Original Article - Comparative Study

Buffered versus Non-buffered Local Anaesthesia in Minor Oral Surgery - A Comparative Study

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Abstract

Introduction: Commercially available local anaesthetics are acidic solutions associated with the vasopressor sting on injection, relatively slower onset of action and pain during palatal injections. The above drawbacks can be addressed by anaesthetic buffering. This prospective study was aimed at comparing the efficacy of buffered and non-buffered local anaesthesia in the extraction of grossly decayed maxillary molar teeth in relation to pain on local infiltration, onset and duration of action of local anaesthesia. **Materials and Methods:** This is a prospective randomised controlled trial done on 100 patients who required bilateral extraction of maxillary molar teeth. In the study group, patients were given buffered local anaesthesia (which was prepared by mixing 2% lignocaine with 1:80,000 adrenaline and 8.4% sodium bicarbonate) before extraction. In the control group, non-buffered local anaesthesia (2% lignocaine with 1:80,000 adrenaline) was given before extraction. **Results:** Statistical data confirmed that buffering reduces pain on infiltration, decreases the onset and increases the duration of action of the local anaesthesia compared to non-buffered local anaesthesia. All the parameters measured were statistically significant ($P = 0.001$). **Discussion:** The study concludes that buffered local anaesthesia was more beneficial than non-buffered local anaesthesia in reducing pain on injection, providing a quicker onset of local anaesthesia and increasing the duration of action of the local anaesthesia. Buffering is a safe, easy and efficient process and should be routinely followed to provide a better experience to the patients.

Keywords: Buffer, infiltration, local anaesthesia, pain, pH

Introduction

Local anaesthetics form the backbone of pain control techniques in dentistry. They are the only drugs that prevent the nociceptive impulse from reaching the patient's brain.[1] Despite numerous advances in dentistry, successful pain control during injection still poses a challenge. Anxiety and fear associated with the pain of local anaesthetic injection still remain one of the main reasons for the refusal of further dental treatment. Reducing pain during surgical procedures is beneficial for patients and surgeons alike. Commercially available local anaesthetics are acidic solutions formed by adding hydrochloride to maximise their water solubility and chemical stability. This increases their shelf life.[2] The pH of local anaesthetic solutions without epinephrine is about 6.5; epinephrine containing local anaesthetic solutions has a pH in the range of about 3.5–4.4. Two ionic forms of the local anaesthesia exist in equilibrium within an anaesthetic cartridge, RN (the uncharged, deionised, active free base form which is lipid soluble) and RNH+ (the charged or ionised cationic form, which is not lipid soluble).[1] It is believed that only the uncharged form of the local anaesthetic is capable of diffusion through interstitial tissues and transport across the nerve membrane.[3,4] The relative amounts of deionised and ionised forms of local anaesthetic are dependent on the pH of the solution, in accordance with the Henderson–Hasselbalch equation. For instance, at a pH of 3.5, 99.996% of the lidocaine hydrochloride is in (RNH+) ionised form, while only 0.004% will be in the (RN) deionised form. Only after the body buffers the pH of the anaesthetic solution closer towards the physiologic range (7.35–7.45) does the anaesthetic action begin to take effect. The time that this transformation requires is a key factor in anaesthetic latency.[1] Most amides are chemically unstable in

