

Comparative Study on Effects of 2% Lidocaine Hydrochloride with Adrenaline (1:200000) on Blood Pressure Among Controlled Hypertensive and Non-hypertensive Patients During Dental Anesthesia

Lujaw Ratna Tuladhar,^{a,e} Meen Bahadur Budhathoki,^{b,e} Anjali Bhattarai,^{b,e} Kushal Bimb,^{b,e} Nikhil Acharya,^{c,e} Eans Tara Tuladhar^{d,f}

ABSTRACT:

Introduction: Local anesthetic used for dental extraction is 2% lidocaine hydrochloride with adrenaline (1:200000). Lidocaine is cardiac depressant and adrenaline is cardiac stimulant; it decreases or increases blood pressure respectively. **Methods:** A total of 100 patients (50 controlled hypertensive and 50 non-hypertensive) were selected. The study was conducted over a period of 14 months from January 2020 to February 2021. Blood pressure was measured for patients who were planned for dental extraction by auscultatory method. Following that, 1.5-3 ml (depending upon the nerve block) 2% lidocaine with adrenaline (1:200000) was injected using 3ml syringe (26 Gauge). Blood pressure was re-recorded after 10 minutes from the time of injection. Visual analog scale pain score was obtained during administration of local anesthesia. Paired t-test was applied to compare blood pressure change before and after administration of local anesthesia in controlled hypertensive and non-hypertensive patients. **Results:** There was a statistically significant increase in both systolic and diastolic blood pressure in non-hypertensive patients ($p = 0.008$, $p = 0.017$). This, however, was not the case with controlled hypertensive patients. There was statistically significant increase in systolic blood pressure ($p < 0.001$). Pain on injection (50% in non-hypertensive and 48% in controlled hypertensive patients) was the only adverse drug reaction that was reported in both groups. **Conclusion:** 2% lidocaine hydrochloride with adrenaline (1:200000) increased systolic but not diastolic blood pressure in controlled hypertensive patients.

Keywords: Adrenaline; Adverse drug reaction; Anesthesia, Dental; Hypertension; Lidocaine

INTRODUCTION:

Local anesthetics used during tooth extraction are 2% lidocaine hydrochloride with adrenaline (1:200000) and 2% plain lidocaine.[1,2] They decrease the unpleasant feeling of pain, however, studies have reported the use of plain lidocaine to

generate more pain compared to lidocaine with adrenaline.[3,4,5]

Lidocaine has cardiac depressant action whereas adrenaline has cardiac stimulant action that can either decrease or increase blood pressure (BP) respectively.[6,7] BP is an important cardiovascular parameter that is measured prior to dental extraction. [8] The normal BP is $\leq 120/80$ mm of Hg and hypertensive patients have BP of greater than 120/80mm of Hg.[9]

The objective of our study was to observe the effect of 2% lidocaine hydrochloride with adrenaline

How to cite this article:

Tuladhar LR, Budhathoki MB, Bhattarai A, Bimb K, Acharya N, Tuladhar ET. Comparative Study on Effects of 2% Lidocaine Hydrochloride with Adrenaline (1:200000) on Blood Pressure Among Controlled Hypertensive and Non-hypertensive Patients During Dental Anesthesia. Journal of Lumbini Medical College. 2021;9(1):6pages. DOI: <https://doi.org/10.22502/jlmc.v9i1.415>. Epub: May 2, 2021.

Submitted: 22 January, 2021

Accepted: 19 April, 2021

Published: 02 May, 2021

- a- Assistant Professor, Department of Pharmacology
- b- Lecturer, Department of Oral and Maxillo-facial Surgery
- c- Lecturer, Department of General Surgery
- d- Assistant Professor, Department of Biochemistry
- e- Nepal Medical College Teaching Hospital, Kathmandu, Nepal.
- f- Maharajgunj Medical Campus, Kathmandu, Nepal.

Corresponding Author:

Lujaw Ratna Tuladhar

e-mail: lujaw3@gmail.com

ORCID: <https://orcid.org/0000-0002-1626-1104>



Licensed under CC BY 4.0 International License which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

(1:200000) on blood pressure among controlled hypertensive and non-hypertensive patients during dental anesthesia.

METHODS:

It was a hospital based cross sectional study conducted in the Department of Oral and Maxillofacial Surgery, College of Dental science, Nepal Medical College Teaching hospital (NMCTH). Ethical approval was obtained from institutional review committee of NMCTH, Kathmandu. The study was commenced from January 2020 to February 2021 for the duration of 14 months. Sample size was calculated taking the reference to the study conducted by Chaudhry S as follows.[10]

$$\text{Sample size (n)} = z^2 \sigma^2 / d^2$$

where z (standard normal value at 95% confidence interval) = 1.96; σ^2 (variance) = $11.08^2 = 122.76$; d (margin of acceptable error) = $136.66 - 133.33 = 3.33$ [10]

$n = 42.53 \approx 43$. However, 50 patients were taken in each group.

The total estimated sample size for the current study was taken as 100 (50 controlled hypertensive and 50 non-hypertensive patients). Patients were explained about the procedure and informed consent was obtained. For participants under the age of 18 years, consent was obtained from accompanying guardian. Controlled hypertensive (121-139/81-89 mmHg) and non-hypertensive ($\leq 120/80$ mm Hg) patients from the age of 16 years and above whose treatment was planned for dental extraction were included in this study. Hypertensive patients with uncontrolled blood pressure ($\geq 140/90$ mm Hg) or patients not under anti-hypertensive medication were excluded from the study. Patients diagnosed with other co-morbid conditions like hyperthyroidism, angina, myocardial infarction, stroke, epilepsy, diabetes and allergic reaction to lidocaine were also excluded to avoid drug interactions.

Patients were asked to relax for five minutes in supine position in the dental chair. Prior to administration of local anesthetic, blood pressure was measured using conventional validated and calibrated Microlife® sphygmomanometer and Microlife® stethoscope using auscultatory method. Following that, 2% lidocaine with adrenaline (1:200000) (XICAINE®) was administered using a disposable aspirating type

3ml single use syringe. Anesthetic solution (1.5-3 ml) was deposited slowly at the rate of 1 ml per minute. Blood pressure was re-recorded after 10 minutes from the time of injection. Visual analog scale pain score rating (0-no hurt, 2-hurt little bit, 4-hurt little more, 6- hurt even more, 8- hurt whole lot, 10- hurt worse) was obtained during administration of local anesthesia. The entire procedure was done by the team of intern doctors under the supervision of the researchers.

Statistical analysis was done by using Statistical Package for Social Sciences (SPSS) version 16. Categorical variables were presented as frequency and age was presented as mean and standard deviation. Paired t-test was applied to compare mean of BP changes before and after the administration of local anesthesia in controlled hypertensive and non-hypertensive patients. p value less than 0.05 was considered as statistically significant.

RESULTS:

A total of 100 patients were included in the study; 50 controlled hypertensive patients (male = 13, female = 37) and 50 non-hypertensive patients (male = 29, female = 21).

The mean age of the controlled hypertensive group was 59.06 ± 8.45 years and non-hypertensive group was 44.22 ± 15.25 years.

Fifty percent (28% had grade 2, 12% had grade 4 and 10% had grade 6) of the non-hypertensive patients and forty eight percent (36% had grade 2 and 12% had grade 4) of the controlled hypertensive patients complained of pain during administration of local anesthetic.

There was a statistically significant increase in systolic ($t = -2.775$, $df = 49$, $p = 0.008$) and diastolic ($t = -2.473$, $df = 49$, $p = 0.017$) BP after administration of lidocaine with adrenaline in non-hypertensive patients though this was not the case with controlled hypertensive patients. We also observed highly significant increase in systolic blood pressure ($t = -3.932$, $df = 49$, $p < 0.001$) but no change in diastolic blood pressure ($t = 0.53$, $df = 49$, $p = 0.958$) in the controlled hypertensive group as shown in Table 1.

DISCUSSION:

Table 1: Mean Blood pressure (BP) before and after administration of local anesthetic with adrenaline in controlled hypertensive and non-hypertensive patients.

