EFFECTS OF VASOCONSTRICTOR ON ARTERIAL BLOOD PRESSURE DURING MINOR ORAL SURGICAL PROCEDURES IN A.K.T.H KANO

BY

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MAY, 2017
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DEDICATION

I dedicated this work to my late father Malam Abubakar Khalid. May his soul rest in peace.
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I am thankful to God Almighty for giving me the ability and strength to accomplish this great task by completing this study.

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GLOSSARY

Adr - Adrenaline

AMSA - Anterior middle superior alveolar

AKTH – Aminu Kano Teaching Hospital

ATP – Adenosine triphosphate

CCLAD- Computer controlled local anesthetic delivery

CNS – Central nervous system

CVS – Cardiovascular system

COMT – Catechol-o-methyltransferase

DA – Dopamine

DBP – Diastolic blood pressure

EMLA – Eutectic mixture of local anesthetic

HCL – Hydrochloric acid

IU – International unit

IV – Intravenous

IM – Intramuscular

INB – Incisive nerve block
IANB – Inferior alveolar nerve block

LA – Local anesthesia

LGA – Local government area

LUTH – Lagos University Teaching Hospital

MAO – Monoamine oxidase

MAOI – Monoamine oxidase inhibitor

NA – Noradrenaline

PABA – Para-amino benzoic acid

pH – the measure of acidity or alkalinity of a solution

pKa – Negative decadic logarithm of the ionization constant (Ka) of an acid

PSANB – Posterior superior alveolar nerve block

PR – Pulse rate

SBP – Systolic blood pressure

TCA – Tricyclic antidepressants
The aim of this study is to evaluate effect of adrenaline contained in dental local anaesthetics on blood pressure and pulse rate of patients undergoing extractions. This was conducted in Oral and Maxillofacial Surgery department of Aminu Kano Teaching Hospital (AKTH), Kano amongst consenting patients aged 18 to 55 years who are either normotensive or known controlled hypertensive.

Simple random sampling method was adopted for the study to allocate the patients into either the study group or the control group using balloting. Sample size of 100(50 per group) was used for the study. The anxiety level was scored using a numerical scale. Baseline blood pressure and pulse rate of the patients were measured 5 minutes before the local anaesthetic injection. Two percent lignocaine with 1:80,000 epinephrine was used in the study group while two percent lignocaine without epinephrine was used in the control group. A maximum of two cartridges was given to each patient. Blood pressure and pulse rate were checked 5 minutes after the local anaesthetic injection, 2 minutes after the commencement of procedure, 15 and 30 minutes after the procedure using a precalibrated non-invasive electronic digital blood pressure monitor (EchoMax Plus manufactured by Hubdic Co. Ltd Korea).

Data collection was done by means of interviewer-administered questionnaire and recorded into a proforma designed for this study. Data was presented using tables, charts and graphs. Quantitative data was summarized using means and standard deviations, while qualitative data was described using frequencies and percentages. Data analysis was performed using Statistical Package for Social Statistics Version 17.0 (SPSS Inc. Chicago, II, USA). The level of significance was
determined using paired t-test. A confidence interval of 95% was used in this study and a p-value of less than 0.05 was considered significant.

Multivariate logistic regression was done to determine the influence of the socio-demographic variables, anxiety level, number of anaesthetic cartridge used, and injection technique on the result of the study.

The results of this study show that there is no statistically significant difference in SBP, DBP, and PR between the study and control group at all intervals (p-value > 0.05) which points to a conclusion that the optimal use of local anaesthetics containing adrenaline does not significantly alter blood pressure in controlled hypertensive and normotensive patients.
CHAPTER ONE

INTRODUCTION:

Minor oral surgery is a broad term referring to surgical procedures to the oral cavity and jaws that can be performed safely and comfortably under general anaesthesia, local anaesthesia, and or sedation in an outpatient setting. In other words, it comprises oral surgical procedures that can be accomplished without necessarily admitting the patient in the hospital. It includes procedures like surgical disimpaction of third molars, biopsies, frenectomies, reduction and immobilization of fractures among others. Most of these procedures are well tolerated under local anaesthesia. In contrast to major oral surgical procedures which require patient admission into the hospital, the minor oral surgical procedures tend to have less mortality rate. Majority of minor oral surgical procedures require the use of local anaesthetics. The currently used local anaesthetic agents consist of vasoconstrictor as part of the composition to improve the biological properties of the solution which may be either adrenergic agonist or felypressin. Of these vasoconstrictors, adrenaline is the most frequently used vasoconstrictor in daily dental practice to achieve the desired properties. Such properties include haemostasis, increased depth and duration of anaesthesia, decreased systemic absorption, decreased dose of anaesthetic agent required and subsequently reduced toxicity. These vasoconstrictors cause some haemodynamic changes which may be either by direct action on the cardiac muscle or by stimulation of the autonomic innervations of the heart. All of these effects may cause, depending on the concentration of the vasoconstrictor an increased heart rate, increased force of cardiac contraction and ultimately increased blood pressure.
However, the occurrence of most adverse reactions is due to inappropriate high dose injection and accidental injection into the vasculature.\textsuperscript{9,10} Apart from these changes, there are physiological responses to adrenaline containing local anaesthetics which includes dysrythmias,\textsuperscript{11,12} ischemic alterations,\textsuperscript{13,14} endogenous catecholamines release\textsuperscript{15} and hypokalemia.\textsuperscript{16,17} These changes are resolved by the net balance between the sympathetic and parasympathetic activity.\textsuperscript{18,19} When this vasoconstrictor-induced physiological response exceeds the normal range, the risk of morbidity and mortality increases especially in patients with background cardiovascular diseases.\textsuperscript{20} Many authors concluded that adrenaline has a safety range,\textsuperscript{21,22} its threshold in cardiovascular patients is not yet clear.\textsuperscript{23,24} These haemodynamic effects of the vasoconstrictor containing local anaesthetics has created fear in the minds of practicing dentists especially when dealing with patients who have background history of cardiovascular disease.\textsuperscript{7,25} The fact that adrenaline is a vasopressor agent has made many authors to implicate it as the causative agent in certain clinical situations of hypertension encountered in the dental office.\textsuperscript{26,27} Hypertensive patients represent an important risk group among patients visiting dental clinic as many of them give a history of high blood pressure.\textsuperscript{28} Not only adrenergic agonists are in use as vasoconstrictors with local anesthetics. Felypressin which is a synthetic analogue of the posterior hypophysal polypeptide hormone, vasopressin (antidiuretic hormone), is available in many countries as a vasoconstrictor.\textsuperscript{29} In contrast to adrenaline, felypressin does not cause significant changes in heart rate as it does not act on adrenergic receptors, rather it has a direct effect on the vascular smooth muscles.\textsuperscript{30} Its action appears to be more prominent on the venous than on the arteriolar circulation.\textsuperscript{31,32}

This accounts for its satisfactory use in prolonging the duration and potency of the anaesthetic block, but may be responsible for its apparent poor control of haemorrhage during surgery.\textsuperscript{33}
Furthermore, the vasoconstrictor effect of felypressin is lower than that of adrenaline but the duration of effect is more or less the same.\textsuperscript{34}

Nonetheless, it offers significant advantage over adrenergic agonist as it has not been found to induce dysrhythmia although some studies have shown that it can increase the systolic blood pressure in controlled hypertensive patients.\textsuperscript{29} It is available only in combination with prilocaine in the concentration of 0.03iu/ml.\textsuperscript{29}

When administering vasoconstrictor containing local anaesthetics, the clinician should take into cognizance drug interactions that may occur. Several drugs have been documented to interact with the vasoconstrictor containing local anaesthetics. These include – inhalational anaesthetics, tricyclic antidepressants, phenothiazines, non-selective beta blockers e.t.c. On several occasions, dental procedures are performed under general anaesthesia with inhalational agents. In these situations, the anesthetic/vasoconstrictor solution is usually used for haemostasis. Some general anaesthetics particularly halothane sensitize the myocardium to the direct myocardial effect of the sympathomimetic amine.\textsuperscript{35} Some controversies exist as regards to the interaction between tricyclic antidepressants and epinephrine in local anaesthetics for dentistry. Tricyclic antidepressants usually prevent neuronal uptake of catecholamines at the adrenergic nerve terminals which results in a higher concentration of catecholamines present at the sympathetic neuroeffector junction.\textsuperscript{29} Some authors have concluded that there is no clinical evidence of significant interactions between tricyclic antidepressants and local anaesthetics containing epinephrine.\textsuperscript{36} However, Jastak and Yagiela\textsuperscript{37} have concluded that there was a two to four fold potentiation of epinephrine by tricyclic antidepressants. The non-selective beta blocking agents commonly used in the treatment of hypertension may enhance the vasopressor action of epinephrine.\textsuperscript{38} The beta blocker inhibits vasodilatation of skeletal muscle; therefore the reflex vasodilatation that would normally occur in
response to the alpha stimulating effects of epinephrine would not take place. Blood pressure rises significantly in most cases.\textsuperscript{38}

Several medical conditions may serve as a contraindication to the use of vasoconstrictor containing local anaesthetics. Depending on the gravity of the untoward effect that may occur, they are classified into absolute and relative contraindications.\textsuperscript{39} The absolute contraindications include – heart diseases (e.g unstable angina, recent myocardial infarction, uncontrolled hypertension, refractory arrhythmias, recent coronary artery bye-pass graft, and uncontrolled congestive heart failure), pheochromocytoma, thyrotoxicosis, sulfite sensitivity, and uncontrolled diabetes.\textsuperscript{39} The relative contraindications include all the aforementioned drug interactions and cocaine abusers.\textsuperscript{39} The use of the vasoconstrictor containing local anaesthetics has become a controversial subject in dentistry due to the clinical effects of the haemodynamic changes assumed to be caused by it.\textsuperscript{40-44}

1.1 STATEMENT OF THE PROBLEM

Many of our colleagues are still overzealous in taking precautions towards avoiding the use of vasoconstrictor containing local anaesthetics in any patient with a history of high blood pressure even if it is controlled to the extent of postponing the procedure if plain local anaesthetic is not at their disposal, even when patients are in acute pain. By so doing, the patients are deprived of the added advantages of using the vasoconstrictor containing local anaesthetics.

Secondly, the use of plain local anaesthetics in longer procedures may lead to the danger of giving more volume of the local anaesthesia than necessary.

1.2 JUSTIFICATION OF STUDY:
This study is designed to evaluate the haemodynamic changes following administration of vasoconstrictor containing local anaesthetics during minor oral surgical procedures. A few studies have been published in international journals as regards the haemodynamic changes following administration of vasoconstrictor containing local anaesthetics. The results of these studies are mixed. However, only few of these studies are from Nigerian authors.

Furthermore, the prevalence of hypertension in patients with oral diseases is increasing in Nigeria,\textsuperscript{45,46} which indirectly means that many hypertensive patients will require dental procedures which are done under local anaesthesia. Therefore, there is need for more studies to determine the association between the vasoconstrictor (adrenaline) and blood pressure in the peri-operative period in Nigeria. The study will add to the quality of care given to our patients.

1.3 **RESEARCH QUESTION:**

Does epinephrine contained in local anaesthetics have significant effect in increasing blood pressure during extractions?

1.4 **HYPOTHESIS:**

Administration of optimal dose of adrenaline containing local anaesthetic agents does not significantly affect the blood pressure on healthy (non-hypertensive) and controlled hypertensive patients.

1.5 **COUNTER OR ALTERNATIVE HYPOTHESIS:**

The administration of optimal dose of vasoconstrictor containing local anaesthetic agents can significantly affect the blood pressure on healthy (non-hypertensive) and controlled hypertensive patients.
CHAPTER TWO

AIM AND OBJECTIVES

2.1 AIM:

The aim of this study is to assess the effect of vasoconstrictor contained in local anaesthetics on arterial blood pressure during minor oral surgical procedures.

2.2 OBJECTIVES:

i. To determine the changes in systolic blood pressure following administration of local anaesthesia containing vasoconstrictor agent.

ii. To evaluate the alterations in diastolic blood pressure following administration of local anaesthesia containing vasoconstrictor agent.

iii. To determine the effect of epinephrine contained in local anaesthetics on pulse rate.
CHAPTER THREE

LITERATURE REVIEW

3.1 HISTORICAL PERSPECTIVE OF LOCAL ANAESTHESIA.

One of the differences which distinguished civilized man from the primitive man is the progress in the art of pain elimination and healing. From time immemorial many researches were done aimed at reducing or even alleviating surgical pain. Various means have been devised in this quest before the advent of local anaesthetics. These include refrigeration, compression, electricity and acupuncture.⁴⁷

It was dentists, not doctors that were responsible for the discovery of anaesthesia due to their close day-to-day contact with pain, and hence their motivation to seek the means of alleviating it.⁴⁸ Doctors focused more on infections than pain because people were dying of pneumonia, diphtheria, gangrene, tuberculosis, tetanus and so on.⁴⁸ Credit was given to the two dentists who first introduced anesthesia: Horace Wells (1815-1848), with nitrous oxide in 1844, and William Thomas Green Morton (1819-1868) with ether in 1846.⁴⁹

Local anaesthesia, the basis of modern local anaesthetics for dentistry and medicine, developed later. The evolution of modern local anaesthetics began from the discovery of the coca leaf. Coca leaves are taken from a shrub of the genus *Erythroxylum*, a member of the erythroxylaceae family, so named by Patricio Browne because of the reddish hue of the
wood of the main species.\textsuperscript{49} \textit{Erythroxylum coca}, one of the species in this genus, contains the highest concentration of the alkaloid known as cocaine in its leaves up to 0.7-1.8\% by weight.\textsuperscript{50}

The first reference to the anaesthetic effects of coca was from Jesut Bernabe Cobo (1582-1657), who in his 1653 manuscript work on the New World, mentioned that toothaches can be alleviated by chewing coca leaves.\textsuperscript{51} However, isolating the active principle of the coca leaf (cocaine) was accomplished by Albert Niemann (1834-1861) in 1860.

From the time cocaine was isolated; several steps were taken to apply it as the first local anaesthetic. Nothing had changed since the early reference of anaesthetic effect of coca by Jesut Bernabe Cobo in 1653.\textsuperscript{51}

The first experimental study on cocaine was conducted by Peruvian Thomas Moreno Y Maiz, who is an ex-naval surgeon as part of his doctoral thesis published in 1868. He found that injecting cocaine solutions caused insensibility in rats, guinea pigs and frogs; he even mentioned its local anaesthetic effects. Nevertheless, he did not mention its use in surgery.\textsuperscript{51}

In 1880 Basil Von Anrep published an interesting article on his experiments on animals (rats, dogs, cats, rabbits and pigeons), animal tissues and organs, and, especially himself. He injected a small quantity of 0.003-0.5 cocaine solution (equivalent to 0.6\%) under the skin on his arm, which left the area insensitive. He did the same with an externally applied 0.005-0.05 solution (equivalent to 1\%) to his tongue, which also caused insensibility. He concluded by recommending cocaine as a surgical anesthetic.\textsuperscript{51}
In 1884, the drug engaged the attention of Sigmund Freud and he listed several possible therapeutic uses of cocaine such as substitution for morphine, general stimulant and local anaesthetic. Later Carl Koller performed some experiments on himself and his assistant with cocaine and found out that 2 percent solution of cocaine hydrochloride produced effective surface anaesthesia of the cornea.\(^{52}\)

Cocaine was soon tested elsewhere on the body and as a surface anaesthetic and in the same year of Koller’s discovery William Steward Halsted in America used a solution of cocaine to produce anesthesia of the inferior alveolar nerve. According to Howe (1972), the first record of the use of cocaine by injection in Britain appeared in the journal of the British Dental Association in 1886, when William Alfred Hund of Yeovil described its use in infiltration techniques.\(^{53}\)

Though cocaine benefits were great, its indiscriminate use coupled with high toxicity and addiction potential led to an intensive search for less toxic substitutes for cocaine. Hundreds of aminoesters of benzoic acid derivatives have been experimented. Two Swedish Chemists, Alfred Einhorn and Euhifelder in 1905 succeeded in synthesizing procaine hydrochloride, which was clinically tested by Hearich Braun and marketed as Novocaine.\(^{54}\) Procaine with or without adrenaline was initially only available as tablets that were dissolved in the appropriate quantity of sterile water by the dental surgeon.\(^{54}\) However, the anaesthetic effects of the drug were weak, and it required high concentration of the adrenaline, particularly when infiltration techniques were used. Moreover, some patients are highly allergic to it.\(^{55}\)
These drawbacks prompted the search for an alternative drug. In 1948, Swedish Chemist, Lofgren, developed a xylidine derivative named lidocaine whose chemical composition is very different from novocaine but which is nonetheless safe and has stronger effect and less allergenic action.\textsuperscript{56} His discovery of lidocaine probably marked a new epoch in local anaesthesia.

3.2 LOCAL ANAESTHESIA IN DENTISTRY

In dental practice, LAs are mainly used for nerve block or for infiltration/regional block techniques to carry out various procedures.\textsuperscript{57}

Less frequently, they are topically applied to painful oral ulcerations and other superficial lesions.\textsuperscript{58}

The total amount of LA injected for dental anaesthesia is generally much smaller (e.g. 20-80mg of lignocaine)\textsuperscript{59} as compared to the amount required for purposes like brachial plexus block, multiple nerve blocks or epidural anaesthesia. As such not much concern is given to the systemic toxicity of dental anaesthesia. Rarely does a serious adverse effect occur;\textsuperscript{59} many side effects that have been described (like palpitation, pallor, sweating, uneasiness, giddiness, fainting, nausea, and tremor) have their origin in the apprehension of the patient to the injection given.

