



Anesthetic efficacy of buffered 4% articaine for mandibular first molar infiltration: a crossover clinical trial

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Background: The limited studies on the effect of buffering on the clinical efficacy of articaine have reported controversial results. The purpose of this study was to clinically compare the pain of injection, anesthetic success, onset, and duration of pulpal anesthesia of buffered 4% articaine with epinephrine 1:100000 versus a non-buffered 4% articaine with epinephrine 1:100000 formulation for buccal infiltration of the mandibular first molar.

Methods: Sixty-three volunteers were enrolled in the study. All volunteers received two injections consisting of a single mandibular first molar buccal infiltration with 1.8 ml of 4% articaine with epinephrine 1:100000 and 1.8 ml of 4% articaine with epinephrine 1:100000 buffered with 8.4% sodium bicarbonate. The infiltrations were applied in two separate appointments spaced at least one week apart. After injection of the anesthetic solution at the examined site, the first molar was pulp-tested every 2 min for the next 60 min.

Results: Successful pulpal anesthesia was recorded in 69.8% of cases using non-buffered articaine solution and 76.2% of cases using buffered articaine solution, with no significant difference between the formulations ($P = 0.219$). The mean time of anesthesia onset for the volunteers with successful anesthetic outcome in both formulations ($n = 43$) was 6.6 ± 1.6 min for the non-buffered articaine solution and 4.5 ± 1.6 min for the buffered solution, which differed significantly ($P = 0.001$). In the same volunteers, the mean duration of pulpal anesthesia was 28.4 ± 7.1 min for non-buffered articaine solution and 30.2 ± 8.5 min for buffered articaine solution, with no significant difference between the formulations ($P = 0.231$). Considering the pain of injection, regardless of the anesthetic success, the mean values of VAS were 11.3 ± 8.2 mm for the non-buffered articaine solution and 7.8 ± 6.5 mm for the buffered articaine solution, which differed significantly ($P = 0.001 < 0.05$).

Conclusion: According to the present study, 4% articaine with epinephrine can benefit from buffering and provide better anesthetic behavior, with improved onset and less pain during injection.

Keywords: Articaine; Buffers; Infiltration Anesthesia; Local Anesthesia.



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INTRODUCTION

Local anesthetic (LA) solutions with epinephrine added to prolong the anesthetic effect have a low pH (3–5) to prevent early oxidation of epinephrine and prolong its shelf life [1,2]. However, this acidity may result in increased pain (burning sensation) due to the injection

and decreased onset of anesthesia [3]. It has been proposed that neutralization of the pH of the LA solution by buffering with sodium bicarbonate immediately before injection may reduce pain, shorten the onset time, and improve the clinical efficacy of LAs [4]. When sodium bicarbonate is mixed with a LA solution, its interaction with the hydrochloric acid in LA creates water and carbon dioxide. Carbon dioxide potentiates local anesthesia

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through three possible mechanisms: a direct depressant effect on the axon, concentrating LA inside the nerve trunk, and decreasing the pH inside the nerve, which leads to greater conversion of the anesthetic to cations inside the membrane [5]. Theoretically, buffering the anesthetic solution increases the pH and, consequently, the anesthetic success, providing a greater number of uncharged base anesthetic molecules [6].

Most research on the buffering of LA solutions in dentistry involves lidocaine and the inferior alveolar nerve block (IANB) technique. However, articaine, which is widely used in dentistry, is fundamentally different from other amide LAs because its thiophene ring has not been extensively researched. Physicochemical properties of articaine, such as increased lipid solubility and protein binding, are related to its increased anesthetic efficacy [7-9]. Commercially available articaine solutions for dentistry are usually provided with epinephrine at a 1:100000 or 1:200000 concentration and have low pH for the reasons explained above. This raises the question of whether buffering can further improve the anesthetic behavior of articaine solutions in terms of success, onset, and duration. Further improvement of the diffusion properties of articaine solutions may lead to useful applications in infiltration anesthesia of mandibular molars as an alternative to IANB. Previous studies on the effect of buffering on the clinical efficacy of articaine have demonstrated controversial results [6,10-11].

The purpose of this study was to clinically compare the pain of injection, anesthetic success, onset, and duration of pulpal anesthesia of a buffered 4% articaine with epinephrine 1:100000 versus a non-buffered 4% articaine with epinephrine 1:100000 formulation for buccal infiltration of the mandibular first molar.

