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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Author’s response to reviews:

Dear Editor,

Re: Manuscript ID PULM-D-16-00483R2

We would like to thank BMC Pulmonary Medicine for giving us the opportunity to revise our manuscript.

We thank the reviewers for their careful reading and thoughtful comments on previous draft.

We have carefully taken their comments into consideration in preparing our revision, which has resulted in a paper that is clearer, more compelling, and broader. The following summarizes how we responded to reviewer comments.

Thanks for all help.

Best wishes,

Dr. Liang Zongan

Corresponding Author
Reviewer reports:

Franco Laghi (Reviewer 1): I thank the investigators for answering most of my questions. Some points, however, still need to be addressed.

1- The investigators wrote to one of my questions that "all the patients used NIPPV directly after extubation". This statement seems to imply that ALL extubated patients undergo NIPPV. In the appendix, however, the investigators list the indications to start NIPPV.

Please: (a) clarify whether ALL patients who are extubated receive NIPPV or whether only those fulfilling the characteristics listed in the list under the heading "Inclusion criteria for patients used NIPPV directly after extubation". (b) If the indications to start NIPPV are those under the heading "Inclusion criteria for patients used NIPPV directly after extubation", please move that list to the body of the manuscript and make it very clear in the methods section that those were the indications for NIPPV.

Answer:

a) only patients fulfilling the characteristics received NIPPV. We have revised our manuscript and made it clearer.

b) Thank you for your advice. We have revised our manuscript.

2- In the methods section make it very clear what was the RASS goal for sedation during NIPPV.

Answer:

We did not set the RASS goal in our study. And the best RASS goal for patients received sedoanalgesia during NIPPV remained unknown. In our study, the RASS score was between -2~2, but we did not control it intentionally. Our goal of sedoanalgesia was when patients did not complain the uncomfortable caused by the interface.

3-The response to my question regarding the fact "That a confounder was associated with a p<0.10 on univariate analysis is not a sufficient reason to generalize the results of this study to other ICUs" is insufficient. That other investigators have used the same strategy does not automatically make that strategy correct. A robust biological justification of the statistical strategy must be provided. Without it, the investigators must recognize that the generalization of their results to future cohort of patients becomes less convincing.

Answer:

We listed a list of confounders which would influence the clinical outcomes according to some papers published before. Actually, whether included confounder with P<0.05, P<0.1 or P<0.2 remains controversial. In our study, there were no confounders with P<0.05. And there were no confounder with P between 0.1 to 0.2. Thus, according to the result of statistic analysis, we included the confounder with P<0.1 in the univariate analysis.
4-Please provide the units for the numbers in the following sentences:

a-Moreover, NIPPV duration was also shorter in the group of sedoanalgesia (46.5 vs. 70, p=0.041).
b-ICU LOS was shorter in patients who received sedation and/or analgesia vs. those who did not receive drugs (5 vs. 8, p=0.030).
c-In our study, we found that sedation and/or analgesia would not influence the oxygenation, and the OI of patients in the sedation and/or analgesia remained unchanged (218.22 ± 65.87 vs. 211.13 ± 44.88, p=0.402).
d-On the contrary, the extraction of CO2 can be facilitated in the patients received sedoanalgesia, which can be seen from the lower PaCO2 after the administration of the drug (51.33 ± 13.49 vs. 48.53 ± 13.54, p=0.019)

Answer:

Thank you for your careful reading, we have revised our manuscript accordingly. But the OI did not have units, so we did not add units for it.

5-In the sentence "Our study showed that sedation and/or analgesia could decline the rate of NIPPV failure and NIPPV duration" change the word "decline" to "reduce"

Answer:

Thank you for your suggestion, and we have revised it.

APPENDIX

Please, specify the level of pressure support used during weaning from mechanical ventilation

Answer:

We have specified the level of pressure support used during the weaning.

Jacek Nasilowski, MD, PhD (Reviewer 3): The following issues have to be fixed before publication:

Firstly, the study was conducted in the very specific cohort: patients after extubation. The study gives impression that all patients after extubation should be treated with NIV, which is not true. This issue should be shown more clearly to justify the use of NIV in included subjects. Following papers should be used: Esteban NEJM 2004, Chien-Ling Su Respiratory Cate 2012, Nava Crit Care Med 2005, Ferrer AJRCCM 2006, Ferrer Lancet 2009, Hess Respir Care 2012.

Answer:

Thank you for your advice, we have read these papers carefully, and added them into our manuscript.
Moreover, indication to NIPPV must be clarified. On the one hand, authors said that the aim of NIPPV was providing respiratory support, but on the other hand they admitted that indication to NIPPV was not respiratory support but low ability of airway protection and cough strength. What does it mean?

Answer:

Sorry for our poor expression. We meant that when NIPPV was used for first line therapy before mechanical ventilation, the aim for it was to provide respiratory support and solve the respiratory failure induced by initiated disease such as COPD and pneumonia. However, when NIPPV was used after extubation, the initiated problems lead to respiratory failure had been released. In this situation, the reason we used NIPPV to provide respiratory support was the low ability of airway protection and cough strength, et al. In order not to be misunderstood, we have revised our expression in the manuscript.

Secondly, there are many other inconsistences in the text. e.g. it is said that all patients used total face mask, but in table 4 the use of oro-nasal mask and facial mask was reported? And the next question arises: whether subjects were proposed a change of interface, if total face mask was not tolerated?

Answer:

Sorry for our carelessness, because when translated into Chinese, total face mask included oral-nasal mask and facial mask. After you asked this question, we have read some papers and consulted some clinicians once worked in America. And finally we made it clear what these three things presented in English. The interface used in our study were oral-nasal mask(90%) and facial mask(10%). So we have revised our manuscript. Thank you again for your careful reading.

Thirdly, the structure of the manuscript is still not perfect. In abstract: the sentence "the use of sedation … could protect … from failure of NIPPV" sounds more like conclusion not result. In Discussion there are data (about OI), which should be given in results.

Answer:

Thank you for our advice, we have revised our paper accordingly.

Fourthly, there are many linguistic errors, unneeded repetitions.

Answer:

Thank you very much for careful reading and meaningful advice. We have polished our manuscript according to your advice, and Professor Dongtao Lin, a specialist in biomedical writing and editing, has copyedited our English expressions in the whole manuscript.