



# **OPEN ACCESS**

**Research Paper** 

# Comparison of different delivery methods of lidocaine and diphenhydramine for anesthesia during suturing of head and facial lacerations

Samad Shams Vahdati<sup>1</sup>, Shima Emami<sup>2</sup>, Alireza Ala<sup>1</sup>, Paria Habibollahi<sup>3</sup>, Sahand Eslami<sup>4</sup>

#### **ABSTRACT**

**Purpose:** Head and facial lacerations often require effective anesthesia for proper repair and healing. This study aims to evaluate the effectiveness of lidocaine and diphenhydramine, administered via injection or margin push, in providing appropriate anesthesia for patients' pain during suturing head and face lacerations.

**Materials and Methods:** This study involved 200 trauma patients with head and face lacerations. All patients had a 15 GCS. Patients were divided into 4 groups of 50. In the first group, lidocaine was injected around the wound, in the second group diphenhydramine was injected around the wound, in the third group lidocaine was pushed through the wound margin, and in the last group, diphenhydramine was pushed. After 5 minutes the pain intensity was evaluated based on the VAS system.

**Results:** Patients had an average age of 34.1 years. Regarding gender distribution, most patients were male (84.5%). The diphenhydramine injection method was the most effective in reducing pain, while the lidocaine push method was the least effective. Regardless of the agent used for anesthesia, the injection method showed better effects than the push method. In the injection methods, the diphenhydramine-injected group experienced lower pain levels than the lidocaine-injected group before and during suturing.

**Conclusion:** Diphenhydramine injection had a superior pain reduction compared to other methods. Considering the lack of substantial difference in the level of anesthesia between lidocaine injection and diphenhydramine injection and diphenhydramine push, diphenhydramine push can be used to prevent pain during the suturing procedure.

Keywords: anesthesia, diphenhydramine, laceration, lidocaine

Emergency and Trauma Care Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>3</sup>Drug Information Center and Pharmacy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran <sup>4</sup>Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

\*Email: sahandeslami1998@gmail.com

https://doi.org/10.5339/jemtac.2025.15

Submitted: 25 September 2024 Accepted: 27 January 2025 Published: 26 March 2025

© 2025 Vahdati, Emami, Ala, Habibollahi, Eslami, licensee HBKU Press. This is an open access article distributed under the terms of the Creative Commons Attribution license CC BY 4.0, which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.



Cite this article as: Vahdati SS, Emami S, Ala A, Habibollahi P, Eslami S. Comparison of different delivery methods of lidocaine and diphenhydramine for anesthesia during suturing of head and facial lacerations. *Journal of Emergency Medicine, Trauma & Acute Care*. 2025(2):15 https://doi.org/10.5339/jemtac.2025.15

#### 1. INTRODUCTION

A lacerated wound that requires sutures is one of the most common problems encountered in the emergency departments. Most of these wounds are on the head and face of the patients. Head and facial lacerations often require effective anesthesia for proper repair and healing due to the high vascularity. Effective local anesthesia is crucial for proper wound repair especially since many patients, particularly children, are afraid of needle injection.

Lidocaine which acts by blocking sodium channels has been the standard approach for providing local anesthesia in these cases. It can also be used for visceral pain, headache, neuralgia, renal colic, and postoperative pains. Despite its effective results in anesthesia, it can be painful, increasing patient discomfort, and reducing compliance. Moreover, it has also been demonstrated that lidocaine can be neurotoxic. Diphenhydramine which is known as an antihistamine has also been used as a local anesthesia due to its ability to block voltage-gated sodium channels. It has also shown positive effects in reducing the acute pain of patients in the emergency department.

These local anesthetics can be administered via injection or pushing through the margin of the laceration to make their impacts. Anesthetic agent push means pushing the substance into the wound margin rapidly through the skin. This method may provide less discomfort for the patient. While all these anesthetic methods can be used in lacerated wound repair, it is important to determine the best technique with the greatest pain reduction and least complications. This study aims to evaluate and compare the effectiveness of lidocaine injection, lidocaine push, diphenhydramine injection, and diphenhydramine push in providing appropriate anesthesia for patients' pain during suturing head and face lacerations.

