

Original Research

Pain intensity after oral mucosal puncture using lidocaine-prilocaine gel and benzocaine: A randomized split-mouth trial



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ARTICLE INFO

Article history:

Received 8 June 2026

Accepted 20 September 2026

Available online 26 October 2026

Keywords:

Anesthesia, local

Benzocaine

Lidocaine, prilocaine drug
combination

ABSTRACT

Objectives: To compare pain intensity associated with oral mucosal puncture after the application of two topical anesthetics in adult patients: a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine gel and a 20% benzocaine gel.

Methods: A randomized, blind, split-mouth clinical trial was conducted in 100 patients aged 25–65 years. Each topical anesthetic was applied to the right or left side, as determined by a computer-generated block randomization sequence with a 1:1 allocation ratio, and the contralateral side automatically received the alternative anesthetic. Bilateral punctures of the anterior maxillary vestibular mucosa were performed. Pain intensity at the puncture site where each topical anesthetic was applied was immediately assessed using a 100-millimeter visual analog scale. Mean paired pain scores were compared using the paired Student's t-test.

Results: Mean pain intensity was lower with the lidocaine-prilocaine gel (9.41 ± 13.14 mm) than with 20% benzocaine gel (14.37 ± 12.90 mm), yielding a mean paired difference of 4.96 mm (95% confidence interval: 2.85 to 7.07; $p < 0.001$). No local or systemic adverse reactions were reported.

Conclusions: The lidocaine-prilocaine gel demonstrated a statistically significant reduction in pain intensity during oral mucosal puncture compared to 20% benzocaine. Although the absolute reduction was modest, it may be clinically relevant for minimizing initial puncture discomfort. (Rev Port Estomatol Med Dent Cir Maxilofac. 2026;67(x):1-8)

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<http://doi.org/10.24873/j.rpemd.2026.12.1591>

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Introduction

Pain control during needle insertion remains a central concern in oral procedures and plays a key role in treatment acceptance. Fear of injections represents one of the main barriers to seeking oral care and is associated with increased anxiety, reduced cooperation, and avoidance of treatment.¹ Despite advances in anesthetic techniques, the use of needles continues to generate discomfort and emotional stress.^{1,2} Pain perception during oral mucosal puncture is a multidimensional experience influenced by several factors, including the patient's baseline anxiety levels, the needle's gauge and bevel design, the anatomical characteristics and keratinization of the mucosal tissue, and the pharmacological properties of the topical anesthetic used.^{3,4}

Topical anesthesia has been introduced as a strategy to reduce pain at the site of puncture. These agents act by blocking nerve conduction through the inhibition of sodium ion permeability across the neuronal membrane, thus preventing the initiation of action potentials.^{5,6} Among the available options, 20% benzocaine is widely used due to its rapid onset and ease of application. However, its analgesic performance may be influenced by limited tissue penetration and short duration of action.^{7,8}

The eutectic mixture of local anesthetics, composed of lidocaine 2.5% and prilocaine 2.5%, has been proposed as an alternative with improved pharmacological properties. Its eutectic formulation lowers the melting point and increases the proportion of the active base form, which enhances tissue diffusion and anesthetic depth.^{9,10} This formulation allows greater penetration through mucosal surfaces and may be associated with lower pain perception during oral procedures.^{11,12}

Pain intensity during oral mucosal puncture is commonly assessed using the Visual Analog Scale (VAS), a validated instrument widely employed in clinical pain research because of its simplicity, reproducibility, and high sensitivity for detecting small differences in pain perception. The VAS provides a continuous measure of pain intensity, whereas numerical and verbal rating scales use discrete response options.¹³

Previous clinical studies comparing eutectic lidocaine-prilocaine formulations with benzocaine have reported inconsistent results regarding pain reduction during oral mucosal puncture.¹⁴ Despite the widespread use of topical anesthetics before oral mucosal puncture, evidence comparing the analgesic effectiveness of 20% benzocaine and the eutectic mixture of 2.5% lidocaine and 2.5% prilocaine remains limited and inconsistent, particularly in adult dental patients.

This study aimed to compare pain intensity during oral mucosal puncture after using a 20% benzocaine gel versus a 2.5% lidocaine and 2.5% prilocaine thermoreversible gel in adult dental patients using a split-mouth design. The study hypothesis was that applying a 2.5% lidocaine and 2.5% prilocaine thermoreversible gel before mucosal puncture would result in a statistically significant and clinically perceptible reduction in pain intensity compared with a 20% benzocaine gel.

