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Research Article

Pain Response and Efficacy of Buffered Versus Non-Buffered Infiltration Local Anesthetics in Maxillary Anterior Region: A Randomized Clinical Trial

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Abstract

Introduction: This study aimed to assess the effectiveness of buffered articaine compared to non-buffered articaine in controlling pain during injection and evaluating anesthesia efficacy in adult patients undergoing injection of the maxillary anterior region.

Methods: Two hundred twenty patients who required maxillary anterior restorative procedures were included in this randomized parallel clinical trial. All patients received local infiltrations using either buffered or non-buffered articaine injections. Pain responses were measured before, during, and after the local anesthetic injection. The anesthesia's efficacy was evaluated with an electric pulp tester. The resulting data were statistically analyzed.

Results: The results of this study showed that patients who received the buffered anesthetic had a lower pain response during injection compared to those who received the non-buffered anesthetic ($P < 0.001$). Pain on palpation and percussion was lower in patients who received the buffered anesthetic ($P < 0.001$). Buffered anesthesia showed better pulpal anesthesia than non-buffered one ($P < 0.001$).

Conclusion: Based on the results of this study, buffered articaine was superior to non-buffered articaine in reducing discomfort during injection and increasing the anesthetic efficacy in patients' upper anterior region.

Keywords: *Buffering; Articaine; Anesthesia; Pain; Adults*

Introduction

The success of any dental procedure relies heavily on the effectiveness of the local anesthetic (LA) used. However, when administering the local anesthetic into the mucosa via infiltration, a stinging sensation may occur, thus increasing the patient's anxiety throughout the procedure. Adding a vasoconstrictor such as epinephrine may increase the patient's pain response [1].

Local anesthetics used in dentistry are acidic with a pH of 3.5-5 [2]. Injecting an acidic solution into the tissue may cause a burning sensation [3]. For that reason, dentists have been buffering local anesthetics with sodium bicarbonate to increase the pH of the injected solution [4, 5]. Raising the pH allows the buffered anesthetic to resemble the pH of the tissues, thus making the injection with a faster onset, less pain, and causing less irritation [4, 6].

Despite the theoretical benefits of buffering, research on the effectiveness of buffered versus non-buffered local anesthetics has been mixed. Several studies have compared buffered and non- buffered solutions, specifically with regard to lidocaine [7, 8, 9]. These studies have shown that while buffered solutions may reduce the discomfort associated with the injection, the overall efficacy in terms of pain relief and clinical outcomes (such as duration of anesthesia or procedural success) has often been found to be similar to that of the non-buffered solutions, especially in certain nerve blocks such as the inferior alveolar nerve block (IANB) [4, 10, 11]. However, most studies have focused on lidocaine, and there is a noticeable gap in research examining other anesthetics, such as articaine, which has become increasingly popular in dental practices due to its favorable pharmacokinetic properties [5, 12, 13].

Articaine, as a more potent local anesthetic, has been shown to have a faster onset and longer duration compared to lidocaine [12]. However, while its efficacy has been documented, little research has specifically compared the pain response associated with buffered and non-buffered articaine, particularly in infiltration anesthesia [13]. Given the growing use of articaine in dental practices, it is crucial to evaluate whether buffering this anesthetic can enhance the patient experience by reducing the pain associated with its injection [6, 13, 14].

The purpose of this study was to evaluate the degree of pain

during injection and efficacy of infiltration anesthesia of buffered versus non-buffered articaine in adult patients before dental procedures in the maxillary anterior region. The null hypothesis was that there is no significant difference in pain perception or pulpal anesthesia outcomes between buffered and non-buffered articaine.

Materials and Methods

Ethical considerations

A consent form was obtained from every participant in the study. This study was approved by the ethical committee of the Cleveland Dental Institute (#CDIOS00010). The study was registered on the clinical trial website (http://www.clinicaltrials.gov) with registration number: NCT06538233. It followed the Preferred Reporting Items for Randomized Trials in Endodontics 2020 (PRISMA 20).

