THE HEMODYNAMIC EFFECTS OF 2% LIGNOCAINE WITH 1:80,000 ADRENALINE VERSUS 1:2,00,000 ADRENALINE IN HYPERTENSIVE PATIENTS UNDERGOING MINOR ORAL SURGICAL PROCEDURES: A PROSPECTIVE, RANDOMIZED AND DOUBLE BLINDED STUDY

Dissertation submitted to

THE TAMILNADU Dr. MGR MEDICAL UNIVERSITY

In partial fulfillment for the Degree of

MASTER OF DENTAL SURGERY

BRANCH III

ORAL AND MAXILLOFACIAL SURGERY

MAY 2019

CERTIFICATE

This is to certify that this dissertation titled **"THE HEMODYNAMIC EFFECTS OF 2% LIGNOCAINE WITH 1:80,000 ADRENALINE VERSUS 1:2,00,000 ADRENALINE IN HYPERTENSIVE PATIENTS UNDERGOING MINOR ORAL SURGICAL PROCEDURES: A PROSPECTIVE, RANDOMIZED AND DOUBLE BLINDED STUDY"** is a bonafide record of work done by **Dr. S. HARSHAD** under my guidance and to my satisfaction during his Post Graduate study period of 2016-2019.This dissertation is submitted to **THE TAMILNADU Dr. MGR MEDICALUNIVERSITY,** in partial fulfillment for the award of the degree of **MASTER OF DENTAL SURGERY** in Branch III- **ORAL AND MAXILLOFACIAL SURGERY.** It has not been submitted (partially or fully) for the award of any other degree or diploma.

_____ _____

Dr. M.S. SENTHIL KUMAR M.D.S.,
Professor and Guide
Department of Oral and Maxillofacial surgery
Sri Ramakrishna Dental College and Hospital
Coimbatore.

Dr. L. DEEPANANDAN M.D.S.,
Professor and HOD
Department of Oral and Maxillofacial surgery
Sri Ramakrishna Dental College and Hospital
Coimbatore.

_____

Dr. V. PRABHAKARAN M.D.S.,
Principal
Sri Ramakrishna Dental College and Hospital
Coimbatore.

DECLARATION BY THE CANDIDATE

NAME OF THE CANDIDATE	**DR. S. HARSHAD**
TITLE OF DISSERTATION	**THE HEMODYNAMIC EFFECTS OF 2% LIGNOCAINE WITH 1:80,000 ADRENALINE VERSUS 1:2,00,000 ADRENALINE IN HYPERTENSIVE PATIENTS UNDERGOING MINOR ORAL SURGICAL PROCEDURES: A PROSPECTIVE, RANDOMIZED AND DOUBLE BLINDED STUDY**
PLACE OF STUDY	**SRI RAMAKRISHNA DENTAL COLLEGE AND HOSPITAL.**
DURATION OF COURSE	**2016 – 2019.**
NAME OF GUIDE	**DR. M.S. SENTHIL KUMAR M.D.S.,**
HEAD OF THE DEPARTMENT	**DR. L. DEEPANANDAN M.D.S.,**

I hereby declare that no part of the dissertation will be utilized for gaining financial assistance for research or other promotions without obtaining prior permission from the Principal, Sri Ramakrishna Dental College And Hospital. In addition, I declare that no part of this work will be published either in print or electronic without permission from the guide who has been actively involved in this dissertation. The author solely has the rights for publishing the work with prior permission from the Principal, Sri Ramakrishna Dental College And Hospital, Coimbatore.

Head of the Department **PG Guide** **Signature of Candidate**

Principal

URKUND

Urkund Analysis Result

Analysed Document:	Thesis corrected.docx (D47181172)
Submitted:	1/24/2019 7:39:00 AM
Submitted By:	dr.harshad22@gmail.com
Significance:	0 %

Sources included in the report:

Instances where selected sources appear:

0

CERTIFICATE – II

This is to certify that this dissertation work titled **THE HEMODYNAMIC EFFECTS OF 2% LIGNOCAINE WITH 1:80,000 ADRENALINE VERSUS 1:2,00,000 ADRENALINE IN HYPERTENSIVE PATIENTS UNDERGOING MINOR ORAL SURGICAL PROCEDURES: A PROSPECTIVE, RANDOMIZED AND DOUBLE BLINDED STUDY** of the candidate **Dr. S.HARSHAD**with registration number **241615301**for the award of **MASTER OF DENTAL SURGERY** in the branch of **ORAL AND MAXILLOFACIAL SURGERY**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 0(zero) percentage of plagiarism in the dissertation

Head of the Department **PG Guide**

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to **Dr. L. Deepanandan, M.D.S., Professor and Head**, Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, for his guidance, patience and knowledge bestowed up on me.

I express my sincere and heartfelt gratitude to my guide **Dr. M.S. Senthil Kumar, M.D.S., Professor**, Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, for his unwavering guidance, for his patience, motivation, enthusiasm, immense knowledge, constant support and encouragement throughout the duration of my course and for the immense scholarly support throughout the study. A mere word of thanks is not efficient to express his unflinching guidance. I am always indebted for his guidance and for sharing his knowledge.

I express my heartfelt gratitude to **Dr. R. Kannan, M.D.S., Professor**, Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, for his innovative ideas, constructive suggestions, valuable criticism and constant encouragement throughout the duration of my course. I extend my heartfelt gratitude for his efficacious guidance, altruistic co-operation and support during my period of study.

A mere word of thanks is not sufficient to express my gratitude to **Dr. M.A.I. Munshi, M.D.S., and Dr. R.S. Karthik, M.D.S., Readers**, Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, for their constant scholarly support, guidance and encouragement throughout the duration of my course.

I express my sincere heartfelt gratitude to **Dr. R. Vijay, M.D.S., Dr. S. Shilpa, M.D.S., and Dr. Ronak Nazir Kaul, M.D.S., Senior Lecturers** Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, for their valuable help, support, guidance and constant encouragement during my study.

I bestow my sincere gratitude to **Dr. N. Paramasivan M.D., D.A., FIDM.,** Sri Ramakrishna Dental College and Hospital for his consent and amenities rendered toward my study.

I owe my sincere gratitude to **Dr. T.R. Nanda Kumar, M.D. (Gen Medicine)., DNB (Cardiology)., AFESC Interventional Cardiologist.**, Department of Cardiology, Sri Ramakrishna Hospital for his timely help and giving me an opportunity to conduct my study under his reference.

I express my sincere thanks to **Dr. Gayathri R Nair, Dr. G. Karthik Rajan, Dr. N. Santhoshi Revathy, Dr. A. Preethi and Dr. M. Shalini** for their support throughout the duration of my course.

I thank **My Patients** for their consent and cooperation towards the preparation of this study.

I thank **My Family and Friends** because of whom I stand to be here today.

Dr. S. HARSHAD

CONTENTS

1. INTRODUCTION 1

2. AIMS AND OBJECTIVES 4

3. REVIEW OF LITERATURE 5

4. MATERIALS AND METHODS 21

5. RESULTS 28

6. DISCUSSION 46

7. SUMMARY & CONCLUSION 52

8. BIBLIOGRAPHY 53

9. ANNEXURES

   I. ETHICAL CLEARANCE CERTIFICATE 64

   II. PATIENT INFORMATION FORM 65

   III. INFORMED CONSENT 66

   IV. STUDY TABLE 67

   V. PATIENT LOG 68

10. GLOSSARY 70

INTRODUCTION

Hypertension is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. High blood pressure typically does not cause symptoms but long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia[1].According to World Health Organization (WHO), persistently elevated blood pressure is a silent killer and is the major cause of premature death worldwide. The prevalence of hypertension rose from 600 million in 1980 to one billion by 2008. In India, males have slightly higher predilection of hypertension when compared to females with percentage of 36% and 34.2% respectively[2].

The American Heart Association (AHA) has formulated a guideline in the year 2017 for classifying hypertension. As per AHA, Systolic Blood Pressure (SBP) 130-139mmHg or Diastolic Blood Pressure (DBP) 80-89mmHg were considered Stage 1 hypertensive and SBP >140mmHg or DBP >90mmHg were classified as Stage 2 hypertensive. While Blood Pressure (BP) <120/80mmHg was considered as normal, SBP of 120-129 and DBP <80mmHg were classified under elevated blood pressure[3].

Local anaesthetic with adrenaline is commonly used in dentistry for all the procedures which require sensory blockage. The technique of diluting vasoconstrictors in local anaesthetics dates back to 1897 when Abel discovered adrenaline[4]. Vasoconstrictors commonly used in dental surgery are of various dilutions of 1: 80,000, 1: 1,00,000 and 1: 2,00,000 having 0.0125 mg/ml, 0.01 mg/ml and 0.005 mg/ml of epinephrine respectively[5]. Although epinephrine is the most used vasoconstrictor in local anaesthetics in dentistry, it is notan ideal drug because epinephrine is absorbed from the site of injection, just as the local anaesthetic and

measurable epinephrine blood levels are obtained, which influence the heart and blood vessels. These are associated with increase in the systolic blood pressure, diastolic blood pressure, cardiac output, stroke volume, heart rate, strength of contraction and myocardial oxygen consumption leading to overall decrease in cardiac efficiency[6].The use of local anaesthetic with adrenaline has shown to have hemodynamic effect on patients by increasing the blood pressure and heart rate[7,8].

Local anaesthesia is defined as loss of sensation in a circumscribed area of the body caused by depression of excitation in nerve endings or inhibition of the conduction process in peripheral nerves without loss of consciousness[6,9].The use of local anaesthetic dates back from 1859 when Neimann used the extracted cocaine from coca beans. It was first introduced in dentistry as regional anaesthesia by Halsted in the year 1884 for the painless removal of third molar[4]. The modern local anaesthetic Lidocaine was first synthesized by Lofgren in 1943 and is widely used in the field of dentistry till date. An essential pre-requisite to success in dentistry is to achieve good quality local anaesthesia and the choice of local anaesthetic should be individualized for each patient. Knowledge of the pharmacology and toxicology of these agents will result in their intelligent and judicious use[10].

Lidocaine hydrochloride is a potent vasodilator, thus when used for pain control, cease to provide a clinical effect when they are absorbed from the site of administration[11,12,13] . The duration of the dental procedure should be weighed against the duration of action of the local anaesthetic; a decision should be made as to whether a vasoconstrictor is needed to prolong its action[10].

Epinephrine is the most commonly employed vasoconstrictor in dentistry. As with the other useful vasoconstrictors, epinephrine produces its effects by stimulating

the alpha adrenergic receptors located in the walls of the arteriole. Epinephrine is also a beta adrenergic stimulator and may cause vasodilatation of arterioles in skeletal muscle due to the predominance of beta receptors in this tissue. Epinephrine's beta adrenergic responses, even at low systemic levels, include skeletal muscle vasodilatation with increased heart rate. The beta adrenergic effects predominate over the alpha because of the greater sensitivity of beta adrenergic receptors to epinephrine[9].

In patients with pre-existing cardiovascular, the side effects of absorbed epinephrine must be weighed against those of elevated local anaesthetic blood levels. It is currently thought that the cardiovascular effects of conventional epinephrine doses are of little practical concern, even in patients with heart disease.Even following usual precautions (e.g., aspiration, slow injection), sufficient epinephrine can be absorbed to cause sympathomimetic reactions/ epinephrine reaction such as apprehension, tachycardia, sweating, and palpitation[8].

The present study was designed to assess and compare the patient comfort, cardiac status and hemodynamic effects of 2% lignocaine with adrenaline in concentrations of 1:80,000 & 1:2,00,000 during routine minor oral surgical procedures and extractions in hypertensive individuals.

AIM AND OBJECTIVES

AIMS:

This study is aimed to evaluate the cardiac status and cardiovascular changes in hypertensive patients reported to Sri Ramakrishna Dental College and Hospital for minor oral surgical procedures injected with 2% lignocaine with 1:80,000 adrenaline in comparison to 2% lignocaine with 1:2,00,000 adrenaline.

OBJECTIVES:

1. To compare the time of onset and the ability to mask pain within the duration of procedure.
2. To compare the difference in changes of clinical parameters like heart rate (HR), respiratory rate (RR), Systolic Blood Pressure(SBP), Diastolic Blood Pressure (DBP), Oxygen Saturation ($SpO_{2)}$, Mean Arterial Pressure (MAP) and cardiovascular indicators like PressureRate Quotient (PRQ) and Rate Pressure Product(RPP).
3. To evaluate and determine any arrhythmic changes before and after administration of local anaesthetic with 2 different concentrations of adrenaline.

REVIEW OF LITERATURE

Vernale et al[11] in 1962, compared the cardiovascular changes in normotensive and hypertensive patients after injection of 2% lignocaine in 1:1,00,000 epinephrine and noticed a rise in systolic pressure and rise or fall in diastolic pressure in both groups. The hypertensive group showed different cardiovascular changes when compared to the normotensive group but the variations were not significant.

The hemodynamic effects of lignocaine in patients with myocardial infarction within 24 hours was studied by Stannard et al[12] in 1968. 100mg of lignocaine was administered for 5 minutes and no statistical change in blood pressure was noted. Hence concluded that lignocaine is safe to be used in ventricular arrhythmias complicating acute myocardial infarction.

In 1982, the study evaluating the effect of third molar extractions without sedation and sedation with intravenous diazepam and inclusion of epinephrine in local anaesthetic on circulatory, physiological and plasma catecholamine by Goldstein et al[13] showed a significant rise in HR and SBP while no changes were noted in DBP in all patients. 60% rise in plasma norepinephrine was noted in non-sedated patients. The rise in mean plasma epinephrine was noted 5 mins after injection of local anaesthetics containing epinephrine. They concluded that there is involvement of the sympathetic nervous system in producing circulatory responses in third molar impactions.