Material and methods

A randomized, blind, split-mouth clinical trial was conducted between December 2006 and July 2007 at the Moche Stomatology Clinic, Faculty of Stomatology, National University of Trujillo, Peru. All study protocols, product formulations, and ethical approvals strictly correspond to the data collection period. This study was originally designed and executed as part of an academic thesis project. The study strictly adhered to the ethical principles of the Declaration of Helsinki and was approved by the local Research Ethics Committee (Approval No. P.I.B. EST.-009). This study is reported in accordance with the CONSORT 2025 statement, supplemented by the methodological recommendations for split-mouth trials.

A total of 120 patients were initially assessed for eligibility. Inclusion criteria were patients classified as ASA I (apparent good general health defined as having no systemic diseases, normal vital signs, and no chronic medications reported during the standardized medical history interview). Exclusion criteria included acute pulpal or periradicular pain; limited mouth opening (<30 mm), which could compromise adequate access, visibility, and standardized needle angulation for the anterior maxillary vestibular puncture; known allergy to local anesthetics; and self-reported chronic alcoholism, due to its potential to alter central pain perception, induce hepatic enzyme changes affecting the metabolism of amide anesthetics, and compromise patient cooperation.¹⁵ Additionally, patients who had taken analgesics within the previous 24 hours and those with contraindications to epinephrine were excluded. Although the topical agents did not contain epinephrine, all participants subsequently required conventional infiltrative local anesthesia with epinephrine (2% lidocaine with 1:100,000 epinephrine) as part of their definitive dental treatment during the same appointment, making this a necessary safety criterion for the overall clinical protocol.

Eligibility assessment excluded 20 patients: 8 due to acute pulpal pain, 5 due to limited mouth opening, 4 due to self-reported chronic alcoholism, and 3 due to contraindications to epinephrine. Consequently, 100 consecutive patients were enrolled and analyzed, as detailed in the participant enrollment and progression diagram (Figure 1). All 100 participants completed the split-mouth protocol without missing data or dropouts. The study population consisted of patients aged 25 to 65 years who required bilateral puncture of the anterior maxillary vestibular mucosa for non-surgical dental procedures.

To control for interindividual variability, a split-mouth design was employed, with the patient as the unit of analysis; each participant contributed two correlated VAS measurements. The computer-generated block randomization sequence (permuted blocks, 1:1 allocation ratio) was produced by the primary investigator using Microsoft Excel 2003 prior to data collection. Based on this sequence, allocations were prepared in advance and concealed in sequentially numbered, opaque, sealed envelopes. The primary investigator, an experienced oral and maxillofacial surgeon, assessed patient eligibility and enrollment without access to the allocation sequence. After obtaining informed consent and confirming eligibility, the primary investigator opened the next sequen-

