Reviewer's report

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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Reviewer: Warwick Ngan Kee

Reviewer's report:

General comments.

This study was performed in a low resource setting and in that respect the investigators are to be congratulated. The question of what induction agent is best for emergency GA caesarean is clinically important and therefore the results of this study have potential value. However, I have important concerns about several aspects of the methodology and interpretation of results.

You do not appear to have defined a clear experimental question. You defined the primary outcome as the incidence of low Apgar scores but your main conclusion that propofol does not improve Apgar scores implies that you were expecting propofol to result in better scores. It is unclear why you would expect that because it would be contrary to what one might expect given the results of older studies in elective cases. On the other hand, looking through the results there seem to be some important real clinical differences in outcome, of which I would highlight the difference in the rate of neonatal intensive care admissions. You appear to have completely glossed over this potentially important outcome. If it is true, it would be a potentially important finding although unfortunately without clearly defined admission criteria much uncertainty remains. I am very concerned that several neonates actually died.

The methodology is inadequately described, particularly the method and standardization of anaesthesia. Statistical methods need better explanation.

Specific comments.

1. Abstract and background. You should stress that this study was performed in emergency cases (as specified in the title). Your conclusion that propofol does not improve Apgar scores implies that you were expecting better results with propofol. Why?

2. Page 3. You have made several statements about the pharmacology with which I do not agree. In line 65 you state that propofol has shorter induction time and smoother induction which is contrary to what clinical experience and the longer time to effect site equilibration of propofol would suggest. Your reference cited to support this (#3) is in Korean – did you really read it?

3. Lines 72-74. In the context of emergency cases the objective of comparing
differences in Apgar scores is clinically relevant but the differences in haemodynamic changes is not really very important. Did you not look at the incidence of awareness which is very important?

4. Overall, the methods are inadequately described. The actual anaesthetic technique needs to be described in clear detail including what steps were taken to standardize. Without this information it is impossible to interpret your findings. This includes all drugs, volatile concentrations, oxygen concentration, use of nitrous oxide, opioids, etc. In lines 106-107 you describe surgical protocols for the administration of general anaesthesia – is this correct?. I am not aware of the WHO recommendations but the actual methods should be described in detail.

5. The selection criteria are important and need better definition and description. You have stated “a variety of indications” but your title suggests that these were emergency cases.

6. The method of randomization needs better description.

7. Informed consent was obtained from all patients. How could you do this adequately in very urgent cases? Was consent written?

8. The sample size calculation is inadequately described. Please define primary outcome, effect size, alpha value. Why was there not allowance for dropouts? Of note your clinical trials registration states a sample size of 162 so why did you only recruit 150?

9. Line 110. How can you measure an Apgar score at 0min? Who made the assessments?

10. Lines 123-126. The statistical methods used should be described in detail, including the actual tests used for all comparisons.

11. Line 154. It is confusing to state the total number of neonates that had an Apgar score <7 at any time rather than describing the number at each assessment time.

12. Neonatal intervention and NICU admission are important clinical outcomes – more important than the Apgar scores. Was there any standardization and did you apply clear admission criteria? The difference in rate of NICU admission is statistically significant so this should be analyzed and described.

13. Haemodynamic changes are of minimal interest in the context of your emergency cases. If you are to include them, then a rigorous comparison should be performed, including analysis of highs and lows and comparison of serial changes. Currently you have analyzed haemodynamic changes according to proportion above or below set values; the latter are very arbitrary. It would be more useful to compare raw values.

14. Many aspects of the discussion need to be carefully reconsidered with regard to the known pharmacology of the drugs. For example, differences in elimination half life are far less important than redistribution (alpha) half life.

15. The main conclusions should be reconsidered. It may be acceptable to report that the incidence of Apgar scores was similar between groups but I think it is incorrect to state that propofol did not improve Apgar scores. More emphasis
should be placed on the clinical outcomes. Do not comment on outcomes such as nausea and vomiting unless they were actually assessed in the study.
Signed by intent.
Warwick D. Ngan Kee

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests