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Use of Alkalinized 2% Lignocaine Hydrochloride with Adrenaline 1:80,000 and Commercial 2% Lignocaine Hydrochloride with Adrenaline 1: 80,000 in Intraoral Nerve Blocks: A Comparative Study

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ABSTRACT

Background: Local anaesthetics are the safest and the most effective drugs in medicine for the prevention and management of pain. Injections of lignocaine as local anaesthetic for pain control in oral and maxillofacial surgery can be painful with onset of anaesthesia is from 3 to 5 min. Sodium bicarbonate has been used worldwide to reduce both these drawbacks to the injection, for making procedures more acceptable.

Material and method: This randomised prospective trial of 55 patients aged above 18years who were given inferior alveolar nerve blocks was designed to assess the effect of alkalinisation of the lignocaine solution with sodium bicarbonate. All patients were given 2% lignocaine hydrochloride with adrenaline 1:80,000 and 55 patients (110 sites) were randomly allocated to be given 8.4% sodium bicarbonate in a 1/10 dilution. Pain was measured on a visual analogue scale (VAS).

Results: Our results have showed the efficacy of the alkalinised local anaesthetic solution in reducing pain on injection and resulting in quicker onset of anaesthesia.

Conclusion: we concluded that bicarbonate alkalinisation is an effective, practical and inexpensive method of decreasing the discomfort experienced by patients receiving local anaesthetic with rapid onset of anaesthesia and increased duration of anaesthesia.

Keywords: Lidocaine, Alkalinisation, Sodium bicarbonate, Pain, Onset of anaesthesia.

INTRODUCTION

Local anaesthetics represent some of the most widely used drugs in medicine and dentistry.[1] Local anaesthetics are the safest and the most effective drugs in medicine for the prevention and management of pain.[2] Injection of local anaesthetics in dental procedure is often painful and therefore is bad enough for some patients to decline further interventions under local anaesthesia.[3] Thus, the patient's ability to tolerate the injection of local anaesthetic is vital. Relatively pain free nerve blocks can be useful for local anaesthetic outpatient procedures (e.g. trans buccal or infraorbital nerve block). Other suggested ways to reduce the pain of local anaesthetic administration include topical use of local anaesthesia, using a thin needle for injection, slow injection, injecting during needle

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withdrawal, altering the temperature of the anaesthetic solution, addition of enzymes, oils which causes blockade of pain and reducing a pain.[4] One of the many reasons for pain during administration of local anaesthesia, is the acidity of the solution which is thought to be the most important, and hence buffered carbonated solutions or alkalinisation of the solutions can be preferred.

Lignocaine has to be used in combination with adrenaline to produce adequate duration of anaesthesia for routine minor oral surgical procedures. Addition of adrenaline (1:80,000) in 2% lignocaine decreases the pH of local anaesthetic solution leading to increased acidity. To decrease photo degradation, aldehyde formation and other denaturing reactions which affect non-ionised lignocaine molecules, lignocaine solutions are marketed as acidic solutions. This prolongs their shelf-life but also makes them painful to inject. Anaesthetic solution acidity may contribute to lengthy anaesthetic waiting periods and cause the burning during injection.[1] Neutralising these acidic solutions has been shown to decrease the pain of administration.[4]

Alkalinizing dental anaesthetic was first studied by Gros and then written about by Laewen in 1910.[1] Two strategies have been employed for alkalinisation: either addition of sodium bicarbonate or carbon dioxide.[5] The use of bicarbonate buffering of local anaesthetics to reduce pain has been evaluated. Sodium bicarbonate is a systemic alkalinizing agent. It increases the plasma bicarbonate concentration, buffers excess hydrogen ions, and raises the pH of blood, thereby reversing clinical sign of acidosis and sodium ions blocking certain sodium channel. Sodium bicarbonate local anaesthetic solution is used to increase the pH to more physiological pH.[3] Raising the pH by the addition of sodium bicarbonate enhanced diffusion of local anaesthetic across nerve membranes resulting in a more rapid speed of onset and therefore an enhanced efficacy when used for regional blockade. Such alkalinisation of lignocaine has been shown in volunteers to reduce the pain of infiltration.[6]

Addition of sodium bicarbonate in commercially (standard) available 2% lignocaine with adrenaline (1:80,000), increases the pH of solution hence reduces the pain during injection, decreases the onset of anaesthesia and increases duration of anaesthesia. So, we conducted a randomized, double blind study compares the efficacy of alkalinized (8.4% sodium bicarbonate) 2% lignocaine hydrochloride with adrenaline 1: 80,000 and commercial (standard) 2% lignocaine hydrochloride with adrenaline 1: 80,000 in intraoral nerve blocks.

MATERIAL AND METHOD

Prospective double blind, randomized study of 55 patients each for both group (110 sites) was conducted on healthy volunteers (ASA-I) irrespective of gender, race and caste to compare the effect of alkalinized 2% lignocaine hydrochloride with adrenaline 1: 80,000 and commercial (standard) 2% lignocaine hydrochloride with adrenaline 1: 80,000 on pain during injection, onset of anaesthesia and duration of anaesthesia in intraoral nerve blocks.

Inclusion criteria: Healthy individuals, aged over 18 years of either sex (ASA Class I and Class II) who were willing for study with informed sign consent.

Exclusion criteria: Patient having clinically significant medical history and falling in category ASA other than I and II, allergic to amide type of local anaesthesia, history of pregnancy, renal failure, respiratory or metabolic alkalosis, hypernatremia, hypoventilation, hypertension, oedema, congestive heart failure, history of urinary calculi, hypocalcaemia and receiving diuretics.

Methodology

Patients attending OPD of Department of Oral and Maxillofacial Surgery indicated for extraction were randomly divided into 2 groups according to the local anaesthetic solution used in which Study Group was received Inj alkalinized 2% lignocaine hydrochloride with adrenaline 1:80,000. Control Group was received Commercial (standard) Inj 2% lignocaine hydrochloride with adrenaline 1:80,000

Anaesthetic Solutions:

In control group Inj 2% lignocaine hydrochloride with 1:80,000 adrenalines and in study group Inj alkalinized 2% lignocaine hydrochloride with 1: 80,000 adrenalines were used. Alkalinized lignocaine was prepared immediately prior to

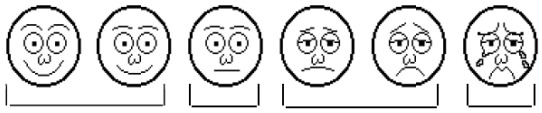
injection by mixing pharmaceutically prepared 1ml 8.4% sodium bicarbonate solution to 10 ml of 2% lignocaine with 1: 80,000 adrenaline. This preparation was used within 1 hour of its preparation in all cases.

Procedure:

After routine blood and radiographic investigations, pre-operative vitals were noted. Facial skin preparation was done with providone iodine solution and standard draping procedure were carried out.

Local anaesthetic solutions were preloaded in non-pyrogenic, non-toxic, presterile single use 2ml syringe with 26G x 38mm long needle by the dental nurse. Required local anaesthetic solution was administered by intra oral nerve block technique. All patients receive anaesthetic solution at same rate. After administration of local anaesthetic, following parameters were recorded:

Pain during injection: Pain during injection was assessed using VAS (four-point scale) 0 = no pain; 1 = mild pain, 2= moderate pain and 3=severe pain by the patient.



VISUAL ANALOGUE SCALE (VAS)

Onset of anaesthesia:

The time of onset of anaesthesia was evaluated by using sharp end of a molt's no.9 periosteal elevator.

Duration of anaesthesia:

The time of duration of anaesthesia was measured from the time subjective symptom (numbness) was positive till the pain in the surgical area was felt. Routine post-operative instructions and medications including analgesics and antibiotics were given to patients.