CONSORT flow diagram for a split-mouth randomized clinical trial

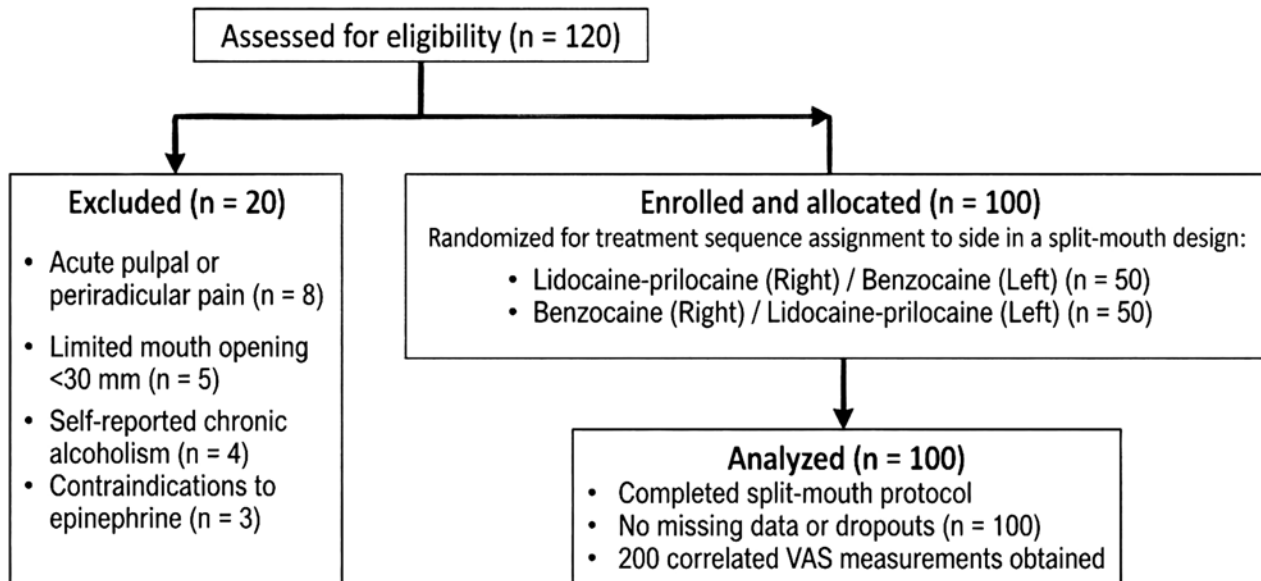


Figure 1. Participant enrollment, randomization, and progression throughout the split-mouth clinical trial. The diagram details the screening process, reasons for exclusion, randomized allocation of the topical anesthetics to the right or left maxillary vestibular mucosa, and the final analyzed sample. All 100 enrolled participants completed the protocol without dropouts, providing 200 correlated visual analog scale (VAS) measurements for the paired analysis.

tially numbered envelope to reveal the treatment allocation for that specific patient.

Trained fourth-year dental students, who did not participate in outcome assessment, implemented the assigned treatment to the right and left sides. Both sides were treated during the same visit. The unblinded students prepared both topical agents out of the sight of the patient and the primary investigator, ensuring the allocation remained concealed from both. The prepared devices were concealed in identical opaque pouches and handled only by the unblinded student. Moreover, during application, the patient's eyes were covered with a sterile surgical drape, the primary investigator was outside the operatory, and the student avoided any verbal or audible information that could reveal the allocated product.

The topical anesthetic agents used were: a 20% benzocaine topical gel (Topical, Dentsply, USA); a 2.5% lidocaine and 2.5% prilocaine thermoreversible periodontal gel (Oraqix, Dentsply International, York, PA, USA) that transitions from a liquid to a gel at body temperature, enhancing mucosal retention. A single-dose 0.17 g cartridge of the lidocaine-prilocaine gel (4.25 mg of each anesthetic) was applied over a standardized mucosal area of approximately 1 cm² in the anterior maxillary vestibular fold using the manufacturer's periodontal dispensing gun, actuated slowly with constant pressure without pressing against the mucosa. An equivalent mass (approximately 0.17 g) of the 20% benzocaine topical gel was applied over a similar 1-cm² area using a sterile cotton swab. Because data were collected between 2006 and 2007, the specific batch/lot

numbers and expiration dates for these commercial products are no longer retrievable from the original institutional records. Therefore, these specific details cannot be reported.

For both agents, the vestibular mucosa was isolated with cotton rolls and dried with gauze for 10 seconds. The agent was applied and left to act for exactly 2 minutes, during which the patients kept their mouths slightly open. Then, the student gently removed any excess residual gel with a dry cotton roll, and patients did not rinse their mouths to avoid displacing the agent. A minimum washout interval of 15 minutes was allowed between the first and second punctures. After the procedure, the student returned the delivery device to the opaque pouch and left the operatory.

Afterward, the primary investigator re-entered the operatory to perform the mucosal punctures, explain the VAS, and record the outcomes while remaining blinded to treatment allocation. This procedure separated the unblinded application phase from the blinded outcome-assessment phase; therefore, neither the patient nor the investigator had visual access to the product or delivery system. The order of the two punctures was independently determined using a secondary random sequence, generated in Microsoft Excel 2003 by the same students immediately before the procedure. This ensured the puncture sequence was not systematically linked to treatment allocation, thereby mitigating potential order effects such as expectation, habituation, sensitization, or reduced uncertainty.

Mucosal punctures were limited to the initial penetration of the mucosa in the anterior maxillary vestibular fold (apical

to the central and lateral incisors and canines). A standardized 30-G × 21-mm needle (BD, Becton Dickinson, Franklin Lakes, NJ, USA) attached to an aspirating dental syringe was used. The needle was inserted to a depth of approximately 2 to 3 mm and at an angle of 45 degrees relative to the mucosal surface. The VAS was recorded immediately after the initial needle penetration and prior to the injection of any local anesthetic solution. The injection of the 2% lidocaine with epinephrine solution (approx. 1.5 mL per side, at a controlled rate of 1 mL/min) was performed only after the VAS was recorded. Pain intensity was assessed using a 100-mm VAS, where 0 indicated “no pain” and 100 represented the “worst pain imaginable.” The explanatory variables included the type of topical anesthetic administered, age group (25–45 years or 46–65 years), sex (male or female), and puncture side (right or left). Participants were monitored throughout the procedure for local or systemic adverse events.

