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Original Article

Dentistry Section

Comparative Effects of Clonidine and Adrenaline with Lignocaine during Maxillary Infiltration Anaesthesia for Dental Extraction

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ABSTRACT

Introduction: Lignocaine is a commonly used local anaesthetic in dental practice. Many practitioners use adrenaline (epinephrine) as additive with lignocaine, and some have used clonidine, instead of adrenaline. Both having benefits and limitations.

Aims: Hence a study was undertaken in our department to evaluate the advantages and disadvantages of using (plain lidocaine local anaesthetic) versus (lidocaine with adrenaline as additive) versus (lidocaine with clonidine as additive).

Study Design: Randomised, prospective, double blind study.

Materials and Methods: Seventy five patients requiring extraction of maxillary molar teeth who fall under ASA I category were included and randomly divided into group – I (n=25) (Lignocaine), group – II (n=25) (Lignocaine ± Adrenaline) and group – III (n=25) (Lignocaine ± Clonidine). The observations recorded were, time of onset of anaesthesia, hemodynamic parameters, blood loss during procedure and duration of post operative analgesia.

Statistical Analysis: The statistical analysis was carried out using SPSS 16 software.

Results: A statistically significant difference was seen in blood loss, being higher in group I and duration of anaesthesia, being shortest in group I. There was no statistical difference between the three groups amongst other parameters.

Conclusion: Adrenaline at 10 µg/ml and clonidine at 15 µg/ml can be safely used as additives with lignocaine, in maxillary infiltration anaesthesia for dental extraction; with addition of either of these two drugs, having an equal advantage over use of plain lignocaine; in terms of lower blood loss and longer duration of anaesthesia; but, with no difference in the onset of anaesthesia and with no significant hemodynamic changes.

Keywords: Additives, Local anaesthesia, Vasoconstrictor

INTRODUCTION

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 [1]. Some centres 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 [1-4] along with lignocaine for intra oral anaesthesia. They have been done in ASA I and ASA II patients.In a study by Patil et al., [1] the onset of anaesthesia was the same in the groups involving both adrenaline and clonidine. We carried out a study in maxillary infiltration anaesthesia, comparing Lignocaine as local anaesthetic without addition of vasoconstrictor, Lignocaine as local anaesthetic with adrenaline and Lignocaine as local anaesthetic with clonidine as vasoconstrictor.

AIMS

To evaluate the advantages and disadvantages of using plain lignocaine local anaesthetic, lignocaine with adrenaline as additive and lignocaine with clonidine.

MATERIALS AND METHODS

It is a randomised, prospective, double blind study and approval from Institutional ethics committee was obtained. Seventy five patients requiring extraction of maxillary molar teeth participated in the study conducted from November 2013 to May 2014 in the Department of Oral & Maxillofacial Surgery, Tagore Dental College & Hospital, Chennai, India.

Inclusion Criteria

Our study included patients between 35 – 45 y, patients with no co morbidities such as hypertension, diabetes mellitus, asthma, bleeding disorders, etc; and who do not have known allergies to any drug under study. Teeth diagnosed with dental caries with apical periodontitis, periapical abscess, chronic pulpitis, teeth which could not be restored and patients who refused conservative management were included in the study.

Exclusion criteria

Pregnant women, known hypertensives, paediatric patients, patients with localized infection, nursing mothers and apprehensive patients were excluded from the study. Patients with impacted or partially impacted molars were excluded from the study. Root canal treated teeth, grossly decayed and mobile teeth were excluded from the study.

Informed consent was obtained from all 75 patients. Data regarding age, gender and clinical diagnosis were collected prior to initiation of the procedure. The patients were divided in to three groups. Randomization was performed using lottery method, and a trainee was asked to pick up the sealed envelope to determine which group the patient will go to. Group I: Maxillary infiltration anaesthesia was carried out using 1ml of 2% Lignocaine as local anaesthetic without addition of any other drug. Group II: Maxillary infiltration anaesthesia was carried out using 1ml containing 2% Lignocaine with 10 µg/ml of adrenaline. Each ampoule of adrenaline contains 1ml = 1mg i.e. 1000 µg of adrenaline. This 1ml of 1mg concentration was diluted to 10ml by adding 9ml 2% lignocaine. Now each ml of

this intermediate preparation contains 1ml=100 µg of adrenaline. The final preparation of 10 µg/ml of adrenaline in 2% lignocaine, is obtained by taking 1 ml of this intermediate preparation containing 1ml=100 µg of adrenaline in 2% lignocaine and diluting it further with 9ml 2% lignocaine. The solution prepared was retained for six hours and any remaining solution discarded.

