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A Comparative Evaluation of Nerve Block Using 2% Lignocaine Hydrochloride with Adrenaline Bitartrate Versus 2% Lignocaine Hydrochloride with Clonidine Hydrochloride in Maxillary Molar Extraction- A Clinical Study

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Abstract

Introduction: The study aimed to compare and evaluate the nerve block using 2% lignocaine hydrochloride with adrenaline bitartrate versus 2% lignocaine hydrochloride with clonidine hydrochloride in maxillary molar extraction.

Method: A total of 30 patients were included in the study with 15 in each group. Patients in group I received 2% lignocaine HCL of 1:80000 adrenaline as the local anesthetic. In group II patient received freshly prepared 2% lignocaine HCL with clonidine (0.015 mg/ml) as the local anesthetic hemodynamic measures were recorded before administration of LA, 5 min after administration of LA and 10 min after completion of extraction. The onset of action of LA was recorded. Data was tabulated and statistical analysis was carried out using paired and unpaired t-tests.

Result: On comparison of mean and SD values of heart rate and mean arterial pressure in group –I and group –II at different time intervals, prior to anesthesia ,5 min after LA administration and 10 min after extraction, significant difference was seen ($p<0.05$). On comparison of the mean and standard deviation of onset of action of group I and group II after LA injection, no significant difference was seen at any time intervals.

Conclusion: The present study indicates that clonidine added to local anesthesia group –II had a definite improvement in the intra-operative vascular parameters as compared to that in group –I. At the same time, there was not much of a difference in the onset of anesthetic action in the clonidine as well as in the adrenaline group.

Keywords: Clonidine, postoperative analgesia, Local anesthesia, Vasoconstrictor, hemodynamic variables.

Introduction

Effective pain control during dental intervention is one of the most important and major prerequisites for

painless dentistry. Several methods and process can be used to control pain, of which the use of local anesthetics is the most commonly used technique in dental practice. The presence of a local anesthetic in the circulatory system means that the drug will be transported or transferred to every part of the body. Local anesthetics can alter or change the functioning of some of these cells. Epinephrine enhances or increases the duration and intensity or potency of anesthesia and also provides desirable hemostasis at the surgical site. Without vasoconstrictors, local anesthetic agents can produce vasodilatation and increase the rate of absorption of local anesthetics from the injection site or area.

Adrenaline is commercially available or accessible in variable concentrations ranging from 1:80,000 to 1:2,00,000 dilution. Nonetheless, it is well recognized that local anesthetic techniques mixed with adrenaline are linked to an increase in plasma adrenaline and either considerable or insignificant modifications to the cardiovascular system. Even with a very little amount of epinephrine, Emanuel S. Troullos et al. have observed and reported that in healthy patients, local anesthetic with epinephrine causes elevated circulatory epinephrine levels, leading to cardiovascular changes [1]. Therefore, in the search for an alternative option for adrenaline as an adjunct to local anesthesia clonidine an alpha-2 adrenoreceptor agonist was studied and tested. Since lignocaine is a popular local anesthetic that is frequently used in dentistry, many practitioners add adrenaline to lignocaine, and some have even used clonidine in place of or in addition to adrenaline. However, there are advantages and disadvantages to each.

Clonidine is a centrally acting anti-hypertensive agent that was studied in the University of Belgrade, Serbia, and Montenegro in 2005 to be used as an adjunct or additive to local anesthesia in 3rd molar surgery[2]. It was also successfully used as an adjunct to LA in regional anesthesia for brachial plexus or supra-clavicular nerve blocks earlier in literature in anesthesia[3, 4, 5]. Literature also shows that using local anesthesia with clonidine significantly increases post-operative analgesia in contrast or when compared to local anesthesia added with epinephrine.[2,10] This helps in improving and boost patient compliance. Alpha-2 adrenoceptor agonist clonidine selectively acts on both the central and peripheral levels, or just one of them. Through central activation of presynaptic alpha-2 adrenoceptors, clonidine decreases blood pressure and causes central analgesic activity as well as sedation. It causes peripheral blood vessel vasoconstriction by activating alpha-2 postsynaptic adrenoceptors in the periphery. This wide spectrum of its use prompted and advised dentists and oral surgeons in particular to use clonidine added with local anesthesia in dental surgeries. The alfa-2 adrenoceptor agonist clonidine, has been shown to improve local anesthetic and analgesia in a range of clinical settings and delivery routes when used as a central antihypertensive medication.[17] A decrease in the central effect of clonidine results in sedation, anxiolysis, and dryness of secretions. It also minimizes the need for anesthetic medications and improves cardiovascular stability and steadfastness during the perioperative period, as demonstrated by Fanini D et al.

