Anesthetic efficacy and safety of 2% lidocaine hydrochloride with 1:100,000 adrenaline and 4% articaine hydrochloride with 1:100,000 adrenaline as a single buccal injection in the extraction of maxillary premolars for orthodontic purposes

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Background: Palatal injection of local anesthetics is the most painful injection. To obviate the need for palatal injections, local anesthetic agents with diffusibility are being investigated. Hence the present study was designed to analyze the anesthetic efficacy of 2% lidocaine hydrochloride (HCl) with 1:100,000 adrenaline and 4% articaine hydrochloride (HCl) with 1:100,000 adrenaline using single buccal infiltration for the extraction of maxillary premolars.

Methods: A prospective, double-blind, crossover, randomized clinical study was performed on 60 consecutive systemically healthy patients with an age range of 15-30 years, requiring extraction of asymptomatic bilateral maxillary premolars for orthodontic purposes. They received 1ml buccal infiltration of 4% articaine HCl with 1:100,000 adrenaline on one side and 2% lidocaine HCl with 1:100,000 adrenaline on the other side. The extraction procedure on either side was scheduled 14 days apart. Parameters assessed were the time of onset of anesthesia, intraoperative discomfort, hemodynamic parameters, and the duration of analgesia. Analysis of the data was done using the Mann-Whitney test, the Wilcoxon test, the Kruskal-Wallis ANOVA test, and the chi-square test. Statistical significance was established at P < 0.05.

Results: Articaine showed a faster time of onset and longer duration of analgesia than lidocaine. However, the difference in the intraoperative discomfort and hemodynamic parameters was statistically insignificant.

Conclusion: Within the limitations of the study, it can be concluded that the extraction of maxillary premolars can be performed with a single buccal infiltration of 2% lidocaine HCl with 1:100,000 adrenaline, which is one of the most commonly used local anesthetic agent.

Keywords: Analgesia; Articaine; Buccal administration; Lidocaine; Local Anesthetics; Maxillary Premolar.

INTRODUCTION

Local anesthetic agents are the backbone of pain control in dentistry and are considered the safest and the most effective drugs available for the prevention and management of pain in any oral surgical procedure. Various amide local anesthetic agents have been studied and reported in the literature [1]. Lidocaine amide local anesthetic agent soon after its synthesis in 1943 by the Swedish chemist Nil Lofgren became a gold standard owing to its minimal side effects, rapid action, and...
effective pain control [2]. Later Rushing et al. (1969) synthesized the first amide local anesthetic agent with a lipophilic thiophene ring instead of the usual benzene ring and an additional ester group called carticaine which was changed to articaine in 1984. The presence of the thiophene ring increases the lipid solubility that gives the molecule better diffusibility than lidocaine, and higher protein binding that increases the duration of anesthesia. It also has less central nervous system toxicity than lidocaine [3].

The extraction of maxillary teeth requires a palatal nerve block. Amongst all the local anesthetic techniques, palatal injection is the most painful as the palatal mucosa is highly dense and has firm adherence to the underlying bone. The maxillary bone is porous, this facilitates diffusion of the anesthetic solution from the buccal to the palatal aspect obviating the need for a palatal injection [4]. Various studies have claimed that articaine diffuses through the soft and hard tissues more reliably than other local anesthetic agents [5,6,7,8]. Only a few studies have evaluated the diffusivity of lidocaine [9,4].

Hence, the present study was conducted to analyze the anesthetic efficacy and safety of 2% lidocaine hydrochloride (HCl) with 1:100,000 adrenaline and 4% articaine hydrochloride (HCl) with 1:100,000 adrenaline using single buccal infiltration for the extraction of maxillary premolars, based on the hypothesis that there would be no significant difference amongst the two local anesthetic agents used as a single buccal infiltration technique in all outcome measures.