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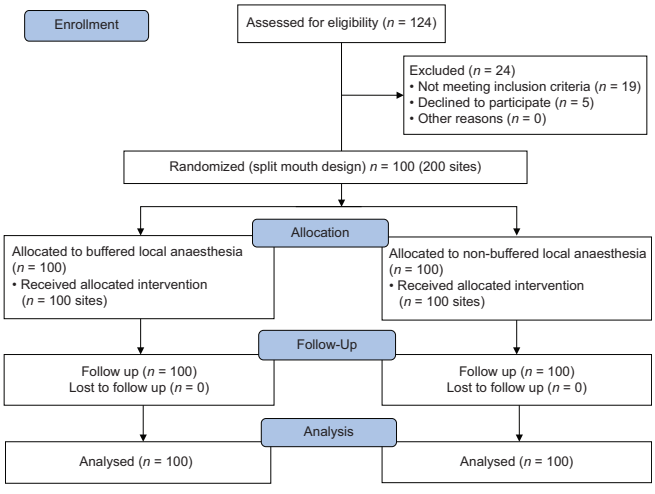
deionised form, being subject to photodegradation, aldehyde formation and other denaturing reactions.[5] This reduces the storage shelf life and solubility of the local anaesthesia. However, due to the acidic nature of the solution, local anaesthetics suffer a number of drawbacks, such as vasopressor sting on injection, a varying degree of post-injection tissue injury, a relatively slower onset and pain during palatal injections due to the tight binding of palatal mucosa to its underlying periosteum.[1,6] A number of methods were suggested to counteract these drawbacks, including the usage of a thin needle for injection, altering the temperature of the anaesthetic solution and buffering or alkalinisation of the local anaesthetic solution.[7] Alkalinisation refers to the addition of a planned amount of a basic solution to the local anaesthetic solution before injecting it into the target tissues.[2] The above drawbacks can be addressed by anaesthetic buffering, which is known to eliminate the sting, decrease tissue injury and reduce latency.[1]

The concept of buffering has not gained popularity in dentistry, although it has been widely used in other medical fields.[8] A few studies related to dentistry reported the usage of buffering in regional nerve blocks.[9,10] Therefore, this study was aimed at comparing the efficacy of buffered and non-buffered local anaesthesia in the extraction of maxillary molar teeth in relation to pain on local infiltration, the onset of local anaesthesia and the duration of action of local anaesthesia.

Materials and Methods

This prospective randomised controlled trial was done in the Department of Oral and Maxillofacial Surgery between 4th January 2021 and 15th July 2021 on 100 patients from the Telangana region who required bilateral extraction of maxillary molar teeth. All procedures performed in the study were conducted in accordance with the ethics standards given in the 1964 Declaration of Helsinki, as revised in 2013. The Institutional Ethical Committee approval for the study was obtained (MNR-EC/INST/2020/1169) and was done in accordance with the consolidated standards of reporting trials [Table 1]. The study was registered under Clinical Trial Registration of India with CTRI number (CTRI/2021/11/038274). An informed consent was taken from all the participants. The study was performed using the split mouth method, where one side maxillary molar tooth extraction was done by giving buffered local anaesthesia (study group) and the contralateral side maxillary molar tooth extraction was done by giving non-buffered local anaesthesia (control group). The control and study groups were assigned to the same patient to rule out bias due to individual variations.

Table 1: Consort flowchart



Inclusion criteria

1. Patients with bilateral grossly decayed maxillary molar teeth indicated for extraction
2. Patients with the American Society of Anesthesiologists status I.

Exclusion criteria

1. Subjects taking any medication such as analgesics, narcotics, sedatives and antidepressants that may affect anaesthetic assessment
2. Subjects who are unable to provide informed consent.

Patients who fulfilled the inclusion criteria were selected and the samples were divided into study and control groups by a computer-generated randomiser. The study and control groups each consisted of 100 grossly decayed maxillary molar teeth which were indicated for extraction. In the study group, patients were given buffered local anaesthesia (which was prepared by mixing 2% lignocaine with 1:80,000 adrenaline and 8.4% sodium bicarbonate) before extraction. In the control group, non-buffered local anaesthesia (2% lignocaine with 1:80,000 adrenaline) was given before extraction. All procedures were done by a single maxillofacial surgeon who was unaware of the type of local anaesthesia given to the patient. All parameters were assessed by a second investigator, who was blinded for the study.

