Original Article - Comparative Study

Clonidine: An Adjuvant to Adrenaline in Local Anesthesia for Third Molar Surgery

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Abstract

Purpose: The aim of the study is to compare the efficacy of anesthesia and hemodynamic parameters of clonidine and epinephrine in lignocaine for lower third molar surgery. **Materials and Methods:** Thirty healthy controls with impacted mandibular third molar were randomly selected from both sexes between the age group of 20–47 years. Patients were divided equally into two groups: Group I (Adrenaline group) and Group II (Clonidine group). Patients received 2.5 ml of 2% lignocaine with adrenaline (12.5 µg/ml) in Adrenaline group and 2.5 ml of 2% lignocaine with clonidine (15 µg/ml) in Clonidine group. 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:** Lignocaine with clonidine intraoperatively and postoperatively decreases SBP and DBP and MAP compared to lignocaine with adrenaline. There was no significant difference in the onset and duration of anesthesia in both the groups. There was a statistically significant difference seen in the visual analog scale, but no statistically significant difference was seen in the verbal rating scale. **Conclusion:** Clonidine has similar efficacy as that of adrenaline with better hemodynamic parameters and can be used as an alternative to adrenaline for third molar surgeries.

Keywords: Clonidine, lignocaine, local anesthesia, verbal rating scale, visual analog scale

Introduction

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). Epinephrine enhances duration and intensity of anesthesia and provides a desirable hemostasis at the surgical site. Goldstein *et al*.[2] have reported that intraoral block anesthesia with 2% lidocaine with epinephrine (1:100,000) in healthy controls, resulted in increased circulatory epinephrine levels associated with cardiovascular changes. Even with a relatively small dosage of epinephrine, it is important to note that in patients having cardiovascular problems (poorly controlled American Society of Anesthesiologists [ASA] III and all ASA IV group), the recommendation is to limit or avoid exposure to vasoconstrictor epinephrine, if possible. 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.[3] 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

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anesthesia and hemodynamic parameters of clonidine and epinephrine in lignocaine for lower third molar surgery.

Materials and Methods

After obtaining permission from the ethical committee, 30 healthy 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 20 to 47 years. Inclusion criteria were healthy patients and minimal to moderately difficult impacted mandibular third molar.[4] 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 (Dispovan 26 × 1.5) 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 30 and age ranging from 20 to 47 years. The Clonidine group contained 46.7% male and 53.3% female, whereas Adrenaline group contained 33.3% male and 66.7% 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 120.0 s and adrenaline was 106.0 s. The mean duration of anesthesia for Clonidine group was 179.3 min, and the adrenaline was 185.3 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 [Figure 1] with $P = 0.03$ was statistically significant, and VRS [Figure 2] with $P = 0.065$ was not statistically significant. In the Clonidine group, 40% had just noticeable pain and 60% had weak pain. In the Adrenaline group, 6.7% had no pain, 73.3% had just

Table 1: Hemodynamic parameters after anesthesia

Hemodynamic parameters	Time intervals	Clonidine group ($n=15$)	Adrenaline group ($n=15$)	*P*	Significance
HR	Preoperative	80.3±2.4	83.4±2.8	0.406	Not significant
	Intraoperative	83.1±3.5	85.6±2.8	0.590	Not significant
	Postoperative	76.4±2.9	80.9±2.6	0.269	Not significant
SBP	Preoperative	129.7±2.3	122.2±3.7	0.104	Not significant
	Intraoperative	122.6±1.9	126.5±2.5	0.244	Not significant
	Postoperative	119.8±1.7	124.2±2.4	0.153	Not significant
DBP	Preoperative	82.2±2.4	80.6±1.9	0.625	Not significant
	Intraoperative	75.6±1.9	81.3±2.5	0.093	Not significant
	Postoperative	75.6±2.0	76.8±2.5	0.701	Not significant
MAP	Preoperative	98.0±2.2	92.5±2.1	0.085	Not significant
	Intraoperative	91.2±1.8	93.1±2.6	0.581	Not significant
	Postoperative	90.4±1.7	91.1±2.1	0.811	Not significant

HR=Heart rate; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; MAP=Mean arterial pressure

noticeable pain, and 20% 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.

Discussion

The cardiovascular safety profile of adrenaline has been a matter of debate, particularly if patients are susceptible to trace amounts of systemic adrenaline in unstable angina, or have a recent history of myocardial infarction or thyroid storm. Lignocaine with adrenaline as vasoconstrictor is common in dental practice. However, changes in HR and blood pressure can be significant during and after extraction, as LA solutions contain adrenaline in different concentrations. Hence, the type and concentration of vasoconstrictors should be considered when selecting a LA solution. 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*.[5] 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.