#### 2. MATERIALS AND METHODS

# 2.1. Study Design

This study is a double-blind intervention study. Two hundred trauma patients who were referred to the emergency department of the hospital between October 2023 and November 2023 with head and face lacerations were included in the study. Inclusion criteria were patients with head and face lacerations and the ones who had a 15 GCS (Glasgow Coma Scale). Patients who did not consent to be included in the study, those with lidocaine and diphenhydramine allergy, and those with GCS under 15 were excluded.

After obtaining informed consent from patients, Excel randomization software divided patients into 4 groups of 50. Numbered drugs and syringes were used, the contents of which were known only to the researcher. In one group, lidocaine was injected around the laceration; in the second group, diphenhydramine was injected around the laceration; in the third group, lidocaine was pushed through the wound margin on the skin and waited to be absorbed; and in the last group, diphenhydramine was pushed. After 5 min, when the wound became numb, the researcher evaluated the pain intensity based on the VAS (Visual Analog Scale) system. The decision to assess pain levels after 5 min was based on the pharmacodynamics of the anesthetic drugs used in the study. According to the properties of lidocaine and diphenhydramine, the onset of their anesthetic effects typically occurs within 5 min of administration, as supported by previous studies.<sup>5,12</sup> Therefore, evaluating pain levels at this time allowed for a reliable measurement of the initial effectiveness of the anesthesia.

For all the studied patients, the required information of the research, including age, gender, wound shape, wound length, type of anesthesia, the amount of anesthesia applied, and the amount of pain endured by the patient based on the VAS system was recorded in the three stages before the anesthesia, during the anesthesia, and at the time of suture.

# 2.2. Statistical Analysis

Patients' data were entered into the SPSS 27.0.0 statistical system. Quantitative data were compared with the ANOVA statistical method, qualitative data were compared based on Mann–Whitney and the post-hoc statistical method was used to investigate the differences between groups. *p*-Value <0.05 was considered to be the significant statistical level.

#### 2.3. Ethical Considerations

The privacy of patients' records was strictly maintained. All the information and data of the patients have been used only in line with the mentioned research and the respect of all members of the research group has been maintained. This investigation has been registered with Iran's Clinical Trials Registration System (IRCT20110814007327N9).

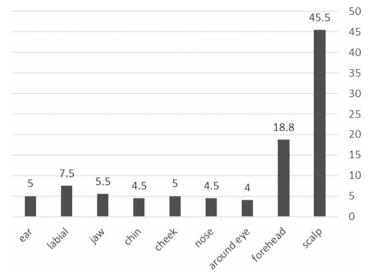


Figure 1. Wound site distribution.

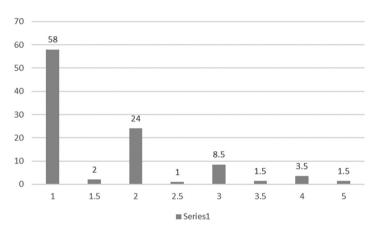


Figure 2. Amount of anesthetic agent used for patients.

#### 3. RESULTS

## 3.1. Demographic and Wound Characteristics of the Study Participants

Two hundred patients were studied among them 169 (84.5%) were male and 31 (15.5%) were female. The age range of studied patients was 18–60 years. The average age was 34.1 ± 12.9783 years, and the median age was 32 years (more information about the profile of each group is available in the supplementary file). The amount of anesthesia used for the patients varied from 1 to 5 cc based on the patient's weight. As shown in Figure 1, most of the patients received 1 cc of anesthesia. In the examination of the site of the lesions, most of the lesions were located on the scalp and forehead while lacerations around the eye were less in number (Figure 2). The wound shape of the studied patients consisted of three linear, dogear, and star models. The lacerations of 165 patients (82%) were linear, 29 patients (15%) had dogear wounds and 6 (3%) had star model wounds.