For the study group, the buffered local anaesthetic solution was freshly prepared just before extraction by adding 0.18 mL of 8.4% sodium bicarbonate (Injection Sodac 8.4% w/v) with 1.8 mL of 2% lidocaine hydrochloride with 1:80,000 adrenaline, which yields a 1:10 dilution, following which it was given at the infiltration site with all aseptic precautions [Figure 1]. For the control group, non-buffered local anaesthesia (2% lignocaine with 1:80,000 adrenaline) was given before extraction, with all aseptic precautions. All the solutions were kept at room temperature.

Pain on infiltration was evaluated using the Visual Analogue Scale (VAS) [Figure 2]. The VAS has markings ranging from 0 to 10, 0 being 'no pain' and 10 being 'worst possible pain'. Patients were asked to rate their pain at the time of infiltration based on the intensity of pain experienced.

The onset of local anaesthesia is defined as the first sensation of numbness or tingling in the anaesthetised region. It was calculated from the point of retrieval of the needle after the injection to the time of onset of numbness, which was demonstrated on probing.

Duration of anaesthesia was calculated as the time lapsed from the time of injection until the patient required taking an analgesic. The patients were instructed not to take any analgesic before they perceived any pain.

Statistical analysis

The data were analysed using SPSS (Statistical Package for Social Sciences) statistical software version 19.0 developed by IBM (International Business Machines New York, USA). The intergroup comparison for the difference in mean scores between the two groups was made using the unpaired *t*-test.

Results

Table 2 describes the intergroup comparison of mean VAS scores of pain between the study group and the control group. The mean pain VAS scores were higher for the control group (3.71 ± 1.24) as compared to the study group (1.04 ± 0.952). The difference between the groups was statistically significant ($P = 0.001$) when analysed using an independent *t*-test at $P < 0.05$ significance level.

Table 3 describes the intergroup comparison of the time of onset of anaesthesia between the study group and the control group. The mean time of onset of anaesthesia was higher for the control group (1.88 ± 0.651) as compared to the study group (0.75 ± 0.160). The difference between the groups was statistically significant ($P = 0.001$) when analysed using an independent *t*-test at $P < 0.05$ significance level. Table 4 describes the intergroup comparison of the duration of anaesthesia between the study group and the control group. The mean duration of anaesthesia was higher for the study group (147.15 ± 15.08) than the control group (124.08 ± 8.597). The difference between the groups was statistically significant ($P = 0.001$) when analysed using independent *t*-test at $P < 0.05$ significance level.

Discussion

Oral anaesthesia is often perceived as a painful experience.[11] This pain is said to be a result of the low pH of the anaesthetic solution. Elevation of pH of local anaesthesia by the addition of sodium bicarbonate was first proposed by Louis Bignon in 1892.[12] Sodium bicarbonate is a systemic alkalinising agent. It increases plasma bicarbonate concentration, buffers excess hydrogen ions and raises the pH of the blood, thereby reversing clinical signs of acidosis.[13]

In the present study, the study group demonstrated a statistically significant reduction in pain on infiltration compared to the control group ($P = 0.001$). The study group reported a mean pain VAS score of 1.04, while the control group reported a mean pain VAS score of 3.71, demonstrating a two- to three-fold increase in pain during infiltration in the control group. This alleviation of pain associated with infiltration of buffered local anaesthesia could be attributed to the raising of local anaesthetic pH towards the physiologic range of 7.0–7.4, which reduces the direct tissue irritation caused by the infiltration of a more acidic compound. This is in accordance with Christoph *et al*.'s study, which reported a statistically highly significant ($P < 0.000001$) result, showing non-buffered local anaesthesia to be 2.8 times more painful than buffered local anaesthesia. Furthermore, Gupta *et al*., reported a mean pain VAS score of 3.4 for non-buffered local anaesthesia and 0.44 for buffered local anaesthesia. Arora *et al*., found a significant difference in the amount of pain on injection between the study and control groups ($P = 0.025$).[14] According to Kattan *et al*., buffering of local anaesthesia has a 2.29 times greater likelihood of achieving successful anaesthesia.[15] Bunke *et al*., and Senthoor *et al*., found a significant decrease in pain with buffered local anaesthesia compared to non-buffered local anaesthesia ($P < 0.05$, $P < 0.1$).[16,17] Furthermore, studies

