ABSTRACT

Local anesthetics are used to alleviate pain and discomfort of the patient during root canal therapy. Effective pain control is an absolute essential for better patient compliance and attitude towards the treatment. The purpose of the study was to observe the onset of action of local anesthesia, its duration of action and pain experienced by the patient during treatment procedure. Patients diagnosed with symptomatic irreversible pulpitis and no changes in the periapical tissues indicated for endodontic management were included in the study. The study was a double blinded randomised clinical trial. The non-randomization procedure allocated 32 teeth with symptomatic irreversible pulpitis, 8 teeth to each control group (group I treated by conventional 2% Lignocaine and group III treated by conventional 4% Articaine HCL) and 8 teeth to each experimental group (group II treated by buffered 2% Lignocaine and group IV treated by buffered 4% Articaine.
The buffering of local anesthetic agent improves the efficacy, onset of action and longevity of the local anesthetic agent. Buffered local anesthetics can be used in place of conventional local anesthetic agents. Long term clinical trials will be required to observe the result and to draw a comment and conclusion.

**Keywords:** Anesthetics; buffered; pain management.

### 1. INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [1]. Pain is one of the most common complaints with which a patient approaches the dental professional [2]. Thus the pain management is an extremely crucial step for the management of patients. Management of endodontic pain is crucial as it improves the patient compliance, improves patient cooperation, reduces postoperative complications and is related to a shorter recovery period.

Although an array of pain management techniques as mentioned by Rosenberg exist that include providing proper information, use of analgesics, pulpotomy, pulpectomy, trephination, etc [3], the most important and foremost step is the successful administration of anesthetic solution [4].

Local anesthesia is the transient loss of sensation in a circumscribed area of the body that is caused by the depression of the excitation of nerve endings or by the inhibition of conduction process occurring in the peripheral nerves [5]. The mechanism by which local anesthetics act is the interruption of neural conduction due to the inhibition of the influx of sodium ions within the neuronal membrane that depolarise the membrane resulting in the depression neurons.

Lignocaine hydrochloride which was made clinically available in 1941 has been the most commonly used local anesthetic agent making it gold standard for comparison [6]. In 1976, a Articaaine HCl, which is an amide based local anesthetic agent was introduced. Articaaine has a long duration of action and is distinctive as it consists of a thiophene group instead of a benzene ring. These properties account for the better performance of articaine over other local anesthetics [7]. Buffering of local anesthetic agents have been suggested to increase the efficacy and decrease pain associated with its injection [8].

We had numerous highly cited publications on well designed clinical trials and lab studies [9–24]. This has provided the right platform for us to pursue the current study. Our aim was to observe for the onset of action of the local anesthesia, its longevity and pain experienced by the patient during the endodontic therapy when different local anesthetic agents were used.

### 2. MATERIALS AND METHODS

This randomized, double-blind study was conducted in the Department of Conservative Dentistry and Endodontics.

The non-randomization procedure allocated 32 teeth with symptomatic irreversible pulpitis, 8 teeth to each control group (group I treated by conventional 2% Lignocaine and group III treated by conventional 4% Articaine HCL) and 8 teeth to each experimental group (group II treated by buffered 2% Lignocaine and group IV treated by buffered 4% Articaine HCL). The criteria for inclusion included symptomatic teeth that were indicated for root canal therapy, patients aged above 18 but less than 50, patients with no systemic illnesses and an initial Visual Analogue Scale (VAS) score of >5.

A VAS score of 5 and above shows distressing miserable pain. Patients with asymptomatic teeth indicated for endodontic therapy, teeth with changes in periapical region, patients aged below 18 and above 50, patients with systemic illnesses and allergic to local anesthetic agents were all excluded from the study.

Preoperative evaluation of the clinical case was done and a preoperative radiograph was taken too. Prior to administration of anesthesia, the base value of pain using VAS score was recorded. The type of anesthesia to be administered was randomly picked up from the lot containing the group number in opaque envelopes by a staff member posted in the outpatient department. While administering the
Inferior Alveolar Nerve Block (IANB), 1.8 mL of the solution was administered over 60 seconds using a 27-gauge needle as recommended by Malamed [5].