Continuous variables were summarized using means and standard deviations. The normality of intraindividual differences was assessed using the Shapiro-Wilk test. The primary comparison was performed using the paired Student's t-test. A sensitivity analysis using the Wilcoxon signed-rank test was also conducted to account for potential skewness.

The sample size of 100 patients was based on a convenience sample of consecutive patients during the data collection period.; however, post-hoc power analysis indicated that this sample provided >99% power to detect a mean paired difference of 5 mm (assuming a standard deviation of differences of 12 mm, $\alpha = 0.05$). Statistical significance was set at $p < 0.05$. Analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Figure 1 details participant enrollment and progression throughout the trial. A total of 100 consecutive patients were enrolled and analyzed, completing the split-mouth protocol without missing data or dropouts. Table 1 summarizes the baseline demographic and clinical characteristics of the study population.

The 100 participants provided 200 correlated VAS measurements (one per side). Mean pain intensity during oral mucosal puncture was significantly lower with the lidocaine-prilocaine gel compared to 20% benzocaine (Table 2). The Shapiro-Wilk test did not detect a departure from normality in the intraindividual differences in pain scores ($p = 0.12$). A statistically significant mean paired difference fa-

Table 1. Baseline demographic and clinical characteristics of the study population: distribution of age, sex, and clinical indication in the enrolled sample.

Characteristic	Total (n = 100)
Age, years	
Range	25 – 65
25 – 45 years, n (%)	69 (69.0%)
46 – 65 years, n (%)	31 (31.0%)
Sex, n (%)	
Male	32 (32.0%)
Female	68 (68.0%)
Clinical indication	
Bilateral anterior maxillary vestibular puncture for non-surgical dental procedures	100 (100.0%)

The split-mouth design inherently controlled for interindividual variability in baseline characteristics. Continuous age data (mean ± SD) were not systematically retained in the final aggregated dataset of this historical thesis project. SD – standard deviation.

vored the lidocaine-prilocaine gel (paired Student's t-test: $t = 5.74$, $p < 0.001$). A sensitivity analysis using the non-parametric Wilcoxon signed-rank test confirmed these findings ($p < 0.001$).

When analyzed by age group, the lidocaine-prilocaine gel achieved lower mean pain intensity values than the 20% benzocaine in both age categories. A formal treatment-by-age interaction test indicated that the treatment effect did not differ significantly between the two age groups ($p > 0.05$), and the differences remained statistically significant within each age subgroup (Table 3).

Both male and female participants showed lower pain intensity values with the lidocaine-prilocaine gel. The treatment effect did not differ significantly between sexes ($p > 0.05$), and the differences remained statistically significant within each sex subgroup (Table 4).

When accounting for puncture side, patients reported lower pain intensity values on both sides with the lidocaine-prilocaine gel. The treatment effect did not differ significantly between the right and left sides ($p > 0.05$), and the differences in pain intensity between topical anesthetics remained statistically significant within each side (Table 5).

No local or systemic adverse reactions (e.g., mucosal erythema, edema, allergic reactions, or neurological symptoms) were observed during the 30-minute postoperative monitoring period, which included direct visual inspection and structured patient questioning.

Table 2. Pain intensity during oral mucosal puncture according to the topical anesthetic administered: primary analysis comparing the eutectic lidocaine-prilocaine gel and the 20% benzocaine gel.

Outcome variable	Total (n=100)				
	Benzocaine 20% (mean ± SD, mm)	Lidocaine 2.5%–prilocaine 2.5% (mean ± SD, mm)	Mean paired difference*, mm (95% CI)	t-value	p-value
Pain intensity (VAS)	14.37 ± 12.90	9.41 ± 13.14	4.96 (2.85 to 7.07)	5.74	< 0.001

SD – standard deviation; CI – confidence interval; VAS – visual analog scale. *

The mean paired difference represents the reduction in pain score when using lidocaine-prilocaine compared to benzocaine. The Shapiro-Wilk test did not detect a departure from normality in intraindividual differences ($p = 0.12$).