Based on the results, the effect of age on the patients of each group independently and at the same time among all patients was not significant (p-value = 0.6, F = 0.624). Moreover, it was demonstrated that the effect of gender, injection site, and wound shape was not significant either. However, the effect of wound length and the amount of anesthetic agent injected were significant regardless of the type of anesthesia and the number of sutures (Tables 1 and 2).

The results indicated that the effect of lidocaine injection was statistically significant compared to diphenhydramine injection, but not in comparison to lidocaine and diphenhydramine push. Additionally, diphenhydramine injection demonstrated a statistically significant difference compared

Table 1. Significant fishers.

Variable	Significant	Fisher (F)
Amount of anesthesia injected	<0.001	13.42
Wound length	<0.001	10.756
Number of sutures	<0.001	12.239

Table 2. Evaluating non-significant parameters (age, gender, wound site, wound shape) among different groups with each other based on *p*-value style.

	Lidocaine injection	Diphenhydramine injection	Lidocaine push	Diphenhydramine push
Age				
Lidocaine injection		0.416	0.544	0.806
Diphenhydramine injection	0.416		0.157	0.57
Lidocaine push	0.544	0.157		0.395
Diphenhydramine push	0.806	0.57	0.395	
Gender				
Lidocaine injection		0.584	0.274	0.784
Diphenhydramine injection	0.584		0.584	0.784
Lidocaine push	0.274	0.584		0.411
Diphenhydramine push	0.784	0.784	0.411	
Wound Site				
Lidocaine injection		0.911	0.222	0.335
Diphenhydramine injection	0.911		0.183	0.283
Lidocaine push	0.222	0.183		0.795
Diphenhydramine push	0.335	0.283	0.795	
Wound Shape				
Lidocaine injection		0.253	0.204	0.19
Diphenhydramine injection	0.253		0.899	0.865
Lidocaine push	0.204	0.899		0.966
Diphenhydramine push	0.19	0.865	0.966	

to lidocaine injection and push, but there no significant difference compared to diphenhydramine push. Further analysis revealed that the effect of lidocaine push was not significant compared to its injection, but was statistically significant compared to the diphenhydramine injection and push. Finally, the study found that diphenhydramine push was only significantly different compared to lidocaine push treatment.

# 3.2. Evaluation of Pain Level by VAS Method Before Anesthesia, During the Anesthesia Process, and Suturing Based on p-Value

Statistical data demonstrated no significant difference in pain intensity between the four groups before anesthesia.

Moreover, comparing the pain levels during the anesthesia process demonstrated that there was no significant difference in pain intensity in the lidocaine-injected group and diphenhydramine-injected group, however, comparison of these two groups separately with the lidocaine-pushed and

Table 3: *p*-Value based on post hoc between groups before anesthesia, during anesthesia, and during suturing.

	Lidocaine injection	Diphenhydramine injection	Lidocaine push	Diphenhydramine push
Before anesthesia				
Lidocaine injection		0.843	0.367	0.913
Diphenhydramine injection	0.843		0.271	0.929
Lidocaine push	0.367	0.271		0.312
Diphenhydramine push	0.913	0.929	0.312	
During anesthesia				
Lidocaine injection		0.073	<0.001	<0.001
Diphenhydramine injection	0.073		<0.001	<0.001
Lidocaine push	<0.001	<0.001		0.774
Diphenhydramine push	<0.001	<0.001	0.774	
During suturing				
Lidocaine injection		0.056	<0.001	0.386
Diphenhydramine injection	0.056		<0.001	0.006
Lidocaine push	<0.001	<0.001		<0.001
Diphenhydramine push	0.386	0.006	<0.001	

diphenhydramine-pushed groups revealed statistically significant differences. Additionally, it was shown that pain levels in lidocaine-pushed and diphenhydramine-pushed groups were not significantly different from each other.