A total of 4 study groups were studied. Group 1 consisted of conventional 2% lignocaine hydrochloride with 1: 200,000 epinephrine (Lox two percent, Neon Laboratories Ltd., Mumbai, India). For the preparation of the buffered local anesthetic solution using Lignocaine, 3 mL of solution was removed using a standard disposable syringe. To this, 3 mL of 8.4% sodium bicarbonate was added, using another sterile, standard disposable syringe to achieve a dilution of 1:10 as mentioned by Frank et al [25]. It was shaken until the solution was clear, to ensure that sodium bicarbonate dissolved completely. The above described anesthetic solution formed the Group 2 for the study. The Group 3 included 4% Articaine Hydrochloride (Septanest with Adrenaline 1/100,000). To the solution in a vial, 40 units of solution was removed using a sterile disposable insulin syringe and the same amount of 8.4% sodium bicarbonate was added [26] to prepare the anesthetic solution for group 4.

The administration of local anesthesia was done. An IANB nerve block at a speed of 1 ml/min with a 25 gauge needle supplemented with local infiltration is given to each patient [6]. The time at which the patient informed of feeling complete numbness at the tongue and lower lip is taken as the time when the anesthetic solution kicks off. Objective evaluation using gingival probing was undertaken. Rubber dam isolation was done and access opening was done under the sterile environment. Biomechanical preparation of the root canal system was done. The root canal procedure was completed and a temporary restoration using zinc oxide eugenol was given and the tooth was restored with a crown on a later date. The patient was asked to report the level of pain using the VAS score experienced during the procedure. Also, the patient was either made to wait or report the time when the effect of anesthesia completely wore off. The data collected was subjected to statistical analysis.

2.1 Statistical Analysis

Descriptive statistics were expressed as mean ± standard deviation (SD) for each groups for VAS scale; Onset of action (Min) and Duration of Action/ Longevity (min). Four groups were compared for 3 factors by Analysis of Variance (ANOVA) followed by paired wise comparison by Tukeys’ post hoc test. Comparison of two groups (lignocaine Vs Articaine ) and (Conventional Vs Buffered ) was done with Independent ‘t’ Test.

Simple/ Multiple Bar charts; were used for data presentation

In the above tests, p value less than or equal to 0.05 (p<0.05) was taken to be statistically significant.

The data was entered into Microsoft Excel 2007. All analyses were performed using SPSS (Statistical Package for Social Sciences) software version 17.

3. RESULTS AND DISCUSSION

It can be inferred that buffering of the local anesthetics not only increases the longevity of the anesthetic effect but also reduces the pain and onset of the anesthetic effect. Dental procedures induce negative responses such as anxiety, stress, fear and pain in children as well as adults. Pain, if not managed properly influences the dropout rates of the patients who opt to not continue undergoing endodontic therapy. The study is an effort taken to find a solution for pain and discomfort associated with the administration of local anesthesia using conventional syringe and needle.

This is the first study to be reported in the literature where conventional and buffered lignocaine as well asarticaine have been used as the study groups. Previous study by Kurien et al used warm, buffered and conventional lignocaine as the study groups [27]. Buffered articaine is statistically significantly a better anesthetic agent when compared to conventional or buffered lignocaine (Tables 1, 2 and 3). However, no statistical significance between anesthetic efficacy of buffered articaine over conventional articaine was found. Buffered Articaine has much less pain during injection as compared to conventional Articaine (Graphs 1, 2 and 3).

The drawbacks of injecting anesthesia in patients include pain during injecting, post injection tissue trauma, unreliable action in areas of inflammation, slow onset of action and burning and stinging of tissue [8]. The reason for this tissue reaction is that the local anesthetic agents are acidic in nature. pH range of 2.86-4.16 has been reported by various researchers [28]. The low pH of solution ensures the shelf life of local anesthetic solutions and keeps the anesthetic molecules intact.
Table 1. Table shows inter-group VAS scores comparison upon administration of local anesthetic agent