Fig 1: Materials: a) 2% Lignocaine hydrochloride with adrenaline 1:80,000 b) inject. of 8.4% sodium bicarbonate solution.

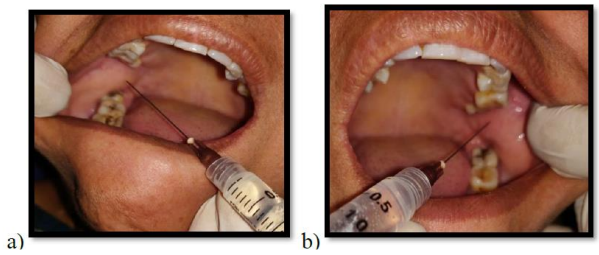


Fig 2: Intra oral nerve block technique: a) Study site b) Control site.

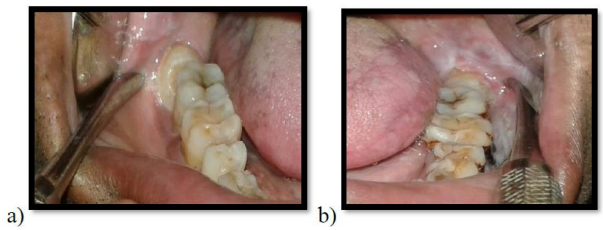


Fig 3: Onset of anaesthesia examine by sharp end of Periosteal elevator: a) Study site b) Control site.

After the administration of local anaesthetic solution, all the observations were noted.

RESULTS

Both sexes with age range 19 to 68 years were equally involved in the study 27 were males and 28 were females. Pain during injection was Checked by VAS scale which shows Statistically significant differences($P < 0.001$) for Group-I was 0.18 (SD: 0.39) versus 2.15 (SD: 0.49) for Group-II (Table – I, Graph- I).Time of onset of anaesthesia checked after giving nerve block which shows Statistically significant differences ($P < 0.001$) for Group-I was 15.25 (SD: 4.63) versus 85.85 (SD: 17.70) for Group-II (Table – II, Graph- II).Duration of anaesthesia was assessed by patient when they first take pain medication which shows Statistically significant differences ($P < 0.001$) for Group-I was 191.58 (SD: 19.49) versus 75.62 (SD: 15.82) for Group-II (Table – III, Graph- III).

Table I: Pain during injection (Checked by VAS scale).

GROUP	N	Mean	Std. Deviation	Std. Error Mean	Mean Difference	P VALUE
STUDY	55	0.18	0.39	0.05	-1.96	<0.001 Statistically significant
CONTROL	55	2.15	0.49	0.07		

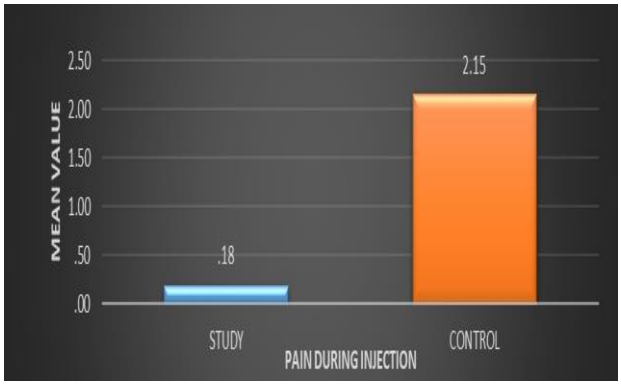
Table II: Time of Onset of Anaesthesia.