Case	Types of BP	Mean \pm SD of BP before and after administration of LA		Mean difference \pm SD	95% confidence interval		t-value	df	p value
		Before	After		Upper	Lower			
Non-hypertensive patients	Systolic	117.16 \pm 7.62	120.98 \pm 10.96	-3.82 \pm 9.73	-6.59	-1.05	-2.78	49	0.008
	Diastolic	75.08 \pm 6.55	78.16 \pm 10.68	-3.08 \pm 8.80	-5.58	-0.577	-2.47	49	0.017
Controlled hypertensive patients	Systolic	133.68 \pm 8.34	139.16 \pm 9.18	-5.48 \pm 9.85	-8.28	-2.68	-3.93	49	<0.001
	Diastolic	84.60 \pm 5.61	84.56 \pm 7.27	0.04 \pm 5.30	-1.55	1.55	0.53	49	0.958

*LA: Local anaesthetic, *SD: standard deviation

The aim of this study was to analyze the effect of 2% lidocaine with adrenaline (1:200000) on BP in controlled hypertensive and non-hypertensive patients during dental anesthesia.

Dental anesthesia minimizes pain and prevents endogenous catecholamine release that can trigger hemodynamic change like alteration in BP and heart rate.[11] The most widely used local anesthetic for dental anesthesia is lidocaine.[12] Lidocaine primary acts by blocking voltage gated inactivated sodium channel.[13] It also possesses additional cardiac depressant action which can decrease BP.[14] The benefits of lidocaine with adrenaline combination are: it slows the rate of absorption, lower systemic blood levels, delays cresting of peak blood level, prolongs duration of anesthesia, intensifies depth of anesthesia, provides bloodless field during procedure and reduces incidence of systemic reactions.[7] The onset of action of lidocaine with adrenaline is five minutes.[7] The most preferred concentration of local anesthetic for dental procedure is 2% lidocaine hydrochloride with adrenaline (1:200000).[12] 1 ml of it contains 2 mg lidocaine and 0.005mg adrenaline, a maximum of 3 ml will contain 6mg lidocaine and 0.015 mg adrenaline.[7] Studies have shown the maximum recommended dose for lidocaine is 500 mg and maximum dose for adrenaline that can be used 0.04mg.[7] Adrenaline has biphasic response i.e. at high concentration it increases BP due to vasoconstriction (α_1 receptor stimulation) whereas at low concentration it decreases BP due to vasodilation (β_2 receptor stimulation).[15] Therefore, lidocaine with adrenaline combination can either increase BP or

decrease BP depending on the plasma concentration of the respective drug.

There are various methods of measuring BP among which oscillometric and auscultatory methods are considered acceptable.[16] Although auscultatory method using mercury sphygmomanometer is regarded as the “gold standard” for blood pressure measurement, wide spread implementation on banning mercury diminished its role by this technique. [17] Calibrated aneroid sphygmomanometer has better accuracy than digital and should be used for proper and better management.[18] American college of cardiology/ American heart association (ACC/AHA) Hypertension guideline has categorized blood pressure of 130-139/80-89 as grade 1[19] and American Society of Anesthesiologists (ASA) physical status classification system (ASAPS) have classified a patient with a mild systemic disease e.g. treated hypertension as ASA 2.[20]

According to international guideline the use of local anesthetic containing adrenaline is safe in patients with controlled hypertension but there are studies that recommend use of plain lidocaine.[21] Pannerselvam E et al. in his study reported that patients who received plain lidocaine perceived less pain during injection of anesthetic solution when compared to patients who received lidocaine with vasoconstrictor. He also reported that post-operative wound healing was better in patients anesthetized by plain lidocaine.[2] In another study conducted by Kalra P et al. reported that lidocaine with adrenaline should be used with caution in diabetic patients as adrenaline suppresses the release of insulin leading

to increase in blood glucose level.[22] Similarly Muntaha S et al. in his study reported that 2% lidocaine with adrenaline is widely used but it should be cautiously used in diabetic patients.[12]

A study conducted by Chardhry S et al. in hypertensive and non-hypertensive patients reported decrease in systolic and diastolic BP after two and five min of injection. The volume of 2% lidocaine with adrenaline (1:100000) deposited was 3.6 ml that contained 0.036 mg adrenaline.[10] Cardiac depressant action of lidocaine and low concentration of adrenaline stimulated beta-2 receptor on the blood vessel leading to vasodilation and drop in blood pressure. The study did not report any adverse drug reaction.[10]