Group III: Maxillary infiltration anaesthesia was carried out using 1ml containing 2% Lignocaine with 15 µg/ml of clonidine. Lidocaine with clonidine mixture was prepared as follows. Each ampoule of clonidine contains 150µg. 1 ml of clonidine was mixed with 9 ml of plain 2% Lidocaine to get a concentration of 15µg clonidine per ml of local anaesthetic solution. The solution prepared was retained for six hours and any remaining solution discarded.

All the patients were sedated with oral Lorazepam 1 mg (Tab ATIVAN, WYETH Ltd) two hours prior to the procedure to reduce anxiety. All the extraction procedures were done by same surgeon. The total anaesthetic mixture volume used in all three groups was 1ml. Infiltration anaesthesia was performed in both buccal and palatal aspect.Aspiration was performed prior to injection of LA to prevent inadvertent intravascular injection. Hemodynamic monitoring was done during infiltration and readings recorded. One minute after the infiltration process was completed, we began the process of determining the onset of anaesthesia using pinprick test [2]. The time when the patient had no pain (NRS score of 0/10) was noted. Numeric Rating Scale (NRS) was used to record pain with scores of 0/10 – no pain, 2/10 – just noticeable pain, 4/10 – weak pain, 6/10 – moderate pain, 8/10 - severe pain and 10/10 extreme pain [5]. In all the three groups, the dental extraction procedure was started five minutes after the infiltration, by which time all patients had an NRS score of 0/10.

Hemodynamic parameters: An observer who was not the surgeon, blinded and not aware of the procedure involved, monitored all the patients by “Philips Multipara monitor” for Heart Rate (HR), Systolic Blood pressure (SBP) and Diastolic Blood Pressure (DBP). Initial measurements were obtained prior to anaesthesia. Additional recordings were made during administration of local anaesthesia, 5 min after administration of anaesthesia, during the procedure and 10 min following completion of the procedure in all three groups. Intraoperative bleeding was calculated using the weight of the gauze pad. Uniform size of (3 ×3 CM) gauze was used in all the patients.

STATISTICAL ANALYSIS

The data from Group I, II and III were subjected to statistical analysis. The statistical analysis was carried out using SPSS 16 software. The sample size calculation was based on a previous study [1] where a minimum of 17 patients in each group was required to have a power of 80% to detect if observed differences are significant. We included 25 patients in each group. The mean, standard deviation and standard error were calculated for the descriptives at 95% confidence limits. The groups were subjected to ANOVA tests. Multiple comparisons between individual groups were carried out using Post Hoc – Tukey HSD tests and the significance calculated. Tests of normality such as Shapiro-Wilk tests were also done. $p < 0.05$ was considered to represent a statistically significant difference.

RESULTS

There was no statistical difference between the three groups in either the age or gender of the participants involved [Table/Fig-1]. There was no statistical difference between the three groups in the onset of anaesthesia [Table/Fig-2,3]. There was also no statistical difference between the three groups in any of the hemodynamic parameters [Table/Fig-4]. None of the patients had any significant hemodynamic variations and hence statistical analysis showed no difference. Statistical analysis of parameters concerning blood loss during procedure, revealed a statistical difference between Group I and Group II, as also between Group I and Group III. The average blood loss was higher in group I [Table/Fig-5]. But there was no statistical difference between Group II and Group III as far as intraoperative blood loss was considered [Table/Fig-6]. There was a statistically significant difference between the three groups in the postoperative analgesia. The mean duration in Group I was 87.60 ± 2.1 mins, Group II 180.49 ± 0.2 mins and 180.51 ± 0.3 mins in Group III [Table/Fig-7]. The longest and almost equal duration of action was in Group II and Group III and the shortest duration of action was in Group I.

