OPEN PEER REVIEW

## Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

## What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

## Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Anesthesiology and Pain Medicine
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# Peer Review Report for "Evaluation of the Effect of Intranasal Lidocaine in the Treatment of Spasticity in Patients with Traumatic Brain Injury"

**Author(s):** Anoush Dehnadi Moghadam, Hamed Hasanzadeh, Fatemeh Dehnadi Moghadam

## Review Timeline:

Submit Date: 8 May 2021
Revised Date: 23 Jul 2021
Accepted Date: 24 Jul 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Reviewer | **Revision** (0) — 30 May 2021

Dear AE,
Comments for the authors:
1- there is lacking of any data about efficacy of intranasal lidocaine to treat neurologic complications in your study and literature review. references 28 and 29 are not related to intranasal route of local anesthetic administration (page 4. paragraph 4. line 11)
2- you didn't have a control group in this study to compare lidocaine with placebo-like normal saline. so relieving of spasticity can not be attributed exclusively to lidocaine in this study.
3- intranasal lidocaine as a continuous infusion for about 7 days seems extravagant. what about the head position of your patients during these seven days?
Thanks.

**REFEREE**: Reviewer | **Revision** (0) — 2 Jun 2021

Dear AE,
1- In the methods section, patients with moderate and severe spasticity had been selected for study, so they must have different Ashworth scales and it affects the amount of

effectiveness of drugs. Did you categorize patients from this point of view?
2- Did the patients get any sedative drugs during the study and what was it and how much?
3- Did the patients have any evaluation for nasal mucous membrane(polyp, integrity,….)?
4- How did you evaluate the toxicity of lidocaine in patients?
Thanks

**REFEREE**: Reviewer | **Revision** (0) 7 Jun 2021

Dear AE,
Method
- Have not the information about instruments that have been used for intranasal infusion and the difficulty for the patient that infusion of intranasal lidocaine can bring 9 days of continuous intranasal lidocaine is not safe.
- At least CSF lidocaine must be detected.
Thanks.

**REFEREE**: Associate Editor | **Revision** (0) 9 Jun 2021

Dear Editor in Chief
Based on reviewers' comments this manuscript needs some corrections. Also, strongly recommend to the author for considering below 11 references:
- Oriby ME. Comparison of Intranasal Dexmedetomidine and Oral Ketamine Versus Intranasal Midazolam Premedication for Children Undergoing Dental Rehabilitation, Anesth Pain Med. 2019;9(1):e85227.
- Saeidi M, Alikhani R, Hormati A, Sabouri SM, Aminnejad R. Propofol-Induced Masseter Muscle Spasm in a Woman with a Major Depressive Disorder. Anesth Pain Med. 2018;8(3):e78748.
- Soltani F, Tabatabaei SK, Janatmakan F, Nasajian N, Amiri F, Darkhor R, et al. Comparison of the effect of haloperidol and dexmedetomidine on delirium and agitation in patients with traumatic brain injury admitted to the intensive care unit. Anesth Pain Med. 2021;11(3):e113802.
- Rimaz S, Ashraf A, Marzban S, Haghighi M, Zia Ziabari SM, et al. Significance of Cardiac Troponin I Elevation in Traumatic Brain Injury Patients. Anesth Pain Med. 2019;9(2):e90858.
- Tully J, Jung JW, Patel A, Tukan A, Kandula S, et al. Utilization of Intravenous Lidocaine Infusion for the Treatment of Refractory Chronic Pain, Anesth Pain Med. 2020;10(6):e112290.
- Imani F, Khajavi M, Gavili T, Pourfakhr P, Shariat Moharari R, et al. Comparison of the Effect of Intra-Rectal Administration of Lidocaine Gel and Lidocaine Plus Fentanyl on Pain Reduction in Prostate Biopsy: A Randomized Clinical Trial, Anesth Pain Med. 2018;8(6):e82778.
- Chandra S, Pryambodho P, Melati AC, Kusuma RI. Comparison Between Lidocaine Inhalation and Intravenous Dexamethasone in Reducing Postoperative Sore Throat Frequency After Laryngeal Mask Insertion, Anesth Pain Med. 2018;8(5):e82131.
- Ghasemi M, Mosaffa F, Hoseini B, Behnaz F. Comparison of the Effect of Bicarbonate, Hyaluronidase, and Lidocaine Injection on Myofascial Pain Syndrome, Anesth Pain Med. 2020;10(3):e101037.