The duration of action of local anaesthesia is largely dependent on the length of time the drug can stay in the nerve to block the sodium channel which varies depending on the region of injection and the presence of a vasoconstrictor in the solution.\textsuperscript{59} Maxillary
infiltration of the LA has a shorter duration than the same drug injected into the mandible which could be explained due to greater vascularity in the maxilla than in the mandible. This difference in duration of action is more marked for plain LA solutions than for those containing vasoconstrictor. After nerve block, the duration of dental pulp anaesthesia is generally 1/4th to 1/3rd that of soft tissue anaesthesia. The plain local anaesthesia may be preferred when a shorter duration of soft tissue anaesthesia without complete pulpal anaesthesia is required, when intra-operative haemorrhage is not a concern, and when vasoconstrictor is contraindicated.

Lignocaine (2%) with adrenaline (1:80,000) is the standard LA preparation used in dental practice. It produces excellent soft tissue as well as pulpal anaesthesia and reduces post-extraction bleeding. After injection pulpal anaesthesia is obtained in 2-3 minutes and lasts for 40-60 minutes, whereas soft tissues remain anaesthetized for 2-3 hours. However, complete pain alleviation may not be achieved in few patients with very sensitive teeth or marked inflammation. In comparison, plain lignocaine (2%) provides soft tissue anaesthesia for 45-90 min, while pulpal anaesthesia is brief (10-20 min). moreover, haemorrhage control is poor due to vasodilatory action of lignocaine. Systemic absorption of lignocaine is very rapid after intra-venous injection due to high lipid solubility and is used clinically in the primary management of ventricular dysrhythmias.

Topically, lignocaine spray formulation may be applied on painful oral ulcers and prior to intra-oral injection of the LA in apprehensive patients.
3.3 TYPES OF ANAESTHESIA

Several modalities have been used to achieve pain control in the medical and dental practice. The choice of a particular modality to be used depends on the nature of the procedure to be performed, time required, invasiveness of the procedure, and the pain associated with it. They include:

1. LOCAL ANAESTHESIA
2. GENERAL ANAESTHESIA
3. SEDATION
   - Minimal sedation
   - Moderate sedation (conscious sedation)
   - Deep sedation

LOCAL ANAESTHESIA

Local anaesthesia has been defined as a loss of sensation in a circumscribed area of the body caused by a depression of excitation in nerve endings or an inhibition of the conduction process in peripheral nerves. One important feature that distinguishes the local anaesthesia from general anaesthesia is that it produces this loss of sensation without inducing loss of consciousness.

Several methods of inducing local anaesthesia have been documented such as:

1. Mechanical trauma
2. Low temperature
3. Anoxia
4. Chemical irritants
5. Neurolytic agents such as alcohol and phenol
6. Chemical agents such as local anaesthetics

However, not all of the above mentioned methods are applicable in clinical practice. It is the ability of a particular method or substance to induce transient and completely reversible state of anaesthesia that will make it relevant in clinical practice.\(^ {65}\)

**GENERAL ANAESTHESIA**

General anaesthesia is defined as a drug-induced depression of consciousness during which the patient is not arousable, even by painful stimulation. Patients often require assistance in maintaining a patent airway and positive pressure ventilation. Cardiovascular function may also be impaired.\(^ {66}\)

**SEDATION**

Sedation is a technique where one or more drugs are used to depress the central nervous system of a patient thus reducing the awareness of the patient to his surroundings.\(^ {63}\) There are three different types of sedation viz: \(^ {63,66,67}\)

1. **Minimal sedation (anxiolysis):** This is characterized by depression of the central nervous system, and cognitive impairment of a patient. However, the patient can still respond to verbal commands and there is no effect on cardiopulmonary status.
2. **Moderate sedation (conscious sedation):** In this, there is depression of consciousness, but patients in this state can respond appropriately to verbal commands, either alone or in conjunction with light tactile stimulation. The patient is able to maintain airway independently, there is adequate ventilation and cardiovascular function is usually unaffected by the drugs administered.

3. **Deep sedation:** Patients are not easily awakened in this state, but they respond purposefully (they do not withdraw) after repeated or painful stimulation. These patients may require assistance maintaining airway and adequate ventilation, but normal cardiovascular status is usually sustained as long as ventilation is appropriate.

Another term **procedural sedation** has emerged by The American College of Emergency Physicians (ACEP). Procedural sedation is defined as "a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardio respiratory function." PSA is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently.¹⁹²

Combating anxiety is the main goal of sedation in dentistry. However, the mainstay of alleviating anxiety is behavioral management, although good doctor-patient rapport is essential. In cases that sedation became necessary, moderate sedation analgesia (known to the dentists as conscious sedation) will suffice.⁶⁹,⁷⁰ This is usually most effective with the combined use of local anaesthesia.⁶⁹
In dentistry, sedation techniques are not pain control techniques and are often overridden when the patient experiences intra-operative pain. To curtail these painful circumstance with sedative agents alone requires the use of very high doses or the addition of a narcotic to the regimen thus producing deeper levels of sedation than might be required coupled with the increasing possibility of side effects.\textsuperscript{69} Common indications for office-based sedation are: young children, stressful procedures (such as third molar extraction, complex periodontal procedures, and dental implants), and behaviorally/medically challenged patients.\textsuperscript{69,70}

The use of drugs to help patients deal with their fears has been extensively researched and a number of techniques have become established in dental practice throughout the world. These are, first, oral sedation with benzodiazepines; second, inhalational sedation with nitrous oxide; and third, intravenous sedation with midazolam alone or with an analgesic.\textsuperscript{69}

\section*{3.4 LOCAL ANAESTHESIA AND METHODS OF ADMINISTERING L.A}
PHYSICAL AND PSYCHOLOGICAL EVALUATION

Prior to commencement of any dental therapy, the doctor or hygienist must determine whether the patient is physically and psychologically fit and can tolerate the procedures in a relative safety. If this is not the case, the specific treatment modifications necessary to decrease the risk presented by the patient must be determined. The doctor must seek to uncover as much information as possible concerning the patient’s physical and mental status before the administration of a local anaesthetic using the patient’s completed medical history questionnaire, the dialogue history, and the physical examination of the patient. Adequate use of these safeguards can lead to an accurate determination of a patient’s physical status and can prevent up to 90% of all life-threatening medical emergencies in dental practice. However, most undesirable reactions to local anaesthetics are not produced by the drugs themselves but as a response to the act of drug administration. The two most commonly occurring psychogenic reactions are vasodepressor syncope and hyperventilation. Other psychogenically induced reactions noted as a response to local anaesthetic administration include tonic-clonic convulsions, bronchospasm, and angina pectoris.

GENERAL METHODS OF LA ADMINISTRATION

There are several methods of obtaining pain control with local anaesthetics. The type of injection to be administered is partly dependent upon the site of deposition of the drug relative to the area of operative intervention. In general, three major types of local anaesthetic injection can be differentiated: local infiltration, field block, and nerve block.
LOCAL INFILTRATION: This involves injecting the local anaesthetic solution into the small terminal nerve endings in the area of dental treatment. The incision (or treatment) is then made into the same area in which the local anesthetic has been deposited.\(^7\)

FIELD BLOCK: Local anaesthetic solution is deposited near the larger terminal nerve branches so the anaesthetized area will be circumscribed, preventing the passage of impulses from the tooth to the central nervous system. Incision (or treatment) is then made in an area away from the site of injection of the anaesthetic. They are commonly referred to as infiltration or supraperiosteal injection.\(^7\)

NERVE BLOCK: In this, local anaesthetic is deposited usually at a distance from the site of operative intervention. Posterior superior alveolar, inferior alveolar, and nasopalatine injections are examples of nerve blocks.\(^7\)

SOME IMPORTANT INJECTION TECHNIQUES IN DENTISTRY

1. INFERIOR ALVEOLAR NERVE BLOCK: The inferior alveolar nerve block (IANB) which is commonly (but inaccurately) referred to as the mandibular nerve block, is the most frequently used and perhaps the most important injection technique in dentistry. It is an especially useful technique for quadrant dentistry. A supplemental block (buccal nerve) is needed if soft tissue anaesthesia in the buccal posterior region is necessary. On rare occasion partial anaesthesia in the lower incisor region may be caused by overlap of sensory fibers from the contralateral side which can be corrected by infiltration. However, it also proves to be the most frustrating with the highest percentage of clinical failures (approximately 15% to 20%) even when administered properly.\(^5\)
The bilateral administration of IANB should be rarely called for in dental treatments other than bilateral mandibular surgeries, as they produce considerable discomfort primarily from the lingual soft tissue anaesthesia, which usually persists for several hours after injection. The patient feels unable to swallow and, because of the lack of all sensation, is more likely to self-injure the anaesthetized soft tissues. The nerve anaesthetized after IANB include the inferior alveolar nerve, the incisive nerve, the mental and the lingual nerve. Two major disadvantages attributed to IANB are the high rate of inadequate anaesthesia (15% to 20%) and highest rate of positive aspiration among all intraoral injection techniques (10% to 15%).