Evaluating pain intensity during the suturing procedure revealed that pain level in the lidocaine-injected group was not significantly different from the diphenhydramine-injected and diphenhydramine-pushed groups but was significantly different compared to the lidocaine-pushed group. Pain intensity in the diphenhydramine-injected group was statistically different from the lidocaine-pushed and diphenhydramine-pushed group, but no significant difference compared to the lidocaine-injected groups. There was a statistically significant difference in the pain level of the lidocaine-pushed group compared to the other three groups. Finally, analysis of the last group, as mentioned, revealed that pain intensity in the diphenhydramine-pushed group was significantly different compared to the lidocaine-pushed group and diphenhydramine-injected group (Table 3).

#### 3.3. Comparison of Pain Level in all Four Groups Based on the VAS Method

Comparing the average amount of pain tolerated during the anesthesia, the lidocaine-injected group reported the highest levels of pain, while the diphenhydramine-pushed group experienced the least pain. Moreover, the analysis revealed that the average pain endured during suturing was the greatest in the lidocaine-pushed group, but the lowest was in the diphenhydramine-injected group.

When comparing the two anesthetic agents, the data showed that diphenhydramine push had a better anesthetic effect than lidocaine push. Moreover, diphenhydramine injection revealed a better anesthetic effect compared to lidocaine injection.

Additionally, regardless of the type of anesthetic agent used, the results demonstrated that the injection method was more effective than the push method in anesthesia.

Finally, comparing the patients' pain levels before anesthesia and during the suturing, the results revealed that the amount of pain tolerated by patients in the diphenhydramine-injected group was lower than lidocaine-injected group, and the lidocaine-injected group had lower pain levels than the lidocaine-pushed group.

#### 4. DISCUSSION

The results of the current study suggest that the choice of anesthetic delivery method and agent can significantly impact the effectiveness of pain management during minor surgical procedures.

Diphenhydramine injections may provide more effective and persistent pain relief than lidocaine, however, there was no significant difference in the amount of diphenhydramine and lidocaine anesthesia.

Laceration, or traumatic skin tear, is one of the main reasons patients visit the emergency department.<sup>13</sup> Generally, almost all tears are treated in the same way. First, the lacerations are anesthetized with anesthetic drugs such as lidocaine, and then the wound should be washed with hydrogen peroxide and then examined. Considering no significant damage to the underlying structures, absorbable sutures are used for suturing the muscle and fascia, and nylon suture is used for skin suturing.<sup>1</sup>

As indicated in recent studies, different local injection methods can greatly affect wound anesthesia by paralyzing the fibers of the sensory nerves and blocking the reception and transmission of pain stimuli, especially in facial lacerations. <sup>14</sup> This is most likely because of improvement in tissue penetration and anesthesia distribution. <sup>15</sup> However, these agents may have potential risks and several side effects revealing the necessity of choosing the best agent and method for anesthetic approaches. <sup>16, 17</sup>

Comparing the two anesthetic agents, our results demonstrated that diphenhydramine push had a better anesthetic effect than lidocaine push, and diphenhydramine injection had a better anesthetic effect than lidocaine injection. This finding is consistent with Eells et al.'s study which showed that different anesthesia delivery methods have different effectiveness.<sup>18</sup> Moreover, Siaffa et al. designed a study comparing regional and local anesthesia and revealed that different anesthesia techniques in different parts of the body have adverse effects.<sup>19</sup> These variations may be due to different pharmacogenetic and pharmacokinetic processes involved in these agents.<sup>20</sup>

Supporting these findings, a study comparing the efficacy of 1% diphenhydramine and 1% lidocaine in healthy volunteers showed that while both agents had similar onset times, lidocaine provided a significantly longer duration of anesthesia (81 min versus 42 min for diphenhydramine) and a deeper level of anesthesia after 30 min.<sup>21</sup> However, despite its shorter duration, diphenhydramine did offer effective short-term pain relief and was shown to be comparable to lidocaine in the initial stages of anesthesia. The same study also reported that diphenhydramine caused skin necrosis in one subject, a side effect that was not observed with lidocaine. This highlights the potential risks associated with diphenhydramine that need to be considered when using it for local anesthesia, particularly in sensitive areas such as the face and scalp.

