Author's response to reviews

Title: Performance of capnometry in non-intubated infants in the Pediatric Intensive Care Unit

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Professor Paola Marchisio
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Dear Professor Marchisio,

We are pleased to respond to the reviewers’ comments regarding our manuscript entitled “Performance of capnometry in non-intubated infants in the Pediatric Intensive Care Unit”. We continue to believe our findings to be of interest to the readers of BMC Pediatrics and feel that your suggestions substantially strengthen the paper.

In response to Referee 1:
1. “Would a receiver operator curve of capnography versus PaCO2 be a better way to analyze the data?”

This is an excellent question and we have discussed it with a statistician. We are comparing two monitoring modalities to examine how one reflects the other with respect to the measured values. We are not establishing sensitivity or specificity, as these are monitoring devices rather than diagnostic tests, nor are we establishing thresholds for normal values. Thus, we believe the Bland-Altman analysis for assessing agreement between clinical measures is the most appropriate (Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1(8476):307-10, 1986 Feb 8). We discussed this question with a statistician, who concurs.

2. “I suggest providing an a typical (not ideal) example of capnography and how you analyzed the wave form.”
Thank you for highlighting this confusing language in our manuscript. Our device gives a waveform for confirmation of CO₂ capture only, and is unfortunately not suitable for waveform analysis. To eliminate confusion, we removed this language from the manuscript and now refer to the reading, not the waveform.

3. “Should there be p values determined for each of the subject group characteristics?”

Since our study was designed to assess the technology, and not attempt to compare the subject groups, we did not determine p values for them. We did, however, control for respiratory rate and weight, as these could impact the performance of the technology.

4. “Please describe the side stream cannula.”

We added the following language to the manuscript: “The sidestream cannula (Philips Microstream EtCo2 circuit, Smart Capnoline O₂), a two prong nasal cannula with a CO₂ detection port that hangs in front of the mouth, was placed on the subject and left in place until a steady state reading was obtained. The sampling rate is 50 ml/min and the sampling line is 100 cm long. Oxygen can be delivered through the nasal prongs, if desired, and was only used as indicated for patient care.”

5. “Did any of these subjects require an intervention that was detected or not detected by the side-stream monitor?”

No.

In response to Referee 2:
1. “Using linear regression analysis, the authors have examined the relationship EtCO2-PaCO2 and EtCO2-PtcCO2 after adjusting for weight and respiratory rate. However, they do not provide any kind of results.”

We are very appreciative of this suggestion and apologize for the omission. We are offering 2 analyses and respectfully request the Referee’s preference. Both were reviewed with a statistician. The first uses the actual sidestream values and the second the log-transformed data. While the actual sidestream values may be more accessible to the clinician, we recognize that log-transformation is appropriate for non-normally distributed data. Since the conclusions are the same, we defer to editorial preferences. We have added the appropriate language in the final paragraph of the methods section, revised the results to add this analysis in the last paragraph of the section, and added a
table as requested by the Referee.

2. “The authors must expand their discussion, including findings from other studies on small infants using both side-stream (Lopez et al. Pediatr Pulmonol 2011; 46: 896-902) and main-stream capnography (Fouzas et al. J Pediatr 2014; 164:283-8).”

We have expanded our discussion to include the references above and highlighted the changes in our revised manuscript.

3. “Perhaps the authors should mention that pulse oximetry is unreliable in detecting hypoventilation, excepting extreme cases.”

We agree. We have included a comment regarding the unreliability of pulse oximetry in detecting hypoventilation in our introduction and have appended our references. Please see highlighted text.

4. “Correlation plots and Bland-Altman comparisons could be presented in one figure (i.e., Fig 1A and B), separately for EtCO2-PaCO2 and EtCO2-PtcCO2.”

Thank you. We have rearranged our figures as recommended, with the correlations in the A panel of Figures 1 and 2 (one for the PaCO2 and one for PtcCO2), and the Bland-Altman plots as the B panels.

5. “Table 1 needs a footnote to explain that those figures are means (median and range).”

Thank you. Clarification has been added to Table 1.

6. “The authors should not repeat the results that are included in Table 1 here.”

Thank you. We have edited our results section so as not to be repetitive of the information presented in Table 1.

7. “The results should be straight. The authors should just report their findings and avoid phrases such as ‘However, because correlation is expected....’ or ‘One of the specific goals ...’.”

Thank you. The intent of this sentence was to remind the reader of the statistical approach explained in the methods, and why we believe that the correlation is less instructive than is the Bland-Altman plot. Therefore, we have modified the methods to read, “Since correlation is expected when two methods attempt to measure the same
physiologic parameter, a Bland Altman analysis was also conducted to analyze the differences between the sidestream reading and either the $P_{tcO2}$ or the $P_{acO2}$. These results are presented in Figures 1 B and 2 B.

Thank you for your ongoing consideration of our manuscript. We look forward to the remainder of the review process.

Sincerely,

Bria Coates, MD