The comparative study by Chernow et al[14] in 1983, comparing the hemodynamic effects of local anaesthesia with and without epinephrine for dental procedures. The MAP, heart rate and plasma catecholamine were measured and notice no significant changes in MAP, heart rate and only sight transient increase in plasma catecholamine from base values in the plain local anaesthetic, whereas

lignocaine with epinephrine showed a significant and sustained increase in plasma catecholamine and heart rate while no changes in MAP were noted. Hence concluded local anaesthetic with vasoconstrictor has no significant hemodynamic effect.

In 1986 the cardiac function of 9 patients with cardiovascular diseases during dental procedures with ECG was studied by Hirota et al[15]. All the patients underwent dental procedures in 2 appointments. Local anaesthetics used were 2% lignocaine in 1:80,000 adrenaline and 3% prilocaine in 0.03IU/ml felypressin in each appointment. They noted increased cardiac output in all patients in the lignocaine group due to increased heart rate in 4 cases and increased stroke volume in the rest. The prilocaine group showed no significant increase in cardiac output except one patient who complained of pain during the dental procedure due to inadequate anaesthesia.

The effect of epinephrine-containing local anaesthetic on plasma catecholamine and cardiovascular changes was studied by Emanuel S. Troullous[16] in 1986. The epinephrine group showed an increase in plasma epinephrine concentration by 27 times and elevation in SBP and pulse rate when 8 dental cartridges of 2% lignocaine with 1:1,00,000 adrenaline was injected. He concluded that the epinephrine injected intraorally alters the cardiovascular status of the patient once a significant amount of epinephrine is absorbed systemically.

The hemodynamic changes in hypertensive and normotensive patients undergoing dental extractions was compared by Meyer F U[17]in 1986. 2% lignocaine with 1:1,00,000 adrenaline was used for all the patients. He noticed changes in blood pressure and heart rate in both the groups which were approximately similar.

Cardiovascular changes in patients above 40 years of age with hypertension was studied by Abraham[18] in 1988. The assessment was done before, during and after

tooth extraction and noticed a greater increase in blood pressure in patients with hypertension compared to normotensive while 2% lignocaine with 1:80,000 adrenaline was injected and in addition, 7.5% patients with hypertension developed significant arrhythmias.

Salonen et al[19] in 1988 studied the role of adrenaline in local anaesthetic used in dental procedures. Hemodynamics and plasma catecholamine levels were evaluated. They noticed that the exogenous adrenaline significantly elevates the heart rate but did not affect the SBP or DBP. They concluded that adrenaline in local anaesthesia is a major source of adrenergic activation during minor oral surgery.

The study comparing the metabolic responses of the local anaesthetics with and without epinephrine was done by Meechan and Rawlins[20] in 1992 . 4.4ml of 2% lignocaine with 1:80,000 adrenaline was injected in one group and the other group with 3% prilocaine with 0.03IU/ml felypressin. The epinephrine group showed a decrease in plasma potassium and increase in blood glucose concentration at 10 mins after injection while the epinephrine free group showed the vice versa. They concluded that epinephrine free and epinephrine containing solution differ in metabolic effects during oral surgical procedures.

Perusse et al[21] in 1992 published a review on contraindications for vasoconstrictors in dentistry. According to the article, unstable angina, recent myocardial infarction, coronary artery bypass surgery, uncontrolled hypertension, uncontrolled diabetes, hyperthyroidism, sulphite sensitivity, and pheochromocytoma were classified under absolute contraindications. Patients under tricyclic anti-depressants, phenothiazine compounds, monoamine oxidase inhibitors, non-selective, and cocaine abusers were classified under relative contraindications. They concluded

that the complications during oral surgical procedures after injection of epinephrine-containing local anaesthetics are not exclusively due to cardiac diseases.

In 1997, evaluation of the local anaesthetic with three different concentration of epinephrine for inferior alveolar nerve block was done by Dagher et al[22]. Anaesthetic success, time of onset and duration of anaesthesia were studied. He concluded that there is no significant difference between the different doses of anaesthesia and should be considered equivalent in inferior alveolar nerve blocks of 50 min duration.

The comparative study of hemodynamic changes and the ECG responses to 2% lignocaine, noradrenaline 1:50,000, vasopressin 0.25 IU/ml and midazolam was done by Middlehurst[23] in 1999. Significant changes in the mean heart rate and mean SBP was noted after administration of the anaesthetic. But comparing the changes in the different solutions proves to be less significant.

The relation between oral mucosal blood flow and plasma epinephrine levels after sub-mucosal infiltration of epinephrine-containing 2% lignocaine was studied by Homma et al[24] in 1999. SBP, DBP, HR and plasma epinephrine concentration were recorded before and after the infiltration. The study showed a peak rise in plasma epinephrine concentration 3 mins after infiltration. This suggests the correlation between the mucosal blood flow in the infiltrated areas.

The drug interactions associated with vasoconstrictor in dental procedures was reviewed by Yagiela et al[25] in 1999. Tricyclic anti-depressants depress the myocardium by blocking muscarinic and α1- adrenergic receptors. Epinephrine along with halothane anaesthesia was associated with ventricular dysrhythmias. Epinephrine intensifies the adrenergic neurotransmitter release and postsynaptic

responses of cocaine. Hence vasoconstrictors should be withheld for 24 hours to allow elimination of the drug.

The hemodynamic response of infiltration anaesthesia and epinephrine infusion was compared with those produced by ergometer exercise by Niwa et al[26] in 2000. Epinephrine was infused to produce the cardiovascular changes similar to that of the response seen in 2%lignocaine with 1:80,000 adrenaline. The changes were evaluated using ECG. The study shows that the cardiovascular changes caused by infiltration of epinephrine-containing local anaesthetic are equivalent to walking speed of 4.8km/hr. They concluded that except pathological conditions like serious arrhythmias, infiltrative anaesthesia with epinephrine is safe to be used for dental procedures.

Tanaka et al[27] in 2000, studied the effect of intravenous injection of epinephrine. Patients under GA were injected with 15μg of epinephrine. HR, BP, and ECG were recorded prior to and after intravenous injection of epinephrine. The results showed an increase in HR between 40 – 80 seconds and a decrease in HR between 160 – 280 seconds. The SBP values increased between 20 -240 seconds. The results indicated that the minimal effective adrenaline dose of epinephrine was 15μg increasing HR by <10 beats/ minute and SBP by <15mmHg compared to the baseline values.

In 2001 the comparative evaluation of the hemodynamic effects of 2% lignocaine with 1:80,000 adrenaline and 3% prilocaine with felypressin was done by Meechan et al[28]. The study results showed an increase in HR 10minutes following the injection and fall in DBP 20mins after the injection of epinephrine-containing local anaesthetic.

The safe dose of epinephrine for patients with cardiovascular disease was studied by Niwa et al[29] in 2001 using ECG. 1.8ml of 2% lignocaine with 1:80,000 adrenaline was injected and the hemodynamic response was noted. The concluded that lignocaine adrenaline is safe to use since the hemodynamic changes are very minimal in patients with cardiovascular diseases.

The comparative study of the hemodynamic effects of local anaesthetic with and without adrenaline was done by FernieiniM et al[30] in 2001, using laser Doppler flowmetry. In both, the group heart rate increased prior to the administration of local anaesthetic and settled back to normal immediately after the administration. In epinephrine containing the heart rate increased once again 5 minutes after injection and sustained for 10 minutes. They concluded that the increase in heart rate prior to injection was due to the release of endogenous catecholamine and the delayed increase in heart rate was due to the adrenaline content in the local anaesthetic.

The efficacy of local anaesthetic with different concentrations of lignocaine and adrenaline was compared by Ohkado et al[31] in 2001. The anaesthetic potency was evaluated on dental pulp by changing the concentrations of lignocaine to that of adrenaline. They noted that the anaesthetic potency was reduced when the concentration of adrenaline was lowered and it remained the same when a higher concentration of lignocaine was used. They concluded that the increase in the concentration of lignocaine does not compensate the anaesthetic efficacy for the lower concentration adrenaline in the local anaesthetic solution.

In 2001, the evaluation of cardiovascular changes after infiltration on the scalp was done by Murthy and Rao[32]. Five different combinations of epinephrine and lignocaine were used. Namely, 0.5% lignocaine, 0.5% lignocaine with 1:1,00,000

adrenaline, 0.5% lignocaine with 1:2,00,000 adrenaline, normal saline with 1:2,00,000adrenaline and normal saline with 1:1,00,000 adrenaline. Plain lignocaine showed no significant changes in BP. SBP, DBP, and MAP increased significantly in NS with 1:1,00,000 adrenaline and episodic increase in DBP in NS with 1:2,00,000 adrenaline. A biphasic diastolic hypotension was noted in both lignocaine with 1:1,00,000 adrenaline and 1:2,00,000 adrenaline at 2 minutes and 9-15 minutes. They concluded that plain adrenaline in 1:1,00,000 adrenaline and 1:2,00,000 concentrations caused significant tachycardia and hypertension. The mixture of lignocaine and epinephrine attenuates hypertension but results in biphasic hypotension.

The cardiovascular effect of epinephrine on hypertensive patients was evaluated by Bader et al[33] in 2002. He noticed that the SBP increased by 4mm/Hg in hypertensive patients, the DBP decreased for both normotensive and hypertensive group and the HR was higher in patients receiving epinephrine than those who received plain lignocaine.

Faraco et al[34] in 2003, conducted a double-blind study to evaluate the cardiovascular changes during dental procedures. The parameters included SBP, DBP, MAP, and HR. One group received no premedication, the second group received 10mg diazepam and the third group was given placebo as premedication. 1.8ml of 2% lignocaine with 1:1,00,000 epinephrine was given to all patients. On evaluation, no significant changes were noted between the groups during dental procedures. They concluded that premedication with diazepam does not have any effect on cardiovascular parameters during dental procedures.

A prospective, randomized study of hemodynamic changes after the administration of saline or 2% lignocaine with 1:2,00,000 adrenaline on patients under GA was conducted by Yang JJ et al[35]. They noticed temporary hypotension and other hypo dynamic changes in patients under GA, none of which lasted longer than 4 minutes in adrenaline group. They explained this mechanism to be the preferential stimulation of β2 receptors at a lower concentration of adrenaline.

Patients undergoing periodontal surgery under local anaesthesia containing 0.06mg adrenaline was evaluated for the changes in BP, HR, and temperature by Gedik et al[36] in 2005. They noticed fall in BP, HR, and temperature during the administration of the local anaesthetic in healthy individuals. They concluded that the patient age, gender, volume of local anaesthetic used, duration of the treatment and the difficulty of the treatment plays a major role in changes of these parameters. They also concluded that these parameters change significantly in medically compromised patients.

The comparison of the effects of local anaesthetic with or without adrenaline on plasma epinephrine and hemodynamic parameters in patients undergoing third molar extractions was studied by Meral et al[37] in 2005. They noticed no significant changes in the hemodynamic parameters like HR and BP in both groups while the plasma epinephrine increased in the adrenaline group. They concluded that adrenaline has minimal effect on hemodynamic parameters.

In 2006, the study observing the hemodynamic effect of local anaesthesia containing 1:80,000 adrenaline for inferior alveolar nerve block was conducted by Haghighat et al[38]. They notice a rise in SBP during injection which returned back to the baseline value 10 minutes after administration of local anaesthetic while the DBP

decreased after administration of local anaesthetic and also at 10 minutes after administration. They concluded that the rise in SBP during injection was due to the anxiety of syringe and returned back to baseline values when the patients get over the phobia of injection. This study shows that one cartridge of local anaesthesia with adrenaline has minimal effect on hemodynamic parameters in healthy individuals.

The comparison of the efficacy of local anaesthetic solution with 2 different concentrations of adrenaline in a patient undergoing third molar was studied by Santos et al[39] in 2007 removal. 4% articaine with 1:1,00,000 adrenaline and 1:2,00,000 adrenaline concentrations were used in a single patient for removal of bilateral third molar removal. Latency, duration of postoperative analgesia, duration of anaesthetic action on soft tissue, intraoperative bleeding and hemodynamic parameters were evaluated. The latency period and duration of action were very similar, intraoperative bleeding assessment by the surgeon was close to minimal and transient insignificant changes in hemodynamic parameters were observed. Hence concluded the concentration of adrenaline does not affect the clinical efficacy of the local anaesthetic and local anaesthetic with a lower concentration of adrenaline are more than sufficient for the lower third molar extraction with or without bone removal.

The effect of anxiety during dental procedures on the cardiovascular response was studied by Liau et al[40] in 2008. Blood pressure, heart rate, oxygen saturation, and ECG were recorded 15 minutes before the injection of local anaesthetic and after the injection. Corah's Dental anxiety scale was used to measure the anxiety. The study showed lower heart rate in patients with mild anxiety when compared to those with moderate and severe anxiety. Heart rate and SBP was higher in patients with severe anxiety after injection of local anaesthetic when compared to the mild and moderate

group. No changes in oxygen saturation were noted in all the three groups. They concluded that anxiety plays a major role on the impact of local anaesthetic on BP and heart rate.

