Author’s response to reviews

Title: Nasotracheal Intubation-Extubation-Intubation and Asleep-Awake-Asleep Anesthesia Technique for Deep Brain Stimulation

Authors:

Wenxi Tang (Drsoup@163.com)
Penghui Wei (weipenghuihui@sina.com)
Jiapeng Huang (jiapenghuang@yahoo.com)
Na Zhang (zhangna0210@163.com)
Haipeng Zhou (hope6968@hotmail.com)
Zhou Jinfeng (zhoujinfengaa@sina.com)
Qiang Zheng (zq4878@163.com)
Jianjun Li (weipenghuihui@sina.com)
Zhigang Wang (wangzhigang367@163.com)

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Author’s response to reviews:

Dear Editor,

Thank you very much for your kind letter and encouragement as well as for the constructive comments by the reviewers concerning our manuscript titled “Nasotracheal Intubation-Extubation-Intubation and Asleep-Awake-Asleep Anesthesia Technique for Deep Brain Stimulation” (BANE-D-18-00477). The language of this manuscript was thoroughly revised and edited by a professor of American medical college, which has improved the overall readability of the manuscript. Additionally, we have thoroughly considered all of the comments of the reviewers and substantially revised our manuscript. We wish to resubmit the revised manuscript for publication in BMC Anesthesiology. A point-by-point response to all of the reviewers’ comments is included below this letter. All changes made to the text are in red so that they can be easily identified.

We have tried our best to address all of the concerns raised by the reviewers. We hope that with the modifications and improvements we have made based on the reviewers’ comments and the quality of
our manuscript will meet the publication standard of this journal.

Once again, thank you very much for your attention and consideration of our manuscript.

Sincerely,

Jianjun Li

Response to reviewers' comments:

Carla Todaro (Reviewer 1):
Comments to the Author
The manuscript needs to be reorganized.

Some part is difficult to read because continually shift between the description of the awake part and the general anesthesia part.

My suggestion is to describes the two part separately so the management during the two different stages appears clear.

The method for this reason seems unclear at some point (please see also comments added to the text).
Reply: Thank you very much for the constructive comments, which have helped improve the quality of our manuscript. We have re-arranged the method and result part of the manuscript into three sections to make reading easier, that is the first asleep stage, the awake stage and the second asleep stage. The detailed revision can be found on lines102-136, page 5-8.

The conclusions are too hasty so need to be discussed in a more broad way.
Reply: Thank you. We have expanded our discussions further. The detailed revision can be found on lines146-150, page 8.

1)Please add the title for each author (for example MD)
- Only corresponding author email address needs to be indicated.
Reply: Thanks. Changes have been made. The detailed revision can be found on lines 3-17, page 1.

2)first time the abbreviation appears in the text needs to be on extended form as well
Reply: Thank you. This has been changed. The detailed revision can be found on lines 25, page 2.

3) above the epiglottis is too generic, I suggest to specify the location using anatomic finding (for example at level of the tongue base) or measures unit as mm.
Reply: Thank you. We have revised to “The nasotracheal tube was retracted to the top of epiglottis
(at level of the tongue base) under the guidance of FB-10V FOB (HOYA Corporation, PENTAX Lifecare Division, Tokyo, Japan) and then kept as a nasopharyngeal airway.” The detailed revision can be found on lines 108-109, page 6.

4) I suggest to add the BMI instead of the weight.
Reply: Thanks for. We have changed to BMI. The detailed revision can be found on lines 66-71, page 4.

5) it was a severe OSA, what AHI index?
Reply: Thank you. AHI was 33 and has been revised in the manuscript. The detailed revision can be found on lines 72, page 4.

6) specify if also a bolus dose was given
Reply: Thank you. We have provided the bolus information. The detailed revision can be found on lines 119, page 7.

7) was always a 6.5 for male and females?
Reply: Thank you. The ETT was 6.0 for female patients and 6.5 for males. The detailed revision can be found on lines 97, page 6.

8) Remember that the most serious perioperative misadventure is the loss of airway control after induction of general anesthesia in patient with OSA. Because of reduced oxygen reserve due to obesity-related decreases in lung volume, morbidly obese patients cannot tolerate a lack of ventilation for appreciable periods before hypoxemia results.
Therefore, I would describe in a more articulate way the reasons why the MAC is a poor choice.
Reply: Thank you. For the third patient, when dexmedetomidine was given to reduce the body movement to complete MRI scan before operation, his head movement caused by OSAS also hampered the MRI scan. Only after the OSAS was eliminated by placing a nasopharyngeal airway, the MRI scan was finished successfully. The related statement can be found on lines 70-77, page 4.

9) The patient with OSA received midazolam?
Reply: Thank you. All patients received small dose of midazolam.