METHODS

The present study was a crossover double-blind clinical trial on healthy adult volunteers approved by the Institutional Review Board of Dental School Aristotle

University of Thessaloniki (11/17-12-2014). The volunteers were retrieved from a pool of young patients who had previously visited our department for the surgical extraction of third molars. The included participants were healthy volunteers aged 18-35 years, with an intact first mandibular molar (free of caries or restoration) and without a history of trauma, sensitivity, or periodontal disease. The exclusion criteria were as follows: use of any medications that could affect anesthetic assessment, allergies to LAs, pregnancy or lactation (for females), and active sites of pathosis in the injection area.

Sixty-three volunteers were enrolled in the study (22 men and 41 women; mean age, 25.6 years), and written informed consent was obtained from each participant. Using a crossover design, all volunteers received two injections consisting of a single mandibular first molar buccal infiltration with 1.8 ml of 4% articaine with epinephrine 1:100000 and 1.8 ml of 4% articaine with epinephrine 1:100000 buffered with 8.4% sodium bicarbonate. The buffered solution was prepared by adding 0.18 ml of 8.4% sodium bicarbonate solution (1.8 ml cartridge to raise the pH to the value of 7.4 at 25°C, as previously described by Goodchild and Donaldson [12-13]. The infiltrations were applied in two separate appointments spaced at least one week apart. The same side chosen for the first infiltration was used for the second infiltration. The type of injected solution was randomly selected by the researcher's assistant, who also prepared the anesthetic formulations and was blinded to the senior author and volunteers. Infiltrations were administered using standard syringes equipped with a 27G 25 mm needle over a period of 1 min. All infiltrations were performed by the senior authors.

Before injection, the first mandibular molar and contralateral canine (control) were tested with an electric pulp tester (model D624, Gentle-Pulse; Parkell Inc., Edgewood, NY, USA) at the middle third of the buccal surface to ensure tooth vitality and obtain baseline information. The analog pulp tester increased the current rate from no output (0) to a maximum (10) manually.

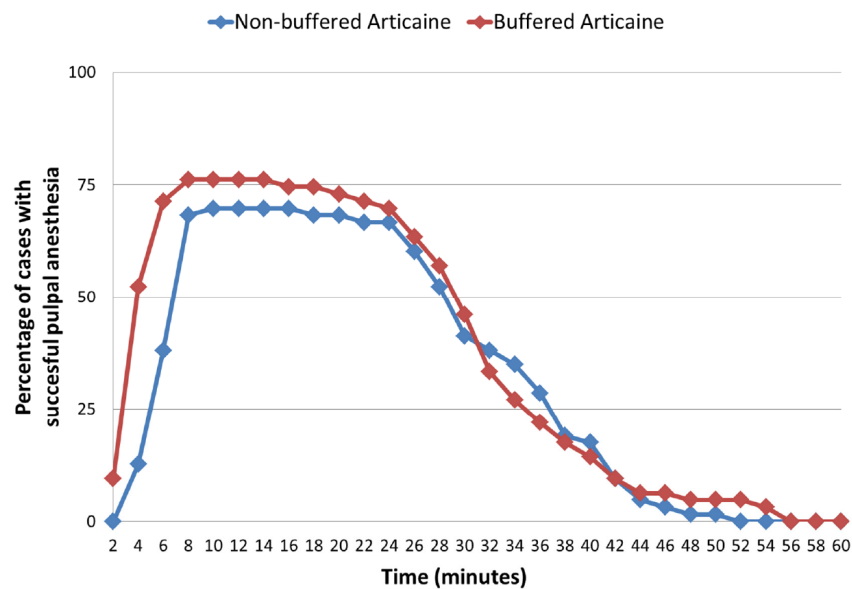


Fig. 1. Percentage of cases with successful pulpal anesthesia of the mandibular first molar at each time interval, as determined by the lack of response to electrical pulp testing at the maximum setting.

The contralateral mandibular canine was used as a control to ensure that the pulp tester responded appropriately. The teeth were isolated using cotton rolls and dried using an air syringe. Toothpaste was applied to the probe tip, and the value of the initial sensation was recorded. After injecting the anesthetic solution into the examined site, the first molar was tested every 2 min for the next 60 min.