In 2008, Vasconcellos et al[41] studied the effect of 4 different local anaesthetics in the amide group used for dental extractions on cardiovascular parameters. The cardiovascular parameters noted were BP, HR, and SpO_2. The study results showed that all the local anaesthetics caused an increase in HR and returned back to normal with no additional treatment. They concluded that the local anaesthetic used in dentistry produce safe hemodynamic changes.

The hemodynamic and haemostatic changes of local anaesthetic with 2 different concentrations of adrenaline in patients undergoing FESS was evaluated by Moshaver et al[42] in 2009. The cardiovascular parameters were noted prior to injection for the baseline values and every minute for 5 minutes after injection of local anaesthetic. In patients injected with 2% lignocaine with 1:1,00,000 adrenaline, significant hemodynamic fluctuations were noted. HR, BP, and MAP were elevated significantly at the first 2 minutes after injection of local anaesthetic with 1:1,00,000 adrenaline and no such fluctuates were noted in patients injected with 2%lignocaine with 1:2,00,000 adrenaline.

The hemodynamic changes in cardiac patients undergoing dental procedures under 2%lignocaine with 1:2,00,000 adrenaline and without adrenaline was compared and analysed by Laragnoit et al[43] in 2009. No significant changes in hemodynamic parameters were noted in all the patients in the 2 groups. They concluded that local anaesthetic with epinephrine did not cause any cardiovascular changes and arrhythmias.

The hemodynamic changes and glucose levels of patients undergoing dental procedures with or without local anaesthetic was compared by Bortoluzzi et al[44] in 2010. The HR, BP, SpO_2 did not change significantly regardless of the use of local anaesthesia. They explained that adrenaline has both β1 (stimulates an increase in BP) and β2 (decreases BP) activity and this is the reason for no change in hemodynamic changes.

The comparison of the hemodynamic effects of lignocaine, prilocaine and mepivacaine without adrenaline in hypertensive patients was analysed by BahadirEzmek et al[45]in 2010 and noted significant changes in DBP in mepivacaine, prilocaine group and heart rate in lignocaine and mepivacaine group. Apart from BP and HR, the author included Rate Pressure Product (RPP) and Pressure Rate Quotients (PRQ) as an indicator for myocardial ischemia and noticed ischemia in 43% of patients after injection if the local anaesthetic agent.

The cardiovascular changes after infiltration of adrenaline with or without lignocaine on the scalp was compared by Tariq et al[46] 2010. The parameters included are BP, HR, and MAP. One group were injected with 2%lignocaine with 1:2,00,000 adrenaline and the other with NS in 1:2,00,000 adrenaline. They noted that the group which received adrenaline without lignocaine showed a significant increase in HR, BP, and MAP while the significant decrease in DBP was noted in the group that received lignocaine adrenaline combination. He concluded that addition of lignocaine reduces the blood pressure.

In 2011, the comparison of the effect of the injection speed of local anaesthetic containing adrenaline on the hemodynamic changes on patients under general anaesthesia was done by Goranovic et al[47]. Local infiltration of the nasal mucosa was

done in 2 different speed. One group were injected at slow speed (>60 seconds) and the other at the rate <60 seconds. No significant changes in HR, SBP, DBP, and MAP were noted in both the group. They concluded that the speed of injection has no effect on cardiovascular changes however lignocaine with adrenaline induced a decrease in blood pressure.

Vnuk et al[48] in 2011, compared hemodynamic effects of epidural lignocaine and lignocaine adrenaline composition in dogs. The study showed an increase in HR and cardiac output in the adrenaline group while a decrease in arterial and pulmonary artery pressure in plain lignocaine group. They suggested that the hypotensive response of the lignocaine is counteracted by the adrenaline added to the lignocaine. But due to a significant increase in heart rate and cardiac output in the elderly, the use of epidural adrenaline should be reconsidered.

In 2011, the clinical features of patients with true or white-coat–resistant hypertension was compared by De la Sierra et al[49]. 8295 patients out of 68045 were treated for resistive hypertension with blood pressure ≥140/90 mm Hg and treated with ≥3 antihypertensive drugs out of which 1 was diuretics. Ambulatory blood pressure was monitored for all the patients and 62.5% were true resistant hypertensive with male predilection, longer duration of hypertension and a worse cardiovascular risk profile and the rest 37.5% were white coat resistance. Hence ambulatory blood pressure monitoring is necessary to diagnose resistive hypertension

The safety of local anaesthetic during dental extractions in hypertensive patients was observed by Silvestre et al[50] in 2011. 4% articaine with adrenaline was injected in one group while mepivacaine was injected in the other. HR, SBP, DBP, MAP, and SpO_2 were evaluated. The study showed an increase in HR and SBP 3

minutes after the injection of local anaesthesia and returned back to the baseline values after the completion of extraction. The rise in values was not significant and hence they concluded that the use of epinephrine is safe for dental extraction in controlled hypertensive patients.

In 2011, the evaluation of the changes in cardiovascular parameters in patients with controlled hypertension receiving dental extractions under lignocaine with and without adrenaline was done by Ogunlewe et al[51]. They observed that the SBP was high in both the groups following injection and fell back to the baseline values. The rise in BP was significant in plain lignocaine group which may be a result of impaired pain control due to loss of effectiveness of local anaesthesia.

The effect of adrenaline containing local anaesthetic on BP and pulse rate in hypertensive patients was studied by Chaudhry et al[52] in 2011. 3.6ml of 2%lignocaine with 1:1,00,000 adrenaline was used in all the patients. The SBP increased 2-5 minutes after the injection of local anaesthetic while the DBP decreased following injection in all patients.

The evaluation of the hemodynamic effects of clinical doses of lignocaine with adrenaline on patients undergoing third molar extractions by Sivamalai et al[53] in 2012 showed a rise in plasma potassium and blood glucose 20 minutes after the injection of the local anaesthetic and no change in HR and BP.

The hemodynamic effects of lignocaine with and without adrenaline was compared by Ketabi et al[10] in 2012, on patients undergoing dental extractions. They noted a decrease in SBP, DBP, and HR in plain lignocaine group and increase in those parameters in patients administered with lignocaine containing adrenaline. They

concluded that the adrenaline in the local anaesthetic showed minor effects on the cardiovascular parameters.

The safety profile of 2 dental anaesthetic solutions on cardiac patients undergoing periodontal surgery was compared by Daniel et al[54] in 2012. Articaine with adrenaline and standard mepivacaine were used in this study. They noted the rise in HR, SBP, and DBP in the adrenaline group while no changes in these parameters were noted in the plain anaesthetic group. They concluded that the use of adrenaline should be as minimal as possible to prevent any hazardous change in the hemodynamic parameters while treating cardiac patients.

The effect of adrenaline in patients undergoing intraocular irrigation during cataract surgery was compared using the balanced salt solution with 1:1,00,000 adrenaline and plain intraocular irrigation by Miratashi et al[55] in 2012. HR, SBP, and DBP were noted prior to irrigation and at 5, 10 and 15 minutes after irrigation. They noted an increase in HR and SBP 5 minutes after irrigation in the adrenaline group while a decrease in DBP after 5 minutes and increase in DBP at 10 and 15 minutes after irrigation. The changes were not significant when compared to the plain intra ocular irrigation group. They concluded that adrenaline has a minimal hemodynamic effect.

In 2014, Managutti A et al[6] compared local anaesthetic with two concentrations of adrenaline (1:80,000 & 1:2,00,000) in normotensive patients and observed no significant changes in the onset of the anaesthesia and pain scale, but local anaesthetic with a higher concentration of adrenaline showed a longer duration of action. And when comparing the cardiovascular changes, there was immediate rise in the heart rate, systolic blood pressure and diastolic blood pressure in local

anaesthetic with higher concentration of adrenaline when compared to local anaesthetic with lower concentration of adrenaline which showed no significant rise in pulse, systolic blood pressure while the diastolic blood pressure decreased from the normal value after administration of the local anaesthetic. Thus they concluded, that lignocaine with 1:80,000 adrenaline and lignocaine with 1:2,00,000 adrenaline had the same efficacy. The local anaesthetic with 1:2,00,000 adrenaline showed more cardiac stability and did not compromise the profundity and success of anaesthesia. Hence lignocaine with 1:2,00,000 adrenaline is safer in cardiac and elderly patients.

The hemodynamic changes caused by interaction between adrenaline and an antipsychotic drug in rats was evaluated by Higuchi et al[56] in 2014. Rats were pre-treated with Chlorpromazine and when 100μg/kg adrenaline was induced, it resulted in significant hypotension and tachycardia. This hypotension was caused by interaction between the adrenalin and chlorpromazine through the activation of the β-adrenergic receptor and showed dose-dependent effect. But when low-dose adrenaline similar to what might be used in dental procedures, no significant hypotension was noted.

The comparative study after the administration of local anaesthetic with three different concentration of adrenaline in normotensive patients and the evaluation of the hemodynamic changes was done by Nedal Abu Mostafa et al[57] in 2015. The patients were divided into 3 groups- G1, G2, and G3 who received 2% lignocaine in 1:80,000 adrenaline, 4% articaine in 1:1,00,000 adrenaline and 4% articaine in 1: 2,00,000 adrenaline respectively. The comparative study showed a significant increase in systolic blood pressure in all the groups and when comparing the SBP within groups, G1 showed significant than G3. The Diastolic blood pressure decreased in all the groups, particularly in G1, heart rate increased in all the groups

and the oxygen saturation decreased in all the groups with a significant reduction in G2. They concluded with local anaesthetic with 1:2,00,000 adrenaline the safer drug since it showed a lesser effect on the systolic/ diastolic blood pressure, heart rate and other parameters.

MATERIALS AND METHODS

The study was conducted in Sri Ramakrishna Dental College and Hospital for evaluating the effects of two different concentration of adrenaline with local anaesthesia. The study was conducted as a prospective, randomized, double-blind study. Patients who reported to department of oral and maxillofacial surgery for minor oral surgical procedures were included in the study. A total of 50 patients were included who satisfied the required criteria.

Inclusion criteria:

- Patients with a known history of essential hypertension and under one drug
- Patient aged between 35yr to 50yr
- Blood pressure:
    - Systolic BP 140mmHg to 160mmHg
    - Diastolic BP 90mmHg to 99mmHg
- No history of other Systemic diseases
- Minor oral surgical procedures
- Procedures that are estimated for a minimum of 30mins
- Patient not under any other medications that alter the blood pressure
- Patients with previous history of Dental extraction

Exclusion criteria:

- The patient above 50 years of age
- Resistant hypertensive patients
- History of other systemic diseases like diabetes mellitus, Chronic Obstructive Pulmonary Disease (COPD), Chronic renal failure etc.
- History of other cardiovascular diseases like myocardial infarction, congestive cardiac failure etc.

- Simple dental extraction procedures
- Severe hypertensive Patients
- Pregnancy & breastfeeding
- Allergic to lignocaine
- Patients under blood thinners
- Mentally challenged patients

Materials Used:

- Multi-parameter monitor (Planet 50 – L&T limited)
- 12 Lead ECG (Welcare ST-300)
- 2 ml single-use syringe (Dispovan, Hindustan Syringes, and Medical Devices, India)
- 26 gauge needle (Dispovan, Hindustan Syringes, and Medical Devices, India)
- Lignocaine 2% adrenaline 1:80,000 (Lignox 2% A 1:80,000, Indoco Remedies, Indore, India)
- Lignocaine 2% adrenaline 1:2,00,000 (Xylocaine 2% Adrenaline 1:2,00,000, Astra Zeneca, India)

Double-blind details:

"Double-blind study is a study in which neither the patients, the experimenter, nor any other assessor of the results, know which participants are subject to which procedure, thus helping to ensure any biases or expectations will not influence results". The patient, operator and the cardiologist are unknown of the type of local anesthetic used on the patient to prevent any bias in the result. The patients are

randomly separated into two groups. The local anesthetic is provided to the operator by the staff nurse in the department.

Procedure

1. Patients who satisfied the criteria underwent detailed clinical examination.
2. The patients were explained about the study, the procedure to be performed, the possible complications of the procedure in their native language and informed consent was obtained for local anesthetic drug administration, ECG and minor surgical procedure.
3. The anaesthetic solutions used in this study are 2% lignocaine with 1:80,000 adrenaline and 2% lignocaine with 1:2,00,000 adrenaline.
4. The local anesthetics were randomly allotted to the patient by randomized lot system.
5. All the procedures were performed by a single operator.
6. In patients who had multiple bilateral extractions, one type of local anesthetic was administered in an appointment and a local anesthetic with other concentration of adrenaline was administered in the subsequent appointment.
7. During each appointment, the patients were made to rest in the casualty ward for 10 minutes prior to the commencement of the procedure. With the assistance of Staff Nurse the ECG leads were placed, BP cuff is tied to the left hand 2 inches above the antecubital fossa and the pulse oximetry was placed in the index finger of the right hand.
8. A mock reading of the ECG, BP and Oxygen saturation (SpO_2) was done to reduce the patient anxiety regarding the procedure.
9. The readings of Systolic and Diastolic blood pressure, Heart rate, Respiratory rate, Oxygen saturation were noted by the staff nurse in the study chart prior to

the administration of the local anesthetic agent and 10 minutes after administration of local anesthetic agent following which Mean Arterial Pressure (MAP), Rate pressure product (RPP) and Pressure rate quotient (PRQ) which was calculated using the formulas,

1. MAP = 2DBP+SBP/3
2. RPP = SBP ×HR
3. PRQ = MAP/HR

10. ECG's recorded before and after the administration of local anaesthetic with adrenaline was submitted to the cardiologist for evaluation.

