Author's response to reviews

Title: Automated FiO2-SpO2 Control System in Neonates Requiring Respiratory Support: a Comparison of a Standard to a Narrow SpO2 Control Range

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Author's response to reviews: see over
Dear Catherine Olino:

RE: Automated FiO2-SpO2 Control System in Neonates Requiring Respiratory Support: a Comparison of a Standard to a Narrow SpO2 Control Range

We are pleased to resubmit our manuscript. We were very encouraged by the positive response reflected in the reviewer comments, and appreciate both their effort. We have attempted to address all the concerns. Our point-by-point response is detailed below.

Additional formatting request:

1. Please remove the Competing Interest section, Author's contribution and Acknowledgement from the end of the Reference section and place it after the Conclusion section.

   A1) We have made this change.

2. Please also ensure that your revised manuscript conforms to the journal style.

   A2) We have carefully reviewed and edited the manuscript to insure conformance with the journal style. This included general editing to correct grammar, and spelling issues noted by reviewer 2. The guidelines call for identifying the department for each of the authors. There are no departments in Economedtrx as there are only 2 employes, so we left that blank.

Reviewer's report: (R1-SN)

Minor Essential Revisions:

C1) Table 1 and figure 1 not clearly marked.

   A1) We have added the appropriate labels.

C2) “In a previous crossover study we compared CLiO2 with two difference manual control strategies in 15 infants during 8-hour test periods.”

   In the above-mentioned sentence, the two difference should be “two different”. spelling mistake

   A2) We have corrected this mistake.
C3) Please mention what evening effects are as pointed by me in the review document and mentioned by the authors in the methods section.

   A3) We have clarified this point in the Methods section.

Major compulsory revision

C4) The narrower range in the intended target range (93-87 SpO2) did increase the time % in the < 80% spo2 as 1.7% (3.1-0.5) p =0.052 . Authors have not mentioned this fact anywhere as 0.052 lies just close on the significant level if p<0.05 is significant.

   A4) This is an excellent point even though the difference was very small. We have addressed it in the Results and Discussion (limitations).

C5) Also worth mentioning about the level of significance , p <0.05 or p<0.01?

   A5) We are not sure exactly what was meant by this comment. The Methods section states the a p< 0.05 would be the threshold for statistical significance. In the results we have expressly state the exact p value rather than only stating it when it was significant.

Reviewer's report: R2-CP

Compulsory Revisions:

1. This is a well-written manuscript on an important subject. However, I am somewhat confused by their terminology: they use the terms “target range” and “control range”, but do not specify unequivocally what is meant with each of these terms (while target range is defined as 87-93%, it remains unclear what is meant by control range)

   A1) Our intent was to differentiate between Control Range, as set on the AVEA-FiO2 controller, and the intended Target Range for SpO2. We agree we have created some confusion, especially since one set control range was the same as the target range. We have addressed this by not only defining it in the Methods section but also being clearer throughout rest of the manuscript.

2. Regarding their results, they should justify why they had only 2 manual FiO2 adjustments/12 h, compared to 10/24 h in Claure’s or 52/24 h in Hallenberger’s study, despite a narrower target range. How can this discrepancy be explained?

   A2) We agree this is an interesting point, so we have added a paragraph in the Discussion to address it. The need to intervene with a manual FiO2 adjustment during automated control is related to several factors. The first is the system itself, different
control algorithms will result in different intervention requirements. That difference is certainly relevant for the systems described by Hallenburger and Claure. In addition setting of the SpO2 alarm delays and thresholds, and the attentiveness of the staff to these alarms is also an important factor. Finally we feel an important factor is the patient, at least in comparing results with the same device. The average rate of severe desaturation in Claure’s two studies was twice that experienced in our study, which we feel is the primary explanation for the difference.

3. If the planned study duration was 3 days, infants completing only 2 days should be excluded.

A3) We mildly disagree and believe there is a trade off to be considered. First the decision to include those subjects that only completed two of the three days was made prospectively, without evaluating the relative impact of exclusion of these three cases. The later would have clearly created the potential for bias in our decision. However studies can also be compromised and reasonably criticized for excluding too much data. So faced with this trade off; we thought it was better to not exclude 3/21 subjects (14%) and accept the missing 72/1512 hours (5%) data. Further with two 12-hour responses from separate days to average, we felt the resultant case, while not complete, was representative. If after considering our perspective you still think exclusion is the best approach, we are willing to comply.

Minor points

1. Methods, para 2: what is an evening effect?

A1) We have edited this comment for clarity.

2. Some spelling mistakes, e.g. “desaurations” or “difference manual control strategies”

A2) We have made the appropriate corrections.

- Quality of written English: Needs some language corrections before being Published

A) An independent American English teacher has reviewed the manuscript for spelling and grammar, in addition to our own careful review. We have corrected it accordingly.

- Declaration of competing interests: I hold rights to a competing FiO2 controller than used here.

A) We suggested Prof Poets as a potential reviewer because of his work in this field, but we were not aware of his commercial interest in another competing device. We found his comments helpful and have no objection to his role as a reviewer.
Sincerely,

Maria Wilinska, on behalf of all the authors