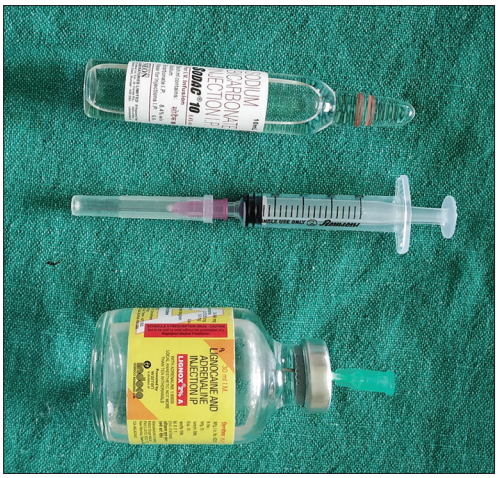
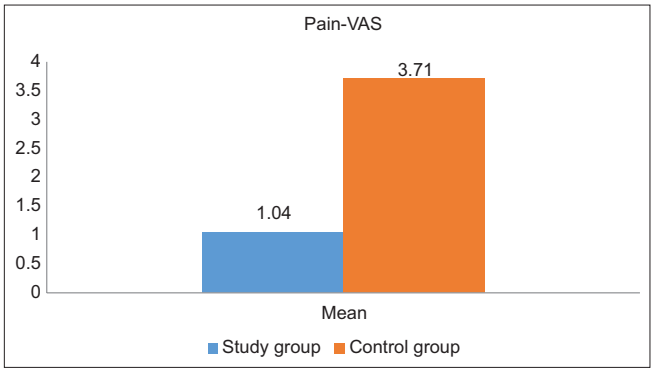


Figure 1: Buffered local anesthesia

Table 2: Intergroup comparison of pain Visual Analogue Scale scores

Group	*n*	Mean	SD	SEM	*P*	Significance
Study group (buffered local anaesthesia)	100	1.04	0.952	0.095	0.001	Significant
Control group (non-buffered local anaesthesia)	100	3.71	1.241	0.124		

Unpaired *t*-test at $P<0.05$ is significant. SD: Standard deviation, SEM: Standard error of the mean



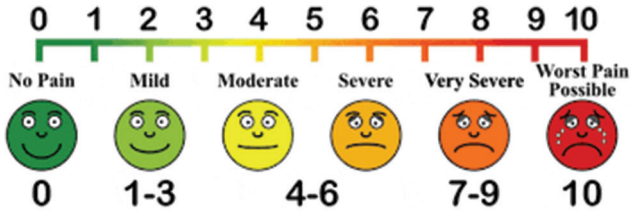


Figure 2: Visual analogue survey scale

done by Sunny Priyatham *et al*., Afsal *et al*., Warren *et al*., Shyamala *et al*., Tole and Neeli and Gandhi *et al*., reported a significantly lower pain score with buffered local anaesthesia ($P < 0.01$).[18-23] Vent *et al*., and Sadananda *et al*., reported the mean pH of buffered solution to be 6.9 ± 0.34, while that without bicarbonate was 3.4 ± 0.26. Sixty-five per cent of their sample reported more pain with non-buffered solution.[24,25] On the contrary, the studies by Whitcomb *et al*., Aulestia-Viera *et al*., Meincken *et al*., Chopra *et al*., Saatchi *et al*., Parirokh and Rabinowitz *et al*., showed that there was no significant difference in the pain on injection between the buffered and non-buffered local anaesthesia ($P > 0.05$).[26-31]

