Comparison of the Effect of 5 and 10% Intranasal Lidocaine Spray on Improving Headache in Patients with Head Trauma Referring to the Emergency Department

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ABSTRACT

Background & Objective: Headache is a common complaint among traumatic patients referring to the emergency department. To improve headache in these patients, an effective, fast-acting, accessible and inexpensive drug without a significant effect on the level of consciousness and vital signs is highly needed.

Materials & Methods: In this double-blind randomized clinical trial (RCT) on patients with head trauma, Group A was given 5% intranasal lidocaine spray while group B was prescribed 10% intranasal lidocaine spray to improve headache. Headache severity was checked based on numeric pain scale (NPS) before drug administration and then at 5, 15, 30 minutes and plus 1 hour post-drug administration, along with patient satisfaction and possible side effects. Finally, the obtained data were analyzed using SPSS 23 software.

Results: According to the data, the maximum reduction in headache occurred 5 minutes after the drug administration. There was a significant difference between the two groups in terms of satisfaction (*P value = 0.022*), where group A had 100% high satisfaction while group B had 87.5% high satisfaction and 12.5% had moderate satisfaction. Of the 80 patients in the study, 3 patients had tearing complications after medication administration, which resolved after 5 minutes, and one case had nasal mucosal anesthesia, which improved after 15 minutes.

Conclusion: According to the results of this study, the use of 5% intranasal lidocaine spray is as effective as 10% intranasal lidocaine spray in relieving headache in traumatic patients and was associated with greater satisfaction and fewer complications.

Keywords: Head trauma - Headache - Intranasal Lidocaine Spray.

Introduction

One of the most important diseases of the nervous system experienced by almost all adults in the world is headache. Primary headaches include migraine, cluster, tension, etc., while secondary headaches include headaches due to head trauma, vascular disorders and homeostasis, headaches related to infection, etc. **(1)**. Head trauma causes primary damage to the brain tissue via direct impact to the head or secondary to hypoxia, edema, inflammation, and oxidative stress. In the direct type, trauma to the head

is due to a physical impact onto the head or pressure on the skull or the movement of the head by a physical stop. However in the indirect type, due to trauma, the contents inside the cranial cavity move because of a force other than direct trauma **(2)**. The mechanism of "acceleration deceleration" and severe shocks are examples of this. Headache is at the forefront of symptoms following concussion or other types of "traumatic brain injury" (TBI). The pathophysiology of the mechanism of symptoms is not fully understood, but it is likely that both anatomical and functional causes are involved **(3)**. In TBI, based on Glasgow Coma Scale GCS (Glasgow GCS Coma Scale), patients are divided into three categories: mild (GCS: 13-15), moderate (GCS: 9-12), and severe (GCS: 3-8) **(4)**.

The most common symptom following mild brain injury (MBI) is headache. According to the Nexus II and New ORLEANS CRITERIA (NOC) criteria **(5)**, MBI patients with should undergo Neuro Imaging. In acute cases, the headache can last from a few hours to a few days after the trauma **(6)**, while in chronic cases, it may last for years and may mimic the form of migraine and tension headaches. According to research, 50% of TBI cases of headache persist along the patient's life **(7)**. Many drugs with various mechanisms are used to treat different types of headaches. Opioids, partial opioid agonists, ergot compounds, antiemetic (combined or alone), serotonin reuptake inhibitors, and NSAIDs are some of the medications used for headaches. Each of these drugs has its own mechanism of action and side effects limiting their use in patients with head trauma **(8-10)**. Lidocaine is an amide derivative of local anesthetic agents. Injectable lidocaine hydrochloride is used as an antiarrhythmic and local anesthetic. Topical lidocaine is available in the market as a local mucosal anesthetic in the form of 10% oral spray, 2% gel and 2% viscous sol. Meanwhile, this drug is made in combination with other drugs in the form of ointment. All forms of the drug are in category B in terms of use in pregnancy **(11)**.