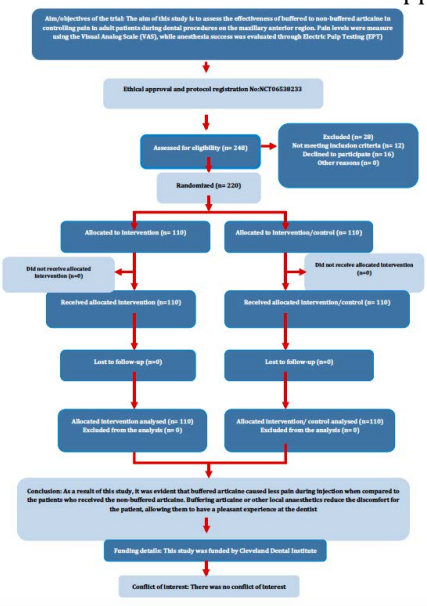
Trial Design

This is a prospective, double-arm randomized controlled trial designed to compare the effectiveness of buffered versus non-buffered articaine in terms of pain management and anesthesia success during dental procedures. The power analysis used pain scores as the primary outcome. Based on the results of Bahrololoomi and Rezaei (2021), the mean and standard deviation (SD) values were 1.64 (1.22) and 2.21 (1.66) in Lidocaine and Articaine groups, respectively [16]. The effect size for the Mann-Whitney test was (d) = 0.391. Using an alpha (α) level of 5% and Power = 80%, the minimum estimated sample size was 109 subjects per group. The sample size was increased to 110 subjects per group. Sample size calculation was performed using G*Power Version 3.1.9.2.

Eligibility Criteria

Participants

A total of 220 participants, aged 20 to 50 years, were enrolled in the study. Participants were recruited from the Cleveland Dental Institute's patient clinic (Figure 1). To ensure the safety and relevance of the study outcomes, the following inclusion and exclusion criteria were applied:



Inclusion Criteria

This study included patients of both genders who were medically healthy individuals with no history of systemic diseases or conditions [American Society of Anesthesiologists class I], aged 20-50 years, with no symptoms of acute pulpitis (pain with cold only which is relieved immediately after removal of the stimulus, related to upper anterior teeth).

Exclusion Criteria

Known allergy to local anesthetics, particularly articaine; pregnant or breastfeeding women; participants taking analgesics or antibiotics 24 hours before the procedure; individuals with a history of significant medical or dental conditions that may interfere with the study or pose safety concerns.

Randomization and Blinding

Eligible patients (n = 220) were randomly assigned in a 1:1 ratio to receive either buffered or non-buffered articaine. Randomization was performed using a computer-generated random sequence (Random.org), ensuring an equal probability of assignment to each group. The preparation of the buffered Articaine was not performed by the operator (another clinician). So, the operator was blinded to the buffering of the Articaine. Participants blindly received either buffered or non-buffered articaine as a local anesthetic for dental procedures involving the maxillary anterior region.

Intervention

The buffered and non-buffered formulations of articaine were prepared to ensure consistency in concentration and delivery. The administration of the anesthetic was conducted by a second-year resident at the Cleveland Dental Institute clinic.

Non-Buffered Articaine Group

Patients in this group received 4% articaine with 1:200,000 epinephrine (Articaine HCl 4%, Henry Schein, Novocol Pharmaceutical Inc., Ontario, Canada) as local infiltration in the maxillary anterior region.

Buffered Articaine Group

Patients in this group received 4% articaine with 1:200000 epinephrine as local infiltration in the maxillary anterior region. Buffering was performed with sodium bicarbonate using the OnPharma Onset Buffering System (Phoenix DeVentures, Morgan Hill, California). Buffering of the anesthetic was done following the manufacturer's protocol [16]. The buffering process involved mixing Articaine HCl 4% with 8.4% sodium bicarbonate in a 10:1 ratio. This adjustment raises the pH of the solution to approximately 7.0-7.3, aiming to reduce the discomfort associated with injection.

The procedure was performed as follows:

1. A single-use cartridge of Articaine HCl 4% was loaded into the Onset® Mixing Pen.
2. system delivers a certain amount of sodium bicarbonate into the cartridge to achieve optimal buffering

3. The buffered anesthetic solution was immediately transferred into a standard dental syringe.
4. Local infiltration was performed in the maxillary anterior region using a 27-gauge short needle, ensuring slow and steady administration of the anesthetic.

Care was taken to aspirate before injection to avoid intravascular administration. All injections were performed by the same clinician to maintain consistency across participants.

Outcome Assessment

Pain levels during the procedure were assessed using the VAS, which ranges from 0 (no pain) to 10 (worst pain imaginable). Pain levels were recorded at predefined time points during the procedure. The effectiveness of the anesthesia was evaluated using the SybronEndo Vitality Scanner Model 2006 electric pulp test machine (EPT) (SybronEndo, Glendora, California), a diagnostic test used to assess the degree of pulpal anesthesia. EPT was performed on the maxillary anterior teeth to assess the success of the anesthesia.