All the patients received 2.5ml of local anaesthesia with adrenaline through standard nerve block technique, either Inferior alveolar nerve block or Posterior superior alveolar nerve block depending on the tooth to be extracted. All the parameters were recorded 10 minutes after the administration of the local anesthetic agent. Other parameters included in this study are the time of onset of anesthesia, visual analog scale for pain and the need for additional anaesthesia within the planned duration of the procedure.

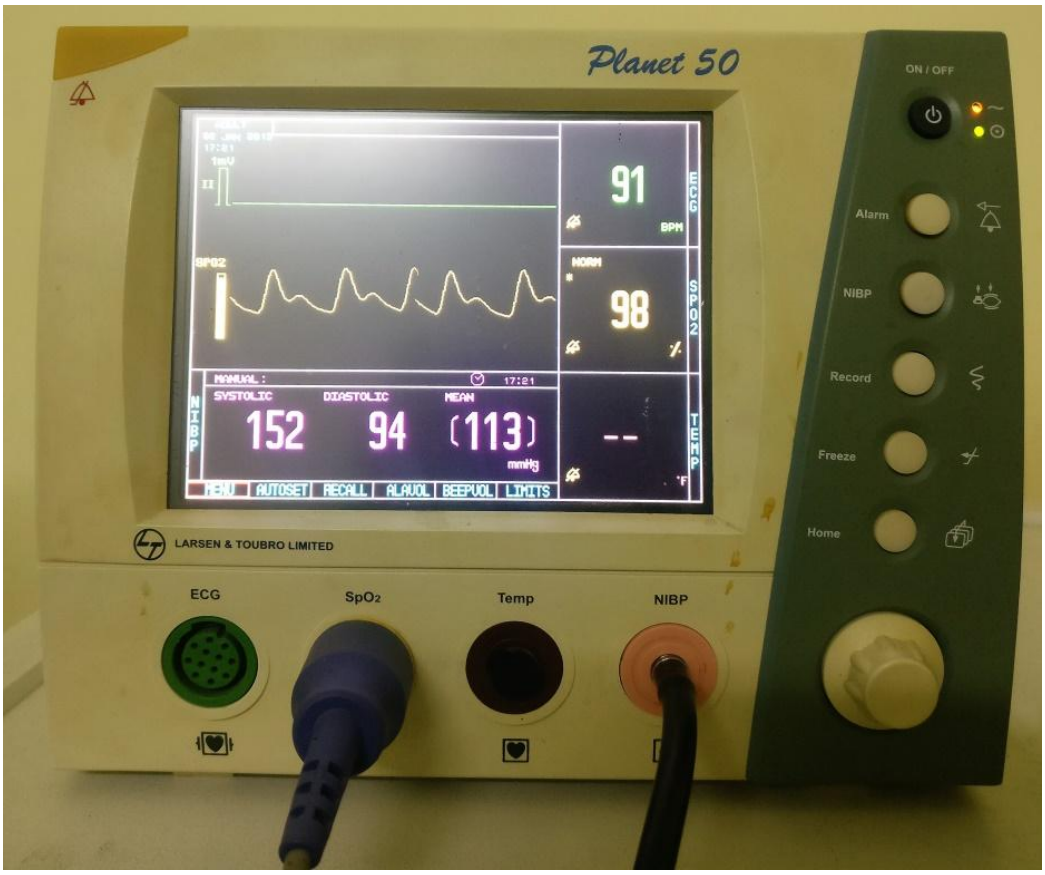


Figure 1: Multi-parameter monitor

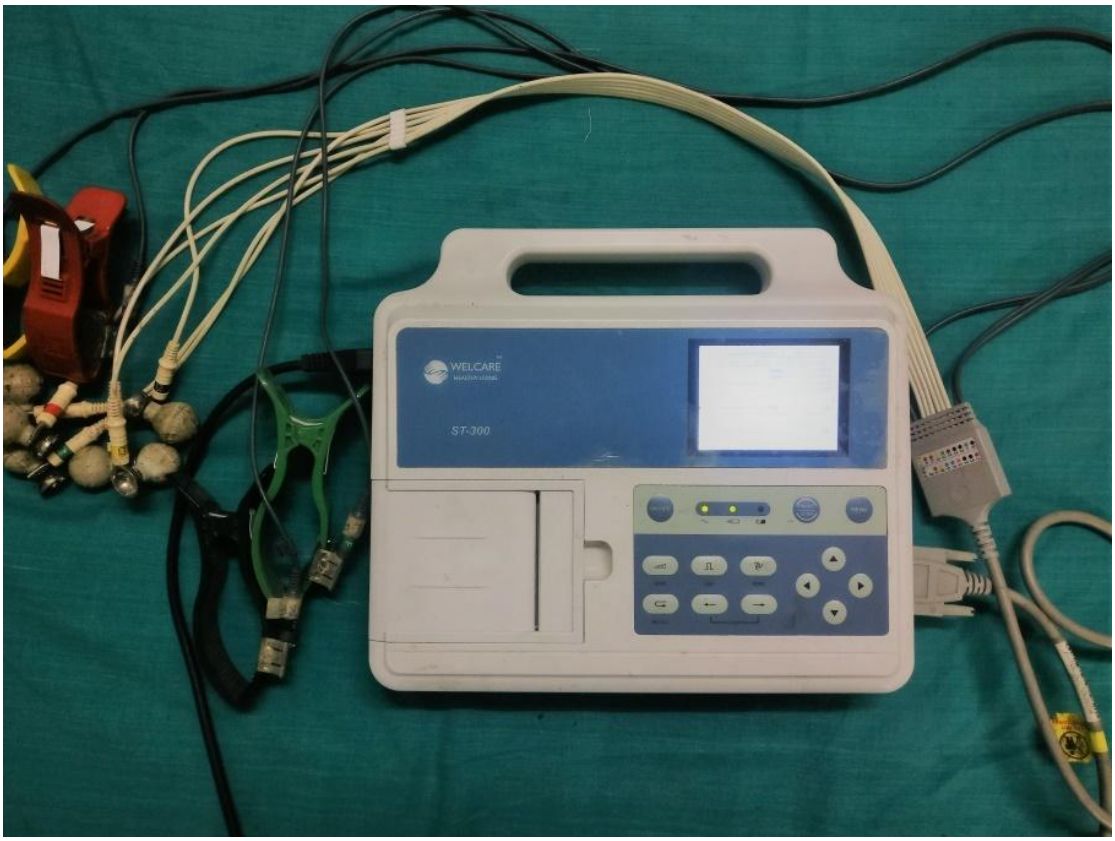


Figure 2: 12 lead ECG

Figure 3: Lignocaine 2% adrenaline 1:80,000 (Lignox 2% Adrenaline 1:80,000)

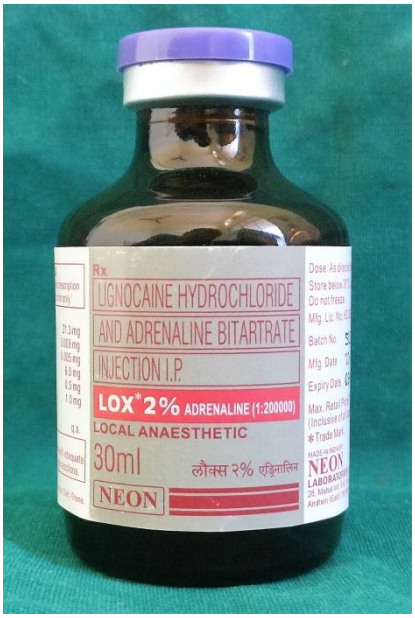


Figure 4:Lignocaine 2% adrenaline 1:2,00,000 (Xylocaine 2% Adrenaline 1:2,00,000)

Figure 5: Dispo Van 2 ml single-use syringe

RESULTS

The hemodynamic parameters prior to and after the administration of local anaesthetic with two different concentrations of adrenaline were recorded and compared. The other parameters recorded were the time of onset and the ability of the local anaesthetic solution to block pain within the procedural time. The cardiovascular parameters were calculated using the clinical hemodynamic parameters recorded. The values were tabulated in the study table and analysed.

Among the study subjects, a majority that is 36 (71%) subjects were smokers and the remaining 14 (29%) reported to have the habit of smoking tobacco. [Diagram1]

Among the study 50%were type 1 hypertensive and 50% were type 2hypertensive. [Diagram 2]

Statistical analysis was carried out using the statistical software SPSS version 20 (IBM.corp.Chicago., USA). Inter-group comparison of data pertaining to smoking habit and prevalence of hypertension was carried out using Pearson's chi-square test. Quantitative data comprising clinical parameters were tested for normality using Shapiro Wilk's test and were found to be parametric in distribution. ($P>0.05$)

Comparison of mean differences pertaining to clinical values between two groups at individual time frames was carried out using independent *t-test*. Intragroup mean differences for the above-mentioned parameters between baseline and after giving LA were carried out using the paired sample t-test. P value less than 0.05 (<0.05) was considered to be statistically significant.

One subject required additional anaesthesia when LA with lower concentration of adrenaline was given whereas none of the subjects who were given LA with higher

concentration of adrenaline required additional anaesthesia. With regard to this, there was no statistically significant difference between LA solutions of 1:80,000 and 1: 2,00,000 concentration. (Table 1)

The mean time of onset of anaesthesia (3.05±1.39 and 3.04±1.53) and the mean pain score (0.05±0.22 and 0.04±0.21)was almost similar was almost similar for both LA solutions. With regard to time of onset of anaesthesia and pain score, there was no statistically significant difference between LA solutions of 1:80,000 and 1: 2,00,000 concentration. (Table 2)

The mean baseline for heart rate was higher among the subjects under Group A (72.85±12.97) compared to the subjects in Group B (71.80±9.26) [Table 3]. After the administration of local anaesthesia mean heart rate in Group A was 78.05±13.29 which is a difference of 5.20±6.45. The p value of <0.001 was obtained that is statistically very highly significant [Table 5]. In Group B the heart rate post anaesthesia was 73.47±12.46 which is a difference of 1.67±0.45 with the p value 0.434 that is statistically not significant [Table 7]. The results show significant changes in heart rate in patients administered with higher concentration of adrenaline but the comparison of mean change among the two groups was not significant. Hence local anaesthetic with both the concentrations of adrenaline can be used on essential hypertensive patients under control.

The baseline respiratory rate was almost similar in patients under both groups i.e., 14.35±1.08 and 14.19±1.24 respectively and no change was noted after the administration of LA with adrenaline in either of the group [Table 5, 6]. The administration of local anaesthetic with adrenaline has no effect on respiratory rate of the patient.

The mean baseline for systolic blood pressure was higher among the subjects under Group B (142.66±13.67) compared to subjects under Group A (137.45±14.28) [Table 3]. After the administration of local anaesthetic a difference of 3.05±1.53 was noted and the mean SBP was 140.50±1.08 in patients under Group A. This is statistically highly significant with the p value 0.04 [Table 5]. A difference of 2.48±1.89 was noted in Group B and the mean SBP after the administration of local anaesthetic with adrenaline was 145.14±14.28 with the p value 0.173 that is statistically not significant [Table 6]. Significant changes in SBP was noted in Group A patients after administration of LA with adrenaline than in patients under Group B, but the comparison of change in SBP between two groups was insignificant. Thus the use of local anaesthetic with higher concentration of adrenaline is advisable for patients with essential hypertension.

The mean baseline for diastolic blood pressure was higher among the subjects under Group B (90.04±9.29) compared to subjects under Group A (83.65±5.46) [Table 3]. After the administration of local anaesthetic a difference of 2.55±0.36 was noted and the mean DBP was 86.20±6.14 in patients under Group A. This is statistically highly significant with the p value 0.044 [Table 5]. A difference of 0.28±0.56 was noted in Group B and the mean DBP after the administration of local anaesthetic with adrenaline was 89.76±9.02 with the p value 0.796 that is statistically not significant [Table 6]. Significant changes in DBP were noted in patients under Group A after administration of adrenaline while the DBP remained almost same in Group B. But the comparison of the mean difference between both the groups remains insignificant statistically. Thus it is safer to use local anaesthetic with both concentration of adrenaline on patients with essential hypertension under control.

The baseline for mean arterial blood pressure was higher among the subjects under Group B (107.91±9.47) compared to subjects under Group A (101.54±6.62) [Table 3]. After the administration of local anaesthetic a difference of 2.56±1.61was noted and the MAP was 104.10±6.69 in patients under Group A. This is statistically highly significant with the p value 0.028 [Table 5]. A difference of 0.76±0.81 was noted in Group B and the MAP after the administration of local anaesthetic with adrenaline was 107.21±9.98 with the p value 0.612 that is statistically not significant [Table 6]. Though significant changes were noted in patients under higher concentration of adrenaline, the MAP was within the normal limits (70 – 100 mmHg) in both the groups.

The mean baseline for oxygen saturation was almost similar in patients under both groups i.e., 97.95±0.38 and 98.00±0.00 in Group A and Group B respectively. After the administration of LA with adrenaline the oxygen saturation remained almost the same i.e.; 97.95±0.22 and 98.00±0.31in Group A and Group B respectively [Table 5, 6]. This is statistically insignificant as the p value obtained were 0.330 for Group A and 0.329 for Group B.