Table 3. Pain intensity during oral mucosal puncture according to age group.

Age group (n)	Total (n=100)			
	Benzocaine 20% (mean $\pm$ SD, mm)	Lidocaine-prilocaine (mean $\pm$ SD, mm)	Mean paired difference (mm)	p-value (within subgroup)
25–45 years (n = 69)	14.42 $\pm$ 14.19	9.06 $\pm$ 14.36	5.36	< 0.001
46–65 years (n = 31)	14.26 $\pm$ 9.61	10.19 $\pm$ 10.05	4.07	< 0.001

SD = standard deviation.

The treatment-by-age interaction test indicated that the treatment effect did not differ significantly between the two age groups ($p > 0.05$).

Table 4. Pain intensity during oral mucosal puncture according to sex.

Sex (total patients, n)	Total (n=100)			
	Benzocaine 20% (mean $\pm$ SD, mm)	Lidocaine-Prilocaine (mean $\pm$ SD, mm)	Mean paired difference (mm)	p-value (within subgroup)
Male (n = 32)	13.09 $\pm$ 16.22	9.44 $\pm$ 14.79	3.65	0.009
Female (n = 68)	14.97 $\pm$ 11.09	9.40 $\pm$ 12.40	5.57	< 0.001

SD = standard deviation.

The treatment-by-sex interaction test indicated that the treatment effect did not differ significantly between male and female participants ($p > 0.05$).

Table 5. Pain intensity during oral mucosal puncture according to puncture side.

Puncture side (total observations, n)	Benzocaine 20% (mean $\pm$ SD, mm)*	Lidocaine-prilocaine (mean $\pm$ SD, mm)*	Mean difference (mm)	p-value (within subgroup)	p-value (interaction test)†
Right (n = 100)	13.82 $\pm$ 11.22	7.35 $\pm$ 9.71	6.47	< 0.001	> 0.05
Left (n = 100)	14.90 $\pm$ 14.42	11.39 $\pm$ 15.59	3.51	0.004	

SD = standard deviation.

* Due to the block-randomized split-mouth design, within each side (n=100 total observations), exactly 50 participants received benzocaine and 50 received lidocaine-prilocaine.

† The treatment-by-side interaction test indicated that the treatment effect did not differ significantly between the right and left sides.

Discussion

Topical anesthetics are widely used to reduce discomfort during oral mucosal puncture and local anesthetic administration in dental practice. Fear of dental anesthesia remains a common source of anxiety and may contribute to avoidance of dental treatment, particularly among individuals with previous painful experiences.¹⁵ Therefore, understanding factors associated with pain perception during puncture procedures may contribute to improving patient comfort and acceptance of dental care.

The analgesic properties of lidocaine-prilocaine gel are related to the eutectic combination of lidocaine and prilocaine, which facilitates diffusion through the oral mucosa and enhances penetration into superficial tissues.^{16,17} This characteristic has supported its use in dermatologic procedures, venous punctures, pediatric interventions, and periodontal therapy. In addition, topical anesthetics appear to influence pain thresholds more than tactile sensitivity, which may explain the lower pain intensity values observed after application of the eutectic lidocaine-prilocaine formulation.¹⁸ The physicochemical properties of the lidocaine-prilocaine periodontal gel are specifically designed for intraoral use. Unlike the eutectic cream formulation (EMLA, Aspen Pharmacare), which was originally

designed for dermal use and has been reported to have limitations related to low viscosity and poor mucosal retention in wet environments, Oraqix is a thermoreversible gel that solidifies at body temperature, enhancing its retention in the periodontal pocket and mucosal surfaces.¹⁷ This characteristic may contribute to its improved anesthetic performance during oral mucosal puncture procedures.

Previous studies evaluating topical anesthetics during intraoral procedures have reported heterogeneous findings. Several authors described lower pain levels during needle penetration and anesthetic administration following application of eutectic lidocaine-prilocaine formulations, whereas others found little or no difference compared with benzocaine or placebo.^{7,19} Such variability may reflect differences in anesthetic formulations, application protocols, puncture techniques, anatomical sites, and pain assessment methods.

In the present study, patients reported lower pain intensity values with lidocaine-prilocaine gel than with 20% benzocaine during oral mucosal puncture. Similar findings have been reported in studies evaluating pain perception during periodontal instrumentation and palatal puncture procedures.^{12,14} These observations may be related to the physicochemical characteristics of the lidocaine-prilocaine formulation, which favor mucosal diffusion and topical anesthetic action.