2. THE GOW-GATES TECHNIQUE OF THE MANDIBULAR NERVE BLOCK: It is frequently more difficult to achieve successful anesthesia of the mandibular teeth and soft tissues than the maxillary structures. Failure rates of up to 20% have been documented with the traditional IANB technique. Primary factors for these failure rates are the greater anatomical variation in the mandible and the need for deeper soft tissue penetration. George Albert Edwards Gow-Gates, a general dental practitioner in Australia, described a new approach to mandibular anaesthesia in 1973. The Gow-Gates technique is a true mandibular nerve block because it provides sensory anesthesia to virtually the entire distribution of V₃. The inferior alveolar, lingual, mylohyoid, mental, incisive, auriculotemporal, and buccal nerves are all blocked in the Gow-Gates injection.

Significant advantages of the Gow-Gates technique over the IANB include its higher success rate, its lower incidence of positive aspiration (approximately 2% versus 10%
to 15% with the IANB) and the absence of problems with accessory sensory innervation to the mandibular teeth.\textsuperscript{74,75}

3. **VAZIRANI-AKINOSI CLOSED-MOUTH MANDIBULAR BLOCK**

After the successful introduction of the Gow-Gates mandibular nerve block in 1973, interest has developed in alternative methods of achieving anaesthesia in the lower jaw. Dr. Joseph Akinosi reported on a closed-mouth approach to mandibular anaesthesia in 1977.\textsuperscript{76} Its primary indication remains those situations in which limited mouth opening precludes the use of other mandibular injection techniques, although it can be used whenever mandibular anaesthesia is desired. Such situations include the presence of spasm of muscles of mastication (trismus) on one side of the mandible after numerous attempts at IANB. The inferior alveolar and Gow-Gates mandibular nerve blocks cannot be attempted when significant trismus is present. The Vazirani-Akinosi technique is an intraoral approach to providing both anaesthesia and motor blockade in cases of severe unilateral trismus.\textsuperscript{77}

In 1992, a modification of the original Vazirani-Akinosi technique was described by Wolfe. The technique he described was similar to the conventional technique except that bending the needle at a 45-degree angle was recommended. This is to enable the needle to remain in close proximity to the medial (lingual) surface of the mandibular ramus as the needle travels through the tissues.\textsuperscript{78}

4. **ANTERIOR MIDDLE SUPERIOR ALVEOLAR NERVE BLOCK**
The anterior middle superior alveolar (AMSA) injection represents a newly described maxillary nerve block injection. It was first reported by Friedman and Hochman in 1997 during development of CCLAD system. This technique provides pulpal anaesthesia for multiple maxillary teeth (incisors, canine, and premolars) from a single injection site. The injection site is on the hard palate about halfway along an imaginary line connecting the midpalatal suture to the free gingival margin. The location of the line is at the contact point between the first and second premolars. The muscles of facial expression and upper lip are not anaesthetized as the local anaesthetic is deposited on the palate. A minimal volume of local anaesthetic solution is enough to provide pulpal anaesthesia from the central incisor to the second premolar.

The AMSA injection may be particularly useful for aesthetic-restorative (cosmetic) dental procedures in which the dentist wishes to evaluate the smile line during treatment. Also, this injection technique has been found to be very effective for periodontal scaling and root planing of the maxillary region. It provides adequate anaesthesia of the attached gingiva and associated teeth. Perry and Loomer demonstrated a patient preference for the AMSA compared with supraperiosteal infiltration injections. Subjects found the AMSA to be as effective as multiple maxillary infiltrations in the maxilla.

**SUPPLEMENTAL INJECTION TECHNIQUES**

1. **INTRAOSSEOUS ANAESTHESIA:**
In this technique, the local anaesthetic solution is deposited into the cancellous bone that supports the teeth. This technique dates back to the early 1900s, a refreshing interest in this technique has taken place over the past 15 years.\textsuperscript{82} There are two modifications to the intraosseous anaesthesia (the periodontal ligament injection and the intraseptal injection).\textsuperscript{83} The intraosseous injection entails deposition of the local anesthetic solution into the interproximal bone between two teeth. Originally it necessitated the use of a half-round bur to provide entry into interseptal bone that had been surgically exposed. Once the hole has been made, a needle would be inserted into it and local anesthetic deposited.\textsuperscript{84}

2. INTRAPULPAL INJECTION:

This involves deposition of the local anaesthetic solution directly into the pulp chamber of a pulpally involved tooth. It provides effective anesthesia for pulpal extirpation and instrumentation where other techniques have failed. The intrapulpal injection provides pain control both by the pharmacological action of the local anaesthetic and applied pressure.\textsuperscript{85}

3.5 PAIN, ANAESTHESIA VERSUS ANALGESIA

Pain is defined by the International Association for the Study of Pain (IASP), as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.”\textsuperscript{86} It is a symptom
that cannot be objectively assessed. Margo Mc Caffery (1968), made an observation about pain and concluded that: "Pain is whatever the experiencing person says it is, existing whenever he says it does."

Pain results from stimulation of nociceptors that are receptors preferentially sensitive to a noxious stimulus. Pain is perceived when nociception reaches the cerebral cortex.

Pain may be abolished by interrupting the pathways that carry the information of the stimulus from the periphery of the body to the central nervous system. Local anaesthetics block sensory neuronal conduction of noxious stimuli from reaching the central nervous system.

Many patients find it difficult to separate pain from dentistry. This perception is very common in those patients who had several dental procedures such as multiple extractions, periodontal surgery or endodontic therapy.

A Dentist who causes little or no discomfort is perceived as a good dentist by the general public. The daily dental practice is therefore based upon achieving adequate local anaesthesia.

Controversies exist as regards to the term – local anaesthesia. Some authors consider the term inappropriate and prefer to call it as local analgesia. Local anaesthesia is defined as a loss of sensation in a circumscribed area of the body, by a depression of excitation in nerve endings or an inhibition of the conduction process in the peripheral nerves. However, the localized loss of pain sensation is desired in clinical practice and is the actual effect observed. Also, some local
anaesthetics such as procaine were administered intravenously for the management of chronic pain and arthritis in the 1940s and 1950s.\textsuperscript{91}

### 3.6 CLASSIFICATION OF LOCAL ANAESTHETIC AGENTS\textsuperscript{29}

A. BASED ON CHEMICAL STRUCTURE OF ANAESTHETIC AGENT:

<table>
<thead>
<tr>
<th>Classification</th>
<th>Anaesthetic Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. ESTERS OF BENZOIC ACID</td>
<td>Butacaine</td>
</tr>
<tr>
<td></td>
<td>Cocaine</td>
</tr>
<tr>
<td></td>
<td>Ethyl aminobenzoate (benzocaine)</td>
</tr>
<tr>
<td></td>
<td>Hexylcaine</td>
</tr>
<tr>
<td></td>
<td>Piperocaine</td>
</tr>
<tr>
<td></td>
<td>Tetracaine</td>
</tr>
<tr>
<td>II. ESTERS OF PARAAMINOBENZOIC ACID</td>
<td>Chloroprocaine</td>
</tr>
<tr>
<td></td>
<td>Procaine</td>
</tr>
<tr>
<td></td>
<td>Propoxycaine</td>
</tr>
<tr>
<td>III. AMIDES</td>
<td>Articaine</td>
</tr>
<tr>
<td></td>
<td>Bupivacaine</td>
</tr>
<tr>
<td></td>
<td>Dibucaaine</td>
</tr>
</tbody>
</table>
Etidocaine
Lidocaine
Mepivacaine
Prilocaine
Ropivacaine

IV. QUINOLINE
Centbucridine

B. BASED ON PRESENCE OR ABSENCE OF VASOCONSTRICTOR
I. Plain local anaesthesia(without vasoconstrictor)
II. Local anaesthesia with vasoconstrictor

3.7 PHARMACOLOGY OF LOCAL ANAESTHETICS

1. CHEMICAL STRUCTURE

Though they differ in many respects, structurally local anaesthetics have specific fundamental features in common. Local anesthetics consist of an aromatic group (benzoic acid or aniline) with an ester or amide linkage to an intermediate hydrocarbon chain, and a secondary or tertiary amino group.\textsuperscript{92}
The local anaesthetic’s hydrophilic properties are due to the secondary or tertiary amino groups, while the lipophilic properties are derived from the aromatic residue which originates from benzoic acid or aniline.\textsuperscript{93}

