Research Article

JRAD Journal of Research and Advancement in Dentistry

J Res Adv Dent 2021;12:2:24-29.

Comparative Analysis of Clonidine and Adrenaline with Lignocaine in Third Molar Extraction

Jeemee Patel[1*] Prafull Pujari[2] Navdeep Singh[3] Dhrumil Sarkar[4] Aastha Choudhary[5] Nadiyapara Priyesh Prafulbhai[6]

[1]Senior Lecturer, Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.
[2]PG Student, Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.
[3]PG Student, Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.
[4]PG Student, Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.
[5]PG Student, Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.
[6]PG Student, Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.

ABSTRACT

Background: There is evidence that clonidine, an alpha-2 adrenoceptor agonist, used as a central antihypertensive agent, enhances local anesthesia and analgesia in a variety of routes of administration and clinical circumstances. The aim of the study was to compare the efficacy of anesthesia and hemodynamic parameters of clonidine and epinephrine in lignocaine for lower third molar surgery

Material and Methods: Forty patients who reported to the Department of Oral and Maxillofacial Surgery requiring removal of impacted mandibular third molar were selected for the study. Patients were randomly divided into two groups, regardless of gender: Group 1 (Clonidine group) received 2.5 ml of 2% lignocaine with clonidine (15 µg/ml) and Group 2 (Adrenaline group) received 2.5 ml of 2% lignocaine with adrenaline (12 µg/ml). Hemodynamic parameters (heart rate, systolic blood pressure [SBP], diastolic blood pressure [DBP], and mean arterial pressure [MAP]) were recorded preoperatively, intraoperatively, and postoperatively. The onset of anesthesia and duration of anesthesia were recorded using pinprick test for both groups. Postoperatively, patients were evaluated for pain experience by the visual analog scale and verbal rating scale.

Results: There was no significant difference between the groups with respect to age, gender distribution, difficulty of impaction, and duration of the procedure. There was a decrease in SBP, DBP, and MAP within the clonidine group when compared to the baseline preoperative values of clonidine group. There was no statistically significant difference in the onset and duration of anesthesia between the groups.

Conclusion: Clonidine when used as an adjuvant to adrenaline in lignocaine can be safe and useful alternative to adrenaline. It is as efficient as adrenaline in respect to onset, duration, and intensity of anesthesia. Hemodynamic parameters are stable and better than adrenaline.

Keywords: Adrenaline, Clonidine, Lignocaine, Systolic Blood Pressure.

INTRODUCTION

Local anesthesia is the main component in dental practice. Local anesthetic produces temporary loss of sensation. Local anesthetic alone has a greater tissue perfusion and shorter duration of action. To overcome the drawback, vasoconstrictor is added. Adding vasoconstrictor to the local anesthesia reduces the rate of absorption from the site of injection or infiltration. The action of vasoconstrictor prolongs the duration of action of

Received: Dec. 1, 2020**: Accepted**: Jan. 12, 2021
***Correspondence Dr. Jeemee Patel.**
Department of Oral and Maxillofacial Surgery, Vyas Dental College and Hospital, Jodhpur, Rajasthan, India.
Email: Not Disclosed
doi: https://doi.org/10.53064/jrad.2021.12.2.07

the anesthetic agent and reduces bleeding at the site of surgery.

When lower third molar surgery is performed under local anesthesia, it is important to achieve adequate anesthesia. This is largely dependent on the presence and concentration of the added vasoconstrictor.[1] Most common local anesthetic (LA) agent available contains epinephrine in different concentration (1:80,000–1:200,000). Lignocaine is a commonly used local anaesthetic in dental practice. Many practitioners use adrenaline as additive with lignocaine, for local infiltration and nerve blocks for intra oral anaesthesia. Changes in heart rate and blood pressure can be significant during and after extraction as the local anaesthetic solutions contain adrenaline in different concentrations. Some centers have also used clonidine with lignocaine instead of adrenaline. Clonidine is α – 2 adrenoreceptor agonist with both central and peripheral action. It is said to decrease the blood pressure and also bring about vasoconstriction of peripheral blood vessels due to activation of postsynaptic α – 2 adrenoreceptors.[2] Clonidine has been used previously in few studies along with lignocaine for intra oral anaesthesia[1-4] They have been done in ASA I and ASA II patients.In a study by Patil et al. the onset of anaesthesia was the same in the groups involving both adrenaline and clonidine.