GROUP	N	Mean	Std. Deviation	Std. Error Mean	Mean Difference	P VALUE
STUDY	55	15.25	4.63	0.62	-70.60	<0.001 Statistically significant
CONTROL	55	85.85	17.70	2.39		

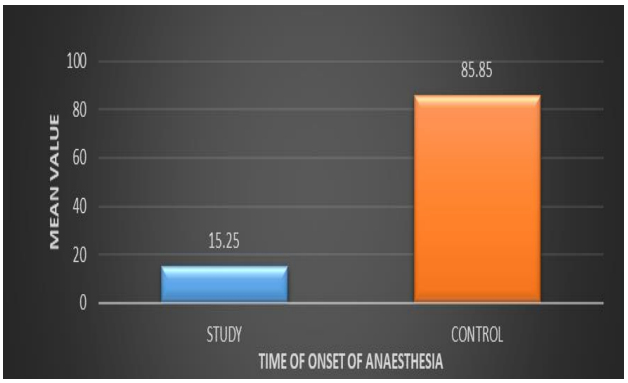
Table III: Duration of Anaesthesia.

GROUP	N	Mean	Std. Deviation	Std. Error Mean	Mean Difference	P VALUE
STUDY	55	191.58	19.49	2.63	115.96	<0.001 Statistically significant
CONTROL	55	75.62	15.82	2.13		

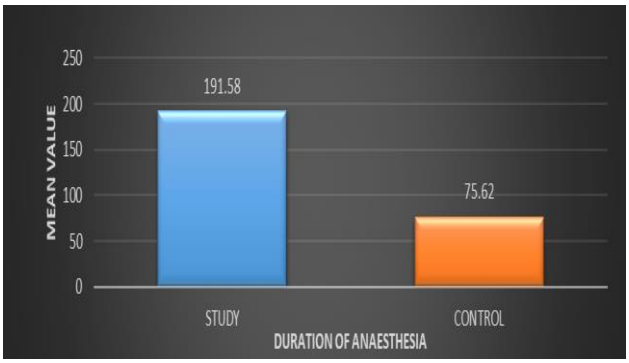
Graph I: Pain during injection (Checked by VAS scale):



Graph II: Time of Onset of Anaesthesia (in seconds)



Graph III: Duration of Anaesthesia (in minutes),



DISCUSSION

Pain is a message to the brain that damage has occurred or is about to occur. A reduction in the pain associated with local anaesthetic injections will reduce the fear of dental treatment, and patients will then be more likely to seek care.[1]

Local anaesthetics have evolved into the safest drugs used in medicine for pain management and they are the most commonly used drugs in dentistry to block the sensation of pain by reversibly blocking nerve conduction when applied to a circumscribed area of the body. However, there are several drawbacks associated with the administration of local anaesthetics. Local anaesthetics are acidic upon injection and cause stinging and burning sensation, they are unreliable in areas of inflammation and infection, they have a relatively slow onset of action, and they can cause post-injection tissue trauma.[10]

Option to reduce the pain of local anaesthesia includes a topical use of local anaesthesia, using a thin needle for injection, slow injection, injecting during needle withdrawal, altering the temperature of the anaesthetic solution, addition of enzymes, oils, avoiding the use of epinephrine and

alkalinizing lidocaine by adding small amounts of sodium bicarbonate solution.[4,10] sodium bicarbonate raises the ph. of local anaesthetic solution which enhanced diffusion of local anaesthetic across nerve membranes resulting in a more rapid speed of onset and therefore an enhanced efficacy.[6] Alkalinizing increases the lipophilic uncharged free base from the lignocaine molecule for diffusion into the nerve membrane. When extracellular pH is increased by alkalinisation, the decreased intracellular pH may increase the effect of local anaesthesia through protonation of intracellular free base local anaesthetics and increase the concentration gradient for free base local anaesthetic across the plasma membrane.[3]

Sodium bicarbonate is available from pharmacy in 7.5% and 8.4% concentration in multidosage cartridge, bulb and vial. For alkalinisation of local anaesthetic solution 1ml of it has to mix with 10ml of commercial 2% lignocaine with adrenaline (1:80,000) immediately prior to its use. The remaining sodium bicarbonate solution can be stored at 4°C in a refrigerator for the next preparation of alkalinized 2% lignocaine with adrenaline solution without altering its pH, stability, sterility and concentration for 14 days.[7]

