RESEARCH ARTICLE

Efficacy of 4% articaine with 1:100000 epinephrine versus 2% lignocaine with 1:100000 epinephrine in infiltration for extraction of maxillary premolars for orthodontic correction – A prospective, randomized, double-blind, crossover study

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ABSTRACT

Background: Unlike other amide local anesthetics (LAs), articaine has better lipid solubility and potency. Very few studies have been done on comparing articaine with other LAs as buccal infiltration among the participants requiring paired extraction of maxillary premolars but limitations of those studies include smaller sample size, lack of washout periods, and diversity in study designs. Aims and Objectives: This study compares the anesthetic efficacy of 4% articaine (1:100,000 epinephrine) with 2% lidocaine (1:100,000 epinephrine) as buccal infiltration. Materials and Methods: This is a randomized double-blinded crossover study conducted at the Department of Oral and Maxillofacial Surgery in collaboration with the Department of Pharmacology, SRIHER, Chennai. This study was done on 59 participants on an outpatient basis. The selected participants received 4% articaine or lignocaine with epinephrine (1:100000) in the mucobuccal fold at the maxillary area during their first visit and the same individual received the other local anesthetic drug on the other side in the same area during the second visit, i.e., 1 week from the date of the first visit. All the statistics were calculated using the software Statistical Package for the Social Sciences 16 version. For all primary and secondary outcomes in the study, the Mann–Whitney U-test was employed to compute the mean and standard deviation. Results: The total mean age of the participants included was 21.69. The volume of drug required was 1.578 ± 0.2760 mL for articaine and 2.2068 ± 0.0984 ml for lignocaine. The onset time was 30–45 s with articaine and 75–90 s with lignocaine. A decrease in pain scores was seen in the articaine group compared to the lignocaine group. Conclusion: This study showed better efficacy of articaine in comparison to lignocaine. Articaine may replace lignocaine in orthodontic corrections with its higher efficacy, faster action, and longer duration.

KEY WORDS: Anesthesia; Dental Procedures; Orthodontic Correction; Analgesia

INTRODUCTION

Safe and effective pain control plays a major role in certain conditions like tooth extraction and in dentistry, local anesthetic is indeed the basis of pain management treatments. It does have an essential role in avoiding pain thereby reducing the fear, anxiety, and discomfort associated
with painful procedures.[2] Orthodontics has always been at the forefront of providing patients with pain-free dental care, from cocaine (1884) to lidocaine (1943).[1] The key local anesthetics (LAs) used in dentistry are classified into amides and esters based on their chemical structure. Examples of ester-linked LAs include cocaine, procaine, tetracaine, and benzocaine which were synthesized between 1891 and 1930, whereas amide-linked LAs such as lidocaine, prilocaine, bupivacaine, dibucaine, articaine were prepared between 1898 and 1972. Because amides generate more quick and efficient profound surgical anesthesia than ester drugs, they are employed more frequently. Still, research is continuing to seek safer and more effective LAs.[1,3,4] Very few studies have been done on comparing efficacy and safety of articaine and lignocaine as buccal infiltration in the participants requiring paired extraction of maxillary premolars but limitations of those studies include smaller sample size, lack of washout periods, diversity in study designs (lack of uniformity). Many anesthetics may be there in the market but they are all lacking the efficacy in treating oral conditions.

The purpose of this current study is to overcome these limitations and compare the safety and efficacy of these two LAs with a randomized, uniform, cross-over design with good sample size. The objectives of this study are to compare the anesthetic potency of 4% articaine versus 2% lidocaine in 1:1 lakh IU epinephrine as buccal infiltration in patients who needed paired maxillary premolar extractions for orthodontic correction, to study onset and duration of anesthesia, and to assess the safety and intra- or post-administration complications of both the drugs.

MATERIALS AND METHODS

This prospective, double-blind, randomized, crossover study was done on 59 participants on an outpatient basis at the Department of Oral and Maxillofacial Surgery, at a tertiary-care hospital from November 2017 to July 2018. The trial was registered with the Clinical Trial Registry of India after receiving institutional ethical committee permission. After explaining the study’s goal, each participant signed a written informed consent form in their native language.

The 4% articaine drug (Septanest, Septodont, USA) was obtained with adrenaline 1:100000 and 2% lignocaine (Xylocaine, Astra Zeneca pharma, India) with 1:100000 adrenaline, standard extraction instruments, disposable syringes, and a 26-gauge needle (1.5 inches) were used in this study. The participants who fulfilled all the inclusion criteria and willing to sign in informed consent were included in the study. Both males and non-pregnant females aged between 12 and 25 years who need bilateral symmetric extraction of maxillary premolars for orthodontic correction and extraction sites free from inflammation and infection were included in the study. The patients with medication that could interfere with the participant’s sensitivity to pain, known history of allergy to any component of the local anesthetic agent, known case of hypertension or diabetes mellitus, pregnancy, and lactation were excluded from the study. The randomization method was done using coverslips. Double-blind was done during the study, and both the principal investigator and dental surgeon were blinded.