There is evidence that clonidine, an alpha-2 adrenoceptor agonist, used as a central antihypertensive agent, enhances local anesthesia and analgesia in a variety of routes of administration and clinical circumstances. Addition of clonidine to LA has been shown to increase its duration of action. Clonidine is a selective alpha-2 adrenoceptor agonist with both central and peripheral action. Through central activation of presynaptic alpha-2 adrenoceptors, clonidine decreases blood pressure and causes central analgesic activity as well as sedation.[5] By the activation of peripheral postsynaptic alpha-2 adrenoceptors, clonidine produces vasoconstriction of the peripheral blood vessels. The aim of the study was to compare the efficacy of anesthesia and hemodynamic parameters of clonidine and epinephrine in lignocaine for lower third molar surgery.

MATERIAL AND METHODS

Forty patients who reported to the Department of Oral and Maxillofacial Surgery requiring removal of impacted mandibular third molar were selected for the study. The study included both genders in the age group of 19 to 49 years. Inclusion criteria were healthy patients and minimal to moderately difficult impacted mandibular third molar. Exclusion criteria were any systemic diseases, pregnancy and lactating mother. Patients were randomly divided into two groups, regardless of gender: Group 1 (Clonidine group) received 2.5 ml of 2% lignocaine with clonidine (15 µg/ml) and Group 2 (Adrenaline group) received 2.5 ml of 2% lignocaine with adrenaline (12 µg/ml). To make the concentration of lignocaine + clonidine of 15 µg/ ml, 9 ml of 2% xylocaine was mixed with 1 ml ampule of 150 µg/ml of clonidine hydrochloride in a 10 ml syringe. Freshly prepared solution was used for every patient

After inducing the nerve block, the patients were evaluated for onset, duration, and intensity of anesthesia. The response to pinprick in the buccal attached gingiva between mandibular canine and first premolar with a 26-G sterile needle was used to determine the onset and duration of anesthesia. The onset of anesthesia was tested every 30 seconds until prick elicited no sensation. The duration was also evaluated by pinprick testing being repeated every 30 min after surgery to the time point when the patient feels blunt sensation, and then continued every 10 min till the return of complete sensation. Intensity of anesthesia was determined by two scores after the completion of the treatment. Patients were given the pain scale visual analog scale (VAS) and verbal rating scale (VRS) and asked to mark.

1. A 100-mm VAS, unmarked except for one end with “no pain” and the opposite end of the scale marked “worst pain”

2. A six-point VRS, the scale marked no pain, just noticeable, weak, moderate, severe, or excruciating pain for describing patient’s comfort during surgery. Hemodynamic changes were recorded pre-, intra-, and post-operatively. The parameters recorded were systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and

mean arterial pressure (MAP) using a standard pulse oximeter with blood pressure cuff attached.

RESULTS

The study comprised patients with a mean age of 29.5 years and age ranging from 19 to 49 years. The Clonidine group contained 45% male and 55% female, whereas Adrenaline group contained 35% male and 65% female. Impactions assessed according to Pederson index were within mild-to-moderate difficulty level. There was no significant difference between the groups with respect to age, gender distribution, difficulty of impaction, and duration of the procedure. The results obtained from the study suggest that clonidine used with lignocaine as a vasoconstrictor produces more stable hemodynamic parameters. There was a decrease in SBP, DBP, and MAP within the clonidine group when compared to the baseline preoperative values of clonidine group. However, there was no statistically significant difference seen when values were compared between the groups [Table 1]. The mean onset of anesthesia in clonidine was 121.05 s and adrenaline was 107.10 s. The mean duration of anesthesia for Clonidine group was 178.25 min, and the adrenaline was 184.10 min. There was no statistically significant difference in the onset and duration of anesthesia between the groups [Table 2]. These criteria strongly depend on the presence of vasoconstrictor effect of local anesthesia, hence supporting the vasoconstrictor action of clonidine when added to lignocaine. Upon comparison of pain score, using VAS with P≤0.05 was statistically significant, and VRS with P > 0.05 was not statistically significant. In the Clonidine group, 41% had just noticeable pain and 59% had weak pain. In the Adrenaline group, 6.9% had no pain, 72.1% had just noticeable pain, and 19% had weak pain. The difference in mean VRS between the two groups was not statistically significant. The pain is multifactorial with individual perception, and pain reaction can vary among individuals.