A study conducted by Karm M et al. observed increase in systolic BP (9.3 ± 7.3 mm Hg) but decrease in diastolic BP (-8.4 ± 6.6 mm Hg) with 2% lidocaine with 1:200000 adrenaline. [23] The study also reported that 2% lidocaine with 1:200000 adrenaline has better safety with regard to hemodynamic parameters than 2% lidocaine with 1:80000 adrenaline.[23]

Another study conducted by Kyosaka Y et al. observed increase in systolic blood pressure at the end of LA injection and decrease in diastolic blood pressure after 5 and 10 minutes of LA injection in participants on anti-hypertensive drugs. The local anesthetic used in this study was 2% lidocaine with 1:80000 adrenaline.[24]

Therefore, different studies have reported different results. This variation in result could be due to difference in volume and concentration of lidocaine and adrenaline, age of patient, co-morbidities, medication and types of nerve block (1.2ml for infraorbital nerve block, 1.8ml for posterior superior alveolar nerve block, 1.8 ml for inferior alveolar nerve block, 0.6ml for greater palatine nerve block, 0.4ml for naso-palatine nerve block).[7]

In our study, we observed the effect of 2% lidocaine with 1:200000 adrenaline on BP in non-hypertensive and controlled hypertensive patients. We investigated in 100 patients, 50 of them were non-hypertensive and 50 were controlled hypertensive patients (Grade 1, 130-139/80-89). We injected 1.5-3ml of 2% lidocaine with adrenaline (1:200000) that contained 0.0075- 0.015mg adrenaline. We observed that there was an increase in systolic and diastolic

blood pressure in non-hypertensive patients. However, controlled hypertensive patients presented with only increase in systolic blood pressure; we did not observe any significant variation in diastolic blood pressure. It is possible that when BP was measured lidocaine was not absorbed systemically (due to adrenaline) to produce cardiac depressant action and only adrenaline was absorbed which could have led to rise in BP. Rise in diastolic BP was not observed in controlled hypertensive patient, this could be due to the action of anti-hypertensive drugs.

In our study, pain on injection was the only adverse drug reaction reported. Fifty percent (28% had grade 2, 12% had grade 4 and 10% had grade 6) of the non-hypertensive patients and forty eight percent (36% had grade 2 and 12% had grade 4) of the hypertensive patients complained of pain during administration of local anesthetic. This difference could be due to difference in age group of the patients, speed of delivery of anesthesia, volume of anesthetic deposited. In a study conducted by Strazar A et al., it was reported that solution selection, topical site preparation with topical anesthetic and procedural technique can be followed to minimize pain on injection.[25] Another study conducted by Kashyap V et al., reported that alkalization of local anesthetic solution with sodium bicarbonate can reduce pain on injection.[26]

The study did not include patient with BP $\geq 140/90$ mm of Hg. The uncontrolled hypertensive patients (121-139/81-89 mm of Hg) were not included. Therefore, safety recommendation may not be applicable for the above group. BP was the only outcome parameter that was monitored.

CONCLUSION:

2% lidocaine hydrochloride with adrenaline (1:200000) increased systolic but not diastolic blood pressure in controlled hypertensive patients.

Conflict of Interest: The authors declare that no competing interests exist.

Financial Disclosure: No funds were available.

REFERENCES:

1. Abu-Mostafa N, Al-Showaikhat F, Al-Shubbar F, Al-Zawad K, Al-Banawi F. Hemodynamic changes following injection of local anesthetics with different concentrations of epinephrine during simple tooth extraction: A prospective randomized clinical trial. *J Clin Exp Dent*. 2015;7(4):e471–6. [PMID: 26535092](#) DOI: <https://doi.org/10.4317/jced.52321>.
2. Panneerselvam E, Balasubramanian S, Raja VBK, Kannan R, Rajaram K, Sharma AR A. ‘Plain lignocaine’ vs ‘Lignocaine with vasoconstrictor’—Comparative evaluation of pain during administration and post-extraction wound healing by a double blinded randomized controlled clinical trial. *Acta Odontologica Scandinavica*. 2016;74(5):374-9. DOI: <https://doi.org/10.3109/00016357.2016.1160148>.
3. Matsumura K, Miura K, Takata Y, Kurokawa H, Kajiyama M, Ade I, et al. Changes in blood pressure and heart rate variability during dental surgery. *Am J Hypertens*. 1998;11(11):1376-80. [PMID: 9832183](#) DOI: [https://doi.org/10.1016/s0895-7061\(98\)00157-5](https://doi.org/10.1016/s0895-7061(98)00157-5)
4. Laragnoit AB, Neves RS, Neves ILI, Vieira JE. Locoregional anesthesia for dental treatment in cardiac patients: a comparative study of 2% plain lidocaine and 2% lidocaine with epinephrine (1:100,000). *Clinics (Sao Paulo)*. 2009;64(3):177-82. [PMID: 19330241](#) DOI: <https://doi.org/10.1590/s1807-59322009000300005>
5. Ketabi M, Shamami MS, Alaie M, Shamami MS. Influence of local anesthetics with or without epinephrine 1/80000 on blood pressure and heart rate: A randomized double-blind experimental clinical trial. *Dent Res J (Isfahan)*. 2012;9(4):437-40. [PMID: 23162585](#) [PMCID: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc3491331/](http://www.ncbi.nlm.nih.gov/pmc/articles/pmc3491331/)
6. Ghavimi MA, Yazdeni J, Zadeh AG, Abdolkarimi A. Comparison of Heart Rate and Blood Pressure administration of anesthesia agent with and without. *International Journal of Current Research and Academic Review*. 2014;2(9):153-8. Available from: <http://www.ijcrar.com/vol-2-9/Mohammad%20Ali%20Ghavimi1,%20et%20al.pdf>
7. Malamed SF. *Handbook of local anesthesia*. 7th ed. Amsterdam: Elsevier; 2019. Available from: <https://www.elsevier.com/books/handbook-of-local-anesthesia/malamed/978-0-323-58207-0>
8. James O, Ladeinde AL, Ogunlew MO, Ajuluchukwu JNA, Adeyemo WL. Hemodynamic response after injection of local anesthetics with or without adrenaline in adult Nigerian subjects undergoing simple tooth extraction. *Journal of Clinical Sciences*. 2015;12(2):90-5. DOI: <https://doi.org/10.4103/1595-9587.169688>.
9. Kibria GMA, Swasey K, KC A, Mirbolouk M, Sakib MN, Sharmeen A, et al. Estimated Change in Prevalence of Hypertension in Nepal Following Application of the 2017 ACC/AHA Guideline. *JAMA Netw Open*. 2018;1(3):e180606. [PMID: 30646022](#) DOI: <https://doi.org/10.1001/jamanetworkopen.2018.0606>.
10. Chaudhry S, Iqbal HA, Izhar F, Mirza KM, Khan NF, Yasmeen R, et al. Effect on blood pressure and pulse rate after administration of an epinephrine containing dental local anaesthetic in hypertensive patients. *J Pak Med Assoc*. 2011;61(11):1088-91. [PMID: 22125984](#)
11. Silvestre FJ, Salvador-Martinez I, Bautista D, Silvestre-Rangil J. Clinical study of hemodynamic changes during extraction in controlled hypertensive patients. *Med Oral Patol Oral Cir Bucal*. 2011;16(3):e354–8. [PMID: 21196862](#) DOI: <https://doi.org/10.4317/medoral.16.e354>.
12. Muntaha ST, Fazal M, Khalida B, Khan K. Evaluation of Blood Glucose Concentration in Patients with Diabetes Undergoing Tooth Extraction after Administration of Local Anesthesia with or without Adrenaline. *Pakistan Oral & Dental Journal*. 2018;38(2):187-90. Available from: http://podj.com.pk/archive/June_2018/PODJ-9.pdf
13. McNulty MM, Edgerton GB, Shah RD, Hanck DA, Fozzard HA, Lipkind GM. Charge at the lidocaine binding site residue Phe-1759 affects permeation in human cardiac voltage-gated sodium channels. *The Journal of Physiology*. 2007;581(2):741-55. DOI: <https://doi.org/10.1113/jphysiol.2007.130161>
14. Torp KD, Metheny E, Simon LV. *Lidocaine toxicity*. Treasure Island (FL): StatPearls Publishing; 2021. [PMID: 29494086](#) Available from: <https://pubmed.ncbi.nlm.nih.gov/29494086/>
15. Lubberding AF, Thomsen MB. Low-