Demographics such as age, gender, weight, and height of all participants in the study were recorded. Blood pressure was measured before and after the extraction procedure following the standardized technique.[5] Blood pressure was measured before and after the extraction procedure following the standardized technique. A Mercury sphygmomanometer was used for the evaluation of blood pressure using a mercury sphygmomanometer with a standard procedure.[5] Pulse rate was recorded as the number of beats per minute.[6] All the participants received both drugs in a cross-over design that is 4% articaine with epinephrine (1:100000) and 2% lignocaine with epinephrine (1:100000) bilaterally with a washout period of 1 week. During the first appointment, all the participants were assigned to receive either drug A (4% articaine with epinephrine (1:100000)) or drug B (2% lignocaine with epinephrine (1:100000)) randomly using the coverslip method. The selected participants received 1.5 mL drug A or 1.5–2.5 mL of drug B in the muco-buccal fold at the maxillary area during their first visit and the same individual received the other local anesthetic drug on the other side in the same area during the second visit, i.e., 1 week from the date of the first visit. This standard technique was followed according to previous studies.[7]

The dental extraction procedure was done by the dental surgeon once the anesthesia was achieved. Pain during and after extraction was also examined using a Visual Analog Scale (VAS). Initially, before giving the local anesthesia, all the participants were educated about indicating the pain using visual analog. Participants were instructed to note the fading time of anesthesia which was recorded through telephonic conversation 3 h post-operatively to measure the duration of action of the local anesthetic agent. VAS is used for assessing pain during extraction and post-operative. The primary outcome of this research was to produce an efficient anesthetic effect after buccal infiltration so that the maxillary premolars could be extracted without pain. The onset, duration, and safety of anesthesia were the secondary outcome measures. The WHO–UMC scale was used to assess adverse drug events, which were then reported according to the institute’s standard operating procedures.

The software used to calculate the sample size was “nMaster 2.0” having the superior margin as two, with observed or expected difference taken as 3.43, the standard deviation taken as 3.4. The sample size calculated in the software with the help of previous literature, power of the study taken as...
Ninety, and considering alpha error as 2.5 results of sample size calculation is Fifty-nine.

All the statistics were calculated using the software Statistical Package for the Social Sciences 16 version. Normality for all the values was evaluated using the Kolmogorov–Smirnov test. For all primary and secondary outcomes in the study, the Mann–Whitney U-test was employed to compute the mean and standard deviation.

RESULTS

Seventy participants were selected for the study out of which fifty-nine have participated. These fifty-nine were randomized as per the protocol into their respective treatment groups [Figure 1]. The total mean age of the participants included was 21.69. The participants included were thirty-seven males and twenty-two females. The mean among study participants was 21.5 and 21.8 years for males and females, respectively. The mean weight of the male and female participants is 63.16 and 50.1, respectively. The mean height of the male and female participants is 176.86 and 158, respectively [Table 1].

The amount of local anesthetic solution administered to achieve appropriate anesthesia was compared in this research. The quantity of drug required was 1.58 ± 0.28 ml and 2.20 ± 0.09 ml for articaine and lignocaine, respectively, which was significantly lower with articaine (P < 0.001) [Table 1].

The onset time was 30–45 s with articaine and 75–90 s with lignocaine. The mean onset time in the lignocaine group was 85.37 ± 2.24 s whereas it was 37.07 ± 3.47 s in the articaine group, as shown in Table 1. The onset time of anesthesia was significantly higher with lignocaine (P < 0.001) [Table 1]. Fading of anesthesia in the articaine group was seen between 90 and 110 min and for the lignocaine group, it was between 55 and 70 min. Mean fading time of anesthesia is more in the articaine group compared to the lignocaine group which was statistically significant. (P < 0.001) [Table 1]. Pain assessment during and after the procedure revealed a significant decrease with articaine (P < 0.001). During the trial period, neither group experienced any intra- or post-operative complications [Table 2].

DISCUSSION

A dental extraction is a painful procedure that might cause dread and anxiety in patients. A painless extraction procedure would immediately benefit patients by lowering their anxiousness and increasing their comfort. One of the most significant components for effective dental procedures is the use of local anesthetic to reduce the pain of the patient. Main factors such as potency, latency, and duration of anesthesia decide the choice or selection of local anesthetic, which may also include the safety and toxicity of the drug.[2] To compare the efficacy of two local anesthetic drugs, standardization of the procedure is essential, thereby eliminating bias during the study. In this investigation, the effectiveness of 4% articaine with vasoconstrictor and 2% lignocaine with vasoconstrictor was compared in the extraction of maxillary premolars bilaterally with uniform study (cross-over) design and having enough washout period during the study.