Materials and Method

The present clinical study was conducted in the Department of Oral and Maxillofacial Surgery, Darshan Dental College and Hospital, Udaipur, Rajasthan. Ethical clearance was obtained from the ethical committee to perform a clinical study on patients.

Test materials used in the study

Clonidine hydrochloride (CLONEON), 2% Lignocaine

hydrochloride with 1: 80,000 adrenaline (XICAINE), 2% Lignocaine hydrochloride (LOX *2%).* 30 subjects within the age group of 18 years to 60 years of either gender who met with the inclusion criteria were divided into 2 groups by random sampling. Each group included 15 patients. Teeth diagnosed with chronic pulpitis, that could not be restored, or patients refused conservative management, failed root canal treated, grossly decayed and mobile teeth and patients who do not have known allergies to any drug under study were included in the study. Medically compromised patients (ASA II and above), pregnant women or lactating women, patients unable to give consent or with impacted or partially impacted teeth and intra-alveolar extraction converting into transalveolar extraction were not included in the study.

The Methodology Was Divided into The Following Steps

All patients underwent routine radiological investigations. Systolic and diastolic blood pressure were measured with the help of a manual sphygmomanometer and heart rate was measured by pulse oximeter and the values were recorded. In Group I, 2% Lignocaine hydrochloride with 1: 80,000 adrenaline (10 µg/ml) was used and in Group II, 2% Lignocaine hydrochloride with clonidine (15µg/ml) was used (the admixture was freshly prepared in the above-mentioned concentrations using *2%* Lignocaine hydrochloride along with clonidine hydrochloride). Nerve blocks as per requirements were administered. The onset of LA was considered at the time when the patient reported no pain while pricking the gingiva of the respected tooth to be extracted by the tip of the syringe or tip of William's probe (Hu Friedy). Then systolic and diastolic blood pressure and Heart rate was measured and the values were recorded. Extraction of the advised maxillary molar was done with a standard extraction instrument performed using the closed method without any complication. A pressure pack using sterile gauze was given. After 10 min of extraction, Systolic and diastolic blood pressure and heart rate was measured and the value were recorded and routine post-operative instructions and medication prescribed.

Statistical Analysis

The results were calculated as mean and standard deviation. The data obtained was compiled systemically and a master table was prepared on a computer using Microsoft Excel 2022. Analysis of obtained data was made by statistical analysis for social science (SPSS) version 22.0, IBM Inc. Data then entered into a Microsoft Excel spreadsheet and was checked for any discrepancies. Paired and unpaired t test was used for categorical variables. The level of statistical significance was set at a p value <0.05.

Results

On comparison of mean and SD values of heart rate in group –I (Adrenaline) and group –II (Clonidine) with time intervals from prior to anesthesia up to 10 min after extraction, showed no significant statistical difference (i.e. $p>0.05$). In group I: it was seen that heart rate increases at 5 min after LA administration from baseline value. Maximum heart rate was found to be at 5 min after administration of LA and minimum heart rate was found to be at prior to anesthesia. Whereas in group-II: the heart rate decreased at 5 min after LA administration to normal value. Maximum heart rate was found prior to LA administration and minimum heart rate was found to be at 10 min after completion of extraction.

