Author’s response to reviews

Title: The Effect of Sedation and/or Analgesia as Rescue Treatment during Noninvasive Positive Pressure Ventilation in the Patients with Interface Intolerance after Extubation

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Reviewer reports:

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Eusebi Chiner (Reviewer 2): I consider that the authors have responded satisfactorily to the reviewers and that the work can be published in the journal in the current format.

Patrick Murphy, PhD (Reviewer 4): The study is an observational cohort study examining the effect of sedation on outcomes of patients with interface intolerance who have been extubated onto NIV. The manuscript has already been reviewed and revised appropriately. I have some minor additional comments. A main limitation of the manuscript, acknowledge by the authors is the study design. Could the authors provide the rationale for the use of sedation in some patients, was there a protocol for indications for sedation or was this clinician preference? This is important as it may provide some insight as to how the populations were separated and thus differences in other aspects that need to be considered when interpreting the results. Further information on sedation administration l=policy should be provided in the manuscript to add information for the reader. Answer:

Thank you for your question. Just as we answered during first revision time in the reviewer 1, there is little evidence about whether sedation and/or analgesia could benefit patients with interface intolerance or not, and in view of the current research status, the present study was conducted to address this question. In order to avoid the selective bias as far as possible, we have searched the medical records from all the ICUs with different medical teams in our hospital.
Although we have collected all the data of the patients recorded as “interface intolerance”, it is a pity that the reason for “someone used the sedoanalgesia while the others did not” was not recorded. As is shown in Table 1, there is no difference between the two groups. We have revised the discussion to remind this limitation. Further random control trial is warranted to reduce the selection bias. And we have added these into the limitation part.

The interfaces are described as oral-nasal or facial; it remains unclear exactly which masks are being discussed. The terms oro-nasal and full face (both covering nose and mouth but not extending to cover the whole face) mask are often used interchangeably but are distinct from total face (covering whole face including eyes) masks. Although this has been revised it remains less than clear and so could the authors add further clarity?
Answer:

Thank you so much for your careful reading and explanation. We have rechecked the term we used in the manuscript. And in order to make it more clear, we have revised our manuscript.

The mortality analysis was adjusted for a range of cofounding variables although age is not listed despite being different between groups. Was age not related to outcome or was it used in the logistic regression but not listed?
Answer:

We did not found significant difference between the one survival and dead(72.5 vs. 71.5, p=0.838), which was listed in the Table 5. Thus, age was not included in the adjusted analysis.

The term OI is used in discussion but is not defined in the manuscript (p13 L12).
Answer:
Thank you for your suggestion. We have revised our manuscript accordingly.

Mean PaCO2 data in discussion should be moved to results section (p13 L18-20).
Answer:

Thank you for your question. All the data about PaCO2 presented in the discussion part were not from our study but from the references, which was used for support our point of view.

The authors refer to a RASS target of +2 to -2 in the discussion (p14 L8-10) however in the response to reviewers comments state that no target was used during the sedation protocol. The authors should clarify this apparent discrepancy.
Answer:

Thank you for your question. Just as we answered during the second revision to Reviewer 1, we did not set the target for the RASS score. The range of RASS score mentioned in our manuscript was just a result instead of target we get from the medical record. In order to not confuse readers, we have revised our manuscript.
The discussion references improved outcomes in patients with hypercapnia rather than hypoxia, however the data provided in this manuscript does not directly support this (p15 L1-2). The higher CO2 in the surviving population does not support the assertion that sedation improves outcomes preferentially in hypercapnic patients as this could relate to differences in diagnosis eg hypercapnic patients may be more likely to have COPD or other factors and a comparison of outcomes based on PaCO2 would be needed to further support this.

Answer:

Thank you for careful reading. The data presented in our manuscript(Table 1) was the ABG measured at half an hour after extubation, which was regarded as basic characteristics between patients who received sedoanalgesia and not. In our study, the sedoanalgesia were used when patients complained for intolerance. Thus, at the time we got the ABG, almost all the patients had not received sedoanalgesia. And just as we answered in the first revision, we did not done the ABG at a time point for all the patients after half an hour. Thus, we could only support our discussion by references.

Table 1: PaCO2 - could the authors check the units (cmH2O)?
Table 1: Consider moving outcomes such as ICU LoS, mortality NIV failure as they are not baseline characteristics to another table or into results text.
Figure 3: Consider changing y-axis name to survival.
Answer:

Thank you for your careful reading. We have revised it item by item.

The manuscript would benefit from final revision from a native speaker.
Answer:

Thank you for your advice. We have polished our manuscript again according to your advice.