Variations in injection speed can have a substantial impact on the outcome. Hence, the drug administration was done by

### Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>N</th>
<th>Mean±SD</th>
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<tbody>
<tr>
<td>Age (mean±SD)</td>
<td>59</td>
<td>21.62±2.26</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Male (n)</td>
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<td>Female (n)</td>
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<tr>
<td>Height (cm)</td>
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<td>169.8±9.6</td>
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<tr>
<td>Weight (kg)</td>
<td>59</td>
<td>58.32±6.76</td>
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<tr>
<td>Volume of anesthetic drug (mL)</td>
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<td></td>
</tr>
<tr>
<td>Articaine</td>
<td>59</td>
<td>1.5±0.3*</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>59</td>
<td>2.2±0.1</td>
</tr>
<tr>
<td>Onset of anesthesia (s)</td>
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<td></td>
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<tr>
<td>Articaine</td>
<td>59</td>
<td>37.07±3.5*</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>59</td>
<td>85.37±2.2</td>
</tr>
<tr>
<td>Fading of Anesthesia (mins)</td>
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<td>Articaine</td>
<td>59</td>
<td>105.2±2.7*</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>59</td>
<td>63±3.2</td>
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</table>

*P<0.05 obtained with Mann–Whitney U-test. SD: Standard deviation
a single operator with recommended standardized injection rate of 1 mL/min for infiltration injection to upsurge evenness in the study.[8] The required dose was lower with articaine (1.58 ± 0.28 mL) than lignocaine (2.20 ± 0.09 mL) to produce effective anesthesia. The onset of anesthetic effect was less than a minute for articaine whereas for lignocaine, it is around 1.5 min. The physicochemical features of articaine, such as the thiophene ring and lipid solubility, contributed to its rapid onset of action among amide LAs. High lipid solubility promotes drug penetration into neuronal membranes, increasing neuronal drug concentration, effective transverse distribution, and improved conduction blockade. The results of the present study were in accordance with the study conducted by Ashwath et al., and Rebolledo et al., who reported the time of onset of anesthesia for articaine as 0.93 min whereas for lignocaine, it was 1.25 min.[7,8] This study showed that fading time of anesthesia for articaine was more (1.5–2 h) compared to lignocaine (1 h) implying a longer duration of action for (former than counterpart) articaine than lignocaine. Duration of anesthesia depends on vasoconstrictor concentration and degree of protein binding of local anesthetic. In this study, the same concentration of vasoconstrictor was chosen for both groups, thereby avoiding bias in the study. Articaine has good protein binding property, comparable to ultra-long-acting LAs such as bupivacaine, ropivacaine, and etidocaine, which also reveals a longer duration of the anesthetic effect of articaine.[9-11] Articaine showed a considerable reduction in pain score in our investigation. The findings of this study agreed with those of other investigations that found articaine to be more effective than lignocaine as infiltration anesthesia.[11,12] In contrary to these results, Hassan et al. reported no significant difference in pain scores for articaine and lignocaine as infiltration in extracting maxillary premolars.[13] In this study, no adverse effects or complications were reported in both groups. According to literature, articaine was shown to cause hypersensitivity, neuropathies, paresthesia, and methemoglobinemia.[14] The ADR incidence was 20% for lidocaine and 22% for articaine, including headache, paresthesia, hypothermia, infection, rash, and pain.[15] Potonick et al. reported non-surgical paresthesia more in 4% of articaine-treated group than in the lignocaine-treated group.[16] However, Rebolledo et al. deemed that robust evidence might be required to reveal the causal factor.[9] Our data showed that the safety of articaine was comparable to that of lignocaine in infiltration anesthesia.

### Table 2: Comparison of analgesic efficacy between articaine and lignocaine

<table>
<thead>
<tr>
<th>Local anesthetic drug</th>
<th>Number of subjects (n)</th>
<th>Pain during procedure</th>
<th>Pain after procedure</th>
<th>Significance (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine</td>
<td>59</td>
<td>Mean: 1.46, SD: 0.750</td>
<td>Mean: 5.44, SD: 0.676</td>
<td>P = 0.001*</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>59</td>
<td>Mean: 2.66, SD: 0.512</td>
<td>Mean: 6.92, SD: 0.816</td>
<td></td>
</tr>
</tbody>
</table>

*P-value obtained with Mann–Whitney U-test. SD: Standard deviation

### CONCLUSION

The variety of local anesthetic agents commercially available necessitates practitioners evaluating the drug based on its pharmacokinetic and clinical presentations undergoing dental procedures. Articaine may replace lignocaine in orthodontic corrections with its higher efficacy, faster action, and longer duration. However, more clinical trials with a greater sample size are needed to ensure the validity of articaine, which may increase its usage in dentistry in India.

### REFERENCES


10. Costa CG, Tortamano IP, Rocha RG, Franciscione CE,


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