In the present study, the mean time taken for the onset of local anaesthesia in the study group was 0.75 min, while the control group reported 1.88 min, which was statistically significant ($P = 0.001$). The onset of action of local anaesthesia is determined primarily by its dissociation constant (pKa) level. It was postulated that buffering lowers the dissociation constant (pKa) of local anaesthesia, which in turn results in a greater number of deionised particles (RN). These deionised particles are lipid soluble and hence diffuse more readily into the nerve, leading to a more rapid and effective inhibition of nerve conduction.[32] When sodium bicarbonate is mixed with a local anaesthetic, it interacts with hydrochloric acid to create water and carbon dioxide. Condouris and Shakalis demonstrated that carbon dioxide possesses an independent anaesthetic effect and caused a seven-fold rise in the action of local anaesthesia.[33] Kashyap *et al*., and Arora *et al*.,[10, 14] found that the buffered group had a significantly faster onset of local anaesthesia when compared to the non-buffered group (34.4 s compared with 109.8 s) (1.06 min and 2.96 min), respectively. Furthermore, the studies by Jing Guo *et al*., Kurien *et al*., Phero *et al*., Bala *et al*., and Koja *et al*., reported a faster onset of buffered local anaesthesia when compared with non-buffered local anaesthesia ($P < 0.001$).[34-38] Whitcomb *et al*., in their study, could not establish a statistically significant difference in the onset of pulpal anaesthesia between the buffered and non-buffered local anaesthesia ($P > 0.05$).

This study showed a statistically significant ($P = 0.001$) increase in the duration of action of the local anaesthesia with a mean of 147.15 ± 15.081 min in the study group and 124.08 ± 8.591 min in the control group. Catchlove postulated that the increased duration of action of local anaesthesia was due to the by-products of the buffering reaction. The free carbon dioxide, which was the by-product of the buffering reaction, potentiates the action of lidocaine hydrochloride by a direct depressant action on the axon and also, the free carbon dioxide increases the concentration of the local anaesthetic within the nerve trunk through ion trapping and also helps in changing the charge of the local anaesthetic inside the nerve

Table 3: Intergroup comparison of onset of local anaesthesia

Group	*n*	Mean (min)	SD	SEM	*P*	Significance
Study group (buffered local anaesthesia)	100	0.75	0.160	0.016	0.001	Significant
Control group (non-buffered local anaesthesia)	100	1.88	0.651	0.061		

Unpaired *t*-test at $P<0.05$ is significant. SD: Standard deviation, SEM: Standard error of the mean

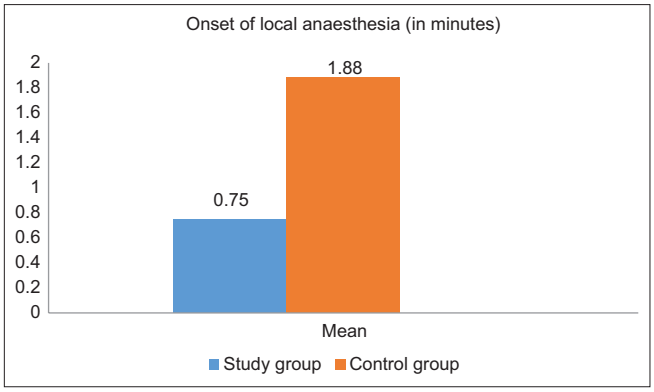
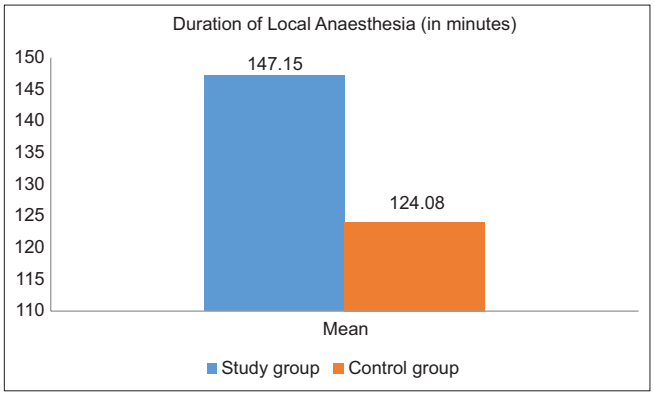