Parameter	Group I	Group II	Group III	Significance
	n=25	n=25	n=25	
Mean Age	41.16 ± 0.8	42.06± 0.62	41.58± 0.97	Not significant
Gender				
Males	20	21	19	Not significant
Females	5	4	6	Not significant

[Table/Fig-1]: Age & gender distribution

Parameter	Group I	Group II	Group III	Significance
	n=25	n=25	n=25	
Onset	1.32 ±0.6 mins	1.41±0.9 mins	1.38 ±0.8 mins	Not significant

[Table/Fig-2]: Onset of anaesthesia among three groups

Groups	‘p’ value	Significance
Gp.I vs Gp.II	0.1038	Not significant
Gp.I vs Gp.III	0.1678	Not significant
Gp.II vs Gp.III	0.1278	Not significant

[Table/Fig-3]: Statistical Analysis of Time of Onset of anaesthesia between individual groups

Parameters	Time sequence	Group I	Group II	Group III	‘p’ value	Significance
		n=25	n=25	n=25		
Heart Rate	Before Anaesthesia	75.4± 6.608	73.2± 5.8	75.5±6.2	0.199	Not significant
	During Anaesthesia	77.3± 3.6	76.1± 6.2	77.6±5.2	0.175	Not significant
	5 min after Anaesthesia	75.3± 5.2	74.1± 4.5	75.1±5.8	0.947	Not significant
	During procedure	81.4± 3.2	83.6± 2.5	80.5±4.3	0.250	Not significant
	10 min after procedure	76.3± 4.1	82.4± 3.6	72.4±5.8	0.473	Not significant
SBP (mmHg)	Before Anaesthesia	121.8± 6.56	120.8± 4.77	122.8± 5.88	0.225	Not significant
	During Anaesthesia	123.6± 5.627	122.1± 3.8	123.3± 4.6	0.969	Not significant
	5 min after Anaesthesia	122.3± 4.9	123.5± 4.76	122.6± 5.16	0.217	Not significant
	During procedure	126.2± 2.76	127.2± 3.56	126.3± 2.3	0.104	Not significant
	10 min after procedure	122.3± 4.3	126.4± 5.5	120.2± 2.36	0.819	Not significant
DBP (mmHg)	Before Anaesthesia	76.1± 2.3	74.3± 3.3	76.3±1.3	0.120	Not significant
	During Anaesthesia	78.5± 2.3	76.8± 3.3	78.5±3.3	0.243	Not significant
	5 min after Anaesthesia	76.7± 4.3	80.5± 6.3	76.6±5.3	0.140	Not significant
	During procedure	80.8± 6.3	82.7± 7.3	78.6±4.3	0.218	Not significant
	10 min after procedure	78.7± 5.3	82.9± 6.3	74.4±3.3	0.349	Not significant

[Table/Fig-4]: Hemodynamic parameters among the three groups

Parameter	Group I	Group II	Group III
	n=25	n=25	n=25
Blood loss	1.5 ± 0.8 ml	0.6 ± 0.2 ml	0.7 ± 0.3ml

[Table/Fig-5]: Blood loss during procedure

Groups	'p' value	Significance
Gp.I vs Gp.II	0.001	Significant
Gp.I vs Gp.III	0.007	Significant
Gp.II vs Gp.III	0.632	Not significant

[Table/Fig-6]: Statistical Analysis of Blood loss

Parameter	Group I	Group II	Group III
	n=25	n=25	n=25
Duration	87.60 ± 2.1 mins	180.49 ± 0.2 mins	180.51 ± 0.3 mins

[Table/Fig-7]: Duration of post operative analgesia

Groups	'p' value	Significance
Gp.I vs Gp.II	0.0003	Significant
Gp.I vs Gp.III	0.0002	Significant
Gp.II vs Gp.III	0.280	Not Significant

[Table/Fig-8]: Statistical Analysis of duration of post operative analgesia

DISCUSSION

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. There was no statistical difference in the 75 patients included in the study regarding gender and age.