Lidocaine inhibits the initiation and conduction of nerve impulses by reducing the permeability of the nerve membrane to sodium ions. This drug prevents the depolarization of the membrane and thus the propagation of its action potential and conduction **(12)**. The duration of action of lidocaine in the form of spray is 10-15 minutes. Up to 10% of the prescribed drug may be excreted unchanged, but mainly as a metabolite and via the kidney **(13)**. Intranasal lidocaine is widely used due to its ease of administration and the lack of side effects. It exerts its function on the sphenopalatine ganglion, which is located at the posterior end of the middle turbine just below the nasal mucosa at a depth of 1-9 mm. This ganglion, along with the internal carotid artery and the cavernous sinus ganglion, provides parasympathetic denervation of the cerebral blood vessels. This ganglion also releases neuropeptides that can cause headaches. The rapid onset of intranasal lidocaine may indicate interference with nerve blocks or neurons. In this method, the thalamic pathway of pain is inhibited **(14)**.

According to studies worldwide, there are reports of rapid reduction of headache with sphenopalatine ganglion nerve block. The study of intranasal lidocaine studies on the improvement of headache has often been done by examining a specific type of headache. Bakbak. B et al. conducted a case report in which a 22-year-old man with a 5-year history of severe cluster headache with ptosis was treated with nasal lidocaine and sphenopalatine ganglion block to improve his headache and ptosis. Has been **(3)**. Blanda. M et al. performed an RCT study on patients with acute migraine headache but at the end it did not consider the use of 4% intranasal lidocaine to be effective in relieving migraine headache **(12)**. Maizels. M et al in their study considered the use of 4% intranasal lidocaine in comparison with placebo to be effective on improving migraines; and in 6-month follow-up of patients, neither lidocaine dependence nor its associated effects were reported **(12)**. In the study by Mohammad Karimi.N, the effect of 10% nasal lidocaine was compared with placebo where the result showed that intranasal lidocaine is a fast effective method in the treatment of headache with minimal side effects **(15)**. In the Avcu study. N et al. they performed bilateral double-blind RCT on patients with acute migraine and found no significant difference between intranasal lidocaine and normal saline, and a new study was recommended in patients whose headache did not last long **(1).**

The aim of this study was to evaluate and compare the effect of 10% intranasal lidocaine spray and 5% intranasal lidocaine spray on the improvement of headache in trauma patients. This study is unique as it was first designed and prepared under the advice of a pharmacologist for nasal lidocaine spray, and with a rapid effect, and minimal side effects on head trauma based on RCTs.

Materials and Methods

This study has been conducted as a double blind randomized clinical trial (RCT).

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Inclusion criteria:

1. Minor head trauma (GCS 14&15) with headache
2. Normal Brain CT Scan
3. Informed consent

Exclusion criteria:

1. Patients under 18 years of age and over 60 years of age
2. Decreased level of consciousness
3. Instability of vital signs
4. Allergy to lidocaine
5. Symptoms of a skull base fracture (racon eye, battle sign, rhinorrhea, otorrhea)
6. Pregnancy and lactation

7. Bleeding and obstruction of the nose
8. Symptoms of common cold or sinusitis
9. History of seizures
10. Patients who had received medication during the current headache in the last two hours and were recovering.

The patients entered the study randomly (using a table of random numbers) with informed consent. Demographic information, vital signs, drug use during the current headache and headache severity were recorded (by the evaluator using the Numeric Pain Scale (NPS) for actual headache).

After examination of the nasal cavity, if the nostril was open, lidocaine spray(nasal spray) 5% or 10% was prescribed by a trained nurse, as one puff inside each nasal cavity at the maximum depth.

The sprays were placed in an indistinguishable cover and were numbered A and B so that the investigator would not be aware of the type of drug; they were administered to the subjects identified according to the crash table. A separate nasal spray was prescribed for each person.

Evaluation: 5, 15, 30 and 60 minutes after administration, the patient was re-evaluated for headache severity based on NPS, improvement of symptoms and possible side effects such as tears, local burning, nasal discharge, which were monitored and items were recorded in a checklist. Finally, the patient's satisfaction was asked and recorded as low, medium and high.

Note that if the headache did not improve within 10 minutes after administration of lidocaine, intravenous morphine sulfate 0.1 mg / kg (maximum 5 mg) would be prescribed as second (rescue) analgesic.

At the end, reduction of 3 scores and more in patient pain would be considered statistically significant.