**METHODS**

The present double-blind, split-mouth, randomized controlled clinical study was prospectively conducted on 60 consecutive systemically healthy patients with an age range of 15-30 years requiring extraction of asymptomatic bilateral maxillary premolars for orthodontic purposes at the outpatient Department of Oral and Maxillofacial Surgery at the Sharad Pawar Dental College and Hospital, Sawangi (M), Wardha between August 2015 to September 2017. The study was performed in accordance with the Declaration of Helsinki and its later amendments or comparable ethical standards and institutional ethical guidelines prescribed by the Central Ethics Committee on Human Research (CECHR) of the Datta Meghe Institute of Medical Sciences. (Ref. No. DMIMS (DU)/IEC/2015-16/1668).

The following formula was used to calculate the sample size required for this study at 95% confidence interval and 80% power of study.

\[
N = \frac{(Z_{\alpha/2} + Z_\beta)^2 \times 2 \times \sigma^2}{d^2}
\]

Where \(Z_{\alpha/2}\) is the critical value of the normal distribution at \(\alpha/2\) (for a confidence level of 95%, \(\alpha = 0.05\) and the critical value is 1.96), \(Z_\beta\) is the critical value of the normal distribution at \(\beta\) (power of 80%, \(\beta = 0.2\) and the critical value is 0.84), \(\sigma^2\) is the population variance, and \(d\) is the difference that you would like to detect.

\[N = 41\]

Taking into account the cases not reporting for the second appointment, a sample size of 60 was devised. Patients having localized infection, systemic diseases, allergy to sulfide or amide local anesthetic agents, and anxiety requiring a sedative or anxiolytic drugs were excluded from this study.

Informed consent was obtained from the patients for this study. Clinical examination was performed, and the patients were subjected to routine blood investigations. Patients were explained about the study and the visual analog scale (VAS) [10]. The preoperative heart rate and blood pressure of each patient were recorded and were considered as the baseline.

The randomization of the side was done by a table of random numbers. The study design demanded the administration of intraoral local anesthesia as a single buccal infiltration for the extraction of bilateral maxillary premolars. The patients were administered 1ml buccal infiltration of 4% articaine HCl with 1:100,000 adrenaline (Septanest®, marketed by Septodont Healthcare India Pvt. Ltd., Maharashtra, India) on one side, and 2% lidocaine
Articaine versus lidocaine

HCl with 1:100,000 adrenaline (Lignospan®, marketed by Septodont Healthcare India Pvt. Ltd., Maharashtra, India) on the other side. The same oral surgeon uniformly administered the anesthetic each time with a slow infusion rate of 1 ml/min. Two independent staff members supporting the study were recruited to ensure randomization and independent observation. These members were not further involved in the statistical analysis to avoid bias. Both the surgeon and the observer were blinded to the drug being administered.

The onset of anesthesia was checked every 30 s using a blunt probe on the buccal and the palatal aspects. A latency period of 5 min was observed to achieve anesthesia. After achieving anesthesia, the first premolar was extracted. The extraction procedure on either side of the upper jaw was scheduled 14 days apart. Post-recruitment exclusion criteria included patients reporting pain > 3 on the VAS during the surgery and patients who did not achieve anesthesia within 10 min and needed re-anesthesia.

The onset of anesthesia was recorded on the buccal and palatal aspects as the time of injection to the time when the effect of anesthesia was first reported. Intraoperative discomfort and postoperative pain were recorded on the 10-point VAS, where 0 indicated no pain and 10 indicated unimaginable pain. Hemodynamic parameters including heart rate, systolic blood pressure, and diastolic blood pressure were recorded at baseline, 10 min following anesthetic administration, and at the end of the procedure. Patients were asked to record their postoperative pain intensity on the VAS and the time of consumption of the rescue analgesic (ketorolac tromethamine tablet, 10 mg). Patients were asked to consume the rescue analgesic when the post extraction pain intensity score on the VAS was > 3, and it was considered as the endpoint of the study. Any adverse effects were observed and recorded.

Data were entered in an MS Excel spreadsheet (Microsoft Corporation, Redmond, Washington, USA) and was analyzed using the computer software Intercooled Stata 9.2 (StataCorp, TX, USA). Analysis of the quantitative data was done using the Mann-Whitney test, the Wilcoxon test, and the Kruskal-Wallis ANOVA test. Analysis of the qualitative data was done using the chi-square test. Statistical significance was established at P < 0.05.