The mean baseline for Rate Pressure Product was higher among the subjects under Group B (10677.19±1647.83) compared to subjects under Group A (10024.60±2186.3) [Table 3]. After the administration of local anaesthetic a difference of 923.65±243.69 was noted and the RPP was 10948.25±2290.67 in patients under Group A. This is statistically highly significant with the p value <0.001 [Table 5]. A difference of 163.38±256.90 was noted in Group B and the RPP after the administration of local anaesthetic with adrenaline was 10840.57±2190.24 with the p value 0.674 that is statistically not significant [Table 6]. The result shows

highly significant changes in patients under Group A while the changes in Group B remained insignificant. Even after the significant increase the values remained in the level of low hemodynamic response making LA with both the concentration of adrenaline safe to use.

The mean baseline for Pressure Rate Quotient was higher among the subjects under Group B (1.49±0.24) compared to subjects under Group A (1.43±0.27) [Table 3]. After the administration of local anaesthetic a difference of 0.07±0.29 was noted and the PRQ was 1.36±0.23 in patients under Group A. This is statistically significant with the p value <0.009 [Table 5]. A difference of 0.01±0.78 was noted in Group B and the RPP after the administration of local anaesthetic with adrenaline was 1.48±0.32 with the p value 0.901 that is statistically not significant [Table 6]. The values after administration of local anaesthesia with adrenaline shows significant changes in Group A, but the values of PRQ still remained >1. No clinical signs of ischemia were present in patients under both groups and it is safer to use local anaesthetic with both concentrations of adrenaline in patients with essential hypertension under control with medication.

Patients with essential hypertension under control were treated with any one hypertensive medication were included in the study. The Calcium channel blockers were the highly preferred drug of choice with 28 patients (56%). Ten patients (20%) were under Angiotensin converting enzyme blocker. Eight patients (16%) were under Angiotensin receptor blocker and two patients were under Diuretics (4%) and Beta blockers (4%) each. The ischemic changes in ECG were noted in 3 patients (10%) under CCB and one patient under ARB. None of the patients under ACE inhibitors, Diuretics and Beta blockers showed arrhythmic changes. [Table 8]

All the patients were evaluated with ECG, before and after the administration of LA. Alteration in T wave was evaluated; normally, the T wave should be in the same direction of QPS complex. In this study, T wave inversion was seen in post administration of LA with adrenaline in four patients. 2 patients in Group A who showed T wave inversion after administration of LA with adrenaline were in the minimum baseline values of Stage 2 HT. [Graph 3] In Group B, one patient who showed T wave inversion was at the maximum range in Stage 2 HT with a long-standing history of HT for up to 7 years. The other patient in Group B showed T wave inversion in both the ECG taken before and after the administration of LA with adrenaline [Graph 4]. Thus this parameter showed that LA with 1:80,000 adrenaline causes more hemodynamic changes than LA with 1:200,000 adrenaline in patients with controlled hypertension.

INTERPRETATION OF RESULTS

In this study, local anaesthetic with both concentrations of LA showed similar time of onset and only one patient under the lower concentration of adrenaline required additional local anaesthesia. The pain scale was also similar in patients under both the groups. Theincrease in Heart rate and SBP was seen in patients under both groups. Patients in Group A showed more increase in heart rate and SBP compared to Group B and this difference is not significant statistically on the comparison.The DBP was increased by 3mm/Hg in Group A while it almost remained equal to the baseline value in Group B. This parameter was not statistically significant.

The RR and SpO_2 remained unchanged before and after administration of LA with adrenaline in both the groups. The MAP was within the normal range even after 3mm/Hg rise was seen in Group A while it almost remained the same in Group B. The RPP values showed low hemodynamic effects of LA with adrenaline and PRQ values showed no signs of ischemia in both the Groups. The ECG revealed arrhythmic changes after administration of LA with adrenaline in three patients. Two patients of which who were in Group A and one patient in Group B. One patient showed arrhythmic change in both the ECG's taken before and after the administration of LA.

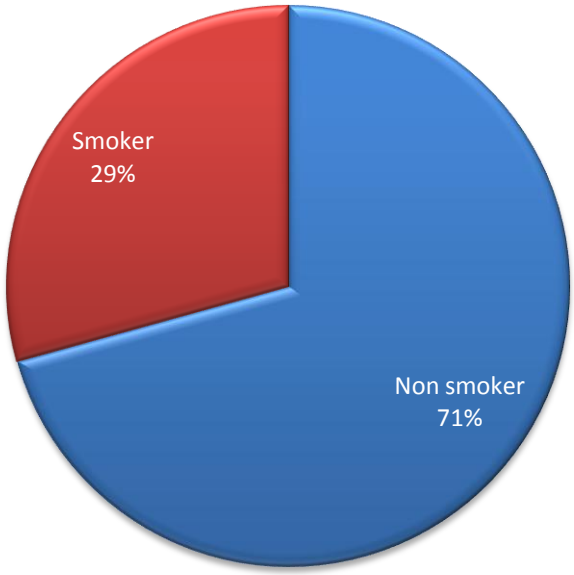


Diagram 1: Distribution of study subjects based on the use of tobacco

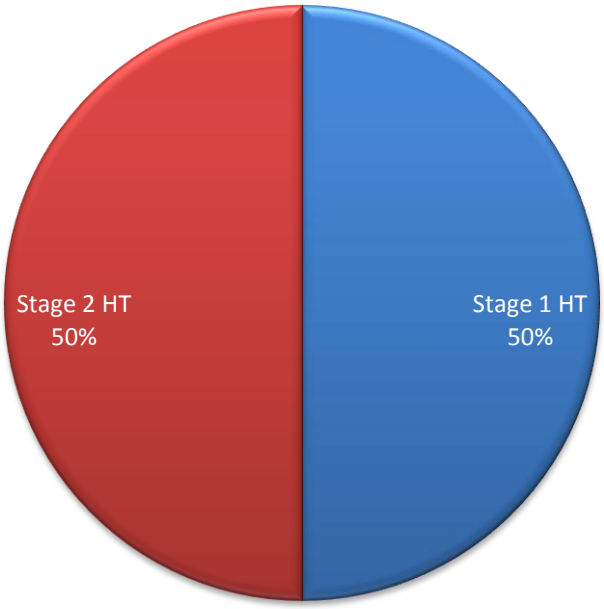


Diagram 2: Distribution of study subjects based on the prevalence of hypertension

Table 1: Comparison of the need for additional anaesthesia between solutions of two concentrations

		Solution		Total	p-Value
		1:80,000	1:2,00,000		
Need For Additional Anaesthesia	No	25	24	49	1.000
	Yes	0	1	1	
Total		25	25	50	

p-value: <0.05 (Significant)

Table 2: Comparison between LA solutions of two concentrations based on time of onset of anaesthesia and pain score

	Solution	N	Mean±SD	p-Value
Time of Onset of Anaesthesia	1:80,000	25	3.05±1.39	0.996
	1:2,00,000	25	3.04±1.53	
Pain Score	1:80,000	25	0.05±0.22	0.973
	1:2,00,000	25	0.04±0.21	

p-value: <0.05 (Significant)

Table 3: Intergroup comparisons of clinical parameters at baseline

Outcome	Solution	N	Mean±SD	p-value
HR	1:80,000	25	72.85±12.97	>0.05
	1:2,00,000	25	71.80±9.26	
RR	1:80,000	25	14.35±1.08	>0.05
	1:2,00,000	25	14.19±1.24	
SBP	1:80,000	25	137.45±14.28	>0.05
	1:2,00,000	25	142.66±13.67	
DBP	1:80,000	25	83.65±5.46	>0.05
	1:2,00,000	25	90.04±9.29	
SpO_2	1:80,000	25	98.00±0.00	>0.05
	1:2,00,000	25	97.95±0.38	
MAP	1:80,000	25	101.54±6.62	>0.05
	1:2,00,000	25	107.91±9.47	
RPP	1:80,000	25	10024.6±2186.3	>0.05
	1:2,00,000	25	10677.19±1647.83	
PRQ	1:80,000	25	1.43±0.27	>0.05
	1:2,00,000	25	1.49±0.24	

p-value: <0.05 (Significant)

Table 4: Intergroup comparisons of clinical parameters after giving Local anaesthesia

Outcome	Solution	N	Mean
HR	1:80,000	25	78.05±13.29
	1:2,00,000	25	73.47±12.46
RR	1:80,000	25	14.35±1.08
	1:2,00,000	25	14.19±1.24
SBP	1:80,000	25	140.50±12.58
	1:2,00,000	25	145.14±14.28
DBP	1:80,000	25	86.20±6.14
	1:2,00,000	25	89.76±9.02
SpO_2	1:80,000	25	97.95±0.22
	1:2,00,000	25	98.00±0.31
MAP	1:80,000	25	104.10±6.69
	1:2,00,000	25	107.21±9.98
RPP	1:80,000	25	10948.25±2290.67
	1:2,00,000	25	10840.57±2190.24
PRQ	1:80,000	25	1.36±0.23
	1:2,00,000	25	1.48±0.32

p-value: <0.05 (Significant)

Table 5: Intragroup comparisons of clinical parameters between baseline after giving LA with 1:80,000 concentration

Outcome	Baseline Mean±SD	After LA Mean±SD	Mean difference ± SD	p-value
HR	72.85±12.97	78.05±13.29	5.20±6.45	<0.001
RR	14.35±1.08	14.35±1.08	0.00±0.00	1.000
SBP	137.45±14.28	140.50±1.08	3.05±1.53	0.04
DBP	83.65±5.46	86.20±6.14	2.55±0.36	0.044
SpO_2	98.00±0.00	0.05±0.36	0.05±0.36	0.330
MAP	101.54±6.62	104.10±6.69	2.56±1.61	0.028
RPP	10024.60±2186.33	10948.25±2290.67	923.65±243.69	<0.001
PRQ	1.43±0.27	1.36±0.23	0.07±0.29	0.009

p-value: <0.05 (Significant)

Table 6: Intragroup comparisons of clinical parameters between baseline after giving LA with 1:2,00,000 concentration

Outcome	Baseline Mean±SD	After LA Mean±SD	Mean difference ± SD	p-value
HR	71.80±9.26	73.47±12.46	1.67±0.45	0.434
RR	14.19±1.24	14.19±1.24	0.00±0.00	1.000
SBP	142.66±13.67	145.14±14.28	2.48±1.89	0.173
DBP	90.04±9.29	89.76±9.02	0.28±0.56	0.796
SpO_2	97.95±0.38	98.00±0.31	0.05±0.66	0.329
MAP	107.91±9.47	107.21±9.98	0.76±0.81	0.612
RPP	10677.19±1647.83	10840.57±2190.24	163.38±256.90	0.674
PRQ	1.49±0.24	1.48±0.32	0.01±0.78	0.901

p-value: <0.05 (Significant)

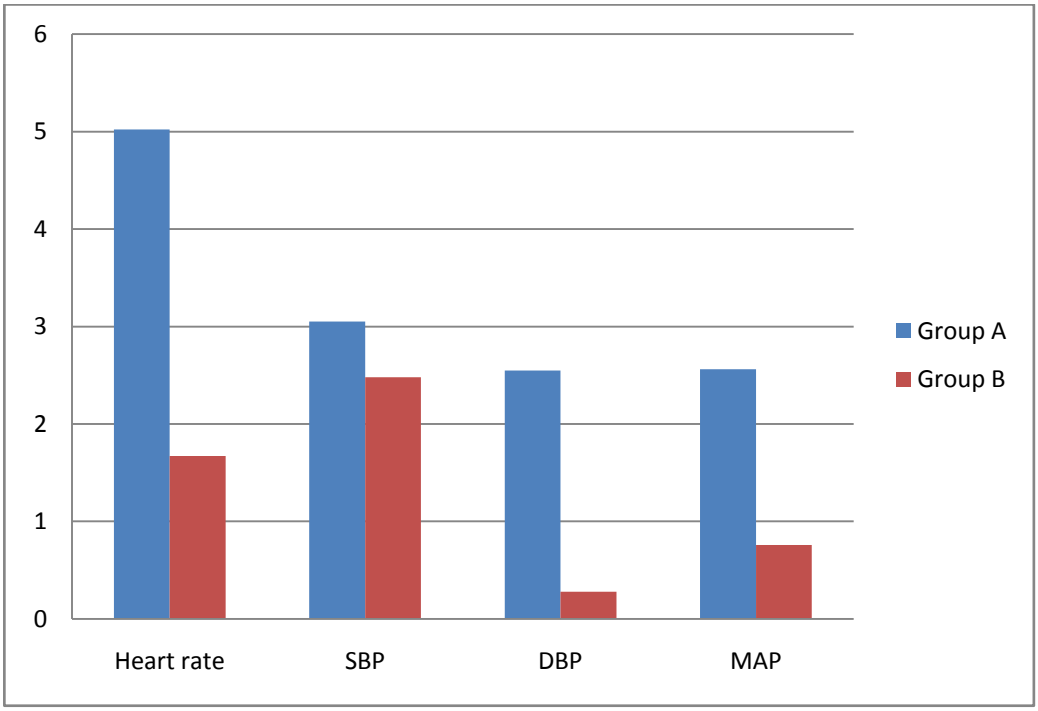
Table 7: Comparison of the mean of Hemodynamic changes in 2 Groups

Outcome	Mean difference ± SD 2% lignocaine in 1:80,000 adrenaline	Mean difference ± SD 2% lignocaine in 1:2,00,000 adrenaline
HR	5.20±6.45	1.67±0.45
RR	0.00±0.00	0.00±0.00
SBP	3.05±1.53	2.48±1.89
DBP	2.55±0.36	0.28±0.56
SpO_2	0.05±0.36	0.05±0.66
MAP	2.56±1.61	0.76±0.81
RPP	923.65±243.69	163.38±256.90
PRQ	0.07±0.29	0.01±0.78