The ester or amide linkage between the aromatic residue and the intermediate carbon chain determines the anesthetic’s metabolism, allergenicity, and classification. It is based on the presence of these amide or ester linkages that they are classified accordingly.\textsuperscript{94}

2. PHARMACOKINETICS:

i. ABSORPTION: The rate of absorption (uptake) of local anaesthetics after parenteral administration (subcutaneous, intramuscular, or IV) is related to both the vascularity of the injection site and the vasoactivity of the drug. IV administration of local anaesthetics provides the most rapid elevation of blood levels and is used clinically in the primary management of ventricular dysrhythmias.\textsuperscript{95} However, rapid IV administration can lead to significantly high local anaesthetic blood levels, which can induce serious toxic reactions. The risk-benefit ratio must always be carefully weighed prior to any intravenous injection.\textsuperscript{96}

When given orally, local anaesthetics are poorly absorbed from the gastrointestinal tract with the exception of cocaine. Most local anaesthetics especially lidocaine undergo a significant hepatic first pass effect after oral administration. Following the absorption of lidocaine from the gastrointestinal tract into the enterohepatic circulation, about 72\% of the dose is biotransformed into inactive metabolites.\textsuperscript{97}

Absorption of local anaesthetics topically largely depends on the region and the sanctity of the skin. When applied to tracheal mucosa, the absorption rate is almost equal to that of
intravenous administration. A eutectic mixture of local anaesthetics (EMLA) has been developed that is able to provide surface anaesthesia of intact skin. \(^{98}\)

ii. DISTRIBUTION:

Local anaesthetics are generally distributed to all the organs in the body once they are absorbed into the blood stream. However, the higher the perfusion of an organ, the greater the concentration of the local anaesthetic distributed to it. Such highly perfused organs include – the brain, liver, kidneys, and lungs. Skeletal muscles, though not as highly perfused as these areas, contain the greatest percentage of local anaesthetic of any tissue or organ in the body as it constitutes the largest mass of tissue in the body. \(^{99}\)

All local anaesthetics readily cross blood brain barrier and can also cross the placenta to enter the circulatory system of a developing fetus. \(^{99}\)

iii. METABOLISM (BIOTRANSFORMATION):

One of the main differentiating factors between the amide and ester local anesthetics is the means they are metabolized into pharmacologically inactive substances. The biotransformation of local anesthetics is paramount because the overall toxicity of drug depends on the rate at which it is absorbed and its rate of removal from the blood. \(^{98}\)

Ester local anaesthetics are hydrolyzed in the plasma by the plasma pseudo-cholinesterase. Different esters are hydrolyzed at different rates and that determines their level of toxicity. Procaine undergoes hydrolysis to para-aminobenzoic acid (PABA), which is excreted unchanged in the urine, and to diethylamine alcohol, which undergoes further biotransformation before excretion. Allergic reactions that occur in response to ester local
anaesthetics usually are not related to the parent compound (e.g procaine) but rather to PABA, which is a major metabolic product of ester local anaesthetic.\textsuperscript{100}

It is not uncommon for some individuals to have an atypical form of pseudo-cholinesterase which causes an inability to hydrolyze ester local anaesthetics and other chemically related drugs (e.g succinylcholine). Approximately 1 of every 2800 persons has such a disorder. This leads to a prolongation of higher local anaesthetic blood levels and an increased potential for toxicity.\textsuperscript{101}

The biotransformation of amide local anaesthetics is more complex than that of the esters. The liver is the primary site where amide local anaesthetic is metabolized. The entire metabolic process occurs in the liver for all amide local anaesthetics except for prilocaine which undergoes metabolism both in the liver and lungs.\textsuperscript{102} Therefore, liver function and hepatic perfusion significantly influence the rate of biotransformation of an amide local anaesthetic. Approximately 70\% of a dose of injected lidocaine undergoes biotransformation in patients with normal liver function.\textsuperscript{98} Patients with lower than normal blood flow or poor liver function are unable to biotransform amide local anaesthetics at a normal rate.\textsuperscript{103} This slower than normal biotransformation rate leads to increased anaesthetic blood levels and a potential increase in toxicity. However, it does not significantly increase the duration of action of locally administered drugs like local anaesthetics. This is so because the duration of action of local anesthetics is determined by redistribution rather than biotransformation. As such a patient with liver disease should be given standard dose of local anaesthetic. However, the total dose is of concern. Therefore it is prudent to minimize the total dose of local anaesthetic given when treating patient with liver dysfunction. Some have suggested the use of an ester local anaesthetic. This does not
offer any advantage as pseudo-cholinesterase which is the enzyme involved in the metabolism of ester local anaesthetic, is also synthesized in the liver.\textsuperscript{104-107}

Articaine has a shorter half-life than other amides because a portion of its biotransformation occurs in the blood by the enzyme plasma cholinesterase.\textsuperscript{108}

One of the amide LAs (Prilocaine) causes a clinical phenomenon called methemoglobinemia. Prilocaine, which is the parent compound, does not produce methemoglobinemia; but orthotoluidine, a primary metabolite of prilocaine, does induce the formation of methemoglobin, which is responsible for methemoglobinemia.\textsuperscript{109}

In some instances, lidocaine is associated with sedation which is attributed to the two metabolites generated – monoethylglycinexylidide and glycine xylidide.\textsuperscript{110}

iii. EXCRETION:

Local anaesthetics are primarily excreted in the kidneys. A percentage of a given dose of local anaesthetic is excreted unchanged in the urine. This percentage varies according to the drug. Esters appear in only very small concentrations as the parent compound in the urine. This is because they are hydrolyzed almost completely in the plasma. Procaine appears in the urine as PABA (90%) and 2% unchanged. Amides usually are present in the urine as the parent compound in a greater percentage than esters, mainly because of their more complex process of biotransformation. Patients with significant renal impairment may be unable to eliminate the parent local anesthetic compound or its major metabolites from the blood, resulting in higher blood levels and increased potential for toxicity.\textsuperscript{111}
i. MECHANISM OF ACTION OF LOCAL ANAESTHETIC AGENTS:

Local anaesthetic agents act primarily by interfering with the excitation-conduction process of the nerve fibers and endings.\textsuperscript{112} These nerve fibers have the ability to respond to a stimulus via excitation and can also propagate same along its full length to the point of termination.\textsuperscript{113} This stimulus conduction can be temporarily interfered with by the action of the local anaesthetics.\textsuperscript{112}

The electrophysiological properties of the neuronal membrane is a function of the permeability of the membrane to specific electrolytes as well as the selective concentration of these electrolytes in the cytoplasmic and extracellular fluid.\textsuperscript{112} A nerve cell membrane is completely permeable to potassium and chloride ions in its resting state and relatively impermeable to sodium ions, amino acids, and proteins.\textsuperscript{112,114} This results in sodium and chloride ions concentrated extracellularly while the potassium and anions other than chloride concentrated intracellularly. The electrophysiological property of the nerve cell membrane is determined by its permeability coupled with the concentrations of the cytoplasmic and extracellular electrolytes.\textsuperscript{112,113} The electrochemical gradient between the inside and outside of the nerve membrane results in an electrical potential of approximately -70 to -90 mV across the cell membrane.\textsuperscript{115} Stimulating the nerves will result in widening of the sodium channels with increased influx of sodium into the interior of the cell resulting in depolarization of the neural cell membrane to a firing threshold of -50 to -60mV. As the firing threshold is reached, the permeability to sodium increases significantly and a rapid
influx of sodium ions occurs. The electrical potential is reversed across the membrane to approximately +40 mV after the depolarization phase.\textsuperscript{112,116}

The permeability of the nerve membrane to sodium ions decreases as soon as the depolarization is over whereas that of potassium ions is increased. This results in movement of sodium ions out and potassium ions in by passive diffusion, restoring the normal resting potential of the nerve.\textsuperscript{115}

The exact mechanism of action of local anaesthetics is unknown. The generally accepted theory is that they prevent depolarization by blocking the transmembrane sodium channels. This is believed to be accomplished by either of the following mechanisms: the specific receptor mechanism and/or the membrane expansion mechanism. The specific receptor theory proposes that there are four binding sites on the sodium channels to which the ionized form of local anesthetic molecules can bind and result in block of the channels, thereby decreasing membrane permeability to sodium and preventing the propagation of action potentials.\textsuperscript{112,114,117} The alternative explanation of local anaesthetic action is the membrane expansion theory. According to this theory, the anesthetic agent acts by penetrating the nerve membrane resulting in an expansion of the membrane and a decrease in the diameter of the channel, thereby preventing sodium permeability.\textsuperscript{112,114} This theory offers an explanation for the action of anaesthetics that do not exist in an ionized form such as benzocaine.\textsuperscript{114}

\textbf{ii. POTENCY OF LOCAL ANAESTHETIC COMPOUNDS}

The potency of local anaesthetic compound is primarily determined by its ability to penetrate the nerve cell membrane, which is directly related to its lipid solubility. Highly
lipid soluble anaesthetic compounds can easily penetrate the nerve membrane. As such, relatively lower concentrations are therefore efficacious.\textsuperscript{112,114} Lidocaine and articaine are considered to be of intermediate potency.