10) Remember that the administration of combination of sedatives, anesthetics and analgesics in OSA patient worsen obstruction of the pharynx.
Reply: Thank you. We understand your concerns, and there is a point in avoiding midazolam or combination of sedatives for OSA patient. However, we avoid hypoxemia for OSA patient during anaesthesia induction in the second asleep phase with three ways: 1. The tracheal catheter retained in the nasal tract which can help maintain the airway unobstructed, and it can be used for high frequency ventilation if necessary. 2. FOB can help the tracheal intubation be completed smoothly when needed. 3. Maintaining a high flow oxygen inhalation throughout the induction of anesthesia.
The goal of small dose of midazolam was to reduce the amount of other respiratory depressing anesthetic agents, such as propofol, thus avoiding severe circulatory fluctuations and respiratory inhibition, and to make sequence induction smoother.

11) use numbers...express it in percentage...
Reply: Thank you. We have tried our best to use numbers or percentage in our revised manuscript.
12) These data can be reported as table
Reply: Thanks for your advice. Due to words limitation, we described them in the main text.

13) extend these comments
Reply: Thanks for your advice. We have expanded these discussions. The detailed revision can be found on lines 71-76, page 4-5 and lines 152-154, page 9.

Kemal Tolga SARACOGLU (Reviewer 2):

Comments to the Author.

1. In the abstract: please explain the abbreviation of PD patients as Parkinson's disease.
Reply: Thanks for your question. Changes have been made. The detailed revision can be found on lines 25, page 2.

2. The standard ASA monitors were placed: please give more details about the monitoring.
Reply: Thanks for your question. Changes have been made. The detailed revision can be found on lines 88-89, page 5.

3. Both blood pressure and heart rate were significantly higher than asleep stage and the second patient needed intermittent injections of low dose nicardipine and esmolol to maintain hemodynamic stability: please give exact numbers to identify the significant difference between two stages. Please also note the dose of nicardipine and esmolol.
Reply: Thanks for your question. We have provided the changes of blood pressures and dosages of nicardipine and esmolol. The detailed revision can be found on lines 117-121, page 7.

4. Discussion: please correct did'nt as did not
Reply: Thanks for your question. Changes have been made. The detailed revision can be found on lines 149, page 8.

5. none of the intubation were finished during patient awake. we believe endotracheal surface anesthesia before intubation is most important whether for making patient tolerable intubation or extubation: the manuscript should be reviewed by a native English speaker.
Reply: Thanks for your question. Language editing has been done.

6. All of our patients were able to wake up quickly and cooperated with neurological tests: this statement is so subjective please give exact mean time values to be more clear.
Reply: Thanks for your question. Exact mean time values have been provided. The detailed revision can be found on lines 113, page 7.

7. Did the authors perform scalp block before the procedure? Please give some information.
Reply: Thanks for your question. Local infiltration was performed, nor scalp blocks. The detailed revision can be found on lines 100-101, page 6.
Sujoy Banik, MBBS, MD, DM (Reviewer 3):

Comments to the Author

1. One thing I always wonder is why did you need to induce the asleep phase after the frame was put on, considering that GA was planned right from the start? The frame can always be put on after the tube is inserted.
   Reply: Thanks for your question. Our surgeons believe it is easier to place the frame while the patient was awake. This is the reason for placement before GA.

2. The dose of remifentanil is quite high during the procedure. Considering that dexmed and propofol were ongoing, I would have anticipated hypotension with these doses; certainly, they are within therapeutic range, but overall looks like overkill.
   Reply: Thanks for your question. We agree with your comments. Although patients have a certain degree of blood pressure drop at these doses, they are within clinically acceptable limits, so we do not mention this in the article.

2. Its also significant to note that even though the first two pts refused MAC, they were happy to proceed with this whole super complex approach, which includes an awake phase during the surgery, which corresponds to MAC. Also, they were happy to answer questions and recordings etc. with something stuck down their nostrils, all looks contradictory.
   Reply: Thanks for your question. Both patients felt that even a small reduction in awake time was better for them than fully awake during the whole case.
   Did they have anterograde amnesia at the end of the procedure? Did they remember their experience, or was it just a subjective experience that was felt by them?
   Reply: Thanks for your question. They remembered the awake portion without discomfort.

3. Prevention of aspiration by this technique is one of the major advantages here. That needs to be more emphasized.
   Reply: Thanks for your question. We have emphasized prevention of aspiration in the revision. The detailed revision can be found on lines 185, page 10.

4. All abbreviations need to be described clearly the first time they are written in the manuscript (PD, DBS, etc.). Kindly do the needful and add abbreviations index as well.
   Reply: Thanks for your question. Changes have been made.

5. If improvements to the English language within your manuscript have been requested, you should have your manuscript reviewed by someone who is fluent in English.
   Reply: Thanks for your advice. Language editing has been provided.