- Fathy W, Hussein M, Khalil H. Comparative Effect of Local Anesthesia with Lidocaine 2% Versus Topical Anesthesia on Cognitive Function in Ophthalmic Surgery, Anesth Pain Med. 2019;9(6):e97172.
Moradi Z, Kokabi R, Ahrari F. Comparison of the Effects of Lidocaine-Prilocaine Cream and Lidocaine Injection on the Reduction of Perineal Pain While Doing and Repairing Episiotomy in Natural Vaginal Delivery: Randomized Clinical Trial. Anesth Pain Med. 2019;9(3):e90207.
- Halili H, Azizkhani R, Tavakoli Garmaseh S, Jafarpisheh MS, Heydari F, et al. Comparing the Effect of Lidocaine-Prilocaine Cream and Infiltrative Lidocaine on Overall Pain Perception During Thoracentesis and Abdominocentesis: A Randomized Clinical Trial, Anesth Pain Med. 2021;11(1):e106275.
Final decision: Major revision
Regards

**REFEREE**: EIC | **Revision (0)** 9 Jun 2021

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (1)

## Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

**Reviewers' Comments:**

| *Reviewer 1* | Response |
|---|---|
| 1- There is lacking of any data about efficacy of intranasal lidocaine to treat neurologic complications in your study and literature review. references 28 and 29 are not related to intranasal route of local anesthetic administration (page 4. paragraph 4. line 11) | I added these references:<br><br>29. Maizels M, Scott B, Cohen W, Chen W. Intranasal lidocaine for treatment of migraine: a randomized, double-blind, controlled trial. JAMA. 1996 Jul 24-31; 276 (4):319-21.<br><br>30. Kanai A, Suzuki A, Kobayashi M, Hoka S. Intranasal lidocaine 8% spray for second-division trigeminal neuralgia, Br J Anaesth, 2006, vol. 97(pg.559-63) |
| 2- You didn't have a control group in this study to compare lidocaine with a placebo like normal saline. so relieving of spasticity cannot be attributed exclusively to lidocaine in this study | Due to the novelty and pilot of this study, it was decided to conduct the study as a single arm and to evaluate the effects of the drug on each patient separately. |
| *3- Intranasal lidocaine as a continuous infusion for about 7 days seems extravagant. What about the head position of your patients during these seven days?* | The position of the patients 'head during the whole study was due to low level of consciousness and mechanical ventilation through endotracheal tube or tracheostomy according to the patients' protocol to prevent ventilator-induced pneumonia 30 degrees above the head that did not interfere with lidocaine infusion |
| *Reviewer 2:* | |
| Method:Have not the information about instruments that has been used for intranasal infusion and the difficulty for patient that infusion of intranasal lidocaine can bring 9 days of continuous intra nasal lidocaine is not safe At least CSF lidocaine must be detected | For intranasal infusion of lidocaine, the usual infusion pump used in the ICU was used and the nasal cannula was used as an interface<br><br>There was no evidence that the drug returned to out of the nose during the study |

| | |
|---|---|
| | Due to the limitations of the study due to the lack of a blood kit level or cerebrospinal fluid lidocaine in the country and the impossibility of obtaining it from abroad, it was decided to use the minimum daily intravenous dose for intranasal treatment, according to available sources. Lidocaine is not mentioned in the pharmacological and cardiac source if administered as a non-toxic.<br><br>dose Tsai PS, Buerkle H, Huang LT, Lee TC, Yang LC, Lee JH. Lidocaine concentrations in plasma and cerebrospinal fluid after systemic bolus administration in humans. Anesth Analg. 1998; 87: 601-604<br><br>Beckett A, Boyes R, Parker B. Determination of lignocaine in blood and urine in human subjects undergoing local analgesic procedures. Anaesthesia. 1965; 20: 294-299.<br><br>Eriksson E, Granberg PO. Studies on the renal excretion of Citanest and Xylocaine. Acta Anaesthesiol Scand Suppl. 1965; 16: 79-85. |
| *Reviewer 3:* | |
| *1-In methods section, patients with moderate and sever spasticity had selected for study, so they must have different Ashworth scale and it affect the amount of effectiveness of drugs. Did you categorized patients from this point of view?* | Because mild spasticity in patients responds relatively well to common medications available for the treatment of spasticity such as baclofen or tizanidine, it was decided to include patients with moderate to severe spasticity in the study |
| *2-Did the patients get any sedative drugs during study and what was it and how much?* | For sedation according to the TBI standard protocol, the same drugs were used for all patients and were evaluated according to the |