Table 4: Intergroup comparison of duration of local anaesthesia

Group	*n*	Mean	SD	SEM	*P*	Significance
Study group (buffered local anaesthesia)	100	147.15	15.081	1.508	0.001	Significant
Control group (non-buffered local anaesthesia)	100	124.08	8.597	0.859		

Independent *t*-test at $P<0.05$ is significant. SD: Standard deviation, SEM: Standard error of the mean



axon.[39] Our result correlates with Savina Gupta *et al*.,'s study, which reported a mean duration of action of local anaesthesia of 133.54 min and 111.76 min with the buffered and non-buffered local anaesthesia, respectively. The result was statistically significant ($P = 0.000$). Valiulla *et al*., Jain *et al*., and Torres-Rojas *et al*., reported the duration of action to be longer for the buffered local anaesthetic group (mean value: 148.24 ± 36.24 min) as compared to conventional local anaesthetic (mean value: 74.03 ± 22.09 min).[40-42] Few other studies compared buffered and non-buffered articaine reported significant results with buffering with respect to the pain and onset parameters.[43-45]

The limitations that were observed with buffered local anaesthetics are, they are not readily available in the market, due to reduced shelf life. As a result, these buffered local anaesthetics need to be freshly prepared just before minor oral surgical procedures. Research should be aimed at improving the shelf life of buffered local anaesthetics so that they are readily available in the market and can be extensively used in minor oral surgical procedures owing to the advantages offered with respect to less pain on injection, faster onset and increased duration of action of local anaesthesia.