On comparison of mean and SD values of systolic blood pressure in group - I and group – II with the time interval from prior to anesthesia up to 10 min after the extraction a statistically significant difference (i.e. $p<0.05$) was

found in systolic blood pressure from prior to anesthesia (p = 0.026), at 5 min after LA administration (p = 0.002) to 10 min after completion of extraction (p=0.000). In group-I: maximum systolic blood pressure was found to be at 10 min after completion of extraction and minimum systolic blood pressure was found to be at prior to administration of anesthesia. Whereas in group - II: maximum systolic blood pressure was found to be prior to administration of anesthesia and minimum systolic blood pressure was found at 10 min after completion of extraction. (Table1:)

During Period	Group –I (Adrenaline) (n=15)	Group –II (Clonidine) (n=15)	t	p-value	Significance
	mean ± SD	mean ± SD			
Prior to anesthesia	134.67 ± 11.356	125.73 ±9.316	2.356	0.026	Significant
5 min after Injection	135.40 ± 13.081	122.53 ±6.300	3.432	0.002	Significant
10 min after extraction	135.93± 10.215	120.93 ±5.599	4.987	0.000	Significant

Table 1: Comparison of mean and SD values of systolic blood pressure in Group -I (Adrenaline) and Group –II (Clonidine) at different time intervals

In group–I: maximum diastolic blood pressure was found to be at 5 min after anesthesia and minimum diastolic blood pressure was found to be at prior to anesthesia. Whereas in group–II: maximum diastolic blood pressure was found to be at prior to anesthesia and minimum diastolic blood pressure was found to be at 5 min after anesthesia.

On comparison of mean and SD values mean arterial pressure in group –I and group –II with time interval from prior to anesthesia to 10 min after extraction significant difference is seen between all the time intervals ($p<0.05$). Prior to anesthesia p= 0.025, 5 min after LA administration p=0.003 and after 10 min of extraction p=0.004. (Table 2).

During Period	Group –I (Adrenaline) (n=15)	Group –II (Clonidine) (n=15)	t	P-Value	Significance
	mean ± SD	mean ± SD			
Prior to Anesthesia	101.511± 7.119	95.777± 6.063	2.375	0.025	Significant
5 min after injection	102.778± 9.687	93.687± 5.243	3.196	0.003	Significant
10 min after extraction	102.200± 9.804	93.199± 5.463	3.106	0.004	Significant

Table 2: Comparison of mean and SD values of mean arterial pressure in Group–I (Adrenaline) and Group –II (Clonidine) at different time intervals.

On comparison of the mean and standard deviation of onset of action of group I and group II after LA injection, no significant difference was seen p=0.22.

Discussion

Research work in Oral and Maxillofacial Surgery continuously strives and struggles to improve and eliminate the side effects or complications of adrenaline

when used as an adjunct to local anesthesia. Secondarily the addition of adrenaline to any local anesthesia has no proven effect on post- operative analgesia which can cause distress or agony in the majority if not in every patient. Therefore, keeping these drawbacks of adrenaline when added to local anesthesia for routine use was carried out. One of the most recent or advanced adjuncts to local anesthesia was found by B. Brkovic in 2005, he used an alpha-2 adrenergic-receptor agonist, clonidine as an adjunct to local anesthesia.

Heart rate

Clonidine has been combined with various local anesthetics like lignocaine, bupivacaine, mepivacaine, and ropivacaine. Research indicates that clonidine effectively lowers intraoperative heart rate and enhances postoperative analgesia by prolonging nerve blockade. A study by Colin et al. (2007) highlighted dose-dependent side effects of clonidine, such as sedation and hypotension, particularly at doses of 150 µg or higher. Other studies, including those by Brakovic et al.[2,10] and Fanini et al[19]., emphasize the importance of understanding cardiovascular reactions linked to local anesthetics containing sympathomimetic vasoconstrictors, especially for patients with pre-existing cardiovascular conditions.