Table 1: Hemodynamic parameters following anesthesia.

Hemodynamic parameters	Time intervals	Clonidine group n=20	Adrenaline group n=20	P value
HR	Preoperative	81.1±2.1	83.2±2.1	0.06
	Intraoperative	82.9±3.1	85.1±2.2	0.4
	Postoperative	77.1±2.1	80.1±2.2	0.3
SBP	Preoperative	128.1±2.5	123.2±2.4	0.2
	Intraoperative	122.1±1.9	127.1±1.9	0.09
	Postoperative	120.8±1.7	123.4±1.4	1.0
DBP	Preoperative	82.9±2.1	80.1±1.2	0.74
	Intraoperative	74.9±1.4	80.9±2.1	0.10
	Postoperative	75.8±2.1	77.4±2.5	0.06
MAP	Preoperative	98.5±2.1	93.1±2.2	0.14
	Intraoperative	91.8±1.4	93.5±2.4	1.0
	Postoperative	90.6±1.4	91.5±2.3	0.54

Statistically significance at p≤0.05

Table 2: Onset and duration of action of anesthesia.

Variables	Clonidine group n=20	Adrenaline group n=20	P value
Onset (s)	121.05±8.4	107.10±8.4	0.25
Duration (min)	178.25±4.4	184.10±3.1	1.0

Statistically significance at p≤0.05

DISCUSSION

Local anesthesia is the main key of successful treatment of for any minor surgical dental procedure. The effectiveness depends on the local anesthetic agents and additive used. Normally, adrenaline is used as a vasoconstrictor to lengthen the duration of anesthetic effect and to reduce the bleeding during the procedure. It appears that clonidine could be a useful alternative to adrenaline

for intraoral anesthesia and may have a role in those with cardiovascular disease or those particularly sensitive to adrenaline.[6] Several studies have been carried out using different concentrations of clonidine for the enhancement of epidural anesthesia, brachial plexus anesthesia, and anesthesia of peripheral nerves.[7] These studies have shown that the effective concentrations of clonidine, without significant side effects, were 150 μg/ml,3 90 μg/ml,4 30 μg/ml,4 10 μg/ml,5 and 5 μg/ml.6 Clonidine at 5 μg/ml can be safely used as additives with lignocaine, in intra-oral anesthesia.

Lignocaine with adrenaline as vasoconstrictor is common in dental practice. But changes in heart rate and blood pressure can be significant during and after extraction, as local anaesthetic solutions contain adrenaline in different concentrations.[4] Hence, the type and concentration of vasoconstrictors should be considered when selecting a local anaesthetic solution. In a study by Brkovic et al., there was no significant difference in the onset of anesthesia between the clonidine and the epinephrine groups, because the onset of anesthesia primarily depends on the characteristics of local anesthetics.[7]

In our study, 1:80,000 (12.5 μg/ml) concentration of adrenaline was compared to (15 μg/ml) concentration of clonidine as an adjuvant for the efficacy of local anesthesia. The clinical significance of cardiovascular and hemodynamic changes caused by the release of endogenous catecholamines and administration of exogenous adrenaline with LA agents has long been a controversial subject in dentistry and medicine and remains a subject of continuing study as well as persistent controversial topic in the etiology of cardiovascular reactions. Alemany-Martínez et al.[8] studied hemodynamic changes during third molar surgery and concluded that although cardiovascular changes were within the normal range, stress and anxiety have an impact on these changes and should be considered. It is essential to avoid pain and minimize patient anxiety to ensure safe clinical practice.