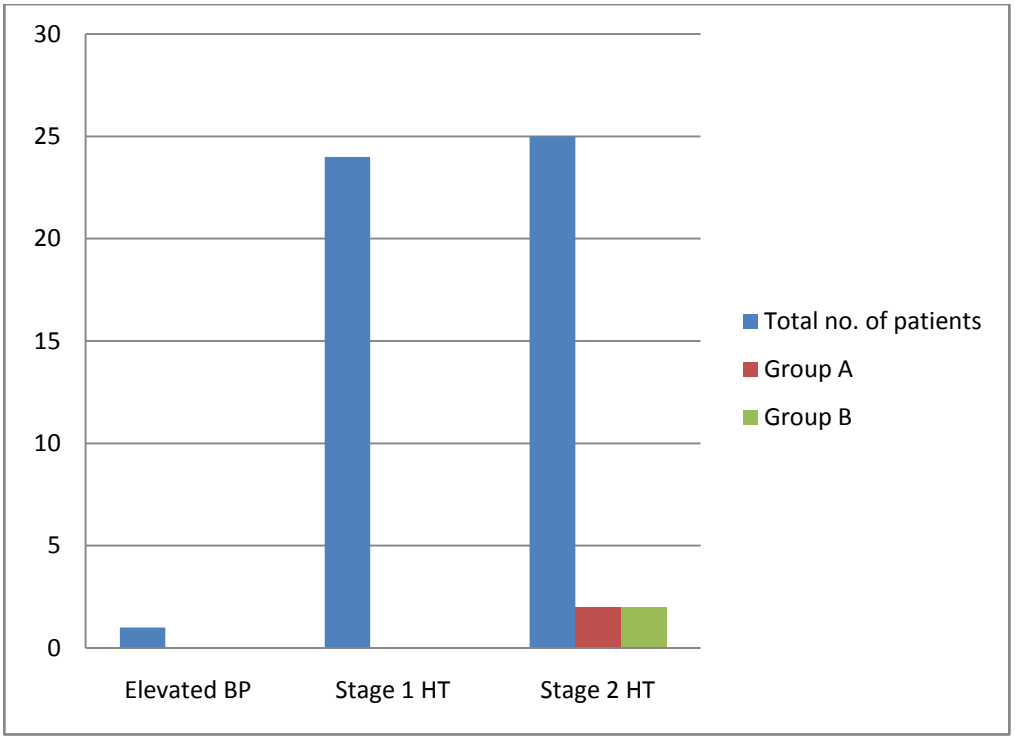
Table 8: Evaluation of the Hypertensive Medication and Arrhythmic Changes

Hypertensive drug	No. Of patients	Patients with arrhythmic changes after administration of LA
Calcium Channel Blocker	28	3
Angiotensin Converting Enzyme inhibitors	10	0
Angiotensin Receptor Blockers	8	1
Diuretics	2	0
Beta Blockers	2	0

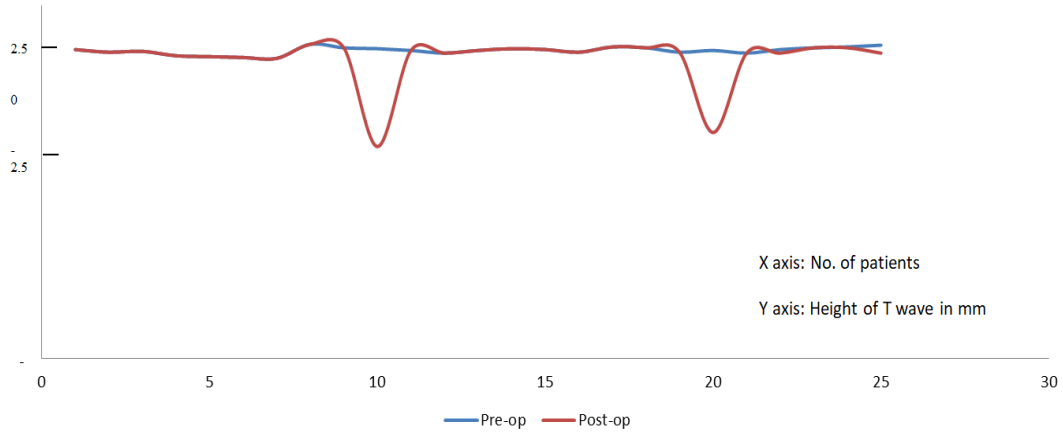
Graph 1: Comparison of the mean difference of hemodynamic changes between Group A and Group B



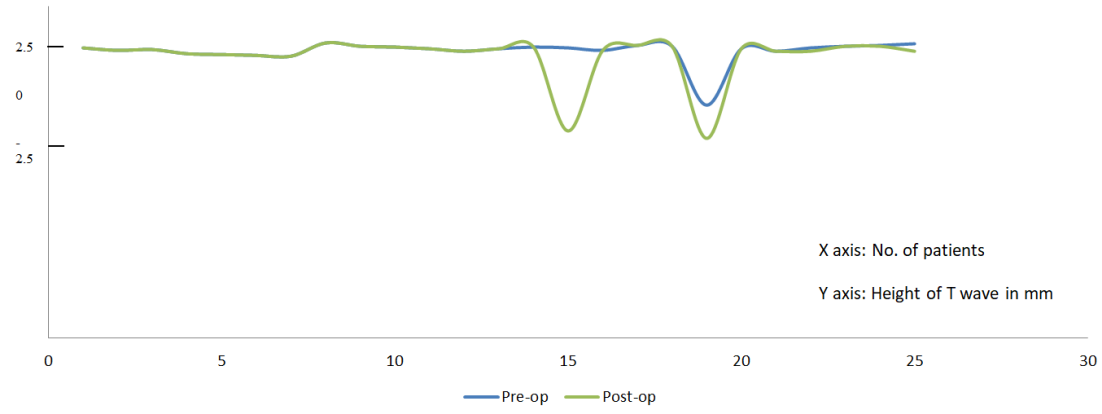
Graph 2: Comparison of the occurrence of arrhythmic changes after administration of local anaesthesia among the hypertensive groups



Graph 3: Representation of T wave inversion in LA with 1:80,000 adrenaline group



Graph 4: Representation of T wave inversion in LA with 1:2,00,000 adrenaline group



DISCUSSION

Local anaesthetics are agents that cause a localized, reversible loss of sensation, upon the area of injection and the technique used. The idea of local anaesthesia is to control pain, provide safe and comfortable dental treatment for patients. The success of a dental procedure depends on the success of the local anaesthesia induced[2]. Local anaesthetics are normally associated with loss of pain in bone and soft tissue during surgical intervention.

Lignocaine is the gold standard and the most commonly used local anaesthetic solution worldwide[13]. They have the property of vasodilation of the blood vessels in the area of administration. Due to this property, the lignocaine gets absorbed into the bloodstream quickly thereby reducing the duration of anaesthesia and increasing the blood concentration of lignocaine. To counteract this action, adrenaline which is a potent vasoconstrictor is added to lignocaine to retard the systemic absorption of local anaesthetic, in the basis of its widespread use. The other advantage of adding adrenaline to the local anaesthetic is to increase the depth and duration of anaesthesia[33]. Adrenaline is known, to have an influence on the heart rate and blood pressure by stimulating the adrenergic receptors namely, alpha-adrenergic and beta-adrenergic receptors. The α adrenergic receptors cause peripheral vasoconstriction, while the β adrenergic receptors cause vasodilatation in muscles and increase in heart rate and force of contraction of the heart.[3] This pharmacological reaction after the administration of local anaesthetic with adrenaline, cause an increase in heart rate and systolic blood pressure while the diastolic blood pressure falls from the baseline values.[44]Meechan et al[51], also reported significant tachycardia in patients with a history of cardiac transplants 10 minutes following the injection of epinephrine-containing local anaesthetic intraorally.

The property of increasing the systolic blood pressure and heart rate leads to the dilemma of using this anaesthetic solution for patients with cardiovascular diseases. This study is done to compare the effect of lignocaine with adrenaline in 2 different concentrations on the cardiovascular parameters. The other parameters studied are their time of onset, ability to block the pain and need for additional anaesthesia within the time of procedure in patients with controlled hypertension.

In this study, the patients in Group A were administered 1:80,000 adrenaline while Group B received 1:2,00,000 adrenaline. When the time of onset was almost the same for both the groups and only one patient in group B received additional anaesthesia within the planned time of the dental procedure. Hence the time of onset and the ability to control pain is almost similar in both 2%lignocaine with 1:80000 adrenaline and 1:200000 adrenaline (Table 2). This is similar to the other studies.

Managutti et al[1] and Caldas et al[42] compared the efficacy of local anaesthetic with 2 different concentration of adrenaline and noticed no difference in the time of onset, the depth or quality of anaesthesia and the duration of anaesthesia produced. Soroghi et al[32] noticed no significant difference was found in the onset or magnitude of vasoconstriction between the concentrations of 1:50,000 to 1:4,00,000 epinephrine.

In our study, a rise in heart rate and systolic blood pressure was observed in both groups. The mean rise of heart rate in Group A was approximately 5±6 while in Group B was 1±0.4 (Table 7). The rise in systolic blood pressure was 3±1.5 and 2±1.9 in Group A and B respectively (Table 7). The changes were not significant which is similar to that of the other studies.

Meral et al[29], compared the local anaesthetic with and without adrenaline and noticed a negligible increase in heart rate and systolic blood pressure in the adrenaline group. Meechan and Rawlins[12]compared 2 different local anaesthetic solutions one of which contained adrenaline and noted an increase in systolic blood pressure and heart rate in the adrenaline group while the reduction in diastolic blood pressure which was insignificant and hypokalemia was also noted. They concluded that local anaesthetic with adrenaline has a negligible effect on the hemodynamic parameters.

In our study, the diastolic blood pressure increased by 2.5mmHg in Group A while it almost remained the same at the end of 15 minutes in Group B (Table 7). This is in contradiction to other studies. This may be attributed to the time of recording the pre-anaesthetic and post anaesthetic parameters. In the study done by Meechan et al[51], Chaudhry et al[44] and Gedik[28] et al. the fall in DBP was seen at 20 minutes in a higher concentration of adrenaline and at 30 minutes in local anaesthetics with 1:2,00,000 adrenaline. In this study increase in the mean arterial pressure (MAP) was seen in both the groups (i.e.) 2.5±1.6 and 0.76±0.81 in Group A and Group B respectively and the mean MAP.

In our study no changes were noticed in the oxygen saturation of the patients in both groups (Table 7). This is in accordance with the other studies by Meral[29] and Vasconcellos[32]. Liau[33] et al compared the oxygen saturation in patients with different levels of anxiety and noticed no significant changes in oxygen saturation even with increase in the SBP and DBP. They concluded that there is no significant co-relation between oxygen saturation and anxiety.

Rate Pressure Product (RPP) and Pressure Rate Quotient (PRQ) remained almost the same in patients under both groups before and after the administration of LA with adrenaline. RPP is the indicator of oxygen consumption[52] of myocardium in non-anaesthetized patients. Patient in Group B showed a very slight increase in value compared to the patients in Group A but the values of the patients in both groups remained under the low hemodynamic response (Table 7). Thus both local anaesthetic with 1:80,000 adrenaline and 1:200,000 adrenaline has low hemodynamic response in patients with controlled hypertension. Pressure Rate Quotient (PRQ) is the indicator of blood supply to the cardiac muscles. The value of PRQ <1 is an indicator of cardiac ischemia[52]. In our study, the values of PRQ remained almost similar in both pre and post injection of local anaesthetic with adrenaline in both the groups (Table 7). Hence the local anaesthetic with different concentrations of adrenaline has no serious effects on the cardiovascular parameters and none of the patients showed signs of cardiac ischemia. Morais et al[52] in 2013 reported similar results. They noted an increase in heart rate, SBP, and RPP while the DBP and PRQ remained the same while comparing the hemodynamic effects of 4% articaine with 2 different concentrations of adrenaline (1:100,000 and 1:200,000).

Bader et al[9], compared the hemodynamic changes before and after administration of plain lignocaine and lignocaine with adrenaline in hypertensive patients and noted no arrhythmic changes after administration of local anaesthetic with adrenaline group using a 6 lead EKG. Hempestal et al, also compared hemodynamic changes using 2 lead ECG and noticed no signs of arrhythmic changes after the administration of local anaesthetic with adrenaline.

In our study, patients having one drug to control essential hypertension were included and evaluated for changes in ECG changes.Out of the 50 patients

included,10 patients (20%) were under Angiotensin Converting Enzyme inhibitors, 28 patients (56%) were on Calcium channel blocker, 8patients (16%) were under Angiotensin Receptor Blockers and 2patients (4%) were under diuretics and beta blockers each. 13% of patients under CCB and none of the patients under ACE inhibitors showed signs of ischemia after the administration of local anaesthetic with adrenaline. CCB acts by blocking the entry of Ca2+ into the smooth muscles of heart and the arterioles there by reduce the excitability of the heart muscles while the ACE inhibitors, inhibits the conversion of Angiotensin I to Angiotensin II there by decreases the arteriolar resistance. There are no known interaction between the calcium channel blocker and adrenaline[8] but according to the study there can be a possibility of interaction due to the ischemic condition noted after the administration of local anaesthetic with adrenaline. In our study, the clinical hemodynamic parameters showed no signs of cardiac ischemia in patients under both the groups. But the Electrocardiography (ECG) showed T wave inversion which is a sign of myocardial ischemia in 4 patients under both the groups. Two patients under Group A whose ECG showed arrhythmic changes were in the minimum baseline value of stage II hypertension. In Group B, one patient who showed arrhythmic changes in ECG was in the extreme baseline value of stage II hypertension with a prolonged history of hypertension and the other patient showed arrhythmic changes both in pre-anaesthetic and post-anaesthetic ECG. This shows that local anaesthetic with 1:80,000 adrenaline causes more hemodynamic changes than the local anaesthetic with 1:2,00,000 adrenaline in controlled hypertensive patients.