Table 2: Onset and duration of action of anesthesia

	Clonidine group	Adrenaline group	*P*	Significance
Onset (s)	120.0±8.2	106.0±8.2	0.240	Not significant
Duration (min)	179.3±4.6	185.3±3.3	0.305	Not significant

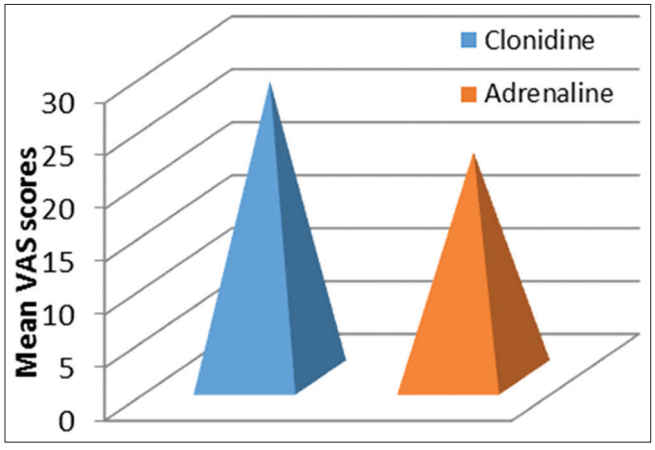

Figure 1: Visual analog scale score

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,[6] brachial plexus anesthesia,[7] and anesthesia of peripheral nerves.[8] Brkovic *et al*.[9] 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.[10-12] 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*.[13] 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 is alpha-2 adrenoceptor agonist with both central and peripheral action. Three mechanisms of action for clonidine additive effects have been proposed. They include (i) direct action on the peripheral nerve, (ii) central alpha-2 receptor-mediated analgesia, and (iii) alpha-2-mediated vasoconstriction.[14] It is known that duration and intensity are parameters that depend on the presence of vasoconstrictor. Concerning the results of Mazoit *et al*.,[15] the addition of clonidine to lidocaine for epidural anesthesia has led to the reduction of the plasma peak concentration of lidocaine. It could be concluded that this effect is the result of vasoconstriction due to clonidine.

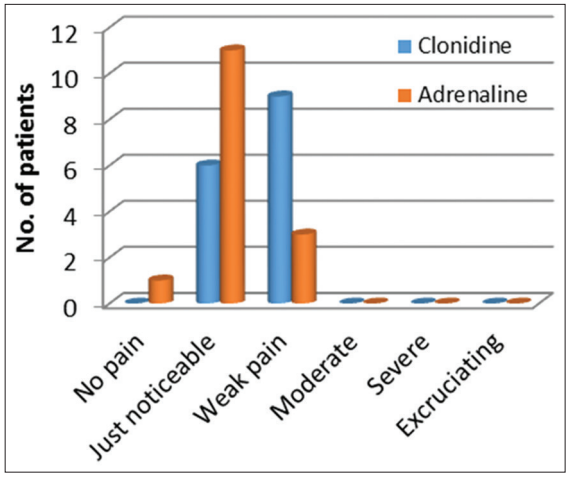

Figure 2: Verbal rating scale scores

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.[16] 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. In our study, we used VAS and VRS for assessing the intensity of anesthesia during the surgical procedure. There was a statistically significant difference in VAS between the groups. VRS showed no statistical significant difference.

Patil *et al*. compared clonidine and epinephrine in poorly controlled, moderate hypertensive patients. 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

Based on the results of the present study, it can be concluded that 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.

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Conflicts of interest

There are no conflicts of interest.

References

1. Yagiela JA. Local anesthetics. Anesth Prog 1991;38:128-41.
2. Goldstein DS, Dionne R, Sweet J, Gracely R, Brewer HB Jr., Gregg R, *et al.* Circulatory, plasma catecholamine, cortisol, lipid, and psychological responses to a real-life stress (third molar extractions): Effects of diazepam sedation and of inclusion of epinephrine with the local anesthetic. Psychosom Med 1982;44:259-72.
3. Ise T, Yamashiro M, Furuya H. Clonidine as a drug for intravenous conscious sedation. Odontology 2002;90:57-63.
4. Gbotolorun OM, Arotiba GT, Ladeinde AL. Assessment of factors associated with surgical difficulty in impacted mandibular third molar extraction. J Oral Maxillofac Surg 2007;65:1977-83.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. Brummett CM, Wagner DS. The use of alpha-2 agonists in peripheral nerve blocks: A review 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.
15. 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.
16. Kiowski W, Hulthén UL, Ritz R, Bühler FR. Alpha 2 adrenoceptor-mediated vasoconstriction of arteries. Clin Pharmacol Ther 1983;34:565-9.