Comparison of Efficacy of 0.75% Ropivacaine and 2% Lidocaine with 1:200,000 Adrenaline in Pain Control in Extraction of Mandibular Posterior Teeth: A Double-blind Study

Abstract

Background: Two percent lidocaine hydrochloride is the gold standard for dental anesthesia against which newer local anesthetic agents may be compared. 0.75% ropivacaine is a newer, long-acting amide local anesthetic agent with inherent vasoconstriction property. Aim: This study aims to compare the efficacy of 0.75% ropivacaine and 2% lidocaine hydrochloride with 1:200,000 adrenaline in pain control in extraction of mandibular posterior teeth. Settings and Design: This is a prospective, double-blind, and split-mouth study. Subjects and Methods: Twenty patients were divided into two groups according to the right and left sides of patient – side A and side B. The side, where 0.75% ropivacaine was to be administered, was randomly selected by flip coin method. Then, the pterygomandibular and long buccal nerve blocks were administered with 0.75% ropivacaine and necessary dental extraction was performed. After 1 week, the same procedure was repeated using 2% lidocaine hydrochloride with 1:200,000 adrenaline. The parameters assessed were pain on injection, onset of anesthesia, pain during the extraction, and duration of anesthesia. Statistical Analysis Used: The nonparametric data were assessed by Mann Whitney “U” test. Results: The mean onset of action for solution A was 7.15 ± 4.934 min and for solution B was 9.75±5.128 min. This was statistically significant. The mean duration of action, pain on injection, and pain during extraction were not significant. Conclusion: This study clearly states that there is no clear advantage of using 0.75% ropivacaine in pterygomandibular nerve block over the gold standard. However, more clinical studies with larger sample size are necessary.

Keywords: Dental extraction, local anesthesia, inferior alveolar nerve block, local anesthetics, lidocaine hydrochloride, ropivacaine

Introduction

Local anesthesia is an effective method of pain control since 1884.[1-6] In dentistry, 2% lidocaine is most frequently used.[7] However, lidocaine is short acting (vasodilator).[8] To increase the depth and duration of anesthesia, epinephrine was added to lignocaine.[9] Nonetheless, epinephrine containing local anesthetic solution is contraindicated in hyperthyroidism and significant cardiovascular diseases (American Society of Anesthesiologists physical status grade 3–4).[8] Furthermore, adding vasoconstrictor reduces the pH of the solution (acidic), rendering the injections uncomfortable to the patients.[9] Hence, search for a long-acting local anesthetic agent with inherent vasoconstrictive property still endures.

Ropivacaine was introduced in 1996 and was found suitable for peripheral nerve blocks in the medical field.[9-14] Limited data are available concerning the dental use of ropivacaine.[15-17] PubMed search revealed no studies comparing 0.75% ropivacaine with 2% lidocaine for pterygomandibular nerve block.

This study aims to compare the efficacy of 0.75% ropivacaine and 2% lidocaine with 1:200,000 adrenaline in pain control in extraction of mandibular posterior teeth.

Subjects and Methods

The research protocol of this study was approved by the institutional ethics committee. This study was funded by the Indian Council of Medical Research as a short-term studentship. In this prospective, double-blind, and split-mouth study, a sample size of 20 participants was considered based on the previous literature with 95% confidence of interval and 80%
power of study. The sample size was calculated using the following formula:

\[ n = \left( \frac{Z_{1-\alpha} + Z_{\beta}}{\delta} \right)^2 \]

where \( n \) = sample size, \( Z_{1-\alpha} = 1.96 \), \( Z_{\beta} = 0.84 \), \( \sigma \) = standard deviation based on El-Sharrawy and Yagiela study and is 0.3, and \( \delta \) = margin of error (0.2).

This formula yielded a result of 17.64 which was rounded off to 20.

Convenient sampling technique was followed. The patients attending the outpatient department of oral and maxillofacial surgery, meeting following inclusion and exclusion criteria, were included in the study.

The inclusion criteria were patients in the age range of 30–60 years and requiring pterygomandibular nerve block for dental extraction of bilateral mandibular posterior teeth of similar grade of mobility. Patients with a history of any systemic diseases, allergy to components of lidocaine or ropivacaine, local malignancies, recent history of consumption of antimicrobial and anti-inflammatory drugs, and those with grossly destructed teeth were excluded from the study.

All the patients were explained about the study and its importance, and valid informed consent was obtained from those who were willing to participate in the study. Routine blood investigations such as hemoglobin, bleeding time, and clotting time were performed. Skin sensitivity test was performed on all the patients 72 h before the procedure.

Patients were divided into two groups according to the right and left sides of patient – side A and side B.

The side where 0.75% ropivacaine [Figure 1 and Table 1] was to be administered was randomly selected by tossing a coin. Then, the pterygomandibular and long buccal nerve blocks were administered with 0.75% ropivacaine. Following the onset of action, tooth extraction was carried out using standard protocol.

After 1 week, the same procedure was repeated using 2% lidocaine with 1:200,000 adrenaline [Figure 1 and Table 1]. All the nerve blocks and necessary procedures were carried out by a single operator.