Additionally, a recent randomized controlled trial comparing a novel topical anesthetic putty with traditional lidocaine infiltration for the repair of lacerations found no significant difference in pain scores between the two groups. Both methods provided effective anesthesia, though the topical anesthetic putty was found to be non-inferior to lidocaine infiltration in terms of pain management. The study also reported no substantial differences in wound healing or adverse events, suggesting that the topical putty method could be a feasible alternative to traditional infiltration methods.<sup>22</sup> This is an interesting development, as it offers a less-invasive option for anesthesia, which may be preferable in certain clinical settings.

Analysis of pain levels at different stages of the procedure provides additional insight into the anesthetic agent's effectiveness. Our data revealed that the lidocaine-injected group had higher pain levels during anesthesia while the lidocaine-pushed group tolerated more pain during suturing procedure. Farahmand et al. designed a study and compared the anesthetic efficacy of diphenhydramine and lidocaine in 202 patients with median nerve injury. The results of their study indicated that lidocaine caused lower pain during injection and patients had more satisfaction levels compared to diphenhydramine<sup>23</sup> which was in contrast with our results. Moreover, Xia et al.'s study compared the anesthetic effects of lidocaine hydrochloride, buffered lidocaine, diphenhydramine, and normal saline after intra-dermal injection and showed that buffered lidocaine was significantly less painful than diphenhydramine injection while lidocaine hydrochloride and diphenhydramine had a superior pain than buffered lidocaine. 24 Moreover, Naghipour et al. designed a study showing that diphenhydramine was associated with improved postoperative analgesia and improved quality of recovery after minor otolaryngology surgery.<sup>25</sup> Additionally, Reisli et al.'s study evaluated diphenhydramine and lidocaine anesthetic effects and demonstrated that diphenhydramine is a safe and useful adjunct in minor procedures of short duration and adding diphenhydramine to lidocaine decreases the risk of local toxicity by reducing the lidocaine dose.<sup>26</sup> Furthermore, a study designed by Apiliogullari et al. compared diphenhydramine and lidocaine efficacy for the prevention of pain after propofol injection and showed that the pain level was significantly lower in both

diphenhydramine and lidocaine groups and no significant difference between these two groups in reducing pain level.<sup>27</sup> However, several studies also revealed that lidocaine is a useful agent for anesthesia after different surgical procedures.<sup>28, 29</sup> These studies' results align with our results offering diphenhydramine and lidocaine, especially when delivered by injection method, may provide more effective and sustained pain relief for patients undergoing different minor surgical procedures.

The results obtained from the current study can help healthcare workers especially those in emergency departments optimize pain management for their patients. By choosing the best anesthesia agent, and best delivery technique, and considering the specific phase of the procedure, healthcare workers can achieve the best anesthetic outcomes for their patients as mentioned in the current study.

Our study has several limitations. First of all, it involved only 200 patients, which is a relatively small sample size, all with a 15 GCS. A larger sample size with patients with more severe injuries may provide more statistical power. Moreover, the current study relied on the VAS system for pain measurement which is a subjective measure. More objective scales can be used to evaluate the exact pain rate. Furthermore, in the current study, we just evaluated pain intensity after 5 min. Longer follow-up periods would have provided more precise results about the anesthetic effects of the administered agents. Additionally, the study was conducted in a specific setting (trauma patients) and may not be generalizable to other patient populations where anesthesia is required for wound repair. Another limitation is that we focused solely on two delivery methods—injection and push—of anesthetic agents. Other methods, such as topical anesthesia or regional nerve blocks, were not assessed in this study but should be evaluated in future research to provide a more comprehensive understanding of optimal pain management strategies in laceration repair. Considering these limitations will help to ensure a comprehensive understanding of the study's outcomes.

