Peer Review File

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Reviewer A

Comment 1:

Abstract

- The authors should state the response to the primary purpose (i.e., evaluation of efficacy intraoperative IANB).

Reply 1: We have added the primary outcome measure.

Changes in text: Please see page 3, line 62

Comment 2:

- Please add data of the diseases.

Reply 2: we have added under results section as well

Changes in text: Please see page 2, line 46

Comment 3:

Methods

- Please explain "aspiration test".

Reply 3: We have added the method of aspiration test.

Changes in text: See page 6, line 158-162

Comment 4:

Results

- P8line185: Please explain "rapid onset of action".

Reply 4: Rephrased the line to rapid onset of anaesthetic activity.

Changes in text: See page 9 line 223

Comment 5:

- P8line187: "all patients in Group B reported numbness of teeth and 9 of them reported numbness in the tongue and 2 of them also were positive for aspiration test"

When did the patients report their numbness? They were under general anesthesia.

Reply 5: It has been already mentioned in the methods section. Sensory loss was checked, which if not achieved in 15 mins were excluded from the study. In addition, now added to results section too.

Changes in text: Please see page 10, line 225-227

Comment 6:

Discussion

- In the first paragraph, please summarize the most important finding in your study.

Reply 6: Added the primary purpose.

Changes in text: See page 10 line 234-236

Reviewer B

The study seems to be interesting. However, there are several points which should be clarified.

Comment 1:

(1) Operation time and bleeding amount are not clear in both groups. It should be shown and analyzed between groups.

Reply 1: We have added the operation time in methods section and blood loss between groups were not determined.

Changes to text: Please see page 7, line 175-176

Comment 2:

(2) Detailed information of mandibulectomy is not clear. Especially, the extent of mandibulectomy is not clear. Was bone graft performed?

Reply 2: Bone graft was not performed; other details are mentioned in the result section now.

Changes to text: Please see page 9, line 211-214

Comment 3:

(3) Procedures of Inferior alveolar nerve block (IANB) should be shown in more detail. Figure or photograph of IANB is required.

Reply 3: We don't have any pictures , as mentioned by one of the reviewers we used standard technique, and it is very difficult to obtain a good picture in an actual patient.

Changes to text: None

Reviewer C

General comments:
I enjoyed reading this manuscript. It is the valuable prospective preliminary study to assess intraoperative opioid and propofol consumption and hemodynamic stability by administrating classical IANB in mandibulectomy.
There are a few unknown points, and I would appreciate the clarification. Regarding the preparation of this manuscript, I also have some advice.

Specific comments:
Comment 1:
1. The primary outcome should be one of either fentanyl consumption or propofol consumption. This is because if two are set as the primary outcome, significant differences are likely to occur due to multiple testing.
Reply 1: Fentanyl consumption is considered as primary objective
Changes in text: Please see page 5, line 109

Comment 2:
2. Whether IANBs in Group B is truly successful is the point of this study. To clear up that issue, the authors checked for loss of sensation after the procedure and excluded block failure. How about a more detailed classification of the successful IANB group? If the loss of sensation is checked in the chin (inferior alveolar nerve), tongue (lingual nerve), and buccal mucosa(buccal nerve), and whether complete or partial sensory blockade was achieved in each area is recorded separately, it would be possible to determine the effectiveness of the IANB in more detail.

IANB is a technique to administer medication to the pterygomandibular space (PMS). The inferior alveolar, lingual, and buccal nerves pass through the PMS, and previous studies using cadavers have shown that 5 mL of medication for the PMS results in the blockade of these nerves (J Anesth. 2022 Feb;36(1):46-51. doi: 10.1007/s00540-021-03004-9.).

Reply 2: The patients self-reported the numbness in buccal mucosa and tongue, and this was confirmed by loss of sensation to pinprick. Only complete sensory blockade was noted as a successful blockade in our study. Franz and Perry attributed that differential rates of blocking among myelinated axons are attributable to difference in critical lengths of axons that must be exposed to blocking concentration than to difference in minimum concentration necessary to block axons of different sizes.

Changes in text: None

IANB is a technique to administer medication to the pterygomandibular space (PMS). The inferior alveolar, lingual, and buccal nerves pass through the PMS, and previous studies using cadavers have shown that 5 mL of medication for the PMS results in the blockade of these nerves (J Anesth. 2022 Feb;36(1):46-51. doi: 10.1007/s00540-021-03004-9.).

Reply: The reason for choosing 2.5 ml of drug for injection.

It's necessary to apply the anaesthetic agent along a distance of no less than 3 inter-nodal lengths of largest fibers. The longest inter-nodal span of inferior dental nerve is 1.8mm. To induce blockade of a whole nerve, atleast 6 mm of the nerve must be deposited. To induce a satisfactory blockade atleast 2ml drug should be deposited. However, studies show 1.0 mL as the effective volume below which consistent success cannot be expected.

Changes in text: None

Comment 3:

3. It is necessary to talk about how long IANB with 0.75% ropivacaine will last. In addition, what was the postoperative hemodynamic course? In addition to the operating and anesthetic times, it would be preferable to describe the postoperative pain score progression or the duration of sensory loss.