Pain perception during dental anesthesia is influenced not only by clinical factors but also by psychological variables. Anxiety, fear, and anticipation of pain have been associated with increased discomfort during oral puncture procedures, whereas placebo effects may modify pain responses.¹ Pain intensity was assessed using a 100-mm VAS, which provides a continuous measure of pain intensity. Although pain perception is influenced by psychological factors such as anxiety and fear, the split-mouth design minimized interindividual variability by allowing each participant to serve as their own control during the same clinical visit.¹³ Even though anxiety levels were not evaluated in this study, they may have contributed to individual variability in pain perception.

Methodological differences among studies may partially explain variations in reported findings. Previous investigations have evaluated different clinical procedures, anatomical locations, and pain assessment approaches. In the present study, pain intensity was assessed immediately after oral mucosal puncture using a VAS under routine clinical conditions. Moreover, a 30 G × 21-mm needle was used because its smaller external diameter reduces tissue displacement during superficial mucosal penetration, potentially decreasing insertion pain. Because puncture depth was limited to 2–3 mm, the greater flexibility of the 30 G needle did not compromise the procedure. To further reduce procedural variability, the same experienced oral and maxillofacial surgeon performed all punctures using a standardized technique, ensuring consistent angle, depth, speed, and bevel orientation throughout the study. The use of standardized 30 G needles and a single experienced operator may have contributed to procedural consistency throughout the study.¹⁹

No local or systemic adverse reactions were recorded during the study period. Previous reports show that topical anesthetics are generally safe when applied over limited mucosal surfaces, at recommended concentrations, and for short periods of time. However, excessive dosing or prolonged exposure may increase the risk of adverse events, particularly among pediatric patients and individuals with systemic conditions.^{10,20}

The observed relative improvement is clinically meaningful in routine dental practice, where patient comfort directly impacts treatment acceptance. While the mean difference of 4.96 mm on the VAS is statistically significant, it represents a modest absolute reduction. In the context of superficial mucosal puncture, where baseline pain scores are relatively low (mean ~10–14 mm), a 5-mm reduction represents a substantial relative decrease (approximately 35%). Furthermore, even minor reductions in the initial sharp pain of needle insertion may theoretically help mitigate anticipatory anxiety and improve the patient's psychological readiness for the subsequent dental procedure, although this hypothesis requires further investigation since anxiety was not directly measured in this study.

Several limitations should be considered when interpreting these findings. Pain intensity was assessed using a subjective VAS and may have been influenced by emotional and psychological factors. Although the VAS is highly sensitive and appropriate for detecting subtle differences in procedural pain, it captures only the unidimensional pain intensity; it does not address its sensory, affective, or cognitive dimensions. Future studies could benefit from incorporating multidimensional

instruments such as the McGill Pain Questionnaire (MPQ) or the Short-Form McGill Pain Questionnaire (SF-MPQ) to provide a more comprehensive assessment of the pain experience. Moreover, anxiety levels were not measured, preventing evaluation of their potential association with pain perception. The split-mouth design reduced confounding by stable between-person characteristics, but changes in anticipatory anxiety between punctures could not be assessed. Future studies should incorporate such instruments to better disentangle the influence of psychological variables on pain perception.

The study was conducted at a single clinical center, which may limit the generalizability of the findings. Also, the sample size of 100 patients was based on convenience and the duration of the data collection period. Although the study achieved sufficient statistical power to detect the observed overall difference, the lack of an a priori power calculation for the subgroup analyses (age, sex, and puncture side) is a limitation, and future studies should be powered specifically for these subgroups.

Other limitations include that the study's primary outcome was strictly limited to pain intensity during the initial mucosal puncture and did not evaluate the duration of the analgesic effect of the topical agents beyond this initial puncture. Future research should assess how long these topical anesthetics remain effective for subsequent intraoral procedures, such as the injection of local anesthetic solutions or minor surgical interventions.

Although the clinical data were collected between 2006 and 2007, the findings remain clinically relevant because the fundamental pharmacological properties of the topical anesthetics evaluated, the standard 30-G needle protocols, and the clinical indications for anterior maxillary vestibular punctures have remained essentially unchanged. Nevertheless, potential temporal shifts in patient demographics, dental materials, or clinical practices should be acknowledged as a contextual limitation when extrapolating these findings to current practice. Future studies incorporating psychological variables, multi-center settings, and larger samples may provide additional evidence regarding factors associated with pain perception during oral mucosal puncture.