Protein binding capacity of the local anaesthetic determines the duration of action. The stronger the binding ability is, the longer the duration of action and vice versa.

Anaesthetic compounds can only act on nerve membranes after they diffuse through non-nervous tissue to reach the nerve. Tissue diffusibility has a direct relationship to the rate of onset. The factors that determine the rate of diffusibility through non-nervous tissues are poorly understood.\textsuperscript{112}

Vasodilator activity of anaesthetic compounds influences their potency and duration. Increased blood flow caused by vasodilatation results in quicker removal of the anaesthetic compound from the injection site, thereby decreasing the amount available to act upon the nerve. With the exception of cocaine, all anaesthetic agents have vasodilator properties.\textsuperscript{115} Both lidocaine and articaine are potent vasodilators and would be ineffective and more toxic if given as plain solution.\textsuperscript{114} Therefore, in order to improve duration and safety, a vasoconstrictor such as epinephrine is added to the cartridges. In contrast, other anaesthetics, such as prilocaine are less toxic and can be given safely as plain solutions.\textsuperscript{118}

iii. RATE OF ACTION:

The onset and duration of action of the local anaesthetic agents can be influenced by a number of factors. The most important factors affecting onset of action are pH of the tissue to be anaesthetized and pKa of the drug to be used.\textsuperscript{111} It has been a well known fact that
infection may cause pH drop and ultimately would lead to delayed action or even prevention of onset of action.\textsuperscript{119} The higher the pKa of the drug the slower the onset of its action. In general, there are no significant differences in pKa among amide local anaesthetics except for the bupivacaine which has a slightly higher pKa and hence a slower onset of action.\textsuperscript{118}

Another important factor affecting the onset of action is the proximity of the deposition of local anaesthetic to the nerve to be anaesthetized. The shorter the distance between the nerve and the area of deposition the faster would be the onset of action. This explains why infiltration is associated with more rapid onset as compared to nerve block.\textsuperscript{120}

Morphology of the nerve also plays a role in determining the onset of action. The relatively thin pain fibres are anaesthetized faster than the thicker ones.\textsuperscript{120}

Within limits, higher concentration and greater lipid solubility improve onset of action to a small degree.\textsuperscript{120}

<table>
<thead>
<tr>
<th>Table 1: Factors affecting onset and duration of action of local anaesthetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. pH of tissue</td>
</tr>
</tbody>
</table>
2. pKa of drug

3. Time of diffusion from needle tip to nerve

4. Time of diffusion away from the nerve

5. Nerve morphology

6. Drug concentration

7. Lipid solubility of drug

On the other hand, the duration of action depends on the length of time that the drug can stay in the nerve to block the sodium channels. Local anaesthetic causes vasodilatation which can lead to rapid diffusion of the local anaesthetic away from the site of action and results in a very short duration of action. Addition of a vasoconstrictor, usually adrenaline can reduce the vasodilatation and improve the duration of action. In general, blocks last longer than pulpal anaesthesia.

Table 2: Expected duration of action of local anaesthetics

<table>
<thead>
<tr>
<th>Duration of action (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>121-123</td>
</tr>
<tr>
<td>Formulation</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Articaine 4% with Epinephrine 1:100,000 or 1:200,000</td>
</tr>
<tr>
<td>Bupivacaine 0.5% with epinephrine 1:200,000</td>
</tr>
<tr>
<td>Lidocaine 2% with epinephrine 1:50,000 or 1:100,000</td>
</tr>
<tr>
<td>Mepivacaine 2% with levonordefrin 1:20,000</td>
</tr>
<tr>
<td>Mepivacaine 3% plain</td>
</tr>
<tr>
<td>Prilocaine 4% with epinephrine 1:200,000</td>
</tr>
<tr>
<td>Prilocaine 4% plain</td>
</tr>
</tbody>
</table>

Table 3: Recommended maximum doses of local anaesthetics with vasoconstrictor
<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum dose</th>
<th>Maximum no. of cartridges</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Articaine</strong></td>
<td>7mg/kg (up to 500mg)</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>5mg/kg in children</td>
<td></td>
</tr>
<tr>
<td><strong>Bupivacaine</strong></td>
<td>2mg/kg (up to 200mg)</td>
<td>10</td>
</tr>
<tr>
<td><strong>Lidocaine</strong></td>
<td>7mg/kg (up to 500mg)</td>
<td>13</td>
</tr>
<tr>
<td><strong>Mepivacaine</strong></td>
<td>6.6mg/kg (up to 400mg)</td>
<td>11 (or 7 if plain)</td>
</tr>
<tr>
<td><strong>Prilocaine</strong></td>
<td>8mg/kg (up to 500mg)</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 4: **Lidocaine disposition (excretion) in various groups of patients**\(^{124}\)
iv. ACTION ON NERVES:

The primary action of local anaesthetics in producing conduction block is to decrease the permeability of the ion channels to sodium ions. Local anaesthetics selectively inhibit the peak permeability of sodium, whose value is normally about five to six times greater than the minimum necessary for impulse conduction (e.g., there is a safety factor for conduction of 5x to 6x). Local anaesthetics reduce this safety factor, decreasing both the rate of rise of the action potential and its conduction velocity. When the safety factor falls below unity, conduction fails and nerve block occurs.

Nerve tissues differ in the way and manner impulse is conducted through them as they differ in their morphology. Approximately 80% of the nerves in the pulp are C-type fibers and the rest are A-delta fibers. The C fibers are unmyelinated and have a diameter of 0.3 to 1.2µm and a conduction velocity of 0.4 to 2m/sec. The conduction of these fibers which are of smaller diameter than the A-delta fibers is slow. These fibers are

<table>
<thead>
<tr>
<th>Group</th>
<th>Lidocaine half-life (hr)</th>
<th>Mean total body clearance (ml/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1.8</td>
<td>10</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.9</td>
<td>6.3</td>
</tr>
<tr>
<td>Hepatic disease</td>
<td>4.9</td>
<td>6</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1.3</td>
<td>13.7</td>
</tr>
</tbody>
</table>
probably distributed throughout the pulp tissue; therefore, they conduct throbbing and aching pain associated with pulp tissue damage.\textsuperscript{127}

The A-delta fibers are myelinated and have a diameter of 2 to 5µm and a conduction velocity of 6 to 30m/sec. The A-delta fibers with a larger diameter than that of the C fibers, conduct impulses at a higher velocity. These impulses are interpreted as sharp and pricking pain.\textsuperscript{127}

The unmyelinated nerve fiber is basically a long cylinder with a high electrical resistance cell membrane surrounding a low-resistance conducting core of axoplasm, all of which is bathed in low-resistance extracellular fluid. The high-resistance cell membrane and low-resistance intracellular and extracellular media produce a rapid decrease in the density of current within a short distance of the depolarized segment. In areas immediately adjacent to this depolarized segment, local current may be adequate to initiate depolarization in the resting membrane. Farther away it will prove to be inadequate to achieve firing threshold. The spread of impulse in an unmyelinated nerve fiber is therefore characterized as a relatively slow process.\textsuperscript{128}

Impulse spread within myelinated nerves differs from that in unmyelinated nerves because of the layer of insulating material separating the intracellular and extracellular charges. The longer the distance between the two charges, the smaller is the current necessary to charge the membrane. Impulse conduction in myelinated nerves occurs by means of current leaps from node to node, a process termed \textit{saltatory conduction}. Saltatory conduction usually progresses from one node to the next in a step wise manner. If conduction of an impulse is blocked at one node, the local current skips over that node and proves adequate to raise the membrane potential at the next node to its
firing potential and produce depolarization. As such a minimum of 8 to 10mm of nerve must be covered by anaesthetic solution to ensure thorough blockade.\textsuperscript{129}