| Dependent Variable: VAS score | (I) 4groups | (J) 4groups | Mean Difference (I-J) | Std. Error | Sig. p value |
|-------------------------------|-------------|-------------|-----------------------|------------|--------------|
| Group 1 Conventional 2% Lignocaine | Group 2 Buffered 2% Lignocaine | .87500 | .50665 | .329 |
| Group 1 Conventional 2% Lignocaine | Group 3 Conventional 4% Articaine | 2.25000* | .50665 | .001* |
| Group 1 Conventional 2% Lignocaine | Group 4 Buffered 4% Articaine | 2.87500* | .50665 | <0.001* |
| Group 2 Buffered 2% Lignocaine | Group 3 Conventional 4% Articaine | 1.37500 | .50665 | .052 |
| Group 2 Buffered 2% Lignocaine | Group 4 Buffered 4% Articaine | 2.00000* | .50665 | .003* |
| Group 3 Conventional 4% Articaine | Group 4 Buffered 4% Articaine | .62500 | .50665 | .611 |

* The mean difference is significant at the 0.05 level

Table 2. Table denotes the inter-group comparison of the onset of anesthetic action when local anesthetic agents are administered

| Dependent Variable: Onset of Action (Minutes) score | (I) 4groups | (J) 4groups | Mean Difference (I-J) | Std. Error | Sig. p value |
|----------------------------------------------------|-------------|-------------|-----------------------|------------|--------------|
| Group 1 Conventional 2% Lignocaine | Group 2 Buffered 2% Lignocaine | .57375 | .24120 | .105 |
| Group 1 Conventional 2% Lignocaine | Group 3 Conventional 4% Articaine | 1.12500* | .24120 | <0.001* |
| Group 1 Conventional 2% Lignocaine | Group 4 Buffered 4% Articaine | 1.66625* | .24120 | <0.001* |
| Group 2 Buffered 2% Lignocaine | Group 3 Conventional 4% Articaine | .55125 | .24120 | .126 |
| Group 2 Buffered 2% Lignocaine | Group 4 Buffered 4% Articaine | 1.09250* | .24120 | .001 |
| Group 3 Conventional 4% Articaine | Group 4 Buffered 4% Articaine | .54125 | .24120 | .136 |

* The mean difference is significant at the 0.05 level

Table 3. Table denotes the inter-group comparison of the duration of anesthetic action when local anesthetic agents are administered

| Dependent Variable: Duration of Action (Minutes) score | (I) 4groups | (J) 4groups | Mean Difference (I-J) | Std. Error | Sig. p value |
|-------------------------------------------------------|-------------|-------------|-----------------------|------------|--------------|
| Group 1 Conventional 2% Lignocaine | Group 2 Buffered 2% Lignocaine | -13.00000 | 4.15197 | .020 |
| Group 1 Conventional 2% Lignocaine | Group 3 Conventional 4% Articaine | -19.62500* | 4.15197 | <0.001* |
| Group 1 Conventional 2% Lignocaine | Group 4 Buffered 4% Articaine | -25.62500* | 4.15197 | <0.001* |
| Group 2 Buffered 2% Lignocaine | Group 3 Conventional 4% Articaine | -6.62500 | 4.15197 | .397 |
| Group 2 Buffered 2% Lignocaine | Group 4 Buffered 4% Articaine | -12.62500* | 4.15197 | .025 |
| Group 3 Conventional 4% Articaine | Group 4 Buffered 4% Articaine | -6.00000 | 4.15197 | .483 |

* The mean difference is significant at the 0.05 level
There is a statistically significant difference among four groups for Mean VAS score with p<0.001. It can be inferred that minimum pain has been reported in cases where buffered articaine was used as an anesthetic agent. Conventional lignocaine when used as an anesthetic agent had the maximum reported pain.

Sterile, non-pyrogenic solution of 8.4% sodium bicarbonate is used as a neutralizing agent. It is compatible with the commonly used amide type of local anesthetic agents [29]. Adjustment of pH of lignocaine reduced pain on injection for both children and adults [30]. Sodium bicarbonate upon mixing with LA interacts with hydrochloric acid which creates water and carbon dioxide.
Graph 3. Comparison for mean Duration of Action (min) among four groups

There is a statistically Significant difference among four groups for Duration of Action (Minutes) score with p<0.001. Buffered articaine has the longest duration of action whereas the anesthetic effect of conventional lignocaine is the shortest.