All patients had their pain evaluation after retrieval of injection needle. Pain was measured by using VAS scale. In our study, the mean pain during injection for Group-I (Study group) was 0.18 (SD: 0.39) versus 2.15 (SD: 0.49) for Group-II (Control group). Statistically significant differences were observed between the two anaesthetic solutions ($P < 0.001$). In this study greater patient comfort and reduce pain during injection were recorded in alkalinized 2% lignocaine hydrochloride compare to commercial (standard) 2% lignocaine hydrochloride during intraoral nerve blocks.

In the comparative study done on the effect of pH adjusted lidocaine [used 8.4% $NAHCO_3$ solution to 2% lidocaine with epinephrine 1: 80,000] and commercial lidocaine for maxillary infiltration anesthesia in 200 patients, pH adjusted anesthesia recorded reduced injection pain and enhanced depth of anesthesia with periapical lesion[5] which coincides with other studies in different concentrations.[2,3,9]

The time of onset of anesthesia was calculated from the point of retrieval of needle after injection, to the time of achieving objective signs of anesthesia instead of subjective symptoms, for the sake of convenience and accuracy. In our study, the mean time of onset of anesthesia for Group-I (study group) was 15.25 (SD: 4.63) versus 85.85 (SD: 17.70) for Group-II (control group). Statistically significant differences were observed between the two anaesthetic solutions ($P < 0.001$). In our study rapid onset of anesthesia was recorded with alkalinized 2% lignocaine hydrochloride anaesthetic solution compare to commercial (standard) 2% lignocaine hydrochloride during intraoral nerve blocks.

In the randomized prospective trial study of 100 patients on the effect of alkalinization of lignocaine [used 8.4% $NAHCO_3$ solution to 2% lidocaine with epinephrine 1: 80,000 (1:10 ratio)] for three nerve blocks (inferior alveolar, lingual, long buccal), alkalinization of lignocaine anaesthetics showed less pain or no pain during injection by VAS scale and increased onset of anaesthesia.[3]

Other study with 20 participants, each receiving non-alkalinized solution (2% lidocaine/epinephrine 1: 100,000 at pH 3.85) and alkalinized solution (2% lidocaine/epinephrine 1: 100,000 alkalinized to pH 7.31) for inferior alveolar nerve blocks, showed reduced anaesthetic onset time and increased patients comfort when alkalinized solution is used.[1]

This coincides with studies on different concentrations of alkalinized lignocaine with adrenaline injections.[2] The time of duration of anesthesia was measured from the time subjective symptom (numbness) was positive till the pain in the surgical area was felt. In our study, the mean duration of anaesthesia for Group-I (study group) was 191.58 (SD: 19.49) versus 75.62 (SD: 15.82) for Group-II (control group). Statistically significant differences were observed between the two anaesthetic solutions ($P < 0.001$). Result of this study showed increased duration of anaesthesia with alkalinized 2% lignocaine hydrochloride compare to commercial (standard) 2% lignocaine hydrochloride after intraoral nerve blocks.

Hence on the basis of the present study and as per the support of the literature, it can be stated that the use of lidocaine hydrochloride in alkalinized or as

commercially available form for local anaesthesia have effect on the pain during injection, onset of anaesthesia and duration of anaesthesia.[2] Reduction of pain during injection, fast onset of anaesthesia and increased duration of anaesthesia are significant with alkalinized then commercial preparation of lignocaine hydrochloride in intraoral nerve blocks.