The results of the present study suggest that clonidine, like epinephrine, is able to increase and prolong the efficacy of lidocaine anesthesia in inferior alveolar nerve block. Several studies have been carried out using different concentrations of clonidine for the enhancement of epidural anesthesia,[9] brachial plexus anesthesia,[10] and anesthesia of peripheral nerves.[11] Brkovic et al. [12] mentions that clonidine (15 μg/ml) added to 2% lidocaine produces an onset, duration, and intensity of intraoral block anesthesia similar to those gained by a solution of 2% lidocaine with epinephrine (12.5 μg/ml). In the present study, there was no significant difference in the onset of anesthesia between the clonidine and adrenaline groups. This mainly depends on the characteristic of LA, thus the presence of adrenaline and clonidine does not have impact on the onset of anesthesia. Similar results were obtained in the other studies for intraoral block.[13-15] Patients in the clonidine group had their SBP and DBP within normal limit and were more hemodynamically stable. There was a significant decrease in SBP, DBP, and MAP in clonidine group when compared with values before administration, while there was increase in SBP, DBP, and MAP in Adrenaline group from preoperative to intraoperative. There were no significant statistical differences in SBP, DBP, and MAP, and HR between Clonidine and Adrenaline group at any time. Shadmehr et al[16] in his study, he concluded that addition of clonidine to lidocaine improved the success rate of inferior alveolar nerve block (IANB) compared to a standard lidocaine/epinephrine solution. Clonidine has been used as an alternative to adrenaline for different types of anaesthesia in major surgeries[2,3] Three mechanisms of action for Clonidine additive effects have been proposed. They include (i) direct action on the peripheral nerve (ii) central α – 2 receptor mediated analgesia and (iii) α – 2 mediated vasoconstriction.[17] It has been proved to provide stable hemodynamic parameters owing to its central hypotensive action. Various studies [1-3,18,19] have demonstrated the ability of clonidine to enhance the central and peripheral neural blockade when added to local anaesthetics during the last two decades. Clonidine has been used with varying success in cervical plexus block when used with ropivacaine.[20] One of the complications of clonidine is hypotension and therefore should be used with caution. Clonidine has shown to reduce cardiac morbidity and mortality improving perioperative outcome in patients at risk for cardiovascular events.[21]

It has been noticed that epidurally injected clonidine induces a reduction in local blood flow and that the decrease in local blood flow correlates

with the injection dose. Experiments on humans have shown that clonidine, infused into a brachial artery, decreased forearm blood flow and that this effect was abolished by phentolamine, a non-selective alpha-1 and alpha-2 adrenoceptor antagonist, but not by prazosin, a selective alpha-1 adrenoceptor antagonist. These results suggest that alpha-2 adrenoceptors are involved in vasoconstriction of human arteries in the forearm region.[22] Pain is an important criterion by which patient comfort can be assessed during the treatment procedure. The VAS, the VRS, and numeric pain scale are the most commonly used scales to assess pain intensity. The validity of all three in a recent study (Lara-Munoz et al. 2004), which tested the VAS, VRS, and NRS in experimental conditions using sound as the variable stimulus. All three tools were found to be reliable and valid, and although the VAS scored highest. Brummett et al. have stated that clonidine when used with short and intermediate-acting local anesthetics prolongs the duration of anaesthesia.[23] Clonidine is said to also cause sedation when used in high doses (100 μg), but the concentration (10 μg) used in our study did not produce any untoward side effects. The results suggested that there were no significant differences between the two agents with regard to the time of onset of action, duration, or intensity of anesthesia, or the vasoconstrictor properties. The clonidine group showed better hemodynamic parameters compared with the epinephrine group. The clonidine group showed significantly lesser postoperative pain and therefore, had lesser analgesic consumption.

CONCLUSION

Clonidine when used as an adjuvant to adrenaline in lignocaine can be safe and useful alternative to adrenaline. It is as efficient as adrenaline in respect to onset, duration, and intensity of anesthesia. Hemodynamic parameters are stable and better than adrenaline.

CONFLICTS OF INTEREST

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

REFERENCES

1. Pavan M Patil SPP. Is Clonidine an Adequate Alternative to Epinephrine as a Vasoconstrictor in Patients With Hypertension? Journal of oral and maxillofacial surgery. 2012;70:257-62.

2. Brkovic LT, D Stojic. Comparison of clonidine and epinephrine in lidocaine anaesthesia for lower third molar surgery. Int J Oral Maxillofac Surg. 2005;34:401-06.

3. Brkovic MG, J Roganovic, N Jovic, L Todorovic, D Stojic. Lidocaine ± clonidine for maxillary infiltration anaesthesia: parameters of anaesthesia and vascular effects. Int J Oral Maxillofac Surg. 2008;37:149-55.

4. Shouvik Chowdhury MS, Anjan Shah. Efficacy of lignocaine with clonidine and adrenaline in minor oral surgical procedure. Contemporary clinical dentistry. 2012;3:227-29.

5. Ise T, Yamashiro M, Furuya H. Clonidine as a drug for intravenous conscious sedation. Odontology 2002;90:57-63.

6. Brkovic B, Gardasevic M, Roganovic J, Jovic N, Todorovic L, Stojic D. Lidocaine clonidine for maxillary infiltration anaesthesia: Parameters of anaesthesia and vascular effects. Int J Oral Maxillofac Surg 2008;37:149-55.