### 3.8 COMPOSITION OF LOCAL ANAESTHETIC SOLUTION

The composition of local anaesthetic solution varies depending on whether or not a vasoconstrictor is included. The \textit{local anaesthetic drug} is the major component of the dental cartridge. It interferes with the propagated nerve impulse, preventing it from reaching the brain.\textsuperscript{125} A \textit{vasopressor drug} is included in most anaesthetic cartridges to increase safety, duration and depth of action of local anaesthetic.\textsuperscript{111} The pH of dental cartridges containing vasopressors is lower (more acidic) than that of cartridges not containing vasopressors. Because of this pH difference, plain local anaesthetics have a more rapid onset of clinical action and are more comfortable.\textsuperscript{130,131} \textit{Antioxidant} is incorporated in cartridges containing vasopressors. Often, \textit{sodium (meta) bisulfite} is used. It prevents the oxidation of the vasopressor by oxygen, which might be trapped in the cartridge during manufacture or diffuse through the semipermeable diaphragm after filling.\textsuperscript{132} Sodium bisulfite reacts with oxygen before the oxygen is able to destroy the vasopressor. Sodium bisulfite is thus converted to sodium bisulfate through oxidation which has an even lower pH.\textsuperscript{132} This is clinically relevant as there is increased burning (discomfort) experienced by the patient on injection of an older cartridge of anaesthetic with vasopressor than with a fresh cartridge. Some patients are allergic to bisulfites and need to be considered before anaesthetic administration. \textit{Sodium chloride} is added to the cartridge to make the solution isotonic with the tissues of the body.\textsuperscript{133} It has been reported that local anaesthetics containing too much sodium chloride (hypertonic solution) have produced tissue edema or paraesthesia lasting for several
months after drug administration. Distilled water is used as the diluent to provide the volume of solution in the cartridge. Mehtylparaben possesses bacteriostatic, fungistatic, and antioxidant properties. It is commonly used in 0.1% concentration (1mg/ml). This has been removed as a component of the dental cartridge in the United States and most other countries. Its removal was based on the fact that dental local anaesthetic cartridge is single-use item meant to be discarded and not recycled. Secondly, repeated exposure to paraben has led to increased reports of allergic reactions in some patients.

3.9 PHYSIOLOGY/METABOLISM OF POPULAR LOCAL ANAESTHETIC AGENTS

1. PROCAINE HYDROCHLORIDE:

It is the first synthetic injectable local anaesthetic. Chemically, it is referred to as 2-diethylaminoethyl 4-amino benzoate hydrochloride. It was prepared by Alfred Einhorn in 1904. It is combined in the dental cartridge with another ester local anaesthetic, propoxycaine. It was used as a local anaesthetic agent until 1996. It has the highest vasodilating property, and as a result of that, the 2% plain procaine solution provides essentially no pulpal anaesthesia and from 15 to 30 minutes of soft-tissue anesthesia. Thus a clean surgical field is more difficult to maintain with procaine because of increased bleeding.
Procaine is of significance in the immediate management of inadvertent intraarterial injection of a drug; its vasodilating properties are used to aid in breaking arteriospasm.\textsuperscript{138}

It has a $pK_a$ of 9.1 as a result of which, it has a slow onset of clinical action (6 to 10 minutes), a reason for the inclusion of propoxycaine in the anaesthetic cartridge. The maximum recommended dose of procaine used for peripheral nerve blocks, is 1000mg.\textsuperscript{139}

Metabolized in the blood by plasma cholinesterase, procaine does not exhibit increased toxicity in patients with hepatic dysfunction.\textsuperscript{136}

Although not very common, the incidence of allergic reaction to both procaine and other ester local anaesthetics is significantly greater than that to amide local anaesthetics.\textsuperscript{140}

3. **LIDOCAINE HYDROCHLORIDE:**

Lidocaine hydrochloride is chemically referred to as 2-Diethylamino 2,6 acetoxylidide hydrochloride and it became the first amide local anaesthetic to be marketed in 1948. Its entry into clinical practice has transformed the dental practice, replacing procaine as the drug of choice for pain control.\textsuperscript{136} When compared to procaine, lidocaine possesses a significantly more rapid onset of action. (2 to 3 minutes versus 6 to 10 minutes), produces more profound anaesthesia, has a longer duration of action, and has a greater potency.\textsuperscript{136}

The maximum recommended dose of lidocaine with epinephrine is 7mg/kg of body weight for the adult patient, within a limit of 500mg. For children, the same dose
for lidocaine with epinephrine is recommended; a dose of 4.4mg/kg, not to exceed 300mg for lidocaine without a vasoconstrictor.\textsuperscript{111}

Lidocaine hydrochloride is metabolized in the liver by the microsomal fixed-function oxidases to monoethylglycerine and xylidide; xylidide is a local anaesthetic and potentially toxic. Excretion occurs via the kidneys as 10% unchanged and greater than 80% into various metabolites.\textsuperscript{128}

Allergy to amide local anaesthetics is virtually nonexistent; true, documented, and reproducible allergic reactions are extremely rare, although possible.\textsuperscript{111}

4. **PRILOCAINE HYDROCHLORIDE:**

It is an amide local anaesthetic that is chemically known as 2-Propylamino-o-propionotoluidide hydrochloride. It was first approved as a local anaesthetic in the United States in 1965. When compared to lignocaine, it is more potent, less toxic, with a slower onset of action.\textsuperscript{128}

Prilocaine undergoes biotransformation more rapidly and completely than lidocaine, taking place not only in the liver, but also to a smaller extent in the kidneys and lungs. Plasma levels of prilocaine decrease more rapidly than lidocaine.\textsuperscript{118,126} Its metabolism differs from that of lidocaine. Being a secondary amine, prilocaine is hydrolyzed straightforwardly by hepatic amidases into orthotoluidine and N-propylanine. Carbon dioxide is a major end-product of prilocaine biotransformation. The efficiency of the body’s degradation of prilocaine is demonstrated by the extremely small fraction of intact prilocaine recoverable in the urine.\textsuperscript{141} Orthotoluidine can induce the formation of methemoglobin, producing methemoglobinemia if large doses are administered.\textsuperscript{142}
3.10 SYSTEMIC ACTIONS/TOXICITY OF LOCAL ANAESTHETICS

Local anaesthetic agents are chemicals that can reversibly block action potentials in all excitable membranes. The central nervous system and cardiovascular system are the most frequently affected among others. Most of the systemic actions of local anaesthetics are related to their blood or plasma level. The higher the level, the greater will be the clinical action.5

Local anaesthetics are absorbed from their site of administration into the circulatory system, which effectively dilutes them and carries them to all cells of the body. The blood level of anaesthetic as well as its toxicity depends on its rate of uptake from its site of administration into the circulatory system and on the rate of distribution in tissues and biotransformation. High blood levels of the drug could result from a single inadvertent intravascular injection or repeated injections. This is one reason why aspiration before every injection is so important.111

1. EFFECTS ON CENTRAL NERVOUS SYSTEM (CNS)

Local anesthetics can easily cross blood brain barrier. The pharmacological action of local anaesthetics on CNS is depression. Some local anaesthetics (e.g. procaine, lidocaine, mepivacaine, prilocaine and even cocaine) have demonstrated anticonvulsant properties. The anticonvulsant property exists at a blood level below that at which the same drug produces seizure activity.6,7 The anticonvulsant blood level of lidocaine is very close to its cardio-therapeutic range (about 0.5 to
Local anaesthetics possess the anticonvulsant effect by virtue of their depressant action on all excitable cells. Epileptic patients on the other hand, have hyper-excitable cortical neurons. Local anaesthetics therefore raise the seizure threshold by decreasing the excitability of these neurons.

Local anaesthetics at low blood levels (therapeutic, nontoxic), possess no significant clinical CNS effects. At a higher dose (toxic overdose), the primary clinical manifestation is a **generalized tonic – clonic** convulsion. Procaine, mepivacaine and lidocaine have been used to terminate or decrease grand mal or petit mal seizures. Other effects of local anaesthetics include – *analgesia and mood elevation*. Many centuries ago till today, some local anaesthetics have been known to be used for mood elevation and rejuvenation. Cocaine has long been used for its euphoria-inducing and fatigue-lessening actions dating back to the chewing of coca leaves by Incas and South Americans.

<table>
<thead>
<tr>
<th>Table 5: Anticonvulsant blood levels of lidocaine&lt;sup&gt;29&lt;/sup&gt;.</th>
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<tr>
<td>Clinical situation</td>
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### 2. EFFECTS ON CARDIOVASCULAR SYSTEM (CVS)

Local anaesthetics have direct effect on the myocardium and peripheral vasculature. However, the central nervous system is more susceptible to the effects of local anaesthetics than the cardiovascular system.\(^{145}\) Local anaesthetics produce myocardial depression that is dose related. Local anaesthetics decrease electrical excitability of the myocardium, decrease the conduction rate and decrease the force of contraction of the heart.\(^{146-148}\) However, therapeutic advantage of these adverse effects are taken to treat any hyperexcitability related cardiac conditions like dysrhythmias among others. Only procaine and lidocaine were successful in clinical trial as regards to antidysrhythmic property. However, lidocaine is the most widely used and intensively studied local anaesthetic in this regard.\(^{149}\) A chemical analogue of lidocaine, Tocainamide was introduced in 1984 as an oral antidysrhythmic drug as lidocaine is ineffective intra-orally due to its high first pass metabolism.\(^{150}\)

The blood level of lidocaine that normally develops after an intraoral injection of one or two dental cartridges (0.5 to \(2\mu g/ml\)) is not associated with cardio-depressant activity.\(^{151}\)
All local anaesthetics produce peripheral *vasodilatation* through relaxation of smooth muscles in the walls of blood vessels except *cocaine and ropivacaine* which produce vasoconstriction. The vasodilatation will in turn increase blood flow to and from the injected area. This is clinically significant however as it will increase the rate of drug absorption leading to decrease in depth and duration of anaesthesia, increased bleeding and increased local anaesthetic blood levels.