The VAS consists of a line with one end "0" representing no pain, and at the other end, with "10" representing the worst pain imaginable. Participants were instructed to mark a point along the line that best represented their perceived level of pain before, during, and after injection.

The EPT is a diagnostic tool used to evaluate the sensory response of the dental pulp, thereby determining the presence or absence of anesthesia. The maxillary anterior teeth targeted for the procedure were isolated and dried, and the probe was placed on the mid-facial surface of the tooth. A gradually increasing electrical stimulus was delivered, and the patient was instructed to raise a hand or signal when any sensation was felt. A lack of response at the maximum output level of the device (80) was considered indicative of successful pulpal anesthesia.

Statistical Analysis

Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). All data showed normal (parametric) distribution except for pain scores and onset of anesthesia time data, which showed non-normal (non-parametric) distribution. Data were presented as mean, standard deviation (SD), median, and range values. For parametric data, a repeated measures ANOVA test was used to compare the two groups as well as to study the changes within each group. Bonferroni's post-hoc test was used for pair-wise comparisons when the ANOVA test was significant. For non- parametric data, the Mann-Whitney U test was used to compare the two groups. The Wilcoxon signed-rank test was used to study the changes within each group. Qualitative data were presented as frequencies and percentages. Chi-square and Fisher's Exact test were used to compare the two groups. The Wilcoxon signed-rank test was also used to study the changes within each group regarding qualitative data. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

Results

Two hundred and twenty patients were recruited for the study. Patients were recruited between the months of January 2024 through January 2025. As a result, buffered articaine showed significantly lower pain scores during anesthetic injection compared to non-buffered articaine (P < 0.001) (Table 1). Post-injection, pain scores remained low in both groups, with no statistically significant changes from the baseline (P = 1 for buffered, P = 0.618 for non-buffered). This suggests that the main benefit of buffering lies in minimizing injection-related discomfort.

Table 1: Comparison between pain scores in the two groups and the Wilcoxon signed-rank test for the changes within each group

Time	Buffered (n = 110)		Non-buffered (n = 110)		*P*-value	Effect size (d)
	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)		
During injection	1 (1, 2)	1.1 (0.31)	7 (5, 8)	7.05 (0.94)	<0.001*	3.303
After injection	1 (1, 2)	1.1 (0.31)	7 (5, 8)	7 (0.97)	<0.001*	3.303
P-value	1		0.618			
Effect size (d)	0		0.112			

*: *Significant at $P \leq 0.05$*

Following injection, the prevalence of pain on palpation and percussion was significantly lower in the buffered group compared to the non-buffered group (P < 0.001) (Table 2, 3). Notably, the non-buffered group exhibited a significant increase in pain on both palpation (P = 0.008) and percussion (P = 0.008) after injection. Whereas the buffered group did not demonstrate any significant change from baseline (Table 2, 3).

Table 2: Comparison between pain on palpation in the two groups and the Wilcoxon signed-rank test for the changes within each group

Time	Buffered (n = 110) Non-buffered (n = 110)				*P*-value	*Effect size (Odds Ratio)*
	n	%	n	%		
During injection	4	3.6	71	65	<0.001*	0.259
After injection	4	3.6	110	100	<0.001*	NC†
P-value	1		0.008*			
Effect size (d)	0		0.592			

*: *Significant at $P \leq 0.05$, NC†: Not computed because all cases in each group had the same value*

Table 3: Comparison between pain on percussion in the two groups and the Wilcoxon signed-rank test for the changes within each group

Time	Buffered (n = 20)		Non-buffered (n = 20)		*P*-value	*Effect size (Odds Ratio)*
	n	%	n	%		
During injection	4	3.6	71	65	<0.001*	0.259
After injection	4	3.6	110	100	<0.001*	NC†
P-value	1		0.008*			
Effect size (d)	0		0.592			

**: Significant at P ≤ 0.05, NC†: Not computed because all cases in each group had the same value*

Regarding the EPT, the average EPT scores were significantly higher in the buffered group than in the non-buffered group post-injection (P < 0.001), indicating more profound pulpal anesthesia. Both groups demonstrated a significant increase in EPT threshold after injection compared to baseline (P < 0.001). When compared to the contralateral untreated tooth, the buffered group maintained significantly higher EPT values (P < 0.001), supporting the clinical efficacy of buffered articaine (Table 4).