7. Brkovic B, Todorovic L, Stojic D. Comparison of clonidine and epinephrine in lidocaine anaesthesia for lower third molar surgery. Int J Oral Maxillofac Surg 2005;34:401-6.

8. Alemany-Martínez A, Valmaseda-Castellón E, Berini-Aytés L, Gay-Escoda C. Hemodynamic changes during the surgical removal of lower third molars. J Oral Maxillofac Surg 2008;66:453-61.

9. Baptista JF, Gomez RS, Paulo DN, Carraretto AR, Brocco MC, Silva JJ. Epidural anesthesia with ropivacaine with or without clonidine and postoperative pain in hemorrhoidectomies. Acta Cir Bras 2014;29:201-8.

10. Gaumann D, Forster A, Griessen M, Habre W, Poinsot O, Della Santa D. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. Anesth Analg 1992;75:69-74.

11. Reinhart DJ, Wang W, Stagg KS, Walker KG, Bailey PL, Walker EB, et al. Postoperative analgesia after peripheral nerve block for podiatric surgery: Clinical efficacy and chemical stability of lidocaine

alone versus lidocaine plus clonidine. Anesth Analg 1996;83:760-5.

12. Brkovic B, Todorovic L, Stojic D. Comparison of clonidine and epinephrine in lidocaine anaesthesia for lower third molar surgery. Int J Oral Maxillofac Surg 2005;34:401-6.

13. Brkovic B, Gardasevic M, Roganovic J, Jovic N, Todorovic L, Stojic D. Lidocaine+clonidine for maxillary infiltration anaesthesia: Parameters of anaesthesia and vascular effects. Int J Oral Maxillofac Surg 2008;37:149-55.

14. Patil PM, Patil SP. Is clonidine an adequate alternative to epinephrine as a vasoconstrictor in patients with hypertension? J Oral Maxillofac Surg 2012;70:257-62.

15. Chowdhury S, Singh M, Shah A. Efficacy of lignocaine with clonidine and adrenaline in minor oral surgical procedure. Contemp Clin Dent 2012;3:227-9.

16. Shadmehr E, Aminozarbian MG, Akhavan A, Mahdavian P, Davoudi A. Anaesthetic efficacy of lidocaine/clonidine for inferior alveolar nerve block in patients with irreversible pulpitis. Int Endod J 2017;50:531-9.

17. Daniel M, Popping NE, Emmanuel Marret, Manuel Wenk, Martin R Trame r. Clonidine as an Adjuvant to Local Anesthetics for Peripheral Nerve and Plexus Blocks A Metaanalysis of Randomized Trials. Anesthesiology. 2009:406-15.

18. Mazoit JX, Benhamou D, Veillette Y, Samii K. Clonidine and or adrenaline decrease lignocaine plasma peak concentration after epidural injection. Br J Clin Pharmacol 1996;42:242-5.

19. Kiowski W, Hulthén UL, Ritz R, Bühler FR. Alpha 2 adrenoceptor-mediated vasoconstriction of arteries. Clin Pharmacol Ther 1983;34:565-9.

20. Giorgio Danelli MN, PF Salcuni, L Caberti MB, E Rossini AC, Fanelli G. Does clonidine 50 lg improve cervical plexus block obtained with ropivacaine 150 mg for carotid endarterectomy? A randomized, double-blinded study. Journal of clinical anesthesia. 2006;18:585–88.

21. Michael T. Ganter CKH, Donat R. Spahn, Marcel Bruggisser TB, Burkhardt Seifert, Thomas Pasch, Marco P. Zalunardo. The effect of clonidine on perioperative blood coagulation. Journal of clinical anesthesia. 2005;17:456–62.

22. Rashmi Madan NB, Dilip Shende, Sudershan K. Khokhar, Hira L. Kaul. A Dose Response Study of Clonidine with Local Anesthetic Mixture for Peribulbar Block: A Comparison of Three Doses. Anesth Analg. 2001;93:1593-97.

23. Brummett CM, Wagner DS. The use of alpha-2 agonists in peripheral nerve blocks: Areview of the history of clonidine and a look at a possible future for dexmedetomidine. In: Seminars in Anesthesia, Perioperative Medicine and Pain. Vol. 25. WB Saunders; 2006. p. 84-92