Lastly, although visual blinding was maintained by concealing the products and delivery systems and separating application from outcome assessment, lidocaine-prilocaine and 20% benzocaine differed in appearance, viscosity, thermoreversible behavior, delivery system, and potentially taste or smell. Because an unblinded student performed the application while the patient's eyes were covered and the blinded investigator was outside the operatory, these measures were intended to reduce the risk of unblinding. However, because the agents differed in physical properties and application method, residual tactile or other sensory cues during application could not be completely excluded.

Conclusions

The lidocaine-prilocaine gel demonstrated a statistically significant, albeit modest in absolute terms, reduction in pain intensity during oral mucosal puncture compared to 20% benzocaine. This relative reduction may be clinically relevant for minimizing initial puncture discomfort in adult patients.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

CREDiT AUTHORSHIP CONTRIBUTION STATEMENT

Manuel Fernando Guillén-Galarza: Investigation; Project administration; Writing – original draft; Writing – review & editing. **Hector Martin Vargas Cornejo:** Conceptualization; Investigation; Writing – original draft; Writing – review & editing. **Cesar Augusto Jiménez-Prado:** Visualization; Writing – review & editing.

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REFERENCES

- Aksoy F, Tosun S. Effects of different topical anesthetics on pain from needle insertion and injection, and the influence of anxiety in patients awaiting endodontic treatment. *Restor Dent Endod.* 2022;47(3):e25.
- Belevcikli M, Altan H, Demir O. Effect of the new needle-free injection system on pain perception and dental anxiety during anesthesia: Randomized controlled split-mouth study. *J Dent Anesth Pain Med.* 2023;23(1):1-8.
- Nadir U, Scaburi IR, Cerci FB, Jeha GM, Tolkachjov SN. How to minimize pain with local anesthesia and improve patient experiences: A review. *An Bras Dermatol.* 2026;101:501366.
- Kiriishi K, Ayuse T, Tanoue N, Komeyama K, Magata N, Takahashi H, et al. Microneedle patch-enhanced palatal anesthesia with benzocaine: Efficacy and safety in a randomized double-blind crossover trial. *Drug Discov Ther.* 2026;20(1):63-70.
- Karnina R, Arif SK, Hatta M, Bukhari A. Molecular mechanisms of lidocaine. *Ann Med Surg (Lond).* 2021;69:102733.
- Körner J, Albani S, Sudha Bhagavath Eswaran V, Roehl AB, Rossetti G, Lampert A. Sodium channels and local anesthetics-old friends with new perspectives. *Front Pharmacol.* 2022;13:837088.
- Miroshnychenko A, Ibrahim S, Azab M, Roldan Y, Diaz Martinez JP, Tamilselvan D, et al. Injectable and topical local anesthetics for acute dental pain: 2 systematic reviews. *J Am Dent Assoc.* 2023;154(1):53-64.e14.
- Karkoutly M, Alatassi L, Azrak L, Bshara N. Efficacy of topical anesthetics of lidocaine, benzocaine, and EMLA in reducing pain during inferior alveolar nerve block in schoolchildren: A randomized controlled trial. *BDJ Open.* 2024;10(1):87.
- Kulkarni MM, Patil AT, Sinha S. A comparative study of 10% lidocaine spray versus eutectic mixture of 2.5% lidocaine and 2.5% prilocaine (EMLA) to attenuate pain of peripheral venous cannulation in children: A prospective randomized control trial at a tertiary care centre. *Indian J Anaesth.* 2023;67(2):167-72.
- Zaki HA, Elarref MA, Iftikhar H, Al-Marri NDR, Masood M, Fayed M, et al. Efficacy of Emla (Eutectic Mixture of Local Anaesthetics) and Let (Lidocaine, Epinephrine, Tetracaine) for topical use in wound management for children: A systematic review and meta-analysis. *Cureus.* 2022;14(11):e31447.
- Lee H, Min HS, Jang M, Kang G, Gong S, Lee C, et al. Lidocaine-loaded dissolving microneedle for safe local anesthesia on oral mucosa for dental procedure. *Expert Opin Drug Deliv.* 2023;20(6):851-61.
- Chugh A, Singh S, Khatana S, Gaur S, Patnana AK, Chugh V, et al. The clinical efficacy of EMLA as a topical anesthetic agent instead of palatal injection during maxillary dental extractions: A randomized controlled trial. *J Maxillofac Oral Surg.* 2023;22(1):172-7.
- Sirintawat N, Sawang K, Chaiyasamut T, Wongsirichat N. Pain measurement in oral and maxillofacial surgery. *J Dent Anesth Pain Med.* 2017;17(4):253-63.
- Maia FPA, Araujo Lemos CA, de Souza Andrade ES, de Moraes SLD, do Egito Vasconcelos BC, Pellizzer EP. Does the use of topical anesthetics reduce the perception of pain during needle puncture and anesthetic infiltration? Systematic review and meta-analysis of randomized controlled trials. *Int J Oral Maxillofac Surg.* 2022;51(3):412-25.
- Navarro-Rodriguez JM, Suarez-Serrano C, Martin-Valero R, Marcen-Roman Y, de-la-Casa-Almeida M. Effectiveness of topical anesthetics in pain management for dermal injuries: A systematic review. *J Clin Med.* 2021;10(11):2522.
- Al-Melh MA, Andersson L. Comparison of topical anesthetics (EMLA/Oraqix vs. benzocaine) on pain experienced during palatal needle injection. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007;103(5):e16-20.
- Chaudhry K, Khatana S, Kaur A, Kumar S, Gigi PG, Aparna G. 2.5% EMLA versus 2% lignocaine with adrenaline injection in small oral mucosal biopsies: A parallel group randomized controlled trial. *J Maxillofac Oral Surg.* 2021;20(4):619-27.
- de Freitas GC, Pozzobon RT, Blaya DS, Moreira CH. Efficacy of benzocaine 20% topical anesthetic compared to placebo prior to administration of local anesthesia in the oral cavity: A randomized controlled trial. *Anesth Prog.* 2015;62(2):46-50.
- Kotian N, Mani G, Ramakrishnan M. Comparative evaluation of two different topical anesthetic agents in controlling pain during intraoral local anesthetic administration in children: A Split-mouth triple-blinded randomized clinical trial. *Int J Clin Pediatr Dent.* 2021;14(2):180-2.
- Gondim DGA, Montagner AM, Pita-Neto IC, Bringel RJS, Sandrini FAL, Moreno EFC, et al. Comparative analysis of the effectiveness of the topical administration of benzocaine and EMLA® on oral pain and tactile sensitivity. *Int J Dent.* 2018;2018:7916274.