The primary outcome was the success rate of pulpal anesthesia, which was considered as such when two consecutive readings of loss of sensation were recorded using the pulp tester. The onset of anesthesia was defined as the first loss of pulpal sensation, and the end of anesthesia was defined as the first reaction to the pulp tester. Before infiltration, each volunteer was instructed on how to rate the pain of the injection using a visual analog scale (VAS) on a special sheet. The VAS consists of a horizontal line 100 mm in length numbered from 0 to 100. Participants were informed that 0 represented the absence of pain and 100 represented the worst pain they had ever sensed. Immediately after the injection of the anesthetic solution, the volunteers rated the pain of the injection on the VAS. They were also asked to record any signs of numbness in the lower lip or neighboring

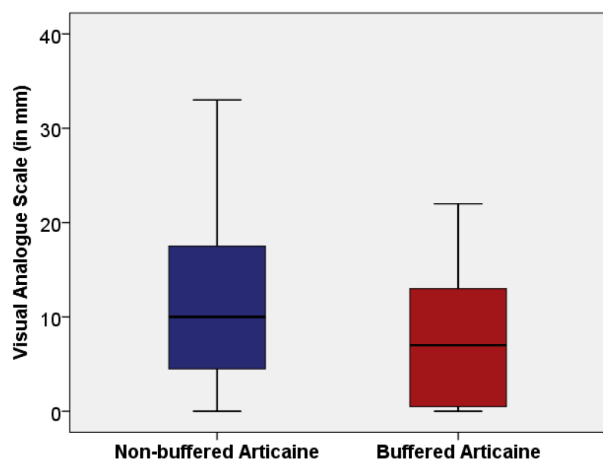
lingual mucosa. In case of a positive reaction, the duration of complete recovery was also recorded.

Based on a previous study [6], we assumed that the primary outcome (success rate of pulpal anesthesia) of the control treatment (non-buffered articaine) would be approximately 70%. We also assumed that the primary outcome of the experimental treatment (buffered articaine) should have a success rate comparable to that of IANB (approximately 90%) to serve as a useful alternative in clinical practice. Considering the aforementioned condition, it was calculated that at least 60 subjects would be needed in the present study to detect a difference of 20% between the success rates of the two treatments, when $\alpha = 0.05$ and $(1 - \beta) = 0.80$. The sample size was calculated using G*Power, version 3.1.9.2 (Frantz Faul, Universität Kiel, Germany).

Statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, United States). Continuous variables are presented as mean \pm SD and categorical variables as percentage and numbers. Success rates of pulpal anesthesia were compared using McNemar's test. Statistical differences in the onset and duration of anesthesia and the VAS score for pain during injection were tested using the Wilcoxon test. Statistical

Table 1. Mean time of anesthesia onset and duration of successful anesthetic outcome within the volunteers in both formulations

	Non-buffered Articaine	Buffered Articaine	P
Onset of anesthesia (in mins)	6.6 ± 1.6	4.5 ± 1.6	0.001
Duration of anesthesia (in mins)	28.4 ± 7.1	30.2 ± 8.5	0.231

**Fig. 2.** Boxplots of VAS for pain on injection in non-buffered and buffered articaine solutions.

significance was set at $P < 0.05$.

RESULTS

All infiltrations were uneventful and well-tolerated by all volunteers without any complications. Successful pulpal anesthesia was recorded in 69.8% (44/63) of the non-buffered articaine solution administrations and 76.2% (48/63) of the buffered articaine solution administrations, with no significant difference between the formulations ($P = 0.219$). The incidence of successful pulpal anesthesia of the mandibular first molar at each time interval for the buffered and non-buffered solutions is presented in Fig. 1.

A comparison of the two solutions among the volunteers with successful anesthetic outcomes in both formulations ($n = 43$) showed that the mean time of anesthesia onset differed significantly, whereas the mean duration of pulpal anesthesia did not differ (Table 1). Considering pain on injection, regardless of the anesthetic success, the mean values of VAS were 11.3 ± 8.2 mm

for non-buffered articaine solution and 7.8 ± 6.5 mm for buffered articaine solution, which differed significantly ($P = 0.001$) (Fig. 2).

All volunteers reported numbness of the lower lip regardless of the delivered anesthetic solution. Interestingly, nine volunteers (14.5%) also reported numbness on the lateral side of the tongue when the buffered articaine solution was injected.

