and NICU admission rates/criteria have been emphasized in text. We however would appreciate further guidance on how to further analyze the difference. Do you mean multivariate analysis?

13. We agree that hemodynamics are of minimal interest and have deleted them from the manuscript.

14. The discussion has been revised and discussed in relation to the redistribution half life instead of elimination half life. Line 306-308

15. The conclusion too has been edited given that the hemodynamics outcomes have been deleted from text and the outcomes that were not assessed for have been removed.

We hope that these corrections are an improvement to the manuscript. We await further guidance.
Dear Malinee Laopaiboon,

Thank you for reviewing our manuscript.

The methodology steps have been reviewed and edited as per reviewer’s suggestions.

1. We calculated the sample size for the different time point and the largest sample size obtained was used which was 150 patients
2. Persons that recorded the data have been stated. Lines 153-157
3. We have described in detail allocation, blinding as it was done during the study period. Lines 103-115

We hope that these corrections are an improvement to the manuscript. We await further guidance.

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Dear Charles Algert,

Thank you for reviewing our manuscript

Discretionary revisions

1. Lines 154-156 have been combined with 157-158
2. Decision to delivery times have been reported in interquatile ranges; analysis made with the non parametric test. Lines 208-223

We hope that these corrections are an improvement to the manuscript. We await further guidance.

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Dear Paolo Silvani,

Thank you for your critical analysis of our manuscript.

We have reviewed the manuscript and made changes as per your suggestion.

In regards to the major compulsory revisions,

1. We do not have an ABG machine to analyse umbilical cord samples and so we chose apgar score as an index to assess fetal condition at birth
2. The time at which the umbilial cord was clamped was taked as time 0. The scores were assessed for by the mid wife
3. To do MAC/hr or EtMAc, one needs inhalational gas analyzers which our anesthetic machines lack. The Isoflurane concentration was varied between 1% and 1.5% with 100% oxygen run at 2.5L/minute

Minor corrections

1. We have added the suggested indications. Lines 54-55
2. A comment has been added in text. Lines 91-94
3. The suggested term induction to umbilical cord clamping has replaced induction to delivery interval

Discretionary revisions

Table 3 has been formatted

We hope that these corrections are an improvement to the manuscript. We await further guidance.

Signed by intent

Janat Tumukunde