RESULTS

The study sample (N = 60) comprised 40 females and 20 males with a mean age of 18.96 ± 3.15 years (15-28 years) (Table 1). The success rate for both groups was 100%. None of the patients required palatal re-anesthesia in both groups (Fig. 1) [11].

The mean time for the onset of anesthesia buccally and palatally with the administration of articaine was 58.70 ± 24.46 s and 64.57 ± 19.97 s and with the administration of lidocaine was 232.83 ± 46.12 s and 247.83 ± 52.32 s, respectively. The difference in the time of onset of anesthesia in the buccal and palatal aspects between the two groups was statistically insignificant (P = 0.211, P = 0.148). No significant difference was noted in terms of discomfort during the extraction of the premolar between the two groups (P = 0.319).

Hemodynamic parameters such as the heart rate, systolic blood pressure, and diastolic pressure were recorded at baseline, 10 min following the administration

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**Table 1. Patient characteristics based on age, gender, weight, height, and physical class**

<table>
<thead>
<tr>
<th>N = 60</th>
<th>Mean ± SD</th>
<th>range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>18.8 ± 3.0</td>
<td>15-28</td>
</tr>
<tr>
<td>Gender</td>
<td>Male : 20, Female : 40</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>160.0 ± 4.9</td>
<td>15-28</td>
</tr>
<tr>
<td>Weight</td>
<td>49.8 ± 3.7</td>
<td>42-60</td>
</tr>
<tr>
<td>ASA PS class</td>
<td>Class I : 60</td>
<td></td>
</tr>
</tbody>
</table>

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Fig. 1. Consort flow chart [11].

Table 2. Heart rate (beats/min) at various intervals between the two groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>N</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(60)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Std. deviation</td>
<td>Mean</td>
<td>Std. deviation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>60</td>
<td>78.65</td>
<td>7.79</td>
<td>77.74</td>
<td>6.97</td>
<td>0.555 (NS)</td>
</tr>
<tr>
<td>10 minutes after injection</td>
<td>60</td>
<td>80.83</td>
<td>7.91</td>
<td>81.30</td>
<td>6.04</td>
<td>0.745 (NS)</td>
</tr>
<tr>
<td>After extraction</td>
<td>60</td>
<td>79.65</td>
<td>7.43</td>
<td>78.13</td>
<td>5.85</td>
<td>0.278 (NS)</td>
</tr>
</tbody>
</table>

of anesthesia, and post extraction. The difference in the heart rate with the administration of articaine and lidocaine at baseline (P = 0.555), 10 min after injection (P = 0.745), and post extraction (P = 0.278) were found to be statistically insignificant (Table 2). The difference in the mean systolic and diastolic blood pressure between the two groups at baseline [(P = 0.587), (P = 0.610)], 10 minutes after injection [(P = 0.565), (P = 0.172)], and post extraction [(P = 0.515), (P = 0.222)] were statistically insignificant (Table 3).

In the present study, a longer duration of analgesia was observed with articaine (202.17 ± 48.35 min) than lidocaine (190.48 ± 38.43 min), but the difference was found to be insignificant (P = 0.886). No adverse effects were found with the use of both the anesthetic agents.
**DISCUSSION**

Pain is a complex, personal, subjective experience, and a psychological phenomenon varying from individual to individual and at different times in the same individual. Local anesthesia is the most effective means of alleviating pain in dentistry. Of all the intraoral local anesthetic techniques, palatal injection is the most painful. The palatal mucosa is dense and is firmly adherent to the underlying bone that resists distension on the deposition of the anesthetic solution causing discomfort to the patient [7]. The diffusibility of a local anesthetic solution is a desirable property that permits the solution to diffuse through the bone and soft tissue, obviating the need for a second injection and minimizing discomfort.