DISCUSSION

The increased liposolubility of articaine results in enhanced diffusion properties and improved LA effects. Although strong evidence to support the claim that articaine is a superior agent compared to other LAs is lacking, its use has been very popular among dental practitioners [14]. The exceptional properties of articaine could possibly benefit from the buffering of the anesthetic solution, and this method could increase its anesthetic behavior in demanding mandibular infiltration as an alternative technique to IANB.

The present clinical study showed that buffering of 4% articaine with epinephrine 1:100000 improves pain of injection and onset of anesthesia, but has no effect on the success rate and duration of pulpal anesthesia of the first mandibular molar after single buccal infiltration. In a similar study by Shurtz et al. [6], no differences were observed in any of these parameters. However, this may be due to the prior application of a topical anesthetic gel (20% benzocaine) at the site of injection in their study, and differences in the time intervals between the measurements with the pulp tester. Interestingly, both the present study and that of Shurtz et al. [6] demonstrated a small increase in the success rate of pulpal anesthesia (approximately 4%–6%); however, this was not

statistically significant in order to be comparable with the success rate of IANB. In contrast, Dhake et al. [10] reported that buffering 4% articaine with 1:100000 epinephrine decreased pain during extraction of primary maxillary molars in children aged 4-10 years. Previous studies using lidocaine have also shown that buffering does not improve the success rate [15-16] or the duration of local anesthesia [17-19].

Considering the onset of anesthesia, theoretically, a higher pH adjusted to the anesthetic solution would rapidly provide more uncharged base available at the site of injection, resulting in a faster onset. Results from previous clinical studies on the effect of buffering on the onset of anesthesia by using different LAs or techniques remain controversial, with some studies supporting a faster onset [10,20-22], whereas other studies refuse this advantage [4,6,11,18,23-25]. In a systematic review and meta-analysis, Aulestia-Viera et al. [26] reported that the magnitude of onset reduction, if any, is about 1-2 min, and this is not a relevant clinical time gain as it is almost the time required to prepare the buffered LA at the chairside, if the concern is regarding saving time.

The acidic pH of LA solutions is considered to be a contributing factor to increased pain during injection [27]. Therefore, another possible beneficial effect of the buffering of LA solutions could be lowering the pain of injection by decreasing the H⁺ ions diffused in the local tissue environment. This beneficial effect was also demonstrated in the present study and is in agreement with that reported by Amorim et al. [11], in which buffered articaine was applied for maxillary infiltrations. However, other studies that used buffered articaine for mandibular [6] or maxillary [10] infiltration did not find any differences in pain after injection. Similarly, controversial results regarding the effect of injection pain have been reported in previous studies that used buffered lidocaine solutions [4,15,18-20,22-23,25,28].

In the present study, all volunteers reported numbness of the lower lip when both anesthetic formulations were administered. This finding can be easily explained by the diffusion of the anesthetic into the buccomandibular

space, which contains the mental foramen and nerve in its anterior part [29]. However, an interesting finding was that a small proportion of volunteers (14.5%) also reported numbness on the lateral side of the tongue when a buffered articaine solution was applied, which was not reported in a similar study by Shurtz et al. [6]. Lingual diffusion of the anesthetic through the inferior border of the mandible is a possible explanation. However, in the first mandibular molar, the lingual nerve lies above the mylohyoid muscle in the sublingual space. Therefore, the most likely way for the anesthetic to reach the lingual nerve could be in the area where the sublingual and submandibular spaces communicate, which is around the posterior free border of the mylohyoid muscle [30]. Moreover, the lingual nerve has fewer fascicles or may even be unifascicular in many individuals [31,32], which could explain why the buffered formulation can easily penetrate it.

The present study had some limitations. For example, the study was conducted in healthy volunteers with an intact first mandibular molar; therefore, the effect of buffering in clinical situations, such as pulpotomy/pulpectomy or extraction, could not be examined. Moreover, the effect of buffering on pain during injection cannot be objectively evaluated because many factors, such as patient anxiety, may be involved.

According to the present study, 4% articaine with epinephrine can benefit from buffering and provide better anesthetic behavior, with improved onset and less pain during injection. There is a trend toward better soft- and hard-tissue diffusion in the demanding area of the mandible in cases where IANB is avoided. As there are only a few studies and varying evidence regarding the effectiveness of buffered articaine, more randomized controlled studies are needed.

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Ioannis Fotopoulos: Methodology, Software, isualization

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