Author’s response to reviews

Title: Perioperative incidence of airway obstructive and hypoxemic events in patients with confirmed or suspected sleep apnea - A prospective, randomized pilot study comparing propofol/remifentanil and sevoflurane/remifentanil anesthesia

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Author’s response to reviews:

Response to the reviewers

Response to reviewer #1

Jonathan Ball (Reviewer 1): Thank you for the invitation to review this manuscript.

The authors describe a prospective, single centre, blinded, randomised study of the effects of 2 different general anaesthetic regimes on the severity of sleep disordered breathing in a cohort of patients with known or suspected mild to moderate OSA. They found no significant effect or either anaesthetic regime on the severity of OSA on the first post-operative night.

We like to thank this reviewer for his important comments to improve our manuscript.

Comments

The power calculation appears to make rather optimistic assumptions and I strongly suspect that this study is significantly underpowered.

The primary statistical analysis comparing the median values of both the 2 regimes before and after is, I believe, flawed. The correct analysis should be to compare the differences between before and after studies in each individual. I would recommend an expert statistical opinion on this point.
The severity of OSA in the sevoflurane group appears to be significantly lower than the propofol group making the comparison between the 2 groups invalid?

I suspect, looking at the presented data that the authors found no effect of any GA regime on any patient thus the above concerns aside, their conclusions may still hold.

We disagree. Obviously, there are no previous studies randomizing different anesthetic regimen with AHI as an end point. Accordingly, in a pilot study exploring this field and comparing anesthetic regimen one wants to see a solid effect, if present, between groups and not chase subtle effects which may be of no clinical importance. This was completely in accordance with a statistician consulted prior to undergoing our pilot study.

We are uncertain, what this reviewer means by saying that the “correct analysis should be to compare the difference between before and after studies in each individual”. This is exactly what we did when comparing each individual’s nocturnal AHI and nadir SaO2 during the postanesthesia night to the preanesthetic night using the Student’s t-test for paired samples or the Wilcoxon matched pairs test, as appropriate. Accordingly, we do not understand this reviewer’s specific critique.

In addition, as the reviewer is well aware, it is also of importance to compare postoperative nocturnal AHI and nadir SaO2 following different anesthetic regimen.

With regard to the reviewer’s assumption that the severity of OSA in the sevoflurane group would appear significantly lower than in the propofol group we like to refer this reviewer to the original manuscript where we clearly stated on page 10: “Patients receiving sevoflurane had a slightly lower nocturnal AHI both pre- and postoperatively (3.8 h-1 (1.8-7.3) vs. 2.9 h-1 (1.2-9.5); p=0.85). However, these differences were not statistically significant (p=0.21, fig. 2).” Thus, this reviewer’s assumption is not correct and had been explicitly addressed.

Additional but unmeasured confounders should be included in the discussion. These include the dose of opiates received post discharge from the PACU and chronic alcohol consumption history.

Thank you for your point well taken. In response, we have addressed potential confounders in the revised discussion section. None of our patients had a history of chronic alcohol consumption.

Changes made in the revised manuscript: On page 16 we added: “Third, we did not assess the doses of analgesics that our patients received after discharge from the PACU, what might be a potential confounder if these doses were significantly different between the groups. However, as the doses of opioids received in the PACU and the types and length of surgery did not differ between the groups, we are confident that unmeasured opioid intake did not affect results. Fourth, another potential confounder would be chronic alcohol consumption, as past and/or current alcohol consumption influences the prevalence and severity of obstructive sleep apnea [26,27]. However, none of our patients revealed such a history on preanesthetic evaluation. “
It would be useful to know if there were any post-operative complications in any of the patients and whether the incidence of these overall compares favourably or unfavourably with expected incidence rates.

All patients were followed up on the first postoperative day by the respective anesthesiologist in charge of clinical care. None of our patients had post-operative respiratory complications, requiring endotracheal intubation, non-invasive ventilation, or unplanned ICU admission. We now have added this information to the revised manuscript, as requested, on page 12.

Again, thank you for your time and effort spent to improve our manuscript.

Response to reviewer # 2

Jan Blaha, M.D., Ph.D. (Reviewer 2): The study by Fassbender and colleagues is an interesting study on patients with OSA undergoing surgery. In a pilot study they compared propofol/remifentanil vs. sevoflurane/remifentanil anesthesia and looked at its effect on postoperative nocturnal apnoea-hypopnea-index. As they pointed out OSA is generally underdiagnosed but has substantial risk in surgical patients. From this perspective this is an important study, but nevertheless I have several points first:

We thank the reviewer for the time and effort spent in reviewing our manuscript and appreciate that he considers this “an important study”.

Major comments:

Type of surgery - should be described in detail also in Methods. It's mentioned only very briefly in Results, but this is an important part of the study. The types of surgery were breast surgery, eye/ENT or urology, and neurosurgery. This needs more detailed description - especially differences in these surgeries between both groups - as there is for example an important difference in position (disc surgery vs. all others); or different types ENT surgeries might have different effects on postoperative occurrence of OSA.

We appreciate this reviewer’s comment and have now added to page 6, methods section, a sentence outlining the number of patients undergoing different surgeries. Specifically, the most frequent surgery was eye surgery including eye enucleation for tumor, musculoskeletal surgery, and gyn/urology surgery. Furthermore, the types of surgery did not differ between the sevoflurane und propofol groups.

Postoperative analgesia - any differences between both groups? Were there any additional requirements for analgesia? What was the average dose of morphine in each group?

As outlined in the original manuscript in table 1 the average morphine dosages were 9.5 mg ±4.4 and 11.5 mg ±6.4 for the two groups, and there was no statistical significant difference between groups.

Minor comments:
Background - there is an explanation of AHI abbreviation missing when used for the first time

Thank you for pointing this out. We apologize and in the revised manuscript have added this information on page 4.

Would monitoring of depth of anesthesia bring any additional information?

Good point but nobody knows. Actually, our pilot study is the first to compare different anesthesia regimen for moderate surgical procedures, not to mention an effort to somehow control for “depth” of anesthesia comparing sevoflurane and propofol based anesthesia.

Data analysis - wrong description of AHI (apnea-hypopnea-indices instead od index)

We apologize. Corrected on page 8.

Again, thank you very much for improving our manuscript.