The time of onset and the ability to mask pain remained the same for both the local anaesthetics with different concentrations of adrenaline.The cardiovascular indicators i.e. PRQ and RPP showed no signs of cardiac ischemia and low

hemodynamic effects of local anaesthetic with two different concentrations of adrenaline respectively.The ECG recorded before and after the administration of local anaesthetic showed signs of myocardial ischemia in 8% of patients in both the groups. This shows that lignocaine with higher concentrations of adrenaline has more effect on the cardiac hemodynamics than the local anaesthetic with lesser concentration of adrenaline.

Limitation of our study is that we have evaluated the hemodynamic changes in a small group of patients with history of controlled hypertension. We suggest a long term study with a large sample size and in different cardiac conditions to obtain a clear and thorough knowledge of the cardiovascular effects of local anaesthetic with adrenaline.A detailed long term study on interaction of adrenaline with individual hypertensive drugs have to be done to obtain a definitive knowledge about the cardiovascular changes.

SUMMARY AND CONCLUSION

To summarize the study conducted to evaluate and compare the local anaesthetic with different concentrations of adrenaline on patients with essential hypertension under control, recording the clinical hemodynamic parameters, calculating the cardiovascular parameters we conclude, the quality of anaesthesia produced by the local anaesthetic with two different concentrations of adrenaline were same, but had more cardiac hemodynamic effect with 1:80,000 concentrations of adrenaline in ECG and but there were no significant changes in hemodynamic and cardiovascular parameters with two different concentrations of adrenaline clinically.

To conclude, 2% lignocaine with 1:80,000 adrenaline has no major advantage over 2% lignocaine with 1:2,00,000 adrenaline for minor oral surgical procedures within the 30-minute duration. Local anaesthetic with 1:2,00,000 concentration of adrenaline provides similar quality of anaesthesia to 1:80,000 adrenaline concentration of local anaesthetic. Hence use of 2% lignocaine with 1:2,00,000 adrenaline should be considered for minor oral surgical procedures in healthy and patients with essential hypertension under control.

BIBLIOGRAPHY

1. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, Prabhakaran D. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. Journal of hypertension. 2014 Jun;32(6):1170.

2. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ. 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: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2018 May 7;71(19):e127-248.

3. Greene NM. Local Anaesthetics Mechanisms of Action and Clinical Use. Anesthesiol J Am Soc Anesthesiol. 1976 Nov 1;45(5):584–584.

4. Malamed .S.F.Handbook of local anaesthesia. Elsevier Health Sciences; 2014 Apr 25.

5. Milam SB, Giovannitti JJ. Local anesthetics in dental practice. Dental Clinics of North America. 1984 Jul;28(3):493-508.

6. Managutti A, Prakasam M, Puthanakar N, Menat S, Shah D, Patel H. Comparative analysis of local anesthesia with 2 different concentrations of adrenaline: a randomized and single blind study. Journal of international oral health: JIOH. 2015 Mar;7(3):24.

7. Pateromichelakis S. Circulatory and respiratory effects of lidocaine administered into the rat maxillofacial circulation. Journal of oral and maxillofacial surgery. 1992 Jul 1;50(7):724-7.

8. Haas DA. An update on local anesthetics in dentistry. Journal-Canadian Dental Association. 2002 Oct;68(9):546-52.

9. Bader JD, Bonito AJ, Shugars DA. A systematic review of cardiovascular effects of epinephrine on hypertensive dental patients. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2002 Jun 1;93(6):647-53.

10. 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. Dental research journal. 2012 Jul;9(4):43-7.

11. Vernale CA. Cardiovascular responses to local dental anesthesia with epinephrine in normotensive and hypertensive subjects. Oral Surgery, Oral Medicine, Oral Pathology. 1960 Aug 1;13(8):942-52.

12. Stannard M, Sloman G, Sangster L. Haemodynamic effects of lignocaine in acute myocardial infarction. British Medical Journal. 1968 May 25;2(5603):46-8.

13. Goldstein DS, Dionne R, Sweet J, Gracely R, Brewer HB, Gregg R, Keiser HR. 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. Psychosomatic Medicine. 1982 Jul Vol. 44:259-272

14. Chernow B, Balestrieri F, Ferguson CD, Terezhalmy GT, Fletcher JR, Lake CR. Local dental anesthesia with epinephrine: minimal effects on the sympathetic nervous system or on hemodynamic variables. Archives of internal medicine. 1983 Nov 1;143(11):2141-3.

15. Hirota Y, Sugiyama K, Joh S, Kiyomitsu Y. An echocardiographic study of patients with cardiovascular disease during dental treatment using local anesthesia. Journal of Oral and Maxillofacial Surgery. 1986 Feb 1;44(2):116-21.

16. Troullos ES, Goldstein DS, Hargreaves KM, Dionne RA. Plasma epinephrine levels and cardiovascular response to high administered doses of epinephrine in local anesthesia. Anesthesia progress. 1987 Jan;34(1):10-13.

17. Meyer FU. Hemodynamic changes of local dental anesthesia in normotensive and hypertensive subjects. International journal of clinical pharmacology, therapy, and toxicology. 1986 Sep;24(9):477-81.

18. Abraham-Inpijn L, Borgmeijer-Hoelen A, Gortzak RT. Changes in blood pressure, heart rate, and electrocardiogram during dental treatment with use of local anesthesia. The Journal of the American Dental Association. 1988Apr 1;116(4):531-6.

19. Salonen M, Forssell H, Scheinin M. Local dental anaesthesia with lidocaine and adrenaline. Effects on plasma catecholamines, heart rate and blood

pressure. International journal of oral and maxillofacial surgery. 1988 Dec 1;17(6):392-4.

20. Meechan JG, Rawlins MD. The effects of two different local anaesthetic solutions administered for oral surgery on plasma potassium levels in patients taking kaliuretic diuretics. European journal of clinical pharmacology.1992Feb1;42(2):155-8.

21. Perusse R, Goulet JP, Turcotte JY. Contraindications to vasoconstrictors in dentistry: Part II. Hyperthyroidism, diabetes, sulfite sensitivity, cortico-dependent asthma, and pheochromocytoma. Oral surgery, oral medicine, and oral pathology. 1992 Nov;74(5):687-91.

22. Dagher FB, Yared GM, Machtou P. An evaluation of 2% lidocaine with different concentrations of epinephrine for inferior alveolar nerve block. Journal of endodontics. 1997 Mar 1;23(3):178-80.

23. Middlehurst RJ, Gibbs A, Walton G. Cardiovascular risk: the safety of local anesthesia, vasoconstrictors, and sedation in heart disease. Anesthesia progress. 1999;46(4):118-123.

24. Homma Y, Ichinohe T, Kaneko Y. Oral mucosal blood flow, plasma epinephrine and haemodynamic responses after injection of lidocaine with epinephrine during midazolam sedation and isoflurane anaesthesia. British journal of anaesthesia. 1999 Apr 1;82(4):571-4.

25. Yagiela JA. Adverse drug interactions in dental practice: interactions associated with vasoconstrictors: part V of a series. The Journal of the American Dental Association. 1999 May 1;130(5):701-9.

26. Niwa H, Satoh Y, Matsuura H. Cardiovascular responses to epinephrine-containing local anesthetics for dental use: a comparison of hemodynamic responses to infiltration anesthesia and ergometer-stress testing. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2000 Aug 1;90(2):171-181.

27. Tanaka M, Goyagi T, Kimura T, Nishikawa T. The efficacy of hemodynamic and T wave criteria for detecting intravascular injection of epinephrine test doses in anesthetized adults: a dose-response study. Anesthesia & Analgesia. 2000 Nov 1;91(5):1196-202.

28. Meechan JG, Cole B, Welbury RR. Anaesthesia: The influence of two different dental local anaesthetic solutions on the haemo-dynamic responses of children undergoing restorative dentistry: a randomised, single-blind, split-mouth study. British dental journal. 2001 May 12;190(9):502-504.

29. Niwa H, Sugimura M, Satoh Y, Tanimoto A. Cardiovascular response to epinephrine-containing local anesthesia in patients with cardiovascular disease. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2001 Dec 1;92(6):610-6.

30. Fernieini EM, Bennett JD, Silverman DG, Halaszynski TM. Hemodynamic assessment of local anesthetic administration by laser Doppler flowmetry. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2001 May 1;91(5):526-30.

31. Ohkado S, Ichinohe T, Kaneko Y. Comparative study on anesthetic potency depending on concentrations of lidocaine and epinephrine: assessment of

dental local anesthetics using the jaw-opening reflex. Anesthesia progress. 2001;48(1):16-20.

32. Murthy HS, Rao GU. Cardiovascular responses to scalp infiltration with different concentrations of epinephrine with or without lidocaine during craniotomy. Anesthesia & Analgesia. 2001 Jun 1;92(6):1516-9.

33. Bader JD, Bonito AJ, Shugars DA. Cardiovascular effects of epinephrine in hypertensive dental patients: Summary.

34. Faraco FN, Armonia PL, Simone JL, Tortamano N. Assessment of cardiovascular parameters during dental procedures under the effect of benzodiazepines: a double blind study. Brazilian dental journal. 2003;14(3):215-9.

35. Yang JJ, Wang QP, Wang TY, Sun J, Wang ZY, Zuo D, Xu JG. Marked hypotension induced by adrenaline contained in local anesthetic. The Laryngoscope. 2005 Feb;115(2):348-52.

36. Gedik RG, Marakoglu I, Demirer S. Blood pressure, heart rate and temperature variability during periodontal surgery. West indian medical journal. 2005 Oct;54(5):329-33.

37. Meral G, Tasar F, Sayın F, Saysel M, Kır S, Karabulut E. Effects of lidocaine with and without epinephrine on plasma epinephrine and lidocaine concentrations and hemodynamic values during third molar surgery. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2005 Aug 1;100(2):e25-30.

38. Haghighat A, Kaviani N, Panahi R. Hemodynamic Effects of 2% Lidocaine with 1: 80000 Epinephrine in Inferior Alveolar Nerve Block. Dental Research Journal. 2008 Jan 20;3(1)4-7.

39. Santos CF, Modena KC, Giglio FP, Sakai VT, Calvo AM, Colombini BL, Sipert CR, Dionísio TJ, Faria FA, Trindade Jr AS, Lauris JR. Epinephrine concentration (1: 100,000 or 1: 200,000) does not affect the clinical efficacy of 4% articaine for lower third molar removal: a double-blind, randomized, crossover study. Journal of oral and maxillofacial surgery. 2007 Dec 1;65(12):2445-52.

40. Liau FL, Kok SH, Lee JJ, Kuo RC, Hwang CR, Yang PJ, Lin CP, Kuo YS, Chang HH. Cardiovascular influence of dental anxiety during local anesthesia for tooth extraction. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2008 Jan 1;105(1):16-26.

41. de Holanda Vasconcellos RJ, do Egito Vasconcelos BC, Genú PR. Influence of local anesthethics with adrenalina 1: 100.000 in basic vital constants during third molar surgery. Med Oral Patol Oral Cir Bucal. 2008 Jul 1;13:E431-7.

42. Moshaver A, Lin D, Pinto R, Witterick IJ. The hemostatic and hemodynamic effects of epinephrine during endoscopic sinus surgery: a randomized clinical trial. Archives of Otolaryngology–Head & Neck Surgery. 2009 Oct 1;135(10):1005-9.

43. Laragnoit AB, Neves RS, Neves IL, 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. 2009 Mar;64(3):177-82.

44. Bortoluzzi MC, Manfro R, Nardi A. Glucose levels and hemodynamic changes in patients submitted to routine dental treatment with and without local anesthesia. Clinics. 2010;65(10):975-8.

45. Ezmek B, Arslan A, Delilbasi C, Sencift K. Comparison of hemodynamic effects of lidocaine, prilocaine and mepivacaine solutions without vasoconstrictor in hypertensive patients. Journal of Applied Oral Science. 2010 Aug;18(4):354-9.

46. Tariq MA, Kamran M, Ali M. CARDIOVASCULAR RESPONSES TO SCALP INFILTRATION, USING ADRENALINE, WITH OR WITHOUT LIGNOCAINE, DURING CRANIOTOMY. Journal of Postgraduate Medical Institute (Peshawar-Pakistan). 2011 Dec 10;24(2).142-146.

47. Goranović, T., Pirkl, I., Parazajder, D., Gudelj, G., Zdilar, B., Vučković, B., ŠIMUNJAK, B. and Šakić, K., 2011. The effect of injection speed on haemodynamic changes immediate after lidocaine/adrenaline infiltration of nasal submucosa under general anaesthesia. Periodicum biologorum, 113(2), pp.217-221.

48. Vnuk D, Nesek-Adam V, Pećin M, Musulin A, Lemo N, Brajenović N, Brčić Karaconji I, Radišić B, Smolec O, Lipar M. Hemodynamic effects of epidural lidocaine vs lidocaine-adrenaline in dogs. Veterinarski arhiv. 2011 Oct 20;81(5):585-95.