Conclusion

Ideally, a good anaesthetic agent should provide no pain or toxicity, should work quickly and allow enough duration for the completion of a minor oral surgical procedure. However, no local anaesthesia can provide a perfect blend of all the above characteristics. The present study concludes that buffered local anaesthesia was beneficial in terms of reducing pain on injection, providing a quicker onset of local anaesthesia and increasing the duration of action of the local anaesthesia. Buffering is a safe, easy and efficient process that should be routinely followed to provide a better experience to patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Malamed SF. Buffering local anesthetics in dentistry. Pulse 2011;44:7-9.
2. Brandis K. Alkalinisation of local anaesthetic solutions. Aust Prescr 2011;34:173-5.
3. Ritchie JM, Ritchie B, Greengard P. The active structure of local anesthetics. J Pharmacol Exp Ther 1965;150:152-9.
4. Strobel GE, Bianchi CP. The effects of pH gradients on the action of procaine and lidocaine in intact and desheathed sciatic nerves. J Pharmacol Exp Ther 1970;172:1-17.
5. Christoph RA, Buchanan L, Begalla K, Schwartz S. Pain reduction in local anesthetic administration through pH buffering. Ann Emerg Med 1988;17:117-20.
6. McArdle BF. Painless palatal anesthesia. J Am Dent Assoc 1997;128:647.
7. Eccarius SG, Gordon ME, Parelman JJ. Bicarbonate-buffered lidocaine-epinephrine-hyaluronidase for eyelid anesthesia. Ophthalmology 1990;97:1499-501.
8. Gupta S, Mandlik G, Padhye MN, Kini YK, Kakkar S, Hire AV. Combating inadequate anesthesia in periapical infections, with sodium bicarbonate: A clinical double blind study. Oral Maxillofac Surg 2014;18:325-9.
9. Whitcomb M, Drum M, Reader A, Nusstein J, Beck M. A prospective, randomized, double-blind study of the anesthetic efficacy of sodium bicarbonate buffered 2% lidocaine with 1: 100,000 epinephrine in inferior alveolar nerve blocks. Anesth Prog 2010;57:59-66.
10. Kashyap VM, Desai R, Reddy PB, Menon S. Effect of alkalinisation of lignocaine for intraoral nerve block on pain during injection, and speed of onset of anaesthesia. Br J Oral Maxillofac Surg 2011;49:e72-5.
11. Gupta S, Kumar A, Sharma AK, Purohit J, Narula JS. "Sodium bicarbonate": An adjunct to painless palatal anesthesia. Oral Maxillofac Surg 2018;22:451-5.
12. Bignon A. On the anaesthetic properties of cocaine. Bull Gen Ther Med Chirurg Obstet Pharma 1892;122:170-2.
13. Dollery C. Therapeutic Drugs. 2nd ed. London: Churchill Livingstone; 1998.
14. Arora G, Degala S, Dasukil S. Efficacy of buffered local anaesthetics in head and neck infections. Br J Oral Maxillofac Surg 2019;57:857-60.
15. Kattan S, Lee SM, Hersh EV, Karabucak B. Do buffered local anesthetics provide more successful anesthesia than nonbuffered solutions in patients with pulpally involved teeth requiring dental therapy? A systematic review. J Am Dent Assoc 2019;150:165-77.
16. Bunke J, Sheikh R, Hult J, Malmsjö M. Buffered local anesthetics reduce injection pain and provide anesthesia for up to 5 hours. J Plast Reconstr Aesthet Surg 2018;71:1216-30.
17. Senthoor P, Janani K, Ravindran C. A prospective, randomized double-blinded study to evaluate the efficacy of buffered local anesthetics in infected and inflamed pulp and periapical tissues. J Maxillofac Oral Surg 2020;19:246-50.
18. Tirupathi SP, Rajasekhar S. Buffered versus unbuffered local anesthesia for inferior alveolar nerve block injections in children: A systematic review. J Dent Anesth Pain Med 2020;20:271-9.
19. Afsal MM, 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.
20. Warren VT, Fisher AG, Rivera EM, Saha PT, Turner B, Reside G, *et al.* Buffered 1% lidocaine with epinephrine is as effective as non-buffered 2% lidocaine with epinephrine for mandibular nerve block. J Oral Maxillofac Surg 2017;75:1363-6.
21. Shyamala M, Ramesh C, Yuvaraj V, Suresh V, SathyaNarayanan R, Balaji TS, *et al*. A comparative study between bupivacaine with adrenaline and carbonated bupivacaine with adrenaline for surgical removal of impacted mandibular third molar. J Maxillofac Oral Surg 2016;15:99-105.
22. Tole N, Neeli A. Evaluation of the efficacy of buffered local anesthetic in extraction of infected teeth-randomized double-blind study. Oral Maxillofac Surg 2024;28:803-7.
23. Gandhi N, Shah N, Wahjuningrum DA, Purnomo S, Nooshian R, Arora S, *et al.* Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis-a randomized clinical study. PeerJ 2022;10:e14187.
24. Vent A, Surber C, Graf Johansen NT, Figueiredo V, Schönbächler G, Imhof L, *et al.* Buffered lidocaine 1%/epinephrine 1:100,000 with sodium bicarbonate (sodium hydrogen carbonate) in a 3:1 ratio is less painful than a 9:1 ratio: A double-blind, randomized, placebo-controlled,