Table 4: Comparison between electric pulp test scores in the two groups and the changes within each group

Tooth	Time	Buffered (n = 110)		Non-buffered (n = 110)		*P*-value	*Effect size* (Partial Eta squared)
		Mean	SD	Mean	SD		
	Before injection	34.1	1.71	31.45	2.93	<0.001*	0.243
	After injection	79.45	0.83	53.7	2.32	<0.001*	0.983
Offending	*P*-value	<0.001*		<0.001*			
	Effect size (Partial Eta squared)	0.994		0.977			
	Before injection	32.1	2.29	28.05	3.97	<0.001*	0.291
	After injection	78.15	1.81	48.9	5.24	<0.001*	0.936
Contralateral	*P*-value	<0.001*		<0.001*			
	Effect size (Partial Eta squared)	0.989		0.946			

**: Significant at P ≤ 0.05*

Discussion

This clinical trial studied whether buffering articaine with sodium bicarbonate enhances patient comfort and pulpal anesthesia effectiveness during maxillary anterior infiltration. The null hypothesis stated that there would be no significant difference in pain perception or pulpal anesthesia outcomes between buffered and non-buffered articaine. Our findings reject the null hypothesis.

Buffered local anesthetics are believed to enhance patient comfort by increasing the pH of the solution. This is done by reducing the proportion of ionized anesthetic molecules and facilitating more rapid diffusion through tissue [17, 18]. Among amide anesthetics, articaine exhibits higher lipid solubility and better bone penetration compared to lidocaine [14, 17]. Buffering may enhance these pharmacologic advantages by increasing the availability of the uncharged base, facilitating faster diffusion through tissue and into the nerve [19].

The pharmacodynamics of local anesthetics are heavily influenced by pH. Local anesthetics are weak bases, existing in equilibrium between ionized and non-ionized forms. At lower pH, the ionized (charged) form dominates, which is less permeable to nerve membranes and results in slower onset.[20]. At physiological pH, a higher fraction of the drug exists in its non-ionized (uncharged) form, facilitating rapid diffusion through lipid bilayers and increasing the efficiency of nerve blockade [21]. Once inside the neuron, the anesthetic must become ionized again to bind to and block voltage-gated sodium channels from the intracellular side.

Local anesthetics exert their effect by reversibly binding to voltage-gated sodium channels, particularly when these channels are in their open or inactivated state [22]. This prevents sodium influx during membrane depolarization, thereby halting the propagation of action potentials along the nerve. The binding affinity and rate of block are also voltage- and frequency- dependent, meaning that nerves firing at higher rates (e.g., during inflammation or pain) are more effectively inhibited by local anesthetics [23]. Buffering enhances the speed with which the anesthetic reaches and enters the nerve, allowing for faster occupation of these channels [24].

Pain was evaluated using both subjective and objective measures, ensuring comprehensive evaluation. The results indicated a statistically significant reduction in pain during injection in the buffered group. This finding is consistent with earlier studies that showed improved patient comfort

with buffered anesthetics [4, 7, 23]. In addition, EPT results depicted significant improvement, indicating that the buffered group offered more profound pulpal anesthesia. These findings suggest that buffering not only enhances patient comfort but improves anesthetic efficacy. The availability of commercial buffering systems like the Onset Mixing Pen from on pharma has made this process more accessible and standardized.

Additional research supports these findings. A recent randomized trial by Bala et al. showed that buffered anesthetics significantly decreased injection pain and increased anesthesia success rates in inferior alveolar nerve blocks [10]. Another study in the Journal of Dental Anesthesia and Pain Medicine reported that buffered 4% articaine resulted in a significantly faster onset of anesthesia and reduced discomfort during maxillary infiltrations compared to its non-buffered counterpart. [18]. More recently, a 2024 clinical trial published in *Biomedicines* demonstrated improved efficacy of buffered articaine in third molar surgeries, further validating our findings [25].

Despite the observed benefits, the relatively small sample size and restriction to maxillary anterior infiltration limit the ability to generalize the results to other regions of the mouth. Additionally, the study did not evaluate onset time or duration of anesthesia, both of which are relevant to clinical practice. Future studies should consider a larger sample size, assessment of other injection techniques, onset time and duration comparisons, and patient-reported anxiety and satisfaction outcomes.

Conclusion

Based on the results of this study, buffered articaine was superior to non-buffered articaine in reducing discomfort during injection and increasing the anesthetic efficacy in patients' upper anterior region. However, post-injection discomfort was similar between the two groups. Both of them showed a minimal response.

Conflict of Interest:

The authors declare that they have no conflicts of interest related to the conduct, authorship, or publication of this research.

Trial registration:

Clinicaltrial.gov, Identifier: NCT06538233

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Authors contributions:

The authors contributed equally to this work.

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The authors deny any conflicts of interest related to this study.

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