Fig. 1. Denotes freshly prepared local anesthetic solution vials. 1 denotes conventional lignocaine, 2 denote buffered lignocaine, and 3 denote conventional articaine while 4 denotes buffered articaine.
Carbon dioxide has a direct depressant action on the nerve axon, increases the concentration of the local anesthetic agent inside the nerve trunk via ion trapping and changes the ionic charge of the LA agent inside the nerve axon. All these mechanisms have been seen to increase the action of buffered local anesthetic agents [31]. Up to seven-fold potentiation in the anesthetic action has been reported [32]. Malamed in his paper mentioned a clinical trial that reported a significant decrease in the time taken for onset of pulpal anesthesia as well as pain upon injection with buffered local anesthetic agents. Hence, buffered LA is more comfortable and faster acting, hence advantageous for both clinician and patient [8].

Many combinations of the sodium bicarbonate and local anesthetic solution have been studied. 1:10 volume ratio of sodium bicarbonate to 2% lignocaine has been finally decided. 4% articaine requires twice the amount of sodium bicarbonate [25].

In cases with symptomatic irreversible pulpitis which are the inclusion cases in the current study, articaine is found to be more effective than lignocaine as reported by Kung [33]. However, no significant difference in the effectiveness of various local anesthetic agents have been reported [34].

Supplementing an incomplete Articaine IANB with infiltration raises the anesthetic success more effectively when compared to Lignocaine [35]. Buffering of Mepivacaine is seen to speed up and potentiate analgesia of median and ulnar nerve blocks performed on horses [36].

Results obtained are consistent with the clinical trials performed previously in the similar kind of set up [27,29,37–39]. Another important finding is that buffered anesthetic solution decreased pain on injection [40]. Less pain and more comfort during endodontic therapy with buffered lignocaine has already been reported too [41].

The longer duration of action of the local anesthetic solution due to buffering of the solution is an important finding of the current study and is consistent with a previously conducted study [42]. A meta-analysis concluded that the efficacy of buffered anesthesia is better than that of conventional [43]. However, a mention of decreased shelf-life of the anesthetic solution has been made which indicates the necessity of preparation and immediate usage of buffered local anesthetics in clinical scenario [43].

Use of various modern methods to increase the efficiency of the local anesthesia has been mentioned. Use of long acting anesthetic agents, single tooth anesthesia, combinant techniques, Anesthetic nanoparticles incorporated materials, etc. Hypothesis suggests a colloidal suspension that contains millions of active analgesic dental robots of micrometer size range to be deposited on the patient's gingiva which release the drug under guided chemical and temperature gradients. The pulpal sensitivity is shut down as soon as the drug reached the internals of the tooth and the nanorobots may be used to restore the function after the procedure is finished [44].

4. CONCLUSION

Buffered local anesthetic solutions have a greater efficiency in respect to onset and duration of action and pain experienced by the patient during treatment procedure than the conventional solutions. Buffered Articaine has proven to be better than buffered lignocaine in all the aspects of efficiency. Utilising buffered local anesthetic solution improves clinical success.

Further comparative clinical studies regarding efficacy of buffered lignocaine and articaine must be done to confirm the findings and bring in to the clinical scenario.

CONSENT

Written informed consent was obtained from the patients before enrolling in the study and only those disagreed to comply with the treatment were excluded from the study.