Dor na punção da mucosa oral com lidocaína-prilocaína e benzocaína: ensaio aleatorizado de boca dividida

R E S U M O

Objetivos: Comparar a intensidade da dor associada à punção da mucosa oral após a aplicação de dois anestésicos tópicos em doentes adultos: um gel com uma mistura eutética de lidocaína a 2,5% e prilocaína a 2,5% e um gel de benzocaína a 20%.

Métodos: Realizou-se um ensaio clínico aleatorizado, cego e com desenho de boca dividida em 100 doentes com idades entre 25 e 65 anos. Aplicou-se um anestésico tópico ao lado direito ou esquerdo, conforme determinado por uma sequência de aleatorização por blocos gerada por computador com razão de alocação 1:1, e o lado contralateral recebeu automaticamente o anestésico alternativo. Efetuaram-se punções bilaterais da mucosa vestibular maxilar anterior. A intensidade da dor associada à punção no local onde foi aplicado cada anestésico tópico foi avaliada imediatamente utilizando uma escala visual analógica de 100 milímetros. As pon-

tuações de dor foram comparadas através do teste t de Student para amostras emparelhadas.

Resultados: A intensidade média da dor foi menor com o gel de lidocaína-prilocaína ($9,41 \pm 13,14$ mm) do que com o gel de benzocaína a 20% ($14,37 \pm 12,90$ mm), traduzindo-se numa diferença média entre pares de 4,96 mm (intervalo de confiança de 95%: 2,85 a 7,07; $p < 0,001$). Não foram registadas reações adversas locais ou sistémicas.

Conclusões: O gel de lidocaína-prilocaína reduziu significativamente a dor na punção relativamente à benzocaína a 20%. Embora a redução absoluta tenha sido modesta, pode ser clinicamente relevante para minimizar o desconforto inicial da punção. (Rev Port Estomatol Med Dent Cir Maxilofac. 2026;67(x):xxx-xxx)

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Palavras-chave:

Anestesia local

Benzocaína

Combinação lidocaína e prilocaína