In Group II, Maxillary infiltration anaesthesia was carried out using Lignocaine as local anaesthetic with addition of 10 µg/ml of adrenaline. 1: 100,000 concentrations of adrenaline when given along with Lignocaine for intra oral anaesthesia in healthy patients can lead to cardiovascular changes even in small dosage [6]. Due to the addition of vasoconstrictors; there is decreased absorption into the systemic circulation and lowered peak plasma concentration.

In Group III, Maxillary infiltration anaesthesia was carried out using Lignocaine as local anaesthetic with addition of 15 µg/ml of clonidine. Clonidine is α – 2 adrenoreceptor agonist with both central and peripheral action. It decreases the blood pressure, produces a central analgesic effect and is a mild sedative due to its central activation of presynaptic α – 2 adrenoreceptor. It brings about vasoconstriction of peripheral blood vessels due to activation of postsynaptic α – 2 adrenoreceptors. When used as a central hypotensive agent, in different routes of administration, it enhances local anaesthesia and analgesia [7].

In a study done in children undergoing orthognathic surgeries, there was a faster recovery and the room stay was also shortened [8]. This indicates that clonidine can be used in oral and maxillofacial surgical procedures.

Administration of local anaesthetic can be stressful for any patient and particularly so for cardiac patients [9]. Cardiovascular system will be affected due to anxiety and pain during injection and hence cardiovascular responses will be difficult to evaluate. However, the effect of anxiety and pain during injection can be reduced with various methods thus making the evaluation a meaningful one [7]. Oral Lorazepam 1 mg was administered two hours prior to the procedure to reduce anxiety in our study. Modified Ramsay Sedation scalewas used to assess the sedation levels of the patients before injection was administered [10].

All the patients were in stage – 2 (Co –operative, oriented and tranquil) at the time of injection. By the induction of antianxiety drug, anxiety was minimised so that it does not influence the haemodynamic parameters adversely. The average duration of the extraction procedure was four minutes. There were seven incidences of root fracture but did not require any transalveolar procedure to remove them. The onset of anaesthesia was observed by testing with a sharp probe (Pinprick test) in the buccal/palatal gingiva adjacent to the tooth to be extracted after a minute for every 30 seconds till the patient gave an NRS of 0/10. The objective change was reported at 1.32 ± 0.6 mins in Group I; 1.41± 0.9 mins in Group II and 1.38 ± 0.8 mins in Group III. Statistical analysis revealed no difference between the groups in onset of anaesthesia. This can be explained by the fact that the local anaesthetic agent used in all three groups were the same and of the same concentration.

Hemodynamic parameters of all the patients were monitored by an observer using "Philips Multipara monitor". Heart Rate (HR), Systolic Blood pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) were noted. The HR, SBP, DBP, and MAP did not show much variations among the groups when recorded before and during administration of local anaesthetic mixture. Similarly the hemodynamic variations recorded at the fifth minute following infiltration and during the dental extraction procedure were also not significant. The hemodynamic variations should be more than 25% - 30% of the baseline value to be significant [11].

This means the heart rate variations at any point of time, within the group, should have increased by more than 19 beats for a baseline of 75/min. This never occurred. Similarly, the systolic blood pressure at any point of time, within the group, should have increased by more than 30 mmHg for a baseline of 120mmHg and diastolic blood pressure should have increased by more than 19 mmHg for a baseline of 76 mmHg. This also never occurred. Hence, the hemodynamic variations were not statistically significant. This can be attributed to the tranquillity attained due to use of T. Lorazepam 1mg prior to procedure. There was an increase in the HR, SBP, DBP, and MAP with the maximum recorded 10 min after the procedure in Group II compared to Group I and Group III. This is due to the presence of Adrenaline which is a vasoconstrictor. It is a sympathomimetic amine with both α and β – adrenergic receptor agonist effects. Different concentrations of adrenaline produce different actions. Low concentrations result in preferential β–2 receptor mediated vasoconstriction in vascular smooth muscle [11]. But when compared to baseline values of the patients in the same group, recorded before infiltration, the average increase was less than 20 % of baseline reading and hence statistically insignificant. Therefore, we can clearly see that at a concentration of 10.0 mic gm/ml, adrenaline does not produce significant hemodynamic changes, when used for local infiltration.