#### 5. CONCLUSION

Our study revealed that age, gender, and type of wound did not have a significant effect on the level of anesthesia and pain during injection. Also, diphenhydramine injection had a superior pain reduction compared to other methods. In addition, there was no significant difference in the level of anesthesia made by diphenhydramine and lidocaine. Considering the lack of substantial difference in the level of anesthesia between lidocaine injection and diphenhydramine injection and diphenhydramine push, diphenhydramine push can be used to prevent pain during the suturing procedure.

### **REFERENCES**

- [1] Mankowitz SL. Laceration management. *J Emer Med*. 2017;53(3):369–82. https://doi.org/10.1016/j.jemermed.2017.05.026
- [2] Yari A, Fasih P, Bagheri A, Aryanezhad SS, Sani MK. Prevalence and pattern of maxillofacial injuries associated with domestic violence: a retrospective study at a major trauma center. *Dent Traumatol.* 2024;40:61–8. https://doi.org/10.1111/edt.12903
- [3] Peluso H, Vega K, Araya S, et al. Incidence and characterization of facial lacerations in emergency departments in the United States. *Craniomax Trauma Reconstr.* 2024:19433875241257572. https://doi.org/10.1177/19433875241257572
- [4] Sørensen K, Skirbekk H, Kvarstein G, Wøien H. Children's fear of needle injections: a qualitative study of training sessions for children with rheumatic diseases before home administration. *Pediatr Rheumatol.* 2020;18:1–12. https://doi.org/10.1186/s12969-020-0406-6
  - [5] Beecham GB, Nessel TA, Goyal A. Lidocaine. 2019.
- [6] Echeverri DCV, Díaz MG, Pachón PB, Valenzuela ĎL, Carreño SP, Erazo-Muñoz M. Lidocaine infusion for malignant visceral pain: case report. *BMJ Support Palliat Care*. 2023;13(e3):e974–e6. https://doi.org/10.1136/spcare-2023-004350
  [7] Mullins C, Fuccaro M, Pang D, Min L, Andreou A, Lambru G. A single infusion of intravenous
- [7] Mullins C, Fuccaro M, Pang D, Min L, Andreou A, Lambru G. A single infusion of intravenous lidocaine for primary headaches and trigeminal neuralgia: a retrospective analysis. *Front Neurol* 2023;14:1202426. https://doi.org/10.3389/fneur.2023.1202426
- [8] Foo I, Macfarlane A, Srivastava D, et al. The use of intravenous lidocaine for postoperative pain and recovery: international consensus statement on efficacy and safety. *Anaesthesia*. 2021;76(2):238–50. https://doi.org/10.1111/anae.15270
- [9] Motov S, Drapkin J, Butt M, Monfort R, Likourezos A, Marshall J. Pain management of renal colic in the emergency department with intravenous lidocaine. *Amer J Emer Med*. 2018;36(10):1862–4. https://doi.org/10.1016/j.ajem.2018.07.021