Drug Preparation: The solution required for preparing nasal spray lidocaine with concentrations of 5% and 10% was prepared through dissolving 5 g and 10 g of lidocaine hydrochloride in 100 cc of water containing methyl paraben and propyl paraben as a preservative and carboxyl methylcellulose as a consistency agent by a professor of pharmacology. Then, to adjust the pH of the desired solutions within the normal pH range, an acidic or alkaline solution was used at about pH equal.

After collecting the data and registering them in the information checklist, they were inputted into the SPSS23 software. Using the software to compare the effect of pain relief in the two groups, t-test and to compare patient satisfaction in the two groups, chi square analysis were performed.

Results

According to the inclusion and exclusion criteria, 80 patients with head trauma and headache complaints were included in the study. According to a random table, 40 subjects were placed in each of the groups A and B. Group A received 5% lidocaine spray while group B received 10% lidocaine spray. In group A, 29 (72.5%) were male and 11 (27.5%) were female. In group B, 27 (67.5%) were male and 13 (32.5%) were female. In this study, a total of 56 men and 24 women were included in the study. Comparison of frequency distribution of gender distribution with chi-square test revealed that there was no statistically significant difference between groups A and B in terms of gender (P Value> 0.05). The mean age of group A was 35.10±275.900 while in group B it was 34.11±225,200. The minimum age was 18 years and the maximum was 59 years. The mean age of the two groups was not significantly different either based on t-test (P Value> 0.05).

During this research, three subjects in group B were excluded from the study due to the lack of 3 scores in pain intensity up to 10 minutes after drug administration, which we included as missing value in the statistics. Mean headache severity in group A at time 0 (before intervention) was 7.1±42.29, at 5 minutes 4.1 ± 12.68, at 15 minutes3.1±62.53 at 30 minutes, 3.1±62.53 and one hour after administration it was 2.1±85.22. In group B, the mean severity of headache at time 0 (before intervention) was 7.1 ±18.37, at time 5 minutes, 3.1±63.36, at 15 minutes, 3.1±29.53, at 30 minutes, 2.1±29.53, and finally at one hour after drug administration it was 2.1±70.36.

The number of subjects in group A was 40 while being 37 in group B. According to the P-Value obtained from the T test, there was no significant difference between the mean scores of headache severity in the two groups at the desired times, suggesting the same effect of nasal spray lidocaine 5% and 10%. According to the results, the maximum reduction of pain in the study groups was found in the first 5 minutes revealing the rapid effect of lidocaine spray in improving headache. Regarding the comparison of patients' satisfaction from group B, 35 (87.5%) mentioned high satisfaction and 5 (12.5%) mentioned moderate satisfaction. In group A, 100% of patients were highly satisfied.

According to the result obtained from chi-square test (P value = 0.022), the level of satisfaction was significantly different between the two groups and showed greater satisfaction in group A (lidocaine 5%). Out of 80 patients, 3 patients entered the study of tearfulness after administration of the drug, which resolved after 5 minutes, and one case complained of numbness of the nasal mucosa, whose symptom improved after 15 minutes. Fortunately, this study was not associated with any serious complications. According to Table 1 and based on P-value obtained from T test, there was no significant difference between the mean age of patients in groups A and B.

According to Table 2, based on P-value obtained from chi-square test, there was no significant difference between groups A and B in terms of gender.

According to Table 3 and P-value obtained from T test, there was no significant difference between the mean pain scores in the two groups in any of the times 0, 5, 15, 30 minutes and 1 hour. This demonstrate sthe same effect of nasal spray lidocaine 5% and 10% where

according to the data, the maximum reduction in pain was in the first 5 minutes. It is necessary to explain that three people from group B were included in the statistics as missing value regarding 3 pain scores in 10 minutes due to lack of pain reduction.

Based on Table 4 and using chi-square test, P-value = 0.022 has been obtained which shows that the level of satisfaction is significantly different between the two groups. The following values were obtianed: Group A: 100% high satisfaction and group B: 87.5% had high satisfaction and 12.5% (5 people) had moderate satisfaction.