There was an decrease in the HR, SBP, DBP, and MAP with the maximum recorded ten minutes after the procedure in Group III compared to Group I and Group II. But when compared to baseline values of the patients in the same group, recorded before infiltration, the average decrease was less than 20% of baseline reading and hence statistically insignificant. Therefore, we can clearly see that at a concentration of 15.0 mic gm/ml, clonidine does not produce significant hemodynamic changes. 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 [12]. It has been proved to provide stable hemodynamic parameters owing to its central hypotensive action [3] Various studies [1-4,6,12,13] 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 [14]. 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 [15].

Weight of gauze pads used in group I was more compared to the other two groups. Blood loss was 1.5 ± 0.8 ml in Group I; 0.6 ± 0.2 ml in Group II and 0.7 ± 0.3 ml in Group III. Statistical analysis

of parameters concerning blood loss during procedure, revealed a statistical difference between Group I and Group II, as also between Group I and Group III as the average blood loss was higher in group I. But there was no statistical difference between Group II and Group III as far as average blood loss was considered. Thus clinically more bleeding was observed in patients in Group I.This is because in Group I, only plain lignocaine was used; whereas in Group II, adrenaline being a vasoconstrictor, decreases blood loss, and in Group III, clonidine decreases blood loss owing to its central hypotensive action [3].

As regards post operative analgesia, it was observed by pinprick test again beginning one hour after initial infiltration. They were recorded every 30 min for one hour and every 15 min thereafter till they complained of pain (NRS Score of 2/10). There was a statistically significant difference between the three groups in the post operative analgesia. The mean duration in Group I was 87.60 ± 2.1 mins, in Group II it was 180.49 ± 0.2 mins and in Group III it was 180.51 ± 0.3 mins. The longest and almost equal duration of action was in Group II group and Group III, and the shortest duration of action was in Group I group. Group I which did not contain any additive and had only lignocaine; had a very short duration of action. The average duration of analgesia increased in Group II due to adrenaline which is a vasoconstrictor. Clonidine is also said to provide excellent postoperative analgesia. In our study, at the concentration of 15 mic gm/ml, it provided good postoperative analgesia which when compared to Group I was statistically significant but not very different from Group II [Table/Fig-8].

Clonidine has also been shown to have a peripheral analgesic effect by releasing enkephalin like substances. Chad et al., [12] has stated that clonidine when used with short and intermediate acting local anaesthetics prolongs the duration of anaesthesia. Clonidine is said to also cause sedation when used in high doses (100 µg) but the concentration (15 µg) used in our study did not produce any untoward side effects [16].

A study by Brokovic et al., [2] states that there are no differences in the enhancement of duration and intensity of intra oral anaesthesia with adrenaline and clonidine whereas clonidine might have hemodynamic advantages over adrenaline as a vasoconstrictor because of its central hypotensive effect. The results of this study is similar to ours, wherein there were no differences in the enhancement of duration of intra oral anaesthesia with adrenaline and clonidine whereas in the 10th min hemodynamic recording, the readings in the adrenaline group II were slightly higher compared to clonidine group III, though none of these hemodynamic changes were statistically significant. All the patients were monitored for four hours following the procedure and discharged without any complaints, side effects and local or systemic adverse reactions to the drug under study. An oral analgesic was given to all the patients at the end of the 4th hour and discharged with a prescription containing analgesic, anti-inflammatory and antibiotic. The patients were followed up over phone after 24 hrs and none of them had any complaints. Clonidine has also been used as a premedication in pediatric patients. This however sedated the patients and also reduced the incidence of vomiting and shivering [17].

CONCLUSION

Adrenaline at 10 µg/ml and clonidine at 15 µg/ml can be safely used as additives with lignocaine, in maxillary infiltration anaesthesia for dental extraction; with addition of either of these two drugs, having an equal advantage over use of plain lignocaine; in terms of lower blood loss and longer duration of anaesthesia but, with no difference in the onset of anaesthesia and with no significant hemodynamic changes.

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