- Dose Adrenaline Reduces Blood Pressure Acutely in Anesthetized Pigs Through a β_2 -Adrenergic Pathway. *J Cardiovasc Pharmacol.* 2019;74(1):38-43. PMID: [31274841](https://pubmed.ncbi.nlm.nih.gov/31274841/) DOI: <https://doi.org/10.1097/FJC.0000000000000682>
16. Muntner P, Shimbo D, Carey RM, Charleston JB, Gaillard T, Misra S, et al. Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association. *Hypertension.* 2019;73(5):35-66. DOI: <https://doi.org/10.1161/HYP.0000000000000087>
17. Ogedegbe G, Pickering T. Principles and techniques of blood pressure measurement. *Cardiol Clin.* 2010;28(4):571-86. PMID: [20937442](https://pubmed.ncbi.nlm.nih.gov/20937442/)
18. Shahbabu B, Dasgupta A, Sarkar K, Sahoo SK. Which is More Accurate in Measuring the Blood Pressure? A Digital or an Aneroid Sphygmomanometer. *J Clin Diagn Res.* 2016;10(3):LC11-4. PMID: [27134902](https://pubmed.ncbi.nlm.nih.gov/27134902/) DOI: <https://doi.org/10.7860/jcdr/2016/14351.7458>
19. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force. *Hypertension.* 2018;71(6):1269–324. DOI: <https://doi.org/10.1161/HYP.0000000000000066>
20. Doyle DJ, Goyal A, Bansal P, Garmon EH. American Society of Anesthesiologists Classification. 2020. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020. PMID: [28722969](https://pubmed.ncbi.nlm.nih.gov/28722969/) Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28722969>
21. Aubertin MA. The hypertensive patient in dental practice: Updated recommendations for classification, prevention, monitoring, and dental management. *Gen Dent.* 2004;52(6):544-52. PMID: [15636281](https://pubmed.ncbi.nlm.nih.gov/15636281/)
22. Kalra P, Rana AS, Peravali RK, Gupta D, Jain G. Comparative Evaluation of Local Anaesthesia with Adrenaline and Without Adrenaline on Blood Glucose Concentration in Patients Undergoing Tooth Extractions. *J Maxillofac Oral Surg.* 2011;10(3):230-5. PMID: [22942593](https://pubmed.ncbi.nlm.nih.gov/22942593/) DOI: <https://doi.org/10.1007/s12663-011-0239-4>
23. Karm MH, Park FD, Kang M, Kim HJ, Kang JW, Kim S, et al. Comparison of the efficacy and safety of 2% lidocaine HCl with different epinephrine concentration for local anesthesia in participants undergoing surgical extraction of impacted mandibular third molars: A multicenter, randomized, double-blind, crossover, phase IV trial. 2017;96(21):e6753. PMID: [28538371](https://pubmed.ncbi.nlm.nih.gov/28538371/) DOI: <https://doi.org/10.1097/md.00000000000006753>
24. Kyosaka Y, Owatari T, Inokoshi M, Kubota K, Inoue M, Minakuchi S. Cardiovascular Comparison of 2 Types of Local Anesthesia With Vasoconstrictor in Older Adults: A Crossover Study. *Anesth Prog.* 2019;66(3):133-40. PMID: [31545671](https://pubmed.ncbi.nlm.nih.gov/31545671/) DOI: <https://doi.org/10.2344/anpr-66-02-04>
25. Strazar AR, Leynes PG, Lalonde DH. Minimizing the Pain of Local Anesthesia Injection. *Plast Reconstr Surg.* 2013;132(3):675-84. PMID: [23985640](https://pubmed.ncbi.nlm.nih.gov/23985640/) DOI: <https://doi.org/10.1097/PRS.0b013e31829ad1e2>
26. Kashyap VM, Desai R, Reddy PB, Menon S. Effect of alkalisation of lignocaine for intraoral nerve block on pain during injection, and speed of onset of anaesthesia. *Br J Oral Maxillofac Surg.* 2011;49(8):e72-5. PMID: [21592633](https://pubmed.ncbi.nlm.nih.gov/21592633/) DOI: <https://doi.org/10.1016/j.bjoms.2011.04.068>