- [10] Sicari V, Zabbo CP. Diphenhydramine. 2018.
- [11] Alsager A, Alsuhaibani A, Nafisah SB. Use of diphenhydramine for pain management in the emergency department: a systematic review and meta-analysis. *J Med Law Publ Health*. 2022;2(3):151–8. https://doi.org/10.52609/jmlph.v2i3.55
- [12] Gallo WJ, Ellis III E. Efficacy of diphenhydramine hydrochloride for local anesthesia before oral surgery. *J Amer Dent Assoc.* 1987;115(2):263–6. https://doi.org/10.14219/jada.archive.1987.0227
- [13] Otterness K, Singer AJ. Updates in emergency department laceration management. *Clin Exp Emer Med.* 2019;6(2):97–105. https://doi.org/10.15441/ceem.18.018
- [14] Rekas-Dudziak A, Mecińska-Jundziłł K, Walkowiak K, Witmanowski H. The use of local anaesthetics in dermatology, aesthetic medicine and plastic surgery: review of the literature. *Adv Dermatol Allergol.* 2023;40(1):22–7. https://doi.org/10.5114/ada.2023.125221
  - [15] Mathison M, Pepper T. Local Anesthesia Techniques in Dentistry and Oral Surgery. 2022.
- [16] Park KK, Sharon VR. A review of local anesthetics: minimizing risk and side effects in cutaneous surgery. *Dermatol Surg*. 2017;43(2):173–87. https://doi.org/10.1097/DSS.000000000000887
- [17] Obokhare J. Local and regional blocks for complex facial wound repair. *Facial Plast Surg*. 2021;37(04):446–53. https://doi.org/10.1055/s-0041-1726442
- [18] Eells AC, Howard BE. Analgesic considerations in facial plastic and reconstructive surgery: a review. *J Oral MaxillofacAnesth*. 2024;3. https://doi.org/10.21037/joma-23-33
- [19] Siaffa R, Bordes J, Vatin L, et al. Effectiveness of regional anaesthesia for treatment of facial and hand wounds by emergency physicians: A 9-month prospective study. *Anaesth Crit Care Pain Med.* 2018;37(6):577–81. https://doi.org/10.1016/j.accpm.2018.02.011
- [20] Cregg R, Russo G, Gubbay A, Branford R, Sato H. Pharmacogenetics of analgesic drugs. *Br J Pain*. 2013;7(4):189–208. https://doi.org/10.1177/2049463713507439
- [21] Dire DJ, Hogan DE. Double-blinded comparison of diphenhydramine versus lidocaine as a local anesthetic. *Ann Emer Med.* 1993;22(9):1419–22. https://doi.org/10.1016/s0196-0644(05)81989-4
- [22] Jenkins MG, Murphy DJ, Little C, McDonald J, McCarron PA. A non-inferiority randomized controlled trial comparing the clinical effectiveness of anesthesia obtained by application of a novel topical anesthetic putty with the infiltration of lidocaine for the treatment of lacerations in the emergency department. *Ann Emer Med.* 2014;63(6):704–10. https://doi.org/10.1016/j. annemergmed.2013.12.012
- [23] Farahmand S, Yazdanbakhsh F, Bagheri-Hariri S, Aliniagerdroudbari E, Abdollahi A, Babaniamansour S. Comparing two different concentrations of diphenhydramine versus lidocaine for median nerve block in emergency department: a double-blind randomized clinical trial. *Euras J Emer Med.* 2021;20(3). https://doi.org/10.4274/eajem.galenos.2021.03779
- [24] Xia Y, Chen E, Tibbits DL, Reilley TE, McSweeney TD. Comparison of effects of lidocaine hydrochloride, buffered lidocaine, diphenhydramine, and normal saline after intradermal injection. *J Clin Anesth*. 2002;14(5):339–43. https://doi.org/10.1016/s0952-8180(02)00369-0
- [25] Naghipour B, Gargari RM. Effect of pretreatment with diphenhydramine on recovery complications in minor ear, nose and throat surgeries: a randomized clinical trial. *Bahrain Med Bull.* 2023;45(1).
- [26] Reisli R, Celik J, Tuncer S, et al. The effects of adding diphenhydramine hydrochloride to lidocaine in intravenous regional anaesthesia. *Pain Clin.* 2003;15(4):441–6. https://doi.org/10.1163/156856903770196836
- [27] Apiliogullari S, Keles B, Apiliogullari B, Balasar M, Yilmaz H, Duman A. Comparison of diphenhydramine and lidocaine for prevention of pain after injection of propofol: a double-blind, placebo-controlled, randomized study. *Eur J Anaesthesiol*. 2007;24(3):235–8. https://doi.org/10.1017/S026502150600202X
- [28] Weibel S, Jokinen J, Pace N, et al. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *Br J Anaesth*. 2016;116(6):770–83. https://doi.org/10.1093/bja/aew101
- [29] Licina A, Silvers A. Perioperative intravenous lidocaine infusion for postoperative analgesia in patients undergoing surgery of the spine: systematic review and meta-analysis. *Pain Med.* 2022;23(1):45–56. https://doi.org/10.1093/pm/pnab210