49. de la Sierra A, Segura J, Banegas JR, Gorostidi M, de la Cruz JJ, Armario P, Oliveras A, Ruilope LM. Clinical features of 8295 patients with resistant hypertension classified on the basis of ambulatory blood pressure monitoring. Hypertension. 2011 May;57(5):898-902.

50. Silvestre FJ, Salvador-Martínez I, Bautista D, Silvestre-Rangil J. Clinical study of hemodynamic changes during extraction in controlled hypertensive patients. Med Oral Patol Oral Cir Bucal. 2011 May 1;16(3):354-8.

51. Ogunlewe MO, James O, Ajuluchukwu JN, Ladeinde AL, Adeyemo WL, Gbotolorun OM. Evaluation of haemodynamic changes in hypertensive patients during tooth extraction under local anaesthesia. West Indian Medical Journal. 2011 Jan;60(1):91-5.

52. Chaudhry S, Iqbal HA, Izhar F, Mirza KM, Khan NF, Yasmeen R, Khan AA. Effect on blood pressure and pulse rate after administration of an epinephrine containing dental local anaesthetic in hypertensive patients. JPMA-Journal of the Pakistan Medical Association. 2011 Nov 1;61(11):1088-1091.

53. Sivanmalai S, Annamalai S, Kumar S, Prince CN. Pharmacodynamic responses of exogenous epinephrine during mandibular third molar surgery. Journal of pharmacy & bioallied sciences. 2012 Aug;4(Suppl 2):5390-5394.

54. Torres-Lagares D, Serrera-Figallo MÁ, Machuca-Portillo G, Corcuera-Flores JR, Machuca-Portillo C, Castillo-Oyagüe R, Gutiérrez-Pérez JL. Cardiovascular effect of dental anesthesia with articaine (40 mg with epinefrine 0, 5 mg% and 40 mg with epinefrine 1 mg%) versus mepivacaine (30mg and 20 mg with epinefrine 1 mg%) in medically compromised cardiac

patients: A cross-over, randomized, single blinded study. Medicina oral, patologia oral y cirugia bucal. 2012 Jul;17(4):655-.

55. Miratashi SA, Behdad S, Ayatollahi V, Ahmadi A. Hemodynamic effects of intraocular epinephrine during cataract surgery: a double blinded placebo controlled randomized clinical trial. Nepalese Journal of Ophthalmology. 2012 Jul;4(2):288-94.

56. Higuchi H, Yabuki A, Ishii-Maruhama M, Tomoyasu Y, Maeda S, Miyawaki T. Hemodynamic changes by drug interaction of adrenaline with chlorpromazine. Anesthesia progress. 2014 Dec;61(4):150-4.

57. Abu-Mostafa N, Al-Showaikhat F, Al-Shubbar F, Al-Zawad K, Al-Zawad F. Hemodynamic changes following injection of local anesthetics with different concentrations of epinephrine during simple tooth extraction: A prospective randomized clinical trial. Journal of clinical and experimental dentistry. 2015 Oct;7(4):471-496.

58. Meechan JG, Thomson CW, Blair GS, Rawlins MD. The biochemical and haemodynamic effects of adrenaline in lignocaine local anaesthetic solutions in patients having third molar surgery under general anaesthesia. British Journal of Oral and Maxillofacial Surgery. 1991 Aug 1;29(4):263-8.

59. Caldas CS, Bergamaschi CD, Succi GD, Motta RH, Ramacciato JC. Clinical evaluation of different epinephrine concentrations for local dental anesthesia. Revista Dor. 2015 Mar;16(1):1-5.

60. de Morais, H.H.A., de Santana Santos, T., da Costa Araújo, F.A., de Freitas Xavier, R.L., Vajgel, A. and de Holanda Vasconcellos, R.J., 2012.

Hemodynamic changes comparing 2% lidocaine and 4% articaine with epinephrine 1: 100,000 in lower third molar surgery. Journal of Craniofacial Surgery, 23(4), pp.1204-1211.

61. Hempenstall PD, Campbell JP, Bajurnow AT, Reade PC, McGrath B, Harrison LC. Cardiovascular, biochemical, and hormonal responses to intravenous sedation with local analgesia versus general anesthesia in patients undergoing oral surgery. Journal of Oral and Maxillofacial Surgery. 1986 Jun 1;44(6): 441-6.

ANNEXURES

ANNEXURE 1

SRI RAMAKRISHNA DENTAL COLLEGE & HOSPITAL
(Educational Service : SNR Sons Charitable Trust)
Affiliated to the Tamilnadu Dr. M.G.R. Medical University, Chennai,
Recognised by Dental Council of India, New Delhi

INSTITUTIONAL ETHICAL COMMITTEE

TO WHOMSOEVER IT MAY CONCERN

This is to certify that the study titled "*THE HAEMODYNAMIC EFFECTS OF 2% LIDOCAINE WITH 1:80000 ADRENALINE VERSUS 1:200000 ADRENALINE IN HYPERTENSIVE PATIENTS UNDERGOING MINOR ORAL SURGICAL PROCEDURES: A PROSPECTIVE, RANDOMIZED AND DOUBLE BLINDED STUDY*" to be done by DR. S. HARSHAD (2016-2019 Batch) in the Department of **Oral and Maxillofacial Surgery** under the guidance of DR. M.S. SENTHIL KUMAR, M.D.S. PROFESSOR is approved by the Institutional Ethical Committee.

DATE : 20.12.2016
PLACE: COIMBATORE

(DR. V. PRABHAKAR, M.D.S.)
Member Secretary

SRI RAMAKRISHNA DENTAL COLLEGE & HOSPITAL COIMBATORE 641 006.

S.N.R. College Road, Navaindia, Coimbatore - 641 006
Phone : 0422 - 2560381 Fax : 0422 - 2564688, E-mail : srdch@dataone.c in., srkdch@gmail.com

ANNEXURE 2

PATIENT INFORMATION

Patient Number: OP Number:

Name:

Age/ Sex:

Habits: Smoking Yes No

Duration (If Yes):

Others:

BMI:

Type Of Hypertension:

Duration:

Drug History:

Total Number Of Drugs:

Associated Systemic Diseases:

History of Previous Surgery:

ANNEXURE 3

INFORMED CONSENT

I (Name)_____ age_____ years, hereby authorize and request the performance of dental services for myself or for Mr/ Mrs/ Ms _____ age ____. I also give my consent to any advisable and necessary dental procedure, medications or anesthetics to be administered by the attending dental surgeon/ supervising staff for the diagnostic purpose or for dental treatment. I have been informed of all the available methods of treatment and I give my consent for the same. I have been explained about all the sequela and complications and I am solely responsible for the opted procedure without shifting any blame or complaint towards the doctor/ staff/ institution/ management.

Signature _____

Address and Phone number: Signature of the Doctor

Date:

தெரிவிக்கப்படும்தகவல்களுக்கானஒப்புதல்மற்றும்அங்கீகாரபடிவம்

நான் (பெயர்) _____ வயது _____ இதன்மூலம் எனக்கோ அல்லது (பெயர்) _____ வயது _____அன்னாருக்கோ தேவையான பல் மருத்துவ சிகிச்சைகளைப்பற்றி அறிந்து அதை அளிக்குமாறு வேண்டுகிறேன் . மேலும் நான் மருத்துவரால் இதரமருத்துவம் சார்ந்த உதவியாளர்களால் அளிக்கப்படும் அறிவுரைகள் , பல் மருத்துவசிகிச்சை முறைகள் மற்றும் மருந்துகள் , என் நோயைக்கண்டறிவதற்கும், சிகிச்சை பெறுவதற்கும் பயன்படுத்தப்படும் என்பதை ஏற்றுக்கோள்கிறேன். தேவையான அனைத்து சிகிச்சை முறைகள், அதன் விளைவாக நேரக்கூடிய பின் விளைவுகள் பற்றியும் எனக்குத்தெரிவிக்கப்பட்ட்து. நான் இந்த சிகிச்சையை முழுமனதாக ஏற்றுக்கொள்கின். எந்த பின்விளைவுகளுக்கும் மருத்துவரோ , மருத்துவ உதவியாளர்களோ, மருத்துவமனையோ அல்லது நிர்வாகமோ பொறுப்பில்லை என்பதை ஏற்றுக்கோள்கிறேன் . எனக்கு இந்த சிகிச்சைஅற்ற செய்முறைபடிப்புபற்றி நன்றாக விளக்கப்பட்டது . நான் இந்த சிகிச்சைஅற்ற செய்முறைபடிப்பில் பங்கேற்க விருப்பம் தெரிவிக்கிறேன்.

கையொப்பம்:_____

முகவரி & தொலைபேசிஎண்: மருத்துவர்கையொப்பம்

நாள்:

ANNEXURE 4: *STUDY TABLE*

S.NO	NAME	AGE (35YRS-50YRS)	OP No.	SMOKER (IF YES, DURATION)	BMI (kg/m^2)	TYPE OF HYPER - TENSION	DURATION OF HYPER-TENSION	DRUG HISTORY	TOTAL NUMBER OF DRUGS (=> 2)	ASSOCIATED SYSTEMIC DISEASES	HISTORY OF PREVIOUS SURGERY

Injection Technique:

Amount of LA: Time of Onset of Anaesthesia: Pain Score:

Tooth Extracted: Need For Additional Anaesthesia:

PATIENT	LOCAL ANESTHETIC SOLUTION: A/B								
TIME	HR	RR	SBP	DBP	SO2	MAP (2DBP+SBP/3)	RPP (SBP*HR)	PRQ (MAP/HR)	ECG
INITIAL BEFORE LA									
5 MINS AFTER LA									

ANNEXURE 5

S.No	Name	Age/Sex	LA Solution	Type of Hypertension	Tooth Extracted
1.	Mr. H	54/M	A	Stage 2	43
2.	Mr.SS	52/M	A	Stage 1	44,42
3.	Mr.SK	48/M	B	Stage 1	37,38
4.	Mr.MS	60/M	B	Stage 1	46,47
5.	Mr.V	68/M	A	Stage 1	18
6.	Mr. K	58/M	B	Stage 1	46
7.	Mr. A	68/M	B	Stage 1	38
8.	Mr. D	66/M	A	Stage 1	14,13
9.	Mr.G	59m	A	Stage 1	48
10.	Mr.R	60/M	A	Stage 2	31,41
11.	Mr. V	75/M	B	Stage 2	31,32,33
12.	Mr. R	26/M	A	Stage 2	16
13.	Mr. R	26/M	B	Stage 2	46
14.	Mr. A	58/M	A	Stage 2	15
15.	Mr.B	65/M	B	Stage 1	22,23,41,32,33,34,35
16.	Mr.B	65/M	A	Stage 1	42,43,44,45
17.	Mr.V	63/M	A	Stage 2	45
18.	Mr.K	72/M	A	Stage 2	34,35
19.	Mr.S	63/M	B	Stage 1	47
20.	Mr.V P	63/M	A	Stage 2	36,37
21.	Mr.SK	44/M	B	Stage 1	27
22.	Mr.AK	60/M	A	Stage 1	36
23.	Mr.R	38/M	B	Stage 1	26
24.	Mr.M	55/M	B	Stage 1	48

25.	Mr.Md.H	61/M	A	Stage 2	42,45
26.	Mr.P	78/M	B	Stage 1	16
27.	Mr.T	56/M	A	Stage 2	37,38
28.	Mr.Md.H	61/M	B	Stage 2	22,23,24
29.	Mr.L	55/M	A	Stage 2	36
30.	Mr.V	62/M	B	Stage 2	45,46
31.	Mr.R	57/M	A	Stage 1	14,17
32.	Mr.S	63/M	B	Stage 1	35
33.	Mr.N	55/M	A	Stage 2	26
34.	Mr.G	31/M	B	Stage 2	35,37,38
35.	Mr.N	55/M	B	Stage 2	15,17
36.	Mr.R	52/M	A	Stage 2	15,17
37.	Mr.N	51/M	A	Stage 1	36
38.	Mr.B	63/M	B	Stage 2	45,46
39.	Mr.SA	65/M	B	Stage 1	48
40.	Mr.R	60/M	A	Stage 2	36
41.	Mr.J	61/M	B	Stage 2	45,46
42.	Mr.V	56/M	B	Stage 1	46
43.	Mr.J	45/M	A	Stage 1	16,17,18
44.	Mr.D	52/M	A	Stage 1	34
45.	Mr.GS	39/M	B	Stage 2	37
46.	Mr.R K	49/M	A	Stage 2	48
47.	Mr.S	51/M	B	Stage 2	38
48.	Mr.P	47/M	B	Stage 1	36
49.	Mr.V	54/M	A	Stage 2	41,43,44
50.	Mr.P	46/M	A	Stage 1	26,28

GLOSSARY

ACE	Angiotensin Converting Enzyme
ARB	Angiotensin Receptor Blocker
ASA	American Society of Anaesthesiologists
BP	Blood Pressure
bpm	beats per minute
CCB	Calcium Channel Blocker
DBP	Diastolic Blood Pressure
ECG	Electrocardiography
HR	Heart Rate
HT	Hypertension
LA	Local Anaesthesia
MAP	Mean Arterial Pressure
Mg	Micro Gram
min.	Minute
ml	Millilitre
mg	Milligram
PRQ	Pressure Rate Quotient
RPP	Rate Pressure Product
RR	Respiratory Rate
SBP	Systolic Blood Pressure
SpO_2	Oxygen Saturation
SPSS	Statistical Package for Social Sciences