| | |
|---|---|
| | RASS criteria |
| *3- Did the patients have any evaluation for nasal mucous membrane (polyp, integrity,)?* | Before starting the study, all patients underwent a history and examination of the head and neck for polyps and other intranasal lesions. |
| *4- How did you evaluate toxicity of lidocaine in patients?* | Clinical signs were monitored for lidocaine toxicity and no cases of seizures, bradycardia, dysrhythmia, or loss of consciousness were observed. |
| *Associate Editor 1:* | |
| *Also, strongly recommend to author for considering below 11 references:* | I added two related references from the ones you mentioned:<br><br>2. Rimaz S, Ashraf A, Marzban S, Haghighi M, Ziabari SM, Biazar G, Rimaz S, Omidi S. Significance of cardiac troponin I elevation in traumatic brain injury patients. Anesthesiology and pain medicine. 2019 Apr;9(2).<br><br>31. Tully J, Jung JW, Patel A, Tukan A, Kandula S, Doan A, Imani F, Varrassi G, Cornett EM, Kaye AD, Viswanath O. Utilization of intravenous lidocaine infusion for the treatment of refractory chronic pain. Anesthesiology and Pain Medicine. 2020 Dec;10(6). |

*Reviewer 1:*
*Dear author*
*1- there is lacking of any data about efficacy of intranasal lidocaine to treat neurologic complications in your study and literature review. references 28 and 29 are not related to intranasal route of local anesthetic administration (page 4. paragraph 4. line 11)*

*2- you didn't have a control group in this study to compare lidocaine with a placebo like normal saline. so relieving of spasticity can not be attributed exclusively to lidocaine in this study*

.
*3- intranasal lidocaine as a continuous infusion for about 7 days seems extravagant.*
*what about the head position of your patients during these seven days?*

*Reviewer 2:*
*Method*
*Have not the information about instruments that has been used for intranasal infusion and the difficulty for patient that*
*infusion of intranasal lidocaine can bring*
*9 days of continuous intra nasal lidocaine is not safe*
*At least CSF lidocaine must be detected*

*Reviewer 3:*
*Dear Author*
*1-In methods section, patients with moderate and sever spasticity had selected for study, so they must have different Ashworth scale and it affect the amount of effectiveness of drugs. Did you categorized patients from this point of view?*
*2-Did the patients get any sedative drugs during study and what was it and how much?*
*3- Did the patients have any evaluation for nasal mucous membrane (polyp, integrity,)?*
*4- How did you evaluate toxicity of lidocaine in patients?*
*Thanks*

## OPEN PEER REVIEW

### Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Associate Editor | **Revision** (1) 18 Jul 2021

Dear EIC,
Fortunately, the author could reply to somewhat about reviewers' and AEs' comments, but they suggest considering all bellow recommendations:
1) Mention IRCT Code.
2) All old added references (before 2010) are not acceptable (following the request of the reviewer), and can be deleted.
2) Follow the AEs' comments including considering and adding ALL suggested references.
Final decision: Minor revision
Regards

**REFEREE**: EIC | **Revision** (1) 18 Jul 2021

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (2)

## Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

**Reviewers' Comments:**

1) Mention IRCT Code.

**Author's response:** This study is not a clinical trial and does not have an IRCT code.

2) The all old added references (before 2010) are not acceptable (following the request of the reviewer), and can be deleted.

**Author's response:** All old references were removed and updated with new related references.

2) Follow the AEs' comments including consider and add ALL suggested references.

**Author's response:** All 10 suggested references were cited.

**OPEN PEER REVIEW**

**Revision (2)**

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

**REFEREE**: Associate Editor | **Revision** (2) 24 Jul 2021

Dear EIC,
I read with interest this revised manuscript. Fortunately, the author could correct the majority of the requested items, and now it is acceptable for publishing.
Final decision: Acceptance
Regards

**REFEREE**: EIC | **Revision** (2) 24 Jul 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.