The following parameters were assessed:

1. Pain on injection: This was measured on 10-mm visual analog scale. This was given immediately after the injection.
2. Onset of anesthesia: Time elapsed from the point of injection till the emergence of numbness and tingling sensation on ipsilateral lower lip and anterior 2/3rd of the tongue. This was measured using a stop watch in minutes.
3. Pain during the extraction: This was also measured on 10-mm visual analog scale. This was given immediately after the extraction of the teeth.
4. Duration of anesthesia: Time elapsed from the point of emergence of numbness and tingling sensation of lower lip and anterior 2/3rd of the tongue till wearing off of the numbness and tingling sensation in the same region. This was measured in hours.

The patient was recalled after 24 h to know when the anesthesia had weaned off.

The results were tabulated and subjected to statistical analysis. The nonparametric data were assessed by Mann Whitney “U” test.

**Observation and Results**

Of 20 patients, 50% of the patients were between 51–60 years of age. The rest 50% of the patients were between 31–50 years of age [Figure 2]. Majority of the patients in this study were males constituting about 80% [Figure 3].

The mean onset of action for solution A was 7.15 ± 4.934 min and for solution B was 9.75 ± 5.128 min. This was statistically significant [Table 2].

The mean duration of action for solution A and solution B came out to be 3.30 ± 1.471 h and 3.50 ± 2.190 h, respectively. However, this was statistically insignificant [Table 2].

However, solution A and solution B did not show any statistically significant results for pain on injection and during extraction [Table 2].

**Discussion**

In drug studies, blinding can achieve higher standard scientific rigor. A double-blind study can greatly lessen the power of preconceived notions and physical cues to distort the results. [18]
### Table 1: Comparison of physical and chemical properties of Lidocaine and ropivacaine

| Properties                              | Lidocaine                                      | Ropivacaine                                   |
|-----------------------------------------|------------------------------------------------|-----------------------------------------------|
| Chemical nomenclature (IUPAC name)      | 2-(diethylamino)-N-(2,6-dimethylphenyl) acetamide | (2S)-N-(2,6-dimethylphenyl)-1-propylpiperidine-2-carboxamide |
| Year of synthesis and of clinical introduction | 1943; 1944                                    | 1957; 1996                                    |
| Prepared by                             | Nils Lofgren                                   | AF Ekenstam                                   |
| Prepared by                             |                                                |                                               |
| 2 D structure                           | ![Lidocaine structure](image)                  | ![Ropivacaine structure](image)               |
| Molecular weight                        | 234.343 g/mol                                  | 274.408 g/mol                                 |
| Specific gravity                        | 1.0056                                         | 1.002-1.005                                   |
| Boiling point                           | 159°C-160°C                                    | 410°C                                         |
| Partition coefficient (LogP)            | 1                                              | 2.9                                           |
| Protein binding                         | 64%                                            | 94%                                           |
| PKa                                     | 7.9                                            | 8.1                                           |
| pH of plain solution                    | 6.5                                            | 5.5                                           |
| pH of vasoconstrictor containing solution | 5.5-5.5                                      | -                                             |
| Relative potency                        | 4                                              | 16                                            |
| Effective dental concentration          | 2%                                             | 0.5%, 0.75%                                   |
| Maximum dose (mg/kg body weight)        | 4.4 (7.1)                                      | 3                                             |
| Target                                  | Sodium channel protein type 10 subunit alpha   | Sodium channel protein type 10 subunit alpha  |
| Enzymes                                 | Cytochrome P450 3A5                            | Cytochrome P450 1A2                           |
| Enzymes (continued)                     | Cytochrome P450 3A7                            | Cytochrome P450 2B6                           |
| Enzymes (continued)                     | Cytochrome P450 2D6                            | Cytochrome P450 2D6                           |
| Enzymes (continued)                     | Cytochrome P450 3A4                            | Cytochrome P450 3A4                           |
| Enzymes (continued)                     | Cytochrome P450 2C9                            | Cytochrome P450 2C9                           |
| Enzymes (continued)                     | Cytochrome P450 2C8                            | Cytochrome P450 2C8                           |
| Enzymes (continued)                     | Cytochrome P450 2C18                           | Cytochrome P450 2C18                           |
| Enzymes (continued)                     | Cytochrome P450 2A6                            | Cytochrome P450 2A6                           |
| Enzymes (continued)                     | Cytochrome P450 2B6                            | Cytochrome P450 2B6                           |
| Byproducts                               | 3-Hydroxylidocaine                             | 3-Hydroxyropivacaine                          |
| Byproducts (continued)                  | Monoethylglycinexylidide                       |                                               |
| Byproducts (continued)                  | Glycinexylidide                                |                                               |
| Byproducts (continued)                  | 2,6-Dimethylaniline (2,6-Xylidine)             |                                               |
| Anesthetic half life                    | 1.6 h                                          | 4.2 h                                         |
| Elimination half life                   | 90-120 min                                     | 111 min                                       |
| Pregnancy classification                | B                                              | B                                             |
| Safety during lactation                 | S                                              | S                                             |
| Routes of administration                | Topical anesthesia                             | Local infiltration                            |
| Routes of administration (continued)    | Local infiltration                             | Nerve block                                   |
| Routes of administration (continued)    | Nerve block                                    | Epidural block                                |
| Routes of administration (continued)    | Epidural block                                 | Spinal and extradural anesthesia              |
| Routes of administration (continued)    | Intravenous injection                          |                                               |
| Routes of administration (continued)    | Spinal and extradural anesthesia               |                                               |
| Routes of administration (continued)    | Transmucosal patches                           |                                               |