ETHICAL APPROVAL

Approval from the Institutional Ethics Committee was obtained before conducting the research. The study was undertaken in full accordance with ethical principles.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. IASP Terminology - IASP n.d. Available:https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698 Accessed August 25, 2019.
2. Al-Johani K, Lamfon H, Abed H, Beyari M. Common chief complaints of dental patients at Umm Al-Qura University n.d.
3. Rosenberg PA. Clinical strategies for managing endodontic pain. Endodontic Topics. 2002;3:78–92.
4. Reader A, Nusstein J. Local anesthesia for endodontic pain. Endodontic Topics. 2002;3:14–30.
5. Malamed SF. Local anesthesia. J Calif Dent Assoc. 1998;26:657-660.
6. Malamed SF. Handbook of local anesthesia. Elsevier Health Sciences; 2004.
7. Ferger P. A new anesthetic in dental prosthetics. Dtsch Zahnarztl Z. 1973;8:87–9.
8. Malamed SF. Buffering local anesthetics in dentistry. Pulse. 2011;44:8–9.
9. Ramarao S, Sathyanarayanan U. CRA Grid - A preliminary development and calibration of a paper-based objectivization of caries risk assessment in undergraduate dental education. J Conserv Dent. 2019; 22:185–90.
10. Poorni S, Srinivasan MR, Nivedhitha MS. Probiotic strains in caries prevention: A systematic review. J Conserv Dent. 2019; 22:123–8.
11. Manohar MP, Sharma S. A survey of the knowledge, attitude, and awareness about the principal choice of intracanal medicaments among the general dental practitioners and nonendodontic specialists. Indian J Dent Res. 2018;29: 716–20.
12. Azeem RA, Sureshbabu NM. Clinical performance of direct versus indirect composite restorations in posterior teeth: A systematic review. J Conserv Dent. 2018;21:2–9.
13. Jenarthanan S, Subbarao C. Comparative evaluation of the efficacy of diclofenac sodium administered using different delivery routes in the management of endodontic pain: A randomized controlled clinical trial. J Conserv Dent. 2018;21:297–301.
14. Nandakumar M, Nasim I. Comparative evaluation of grape seed and cranberry extracts in preventing enamel erosion: An optical emission spectrometric analysis. J Conserv Dent. 2018;21:516–20.
15. Sureshbabu MN, Selvarasu K, V JK, Nandakumar M, Selvam D. Concentrated growth factors as an ingenious biomaterial in regeneration of bony defects after periapical surgery: A report of two cases. Case Rep Dent. 2019; 7046203.
16. Siddique R, Nivedhitha MS, Jacob B. Quantitative analysis for detection of toxic elements in various irrigants, their combination (precipitate), and para-chloroaniline: An inductively coupled plasma mass spectrometry study. J Conserv Dent. 2019;22:344–50.
17. Teja KV, Ramesh S, Priya V. Regulation of matrix metalloproteinase-3 gene expression in inflammation: A molecular study. J Conserv Dent. 2018;21:592–6.
18. Rajakeerthi R, Ms N. Natural Product as the Storage medium for an avulsed tooth – A systematic review. Cumhuriyet Dental Journal. 2019;22:249–56.
19. Siddique R, Nivedhitha MS. Effectiveness of rotary and reciprocating systems on microbial reduction: A systematic review. J Conserv Dent. 2019;22:114–22.
20. Janani K, Sandhya R. A survey on skills for cone beam computed tomography interpretation among endodontists for endodontic treatment procedure. Indian J Dent Res. 2019;30:834–8.
21. Siddique R, Sureshbabu NM, Somasundaram J, Jacob B, Selvam D. Qualitative and quantitative analysis of precipitate formation following interaction of chlorhexidine with sodium hypochlorite, neem, and tulsi. J Conserv Dent. 2019; 22:40–7.
22. Rajendran R, Kunjusankaran RN, Sandhya R, Anilkumar A, Santhosh R, Patil SR. Comparative evaluation of remineralizing potential of a paste containing bioactive glass and a topical cream containing casein phosphopeptide-amorphous calcium phosphate: An in vitro study. Pesqui Bras Odontopediatria Clin Integr. 2019;19:1–10.
23. Govindaraju L, Neelakantan P, Gutmann JL. Effect of root canal irrigating solutions on the compressive strength of tricalcium silicate cements. Clin Oral Investig. 2017;21:567–71.
24. Khandelwal A, Palanivelu A. Correlation between dental caries and salivary
albumin in adult population in Chennai: An in vivo study. BDS. 2019;22:228–33.

25. Frank SG, Lalonde DH. How acidic is the lidocaine we are injecting and how much bicarbonate should we add? Can J Plast Surg. 2012;20:71–3.