Reply 3: This is an interesting research question which can direct further studies , however it was not possible in our pilot study, as our patients after the mandibulectomy had a variety of procedures like neck dissection, Pectoralis major myocutaneous flap, nasolabial flap and so on. For comparing post operative hemodynamic course and post operative pain the entire surgery in both the groups will have to be standardised. Hence, we chose to close our study after mandibulectomy.

Changes in text: None

Comment 4:

4. Surgery-related blood loss may be decreased by IANB's intraoperative hemodynamic stabilization. Therefore, please describe the intraoperative blood loss for both groups.

Reply 4: We acknowledge this as a limitation of our study, that blood loss between the two groups was not documented. A marginal mandibulectomy could logically have a different amount of blood loss vs. segmental mandibulectomy vs. hemi-mandibulectomy. For accurate estimation of blood loss between the two groups the surgical procedure will have to standardised.

Changes in text: Added as limitation. Please see page 12, line 286-290

Comment 5:

5. Please describe the intraoperative infusion volume, type of infusion, urine output, and ventilator setting conditions.

Reply 5: Intraoperative infusion volume is already mentioned in methods section.

Urine output was not compared amongst the two groups because not all patients were catheterized.

Other details are added in the methods section.

Changes in text: Please see page 7, line 165-172

Reviewer D

Comment 1:

Due to the small sample size of 22 subjects, the authors agree that this trial should be considered a pilot study. So please add this essential feature to the title.

Reply 1: Rephrased the title

Change in text: Page 1 Line 1

The background is inadequate for me:

Comment 2:

• It seems unnecessary to define well-known techniques such as the mandibular nerve block or the mandibulectomy. All these sentences are superfluous and can be deleted. For example, lines 69-74 and cites 4 and 5 are too general and lack consistency with the background.

Reply 2: Removed these lines.

Changes in text: removed lines from page 4, introduction.

Comment 3:

• Nevertheless, the background should refer to the trend of 'multimodal anesthesia,' combining different anesthetic approaches to get a more balanced result. It would be appropriate to report the documentation about using IANB in a multimodal approach to improve postoperative pain control and opioid requirements after orthognathic surgery (Vetter M, et al., 2020; Bertruit M, et al., 2021).

Reply 3: Added relevant references and edited background.

Changes in text: See page 4 lines 84-87

Comment 4:

• The authors would better explain to the general reader why it is advisable to use intraoperative analgesia concomitantly with general anesthesia. The preemptive anesthesia approach could be explained by its effects of decreasing physiological stress and its hemodynamic repercussions (Chen YA, et al., 2016) .

Chen YA, Rivera-Serrano CM, Chen C, Chen YR. Pre-surgical regional blocks 1 in orthognathic surgery: prospective study evaluating their influence on the intraoperative use of anesthetics and blood pressure control. Int J Oral Maxillofac Surg, 2016;45(6):783-6.)

Reply 4: Added relevant explanation.

Changes in text: See page 4 and lines 93-99.

Comment 5:

Regarding the material & methods section, some clarifications need to be made.

• In the study population, the treatment prescription should be precise. Which mandibulectomies do enter the study?

Reply 5: Added in methods section.

Changes in text: Please see page 5, line 121-122

Comment 6:

• Opioids and propofol consumption is closely related to the extension and duration of the operation. To this end, it could have been helpful to control the duration of surgeries. Is the surgical burden equal for all patients? The authors recognize these surgical differences in lines 238-240.

Reply 6: Since the reading were only taken for one hour until mandibulectomy was completed , the surgical burden was similar for both the groups.

Change in text: None

Comment 7:

• In the sample size calculation, what does a medium effect size of 0.5 stand for? If it is a difference in medication consumption, it may be expressed in mcg/kg of fentanyl or the number of propofol boluses. Please, specify.

Reply 7: Medium effect size is assumed for primary outcome difference between the two groups, i.e., amount of fentanyl consumption. We have added the units now.

Change in text: Added units under sample size calculation

The results section seems well-written to me.

In the discussion section,

Comment 8:

• Although mandibular nerve injection is generally safe, if its potential complications are included in the discussion, some are to be mentioned. (Aquilanty L, et al., 2022).

Aquilanti L, Mascitti M, Togni L, Contaldo M, Rappelli, G, Santarelli A. A Systematic Review on Nerve-Related Adverse Effects following Mandibular Nerve Block Anesthesia. Int J Environ Res Public Health 2022;19:1627.

DOI:10.3390/ijerph19031627

Reply 8: Complications have been added as part of further research suggestions.

Change in text: See pages 12, lines 277-279.

Comment 9:

• Lines 204-6 introduce a general comparison with a cross-sectional study. I can't see where this comparison leads us. The same can be said about the comparison with cite number 16.

Reply 9: Removed irrelevant comparisons.

Changes in text: Removed lines from discussion

Comment 10:

• Can the authors explain why they recorded a decrease in mean arterial pressure in group B being ropivacaine vasoconstrictive? It seems not discussed enough.

Reply 10: We added few lines as why the mean MAP could be low.

Changes in text: Please see page 11, 12, line 272-274

Comment 11:

Finally, the conclusion is well-formulated, but the order of the two sentences should be changed. The second should be moved to the first place, and the lack of statistical power

as a pilot study is an aspect to be added. The first sentence, unchanged, could move to second place.

Reply 11: Made the mentioned changes

Changes in text: Conclusion section Please see page 12, line 293-295