Author's response to reviews

Title: Role of sedation for agitated patients undergoing noninvasive ventilation: clinical practice in a tertiary referral hospital

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Dr. Antonio Esquinas
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Title: Role of sedation for agitated patients undergoing noninvasive ventilation: clinical practice in a tertiary referral hospital

Dear Ms Hazel Joyce Delos Santos and Dr. Antonio Esquinas

We wish to thank you for your email of June 3, 2015, regarding our manuscript, "Role of sedation for agitated patients undergoing noninvasive ventilation: clinical practice in a tertiary referral hospital" and for the careful reading of our manuscript and the very instructive comments. We have revised the manuscript on the basis of your comments.

The attached paper entitled “Role of sedation for agitated patients undergoing noninvasive ventilation: clinical practice in a tertiary referral hospital” has been carefully reviewed by an experienced editor whose first language is English and who specializes in editing papers written by physicians whose native language is not English.

Sincerely yours,

Responses to the comments of the editor

Editor's Comments:

I would like to thank the authors for their further appreciated efforts in addressing all the raised comments and criticisms. The manuscript is really much improved.

However, at that point, I would be able to accept the paper only if the following minor requests will be sorted out in order to improve the message and clarity of the manuscript:

1) I have still some problems in understanding what underlined by the authors (page 10, lines 161-165)? In this study, the avoidance of NIV...
failure was considered to indicate the efficacy of sedation." I guess that they meant "failure of sedation consists in the need for withdrawal NIV because of absolute intolerance of patients (RASS>=1) despite the maximized analgo-sedative strategy". The authors well know that failure of NIV could occur for other reasons that patients intolerance/agitation (e.g. impossibility to correct gas exchange, haemodynamic instability, excessive burden of secretions, multi-organ failure): I invite the authors to report the different patterns of NIV failure (failure due to lack of efficacy of sedation and failure not due to sedation inefficiency)

Thank you very much for your review and valuable comments.
As you pointed out, the definition of failure of sedation in the former manuscript was insufficient and unclear. Failure of NIV could occur for reasons other than sedation insufficiency. In this study, there were 11 patients among the non-DNI patients who failed to continue NIV treatment and were intubated. In 2 this was due to agitation while in 9 it was due to other reasons such as exacerbation of the respiratory status or hemodynamic instability (Table 5).
We changed the Methods section as follows (page 10, line 166-page 11, line 171).
“In this study, failure of sedation consisted of the need for withdrawal of NIV because of absolute intolerance by patients despite the maximized analgo-sedative strategy. That is, in the non-DNI group, failure of sedation was declared when a patient was intubated due to agitation in spite of sedation, and failure of sedation in the DNI group was declared when NIV treatment could not be continued due to agitation.”

Also, we changed the Discussion section as follows (page 17, lines 290-292).
“In this study, 9 (23%) non-DNI patients were intubated for reasons other than sedation insufficiency, such as exacerbation of the respiratory status or hemodynamic instability (Table 5).”

2) Despite the encouraging results of this paper that mirrors previous experience, as opportunely stated by the authors in the discussion (page 17, lines 278-284), I recommend to stress this concept in the conclusions (page 20: line 339) "Continuing NIV under sedation is not appropriate in case of failure of controlling agitation both in DNI patients for the risk of prolonging distress and agony and in non-DNI patients for the risk of unduly delay the intubation”
Thank you very much for your instructive comment.
As you recommended, we should stress the negative sides of sedation under NIV.
We added the following sentence in the Conclusion (page 21, lines 351-354).
“Also, continuing NIV under sedation is not appropriate in cases of failure to control agitation both in DNI patients in consideration of the risk of prolonging distress and agony, and in non-DNI patients considering the risk of unduly delaying intubation.”

3) Again, due to the uncontrolled design of the study, I strongly suggest to add in the conclusions (both abstract and discussion: last paragraph) that "larger controlled studies are needed to better clarify the role of sedation in improving NIV outcomes in intolerant patients"

Thank you again for your instructive comment.
As you pointed out, a further larger study with controls is needed to clarify the role of sedation under NIV. This study was a retrospective study without control subjects.
As you suggested, we added the following sentence in the Abstract (page 4, lines 56-57).
“Larger controlled studies are needed to better clarify the role of sedation in improving NIV outcomes in intolerant patients.”

We also added the following sentence in the Discussion (page 20, lines 341-343).
“In consideration of these limitations, larger controlled studies are needed to better clarify the role of sedation in improving NIV outcomes in intolerant patients.”

4) Concerning the still contrasting role of NIV as pure palliation (see: page 17, line 295-page 18, line 302), I would change the sentence as follows "Therefore, we often had to continue NIV with sedation as palliative care, which might on one hand contribute in some degree to the high mortality rate and on the other hand to prolong usefulness an agony. To avoid the latter, we discontinued NIV in DNI-subjects in accordance with patient and or family decision in case of persistent agitation/intolerance”

Thank you very much for your useful suggestion.
Your suggested explanation is much more comprehensive and informative compared with our previous explanation. As you suggested, we changed the Discussion section as
follows (page 18, lines 307-311).

“Therefore, we often had to continue NIV with sedation as palliative care, which might on one hand contribute in some degree to the high mortality rate, and on the other hand contribute to prolonging useless agony. To avoid the latter, we discontinued NIV in DNI patients in accordance with patient’s and/or family’s decision in cases of persistent agitation.”

5) It’s not clear what "When NIV treatment was not needed for 12 consecutive hours..." means (see page 8, lines 130-132): blood gases and respiratory rate during a spontaneously breathing trial?

We apologize for the insufficient explanation of the criteria for NIV discontinuation. We discontinued NIV treatment in patients that met all of the following criteria: 1) SpO\textsubscript{2} was >90% with the inhalation of oxygen <10 l/min via reservoir mask; 2) PaCO\textsubscript{2} levels were <45 mmHg or patients did not suffer acute respiratory acidosis; and 3) patients had no signs of respiratory distress, including a respiratory rate >24 and increased accessory respiratory muscle use.

We added the following explanation in the Methods section (page 8, line 131-page 9, line 137).

“At first NIV treatment was performed all day. However, we discontinued NIV treatment in the cases that met all the following criteria: 1) SpO\textsubscript{2} was >90% with the inhalation of oxygen <10 l/min via reservoir mask; 2) PaCO\textsubscript{2} levels were <45 mmHg or patients did not suffer acute respiratory acidosis; and 3) patients had no signs of respiratory distress, including a respiratory rate >24 and increased accessory respiratory muscle use. When NIV treatment was not needed consecutively for 12 h, NIV treatment was considered to be finished.”

Thank you again for your valuable comments on our paper. We trust that the revised manuscript is suitable for publication.

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