crossover trial. J Am Acad Dermatol 2020;83:159-65.
25. Sadananda V, Jubana M K, Hegde M, Shetty A, Gatti P. Comparison of buffered and non-Buffered lidocaine: PH and pain perception. World Acad Sci J 2022;4:37.
26. Aulestia-Viera PV, Braga MM, Borsatti MA. The effect of adjusting the pH of local anaesthetics in dentistry: A systematic review and meta-analysis. Int Endod J 2018;51:862-76.
27. Meincken M, Norman C, Arevalo O, Saman DM, Bejarano T. Anesthesia onset time and injection pain between buffered and unbuffered lidocaine used as local anesthetic for dental care in children. Pediatr Dent 2019;41:354-7.
28. 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.
29. Saatchi M, Khademi A, Baghaei B, Noormohammadi H. Effect of sodium bicarbonate-buffered lidocaine on the success of inferior alveolar nerve block for teeth with symptomatic irreversible pulpitis: A prospective, randomized double-blind study. J Endod 2015;41:33-5.
30. Parirokh M. Buffered lidocaine with sodium bicarbonate did not increase inferior alveolar nerve block success rate in patients having symptomatic irreversible pulpitis. J Evid Based Dent Pract 2016;16:59-61.
31. Rabinowitz Y, Williams S, Triana RR, Khan MT, Hooker KJ, Dubey A, *et al.* Assessing the efficacy of buffered versus nonbuffered lidocaine in dental extractions: A double-blinded randomized controlled trial. J Oral Maxillofac Surg 2024;82:684-91.
32. Ritchie JM, Greengard P. On the mode of action of local anesthetics. Annu Rev Pharmacol 1966;6:405-30.
33. Condouris GA, Shakalis A. Potentiation of the nerve-depressant effect of local anaesthetics by carbon dioxide. Nature 1964;204:57-8.
34. 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. J Dent Anesth Pain Med 2018;18:129-42.
35. 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.
36. Phero JA, Nelson B, Davis B, Dunlop N, Phillips C, Reside G, *et al.* Buffered versus non-buffered lidocaine with epinephrine for mandibular nerve block: Clinical outcomes. J Oral Maxillofac Surg 2017;75:688-93.
37. Bala M, Taiwo AO, Ibikunle AA, Olasoji HO, Sulaiman AO, Chukwuma BC, *et al.* Effectiveness of buffered and non-buffered local anaesthetic in inferior alveolar nerve block: A randomised study. Br J Oral Maxillofac Surg 2023;61:351-5.
38. Koja DB, Bede SY. Evaluation of buffered local anaesthesia in dental extraction: A randomized controlled study. Oral Surg 2022;15:489-95.
39. Catchlove RF. The influence of CO 2 and pH on local anesthetic action. J Pharmacol Exp Ther 1972;181:298-309.
40. Valiulla MU, Halli R, Khandelwal S, Mittal A, Singh A, Bhindora K. Efficacy of sodium bicarbonate-buffered local anesthetic solution in cases requiring bilateral maxillary premolar orthodontic extraction: A comparative split-mouth study. Cureus 2023;15:e37934.
41. Jain TK, Jha R, Tiwari A, Agrawal N, Mali S, Sinha A, *et al*. A comparative study to evaluate the anesthetic efficacy of buffered versus non-buffered 2% lidocaine during inferior alveolar nerve block. Cureus 2022;14:e31855.
42. Torres-Rojas K, Chumpitaz-Cerrate V, Chávez-Rimache L, Núñez-Díaz D, Pérez-Jimenez V. Comparison of the anesthetic effect of alkalized lidocaine versus non-alkalized lidocaine administered at a slow rate in mandibular primary molars. J Dent Res Dent Clin Dent Prospects 2023;17:47-53.
43. Dhake P, Nagpal D, Chaudhari P, Lamba G, Hotwani K, Singh P. Buffered articaine infiltration for primary maxillary molar extractions: A randomized controlled study. J Dent Anesth Pain Med 2022;22:387-94.
44. Manta K, Dabarakis N, Lillis T, Fotopoulos I. Anesthetic efficacy of buffered 4% articaine for mandibular first molar infiltration: A crossover clinical trial. J Dent Anesth Pain Med 2023;23:135-41.
45. Kalra G, Makkar S, Menrai N, Kalia V, Suri N, Gupta S. Comparative evaluation of the efficacy and onset of local anesthesia using buffered 2% lidocaine with 1:100,000 adrenaline, non-buffered 2% lidocaine with 1:100,000 adrenaline, buffered 4% articaine with 1:100,000 adrenaline and non-buffered 4% articaine with 1:100,000 adrenaline in dental extraction. J Maxillofac Oral Surg 2023;1-6. DOI:10.1007/s12663-023-01945-0.