CONCLUSION

Based on all the observations and statistical analysis, the results of this study concluded that bicarbonate alkalinisation is an effective, practical and inexpensive method of decreasing the discomfort experienced by patients receiving local anaesthetic with rapid onset of anaesthesia and increased duration of anaesthesia. It does not delay the flow of patients through local anaesthetic lists and is of particular benefit. Further researches with larger samples and double blinded studies are required to develop newer anaesthetic protocol.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

REFERENCES

1. Stanley F. Malamed, Susan Tavana, Mic Falkel. Faster Onset and More Comfortable Injection with Alkalinized 2% Lidocaine with Epinephrine 1:100,000. Compendium Supplement – Research February 2013, Volume 34, Issue 2 Published by AEGIS Communications.

2. Stanley F. Malamend. Buffering Local Anaesthesia in dentistry. The pulse volume 44 issue 1 2011.

3. Vinay Mohan Kashyap, et al. Effect of alkalinisation of lignocaine for intraoral nerve block on pain during injection, and speed of onset of anaesthesia. British Journal of Oral and Maxillofacial Surgery 49 (2011) e72–e75.

4. J.E. Masters. Randomised control trial of Ph buffered lignocaine with adrenaline in outpatient operation. British journal of plastic surgery (1998) 51 385-387.

5. Fa'iz A Al–Sultan. Effectiveness of pH adjusted lidocaine versus commercial lidocaine for maxillary infiltration anesthesia. Al–Rafidain Dent J Vol. 4, No. 1, 2004.

6. A. R. Fitton et al. The use of pH adjusted lignocaine in controlling operative pain in the day surgery unit: a prospective, randomised trial. British Journal of Plastic Surgery (1996), 49, 404-408.

7. Jack T Seki et al. Stability of sodium bicarbonate injection 8.4% in syringes over a six-week period in refrigerated temperature. J Oncol Pharm Practice 2017; DOI: 10.1177/1078155217694493.

8. Kenneth d. Thompson, Sophia Welykyj, Mary C. Massa. Antibacterial Activity of Lidocaine in Combination with a Bicarbonate Buffer. J Dermatol Surg Oncol 1993:19:216- 220

9. Shelley M. Parham, Janice L. Pasieka. Effect of pH Modification by Bicarbonate on Pain after Subcutaneous Lidocaine Injection. cjs, Vol. 39, No. 1, February 1996.

10. Stacy martin, Jeffrey S. Jones, Barbara N. Wann. Dose warming local anesthetic reduce the pain of subcutaneous injection?. American journal of emergency medicin 1996 volume 14 number 1.

11. Gerard X. Brogan, Adam J. Singer, Sharon M. Valentine, Henry C. Thode, Edward Giarrusso, Judd E. Hollander. Comparison of wound infection rates using plain versus buffered lidocaine for anesthesia of traumatic wounds. American journal of emergency medicine 1997, volume 15 number 1.

12. Amy a. Ernst, Eduardo Marvez-Valla, Todd G. Nick, Trevor Mills, Lucia Minvielle, Debra Houry. Topical Lidocaine Adrenaline Tetracaine (LAT Gel) Versus Injectable Buffered Lidocaine for Local Anesthesia in Laceration Repair. West j Med 1997 August; 167:79-81.

13. Shoichiro lbusuki, Hiroshi Katsuki, Mayumi Takasaki. Reducing the Pain associated with local anaesthetic infiltration for Open Carpal tunnel decompression. Journal of Hand Surgery (British and European Volume, 2004) 29B: 4: 399–401.

14. Michele Curatolo, Steen Peter-Felix, Lars Arendt-Nielsen, Rolf Lauber, Henrik Hogstrom, Pasquale Scaramozzino, Martin Luginbuhl, Thomas J. Sieber, Alex M. Zbinden. Adding Sodium Bicarbonate to

Lidocaine Enhances the Depth of Epidural Blockade. Article in Anesthesia & Analgesia March 1998; DOI: 10.1097/00000539-199802000-00024.

15. Catherine J. Sinnott, Joseph M. Garfield, Johannes G. Thalhammer, Gary R. Strichartz. Addition of Sodium Bicarbonate to Lidocaine Decreases the Duration of Peripheral Nerve Block in the Rat. American Society of Anesthesiologists 2000; 93:1045–52.