Amongst all the local anesthetic agents, articaine, an amide local anesthetic agent is believed to diffuse through soft and hard tissues due to the presence of a thioephene ring that allows for higher lipid solubility, thus making it superior when used to alleviate pain. The property of diffusion makes it suitable for a single buccal injection in avoiding a painful palatal injection [5,6,8]. However, there is insufficient literature regarding the diffusion of lidocaine, which is a commonly used drug and considered as the gold standard [4,9]. Therefore the present study was conducted to compare the efficacy and safety of 2% lidocaine HCl with 1:100,000 adrenaline and 4% articaine HCl with 1:100,000 adrenaline using single buccal infiltration for the extraction of bilateral maxillary premolars, with the hypothesis that there would be no significant difference amongst the two local anesthetic agents used as a single buccal infiltration technique in all outcome measures.

All interventions in both groups were successful (100%), and there were no dropouts in the study. The present study employed a randomized, split-mouth study design, wherein, patients served as their control, thereby eliminating bias arising out of interpersonal variation and reaction to pain. The surgeon who conducted the procedure was blinded to eliminate surgeon sensitivity to the difference in the injection protocol. A total of 60 subjects were recruited in this study. All extractions were performed in a standardized, controlled, peaceful, and patient-friendly environment by the same surgeon. The washout period between the interventions on both sides was 14 days. Other studies have reported a success rate of 92% in buccal infiltration with lidocaine for orthodontic extractions in the premolar region without a palatal injection [4,12].

The time of onset of anesthesia or latency time was measured from the time of injection to the time when effective anesthesia was achieved, and it depends on the intrinsic properties of the drug, anesthetic technique, and the pKa value. Latency is directly proportional to the pKa, smaller the pKa value shorter the onset time. Both articaine and lidocaine have similar a pKa of 7.8. Also, the time interval after injection and the amount of drug used affects the diffusion rate, which thereby affects the time of onset [13]. The anterior region of the maxilla has a higher density of bone, and therefore a longer latency period may be required for the diffusion of the solution through the bone. To evaluate the palatal anesthesia, we standardized the waiting period to 10 min, during which the buccal and palatal aspects were assessed for the adequacy of anesthesia. In the present study, the time of onset of anesthesia on the buccal aspect with the administration of articaine and lidocaine was 58.70 ±

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**Table 3.** Systolic and diastolic blood pressure (BP) (mmHg) at various intervals between the two groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>N (60)</th>
<th>Systolic BP</th>
<th></th>
<th>Diastolic BP</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Articaine</td>
<td>Lidocaine</td>
<td>P-value</td>
<td>Articaine</td>
</tr>
<tr>
<td>Baseline</td>
<td>60</td>
<td>117.61 ± 7.40</td>
<td>116.74 ± 7.52</td>
<td>0.578 (NS)</td>
<td>76.52 ± 6.50</td>
</tr>
<tr>
<td>10 minutes after injection</td>
<td>60</td>
<td>120.61 ± 6.36</td>
<td>119.82 ± 6.62</td>
<td>0.565 (NS)</td>
<td>76.65 ± 6.18</td>
</tr>
<tr>
<td>After extraction</td>
<td>60</td>
<td>119.61 ± 6.42</td>
<td>118.74 ± 6.36</td>
<td>0.515 (NS)</td>
<td>76.13 ± 5.88</td>
</tr>
</tbody>
</table>

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24.46 s and 64.57 ± 19.97 s, respectively. The mean time of onset of palatal anesthesia with articaine was 232.83 ± 46.12 s and with lidocaine was 247.83 ± 52.32 s. An insignificant difference was observed in the time of onset of anesthesia in the buccal and palatal aspects between the two groups (P = 0.211, P = 0.148), showing diffusion of articaine and lidocaine to the palatal aspect. This result was in accordance with the previous studies that showed similar results [4,6,8]. In contrast, Ozec et al. (2010) [14] could not establish the presence of palatal anesthesia with articaine after buccal injection, and Mittal et al. (2015) [15] failed to determine the effectiveness of both articaine and lidocaine in providing palatal anesthesia.