Table 1. Basic information of patients (determination and comparison of mean age in the two study groups)

Desired Variable	Group B	Groups A	P value
Average Age (years)	34.11 ± 2.2	35.10 ± 2.9	0.88

Table 2. Determining and comparing the frequency distribution of gender by study groups

Desired Variable		Groups A	Group B	P value
Gender	Men	29 (42.5 %)	27 (67.5 %)	0.626
	Women	11 (27.5 %)	13 (32.5 %)	

Table 3. Comparison of the mean pain score at the desired times in groups A and B

Variable	Group B	Group A	P value
0min	37 (7.1 ± 18.37)	40 (7.1 ± 42.29)	0.884
5 min	37 (3.1 ± 63.36)	40 (4.1 ± 12.68)	0.15
15 min	37 (3.1 ± 29.53)	40 (3.1 ± 62.53)	0.351
30 min	37 (2.1 ± 86.35)	40 (3.1 ± 20.39)	0.905
1 h	37 (2.1 ± 70.36)	40 (2.1 ± 85.22)	0.152

Table 4. Comparison of patients' satisfaction in groups A and B

Study group	High	Medium	Low	P value
A	100 % (40 people)	0	0	0.022
B	87.5 % (35 people)	12.5% (5 people)	0	

Discussion

Given the high prevalence of accidents that lead to trauma and head injury, and the fact that the most common complaint in patients with mild traumatic brain injury is headache, one of the concerns of the emergency medical team is to reduce headache in these patients. Thus, the healthcare team hope to control headache in a fast and uncomplicated way and without affecting the GCS as well as the vital signs of trauma patients. The use of NSAIDs is associated with limitations due to the possibility of simultaneous injury to the head and other organs in trauma patients. Opioid use to control headaches can be associated with hypotension, apnea, or the possibility of dependence. Meanwhile, opioids are not always available.

Researchers around the world have done similar studies to find a new way to reduce headaches. In the Maizels. M study, intranasal lidocaine was effective on migraine headache, but this effect did not diminish at 6-month follow-up **(12)**. The study of Bakbak. B et al. found that the use of nasal lidocaine and sphenopalatine ganglion block was effective on improving headache and ptosis in cluster patients **(2).** Mohammad Karimi. N's study in 2014, which was performed as an RCT on 90 patients referring to the emergency department with headache complaints, evaluated the effect of 10% nasal lidocaine with placebo on primary and secondary headaches. The 10% nasal lidocaine method was reported as a suitable and effective method on improving primary and secondary headaches. Since then, similar studies have been published with some disagreements about the effect of nasal lidocaine spray, though most studies have been performed on primary headaches such as migraine and cluster headache **(15).**

The present study has been unique as it was performed specifically on headache patients with head trauma. In this study, 80 patients were enrolled via a double-blind RCT method and were divided into two groups A and B based on a random table. Group A received 5% lidocaine spray while group B received 10% lidocaine spray. The results of this study revealed that there was no statistically significant difference between the two groups in terms of mean age and gender. The mean severity of headache in groups A and B at the desired times was not statistically significant either, but the satisfaction of patients in the lidocaine group was 5% (A) higher than in group 10 (B). Meanwhile, the maximum reduction of headache in both groups was achieved in 5 minutes.

Conclusion

Overall, this study found that not only is the use of 5% intranasal lidocaine spray as effective as 10% intranasal spray in improving head trauma patients, but it has also been associated with greater satisfaction and fewer complications. Therefore, 5% intranasal lidocaine spray can be used as a suitable alternative to morphine sulfate and NSAIDs in the hospital emergency room as a safe, fast and effective way to improve headache in trauma patients. As future suggestions, the following can be mentioned:

- Use of lidocaine nasal spray in combination with other drugs to improve headache in trauma patients
- Use of long-acting anesthetics as nasal sprays
- Comparison of the reduction of headache severity in blunt and penetrating head trauma
- Comparison of reduction in headache severity in patients with cerebral hemorrhage and concussion (diffuse axonal injury)
- Study on the shelf life of the effect of intranasal lidocaine spray on headache relief.

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Conflict of Interest

The authors declare no conflict of interest.

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Ethics and RCT code

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Authors' Contributions

Design of the work : AE, NM,Analysis: M N.Interpretation of data for the work: FT, AM,Drafting the work and reviewing it critically for important intellectual content: FT, AM, Final approval of the version to be published: AE, Agreement to be

accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: AE, FT, AM

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