*Contd...*
A split-mouth designed study was used because it allowed for intraindividual comparison, and the assessment of postoperative complications following extraction of tooth can be done with great confidence. Furthermore, the left and right sides could behave differently, and the second extraction in the same mouth would be easier and thereby less traumatic. These possible causes of bias were controlled by randomly assigning the cases to each of the possible combinations.\(^{[19]}\)

The onset of 2% lidocaine with 1:200,000 epinephrine came out to be much faster as compared to 0.75% ropivacaine. This was in concurrence with Ernberg and Kopp and Oliveira \textit{et al.}\(^{[17,20]}\). This delay in onset of action may be attributed to the highest pKa value of ropivacaine, intermediate lipid solubility of ropivacaine, and complexity of injection.\(^{[17,21]}\) However, El-Sharrawy and Yagiela showed rapid onset of action with 0.75% and 0.5% of ropivacaine for inferior alveolar nerve block.\(^{[22]}\) However, in one of the cases, 0.75% ropivacaine did not cause anesthesia even after waiting for 25 min, so we excluded the same from our study.

The duration of anesthesia for 2% lidocaine with 1:200,000 epinephrine was less as compared to 0.75% ropivacaine. However, this result was statistically insignificant. The result of this study was in concurrence with Ernberg and Kopp and El-Sharrawy and Yagiela.\(^{[17,22]}\) This may be because ropivacaine has greater protein binding capacity as compared to lidocaine \([\text{Table 1}]^{[21]}\).

Reduction in the injection pain can help provide overall comfort and well-being during the dental treatment; the pain on injection usually depends on the pH of the solution.\(^{[21,23]}\) In this study, both the drugs showed similar pain on injection. This may be attributed to the complexity of injection technique and the experience of the operator, in spite of higher pH of ropivacaine \([\text{Table 1}]^{[21]}\). After onset of anesthesia, both the drugs showed statistically

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**Table 2: Statistical analysis of onset of anesthesia, duration of anesthesia, pain on injection, and pain during procedure**

| Parameters                        | Solutions  | \(n\) | Mean±SD      | Mann–Whitney U-test | \(P\) | Inference |
|-----------------------------------|------------|-------|--------------|---------------------|-------|-----------|
| Onset of anesthesia (min)         | Solution-A | 20    | 7.15±4.934   | 115.500             | 0.021 | S         |
|                                   | Solution-B | 20    | 9.75±5.128   |                     |       |           |
| Duration of anesthesia (h)        | Solution-A | 20    | 3.30±1.471   | 167.000             | 0.383 | NS        |
|                                   | Solution-B | 20    | 3.50±2.190   |                     |       |           |
| Pain on injection                 | Solution-A | 20    | 0.95±1.145   | 168.500             | 0.398 | NS        |
|                                   | Solution-B | 20    | 1.25±1.118   |                     |       |           |
| Pain during procedure             | Solution-A | 20    | 1.95±1.356   | 145.500             | 0.142 | NS        |
|                                   | Solution-B | 20    | 1.3±0.978    |                     |       |           |

Solution A=2% lidocaine with 1:200,000, Solution B=0.75% ropivacaine, \(n\)=Sample size. S=Significant \((P\leq0.05)\), NS=Not significant \((P>0.05)\), SD=Standard deviation

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**Table 1: Contd**

| Properties   | Lidocaine | Ropivacaine |
|--------------|-----------|-------------|
| Brand names  | Xylocaine, Dilocaine, Nervocaine, G-Lidocaine, Jasocaine, Xylone, lox, Themicaine | Naropin, Ropivacaine Hydrochloride |

IUPAC=International Union of Pure and Applied Chemistry

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**Figure 2: Age distribution of the study population**

**Figure 3: Gender distribution of the study population**
insignificant results for pain during extraction. This was similar to the results of Bhargava et al. This study did not show any clear-cut advantages of ropivacaine over 2% lidocaine with 1:200,000 epinephrine.

**Conclusion**

This prospective, split-mouth, double-blind study revealed the following inferences:

- The onset of action of 2% lidocaine with 1:200,000 epinephrine is rapid than 0.75% ropivacaine.
- Although statistically insignificant, 0.75% ropivacaine showed prolonged duration of action comparatively.
- The pain on injection and pain during extraction were insignificant both clinically and statistically.

Thus, this study clearly states that there is no clear advantage of using 0.75% ropivacaine in pterygomandibular nerve block over the gold standard. However, multicentric studies with larger sample size and assessing cardiovascular parameters are necessary.

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**Conflicts of interest**

There are no conflicts of interest.

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