The depth of anesthesia was measured as discomfort on surgical stimulus on the VAS following the confirmation of anesthesia objectively on both the buccal and palatal aspects. None of the patients in either of the groups experienced discomfort during the procedure. The results are in accordance with the previous studies [8,12,15,16].

A local anesthetic agent combined with a vasoconstrictor counteracts the vasodilation caused by the local anesthetic agent, delays its absorption into the cardiovascular system, increases the duration of local anesthesia, diminishes the risk of toxicity, and also transiently affects hemodynamic parameters such as blood pressure and heart rate. The heart rate provides an indirect measurement of pain, anxiety, and apprehension that are not subject to observer bias. An increase in the variation of the heart rate and blood pressure are observed during stressful situations. However, other factors such as anxiety, apprehension, alcohol, smoking, and drugs (anti-hypertensives, sedatives, and anti-depressants) may also lead to changes in the hemodynamic parameters [15]. The heart rate and the blood pressure (systolic and diastolic) were recorded at baseline, 10 min following injection, and post extraction.

In the present study, the heart rate transiently increased following the administration of articaine as well as lidocaine and returned to normal post extraction. The difference in the two groups was statistically insignificant (P = 0.555, P = 0.745, P = 0.278). These results correspond to the results of the previous studies [17]. On the contrary, Nusstein et al. (2004) [18] could not record any increase in the heart rate following the administration of both the solutions.

The systolic and diastolic blood pressure following the administration of articaine and lidocaine at baseline [(P = 0.587), (P = 0.610)], 10 min after injection [(P = 0.565), (P = 0.172)], and post extraction [(P = 0.515), (P = 0.222)] were statistically insignificant. The systolic blood pressure following the administration of both the agents showed a subtle increase at 10 min after injection and returned to the baseline values after extraction. Similar results were observed in other studies [15,17].

In the present study, the administration of articaine helped achieve a longer duration of anesthesia (202.17 ± 48.35 min) than lidocaine (190.48 ± 38.43 min), but there was no significant difference between the two agents (P = 0.886). The duration of analgesia is proportional to the degree of protein binding, and it depends on the individual response to a drug, the status of the tissue at the site of drug administration, the concentration of the vasoconstrictor, and the amount and concentration of the drug administered. The reported protein binding values for lidocaine and articaine are 65% and 95%, respectively. Clinical trials have shown 4% articaine HCl to provide a significantly faster onset, longer duration of action, and lower toxicity than 2% articaine HCl. Darawade et al. (2014) [6] showed similar results as observed in the present study. No adverse effects were noted with the administration of both the drugs.

Maxillary tooth extraction without palatal anesthesia has been a topic of much research. The diffusibility of articaine across the alveolar bone to anesthetize the palatal mucosa with a single buccal infiltration is well established; however, the use of lidocaine as a single buccal infiltration to anesthetize the palatal mucosa have been demonstrated with inconsistent results. The present research attempts to highlight the results with the use of lidocaine with comparable efficacy, albeit with greater latency.
The results of the present study indicate that 4% articaine HCl with 1:100,000 adrenaline produced more effective and faster bucco-palatal anesthesia than 2% lidocaine HCl with 1:100,000 adrenaline. Similarly, lidocaine also showed diffusibility to the palatal tissue when only buccal infiltration was given and 5 min was allowed between the administration of local anesthesia and initiation of the procedure.

Hence, within the limitations of the study, it can be concluded that the extraction of maxillary premolars can be performed with a single buccal infiltration of 2% lidocaine HCl with 1:100,000 adrenaline which is one of the most commonly used local anesthetic agent, but with a longer latency period. Multi-centric trials with a larger sample size are needed to arrive at a logical conclusion.

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Anendd Jadhav: Conceptualization, Methodology, Supervision, Validation, Writing - review & editing  
Nitin Bhola: Conceptualization, Supervision, Validation, Visualization, Writing - review & editing  
Manan Gupta: Investigation, Methodology, Project administration, Writing - review & editing

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**REFERENCES**