16. Dr. Ruby Mehta, Dr. D. D. Verma, Dr. Veena Gupta, Dr. A. K. Gurwara. To Study the effect of Alkalinization of Lignocaine hydrochloride on Brachial plexus block. Indian J.Anaesth. 2003;47(4) : 283-286.

17. I. C. Vossinakis, P. Stavroulaki, I. Paleochorlidis, L.S. Badras. The effect of extracellular pH and without bicarbonate on intracellular procaine concentration and anesthetic effects in crayfish giant axons. Anesthesiology 1998; 88; 1549-57.

18. C. K. Yiannakopoulos. Carpal Ligament Decompression under Local Anaesthesia: The Effect of Lidocaine Warming and Alkalinisation on Infiltration pain. Journal of hand surgery (British and European volume, 2004) 29b: 1: 32–34.

19. Simon G Frank MD, Donald H Lalonde. How acidic is the lidocaine we are injecting, and how much bicarbonate should we add?. J Plast surg 2012;20(2):71-74.

20. Demetra Daskalos Logothetis. Anesthetic Buffering: New Advances for Use in Dentistry. ID# 320452 rdhmagazine.com January 2013.

21. A. Robert Strazar, Peter Strazar, Donald H. Lalonde. Minimizing the Pain of Local Anesthesia Injection. Plast. Reconstr. Surg. 132: 675, 2013.

22. Oluwatola Afolabi, Amanda Murphy, Bryan Chung, Donald H Lalonde. 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(4):209-212.

23. Ravi Ranjan, Sriti Sinha, Ratanendra Kr. Mishra. Comparison of role of sodium bicarbonate (7.5%) as an alternative of hyaluronidase in ocular anaesthesia for cataract surgery. J of Evolution of Med and Dent Sci/ eISSN- 2278-4802, pISSN- 2278-4748/ Vol. 3/ Issue 22/June 02, 2014.

24. Mrinal Kumar, Ranmeet Batra, Sumit Chopra, Gaurav Verma, Ankit Aggarwal, Abhinav Garg. Role Of Alkalinization In Enhancing Efficacy Of The Local Anesthetic – A Clinical Study. Indian Journal of Dental Sciences. (March 2015, Issue:1, Vol.:7).

25. Vijetha Devaram, T. Padma, S. Sreenivas Rao. Study & Evaluate the Comparison of Plain Lignocaine and Lignacaine with Sodium bicarbonate effects in Supraclavicular Brachial plexus block. Journal of evidence based medicine and healthcare; volume 2, issue 35, august 31 2015; page: 5414-5425, doi: 10.18410/jebmh/2015/753.

26. Andrew W. Comerci, Steven C. Maller, Richard D. Townsend, John D. Teepe, Kraig S. Vandewalle. Effect of a new local anesthetic buffering device on pain reduction during nerve block injections, Published with permission of the Academy of General Dentistry. © Copyright November/December 2015 by the Academy of General Dentistry.

27. Aminah M, Priya Nagar, Parul Singh, Monali Bharti. Comparison of Topical Anesthetic Gel, Pre-Cooling, Vibration and Buffered Local Anesthesia on the Pain Perception of Pediatric Patients during the Administration of Local Anesthesia in Routine Dental Procedures. International Journal of Contemporary Medical Research Volume 4 | Issue 2 | February 2017 | ICV (2015): 77.83 |.

28. Charles D. Schlesinger. Buffered anesthetic usage in inferior alveolar blocks for 3rd-molar removal. Journal of Clinical and Experimental Dentistry dentaltown.com, july 2017.

29. Reenu Sarah Kurien, Mousumi Goswami, Sanjay Singh. 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 Prospect 2018; 12(2):102-109| doi: 10.15171/joddd.2018.016.

30. Jing Guo, Kaifeng Yin, Rafael Roges, Reyes Enciso. 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(3):129-142.