In the present study, heart rates were monitored using a multiparameter pulse oximeter in two groups: one receiving clonidine and the other adrenaline. Measurements were taken before local anesthesia (LA), five minutes post-LA, and ten minutes post-extraction. The results showed that the postoperative heart rate in the clonidine group (Group II) significantly decreased compared to pre-LA levels ($p<0.05$). Conversely, the adrenaline group (Group I) exhibited a marked increase in heart rate five minutes after LA administration (82.33 ± 10.880), with slight decreases noted ten minutes after extraction (80.87 ± 11.090).

The study concluded that adrenaline causes a notable rise in intraoperative heart rate, particularly within the first five minutes post-injection, while clonidine was associated with a significant reduction in heart rate after ten minutes of extraction ($p<0.05$). These findings align with earlier studies indicating that the heart rate in the adrenaline group consistently exceeded baseline values, while clonidine led to lower heart rates during and post-surgery.

Ultimately, the study suggests that clonidine, when added to lignocaine, significantly reduces postoperative heart rate compared to adrenaline-lignocaine combinations, highlighting the systemic absorption of adrenaline even with peripheral injections.

Systolic, diastolic and mean arterial blood pressure

Brkovic et al. (2005) studied the addition of adrenaline or clonidine to lidocaine for inferior alveolar nerve blocks and found no significant differences in systolic or diastolic blood pressures between the two groups. Similarly, Chaudhary et al. (2012) assessed the efficacy of lignocaine with adrenaline versus clonidine in 30 patients undergoing bilateral mandibular third molar extractions. They observed that the group receiving lignocaine with clonidine had significantly lower heart rates and mean arterial blood pressures during and after surgery.

In our study, the mean systolic blood pressure at the procedure's start was 134.67 ±11.356 in the adrenaline group and 125.73 ±9.316 in the clonidine group, indicating a significant difference ($p< 0.05$). At 5 minutes post-local anesthetic (LA) administration, systolic blood pressures were 135.40 ±13.081 (adrenaline) and 122.53 ±6.300 (clonidine), again showing significant differences ($p< 0.05$). Ten minutes

post-extraction, these values were 135.93±10.215 (adrenaline) and 120.93±5.599 (clonidine), also significant ($p < 0.05$).

For diastolic blood pressure, the values at the procedure's start were 84.93±7.554 (adrenaline) and 80.80±5.545 (clonidine), with no significant difference ($p > 0.05$). At 5 minutes post-LA, the diastolic pressures were 86.47±9.062 (adrenaline) and 79.27±5.637 (clonidine), showing significant differences ($p < 0.05$). Ten minutes after extraction, the values were 85.33±10.728 (adrenaline) and 79.33±5.790 (clonidine), with no significant difference ($p > 0.05$).

Throughout the procedure, the adrenaline group showed stable blood pressures, while the clonidine group maintained lower values after 5 minutes compared to their baseline and the adrenaline group. Significant changes were noted in mean arterial pressures ($p<0.05$) from pre-anesthesia to 10 minutes post-extraction.

In conclusion, clonidine appears to be a safe and effective alternative to adrenaline in intraoral block anesthesia, significantly affecting intra-operative systolic and diastolic blood pressures without inducing hypotension, which remained within normal limits. This suggests that the hypotensive effects of clonidine are dose-dependent.

Onset of action

The mean of onset of action of anesthesia's time observed in the group I sample was 250.00±65.860 and in the group II sample was 279.60±65.506 and had a p-value>0.05 which suggested no significant changes were seen in either of the groups. So we can conclude that both solutions have the same onset of action. This makes sense because the properties of the local anesthetic largely determine when anesthesia begins (the induction time). MOLNAR et al.[16] reported similar outcomes, demonstrating that the 1.5% lidocaine with clonidine (5 mg/ml) method did not vary from the 1.5% lidocaine with epinephrine (5 mg/ml) method in terms of the cervical plexus block onset. Interestingly, though, when anesthesia was subjectively assessed, the clonidine group's anesthesia onset occurred much faster[16].

Scope for Future Research

More studies with larger sample size is required. Further dose dependent study should be conducted. Further study should be conducted on cardiovascular patients to assess the clonidine's effects.

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