26. Shurtz R, Nasstein J, Reader A, Drum M, Fowler S, Beck M. Buffered 4% articaine as a primary buccal infiltration of the mandibular first molar: A prospective, randomized, double-blind study. J Endod. 2015;41:1403–7.

27. Kurien RS, Goswami M, Singh S. Comparative evaluation of anesthetic efficacy of warm, buffered and conventional 2% lignocaine for the success of inferior alveolar nerve block (IANB) in mandibular primary molars: A randomized controlled clinical trial. J Dent Res Dent Clin Dent Prospects. 2018;12:102–9.

28. Becker DE, Reed KL. Essentials of local anesthetic pharmacology. Anesth Prog. 2006;53:98–108; quiz 109–10.

29. Comparison of Pain of Conventional to Buffered Local Anesthesia During Injection in Pediatric Dental Patients - Full Text View - ClinicalTrials.gov n.d.

30. Cepeda MS, Tzortzopoulou A, Thackrey M, Hudcova J, Gandhi AP, Schumann R. Adjusting the pH of lidocaine for reducing pain on injection. Cochrane Database Syst Rev. 2010;CD006581.

31. Catchlove RFH. The influence of CO2 and pH on local anesthetic action. J Pharmacol Exp Ther. 1972;181:298–309.

32. Condouris GA, Shakalis A. Potentiation of the nerve-depressant effect of local anaesthetics by carbon dioxide. Nature. 1964;204:57–8.

33. Kung J, Mc Donagh M, Sedgley CM. Does articaine provide an advantage over lidocaine in patients with symptomatic irreversible pulpitis? A systematic review and meta-analysis. J Endod. 2015;41:1784–94.

34. Ramadurai N, Gurunathan D, Subramanian E, Samuel A. Local anesthetic used for dental treatment in children- Systematic review. British Journal of Medicine and Medical Research. 2016;13:1–9.

35. Ashraf H, Kazem M, Dianat O, Noghrehkar F. Efficacy of articaine versus lidocaine in block and infiltration anesthesia administered in teeth with irreversible pulpitis: A prospective, randomized, double-blind study. J Endod. 2013;39:6–10.

36. Boone L, Schumacher J, De Graves F, Cole R. Buffering mepivacaine with sodium bicarbonate speeds and potentiates analgesia of median and ulnar nerve blocks performed on horses. Vet Rec. 2019;184:155.

37. Chopra R, Jindal G, Sachdev V, Sandhu M. Double-blind crossover study to compare pain experience during inferior alveolar nerve block administration using buffered two percent lidocaine in children. Pediatr Dent. 2016;38:25–9.

38. Guo J, Yin K, Roges R, Enciso R. Efficacy of sodium bicarbonate buffered versus non-buffered lidocaine with epinephrine in inferior alveolar nerve block: A meta-analysis. Journal of Dental Anesthesia and Pain Medicine. 2018;18:129.

39. M MA, Khatri A, Kalra N, Tyagi R, Khandelwal D. Pain perception and efficacy of local analgesia using 2% lignocaine, buffered lignocaine, and 4% articaine in pediatric dental procedures. J Dent Anesth Pain Med. 2019;19:101–9.

40. Christoph RA, Buchanan L, Begalla K, Schwartz S. Pain reduction in local anesthetic administration through pH buffering. Ann Emerg Med. 1988;17:117–20.

41. Mutalik S. How to make local anesthesia less painful. J Cutan Aesthet Surg. 2008;1:37–8.

42. Afolabi O, Murphy A, Chung B, Lalonde DH. The effect of buffering on pain and duration of local anesthetic in the face: A double-blind, randomized controlled trial. Can J Plast Surg. 2013;21:209–12.

43. Kattan, S. et al. Do buffered local anesthetics provide more successful anesthesia over non-buffered solutions in patients requiring dental therapy? – A
systematic review & meta-analysis.
University of Pennsylvania; 2017.
Available: https://repository.upenn.edu/dental_theses/19

Accessed: 2 August 2020.

44. Lumbini P, Agarwal P, Kalra M, Krishna KM. Nanorobotics in dentistry. Ann Dent Spec. 2014;2:95–6.

© 2020 Hemmanur and Nasim; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/59718