3. **EFFECTS ON RESPIRATORY SYSTEM**

Effect of local anaesthetic on respiratory system is dependent on the dose. At optimal levels it has a direct relaxant action on bronchial smooth muscle, whereas at overdose levels it may produce respiratory arrest as a result of generalized CNS depression.

4. **MISCELLANEOUS ACTIONS**

   a. **Neuromuscular blockade**

   This happens as a result of the inhibition of sodium diffusion through a blockade of sodium channels in the cell membrane. When this happens after muscle relaxant administration (e.g succinylcholine, atracurium), it may lead to prolonged muscle relaxation. However, such actions are unlikely to occur in the dental outpatient.

   b. **Malignant hyperthermia**

   This is a pharmacogenic disorder in which a genetic variant in the individual alters his response to certain drugs. It manifests with tachycardia, tachypnea, unstable
blood pressure, cyanosis, respiratory and metabolic acidosis, high fever (up to 108°F (42°C) or more), muscle rigidity and death.\textsuperscript{5}

c. Allergic reactions

Allergic reactions to local anaesthetics are fairly common.\textsuperscript{10,11} True allergy to amide anaesthetics is exceedingly rare, whereas the ester procaine is somewhat more allergenic. An allergy to one ester rules out the use of another ester as the allergenic component is the breakdown product of para-aminobenzoic acid and metabolism of all esters yields this compound. In contrast, an allergy to one amide does not rule out the use of others. Other components of local anaesthetic that may trigger allergic reaction include preservative (methylparaben), sodium metabisulfite.\textsuperscript{12} Until recently, the amide local anaesthetics were thought to be capable of provoking malignant hyperthermia and were considered to be absolutely contraindicated in such patients. However, the Malignant Hyperthermia Association of the United States has concluded that there are no documented cases in the medical or dental literature supporting the concept of amide anaesthetics triggering malignant hyperthermia.

d. Methemoglobinemia

This is an uncommon adverse reaction which is associated more with prilocaine but may also occur with articaine or the topical anaesthetic benzocaine. Methemoglobinemia manifests as cyanotic appearance which does not respond to the administration of 100% oxygen and is induced by excessive metabolites of the
above mentioned drugs. These drugs are best avoided in patients with congenital methemoglobinemia.\textsuperscript{152}

3.11 PHARMACOLOGY OF VASOCONSTRICTORS

Vasoconstrictors that are commonly used in combination with dental local anaesthetics are chemically identical or similar to the sympathetic nervous system mediators epinephrine and norepinephrine both of which are catecholamines. The other less commonly used vasoconstrictor is felypressin which is a synthetic analogue of the polypeptide vasopressin (antidiuretic hormone) and is only used in combination with prilocaine.\textsuperscript{5,22}

PHARMACOKINETICS

Catecholamines are synthesized from the amino acid phenyl-alanine. Synthesis of NA occurs in all adrenergic neurones, while that of Adrenaline occurs only in the adrenal medullary cells and probably requires high concentration of glucocorticoids through intra-adrenal portal circulation for induction of the methylating enzyme.\textsuperscript{99} Noradrenaline is stored in synaptic vesicles or granules within the adrenergic nerve terminal. The granular membrane actively takes up dopamine from the cytoplasm and the final step of synthesis of noradrenaline takes place inside the granule which contains dopamine $\beta$-hydroxylase.\textsuperscript{99}

Catecholamines are released by exocytosis, all the granular contents (NA, Adr, ATP, dopamine $\beta$-hydroxylase, chromogranin) are poured out as a result. Uptake of
catecholamines after release occurs either by axonal uptake or granular uptake both of which act via an amine pump.\textsuperscript{99}

Catecholamines are metabolized in two ways. NA leaking out from the granules into the cytoplasm as well as that taken up by axonal transport is first attacked by MAO (monoamine oxidase), while that which diffuses into circulation is initially acted upon by (COMT) catechol-o-methyltranferase. Both the MAO and COMT are present in the liver. The other enzymes can subsequently act to produce VMA (vanillylmandelic acid). All the metabolites so produced are conjugated with glucoronic acid or sulfate before excretion in the urine. Only small amounts (approximately 1\%) of epinephrine are excreted unchanged in the urine. However, metabolism does not play an important role in terminating the action of endogenous CAs as much as its reuptake by adrenergic nerves does.\textsuperscript{99,153}

**PHARMACODYNAMICS**

**THE ADRENERGIC RECEPTORS:**

There are different types of adrenergic receptors as described by Ahlquist in 1948. He described them as \textit{alpha (a) and beta (b)} receptors. Alpha receptors are further classified into $\alpha_1$ and $\alpha_2$, also beta receptors are classified into $\beta_1$ and $\beta_2$. The alpha receptors are found in the smooth muscles of blood vessels and stimulation of which produces vasoconstriction with attendant increase in blood pressure. Both alpha 1
and alpha 2 receptors are postsynaptic. The only difference is that alpha 1 receptors are postsynaptic excitatory while alpha 2 receptors are postsynaptic inhibitory receptors.\textsuperscript{29}

Activation of beta receptors leads to smooth muscle relaxation (vasodilatation and bronchodilatation) and cardiac stimulation (increased heart rate and strength of contraction).\textsuperscript{154}

The beta\textsubscript{1} receptors are found in the heart and small intestines and are responsible for cardiac stimulation and lipolysis. The beta 2 receptors are found in the bronchi, vasculature, and uterus and their stimulation leads to bronchodilation, vasodilation and uterine contraction.\textsuperscript{155}

In general, the actions of beta-adrenergic system are mainly systemic whereas the actions of alpha-adrenergic system are peripheral with some few systemic actions.\textsuperscript{29}

The beta 1 stimulation tends to increase blood pressure while beta 2 tends to decrease blood pressure. Systemic alpha stimulation will increase blood pressure though not significantly.\textsuperscript{29,154,155}

The two common catecholamines (adrenaline and noradrenaline) have different actions. Noradrenaline preferentially stimulates beta 1 adrenergic receptors, with very little beta 2 activity leading to an increase in blood pressure when used as local anaesthetic vasoconstrictor. But because adrenaline stimulates both beta 1 and beta
2 adrenergic receptors equally, it does not tend to increase blood pressure because the two different effects on different beta receptors balance each other. 29,155.

3.12 RATIONALE FOR INCLUSION OF VASOCONSTRICTORS IN LOCAL ANAESTHETICS.

All local anaesthetics used clinically possess some degree of vasodilatation activity except for cocaine and ropivacaine which produce vasoconstriction.9 Immediately after injection of local anaesthetic solution into the tissues, there is vasodilatation of the blood vessels in the area with attendant increased perfusion which leads to the following consequences:

1. An increased rate of absorption of local anaesthetic into the cardiovascular system which in turn removes it from the injection site.
2. Decreased depth and duration of action of anaesthesia as the local anaesthetic agent has diffused away from the injection site rapidly.
3. Increased bleeding at the operation site because of increased perfusion.
4. Increased risk of local anaesthesia toxicity due to higher plasma levels of the local anaesthetic.13

Vasoconstrictors are drugs that are added to local anaesthetic to counteract the vasodilating effect of the local anaesthetics. The following benefits are achieved:
1. Decreased blood flow to the site by constricting blood vessels at the site of administration.

2. Reduced absorption of local anaesthetics into the cardiovascular system resulting in lower anaesthetic blood levels.\textsuperscript{24,25}

3. Local anaesthetic blood levels are lowered, thereby minimizing the risk of local anaesthetic toxicity.

4. Increased amounts of the local anaesthetic remain in and around the nerve for longer periods, thereby increasing the duration of most local anaesthetics.

5. Decreased bleeding at the operative site\textsuperscript{16,17}

6. Decrease in the minimum concentration of local anaesthetic agent needed for nerve block.\textsuperscript{18,19}

In addition, dental treatment with insufficient vasoconstriction within the local anaesthetic formulation may lead to less than adequate pain control and thus increased levels of endogenous catecholamines and particularly norepinephrine.\textsuperscript{124} Pain control was significantly impaired in those patients receiving the local anaesthetic without the vasoconstrictor as compared to those patients receiving the local anaesthetic with vasoconstrictor.\textsuperscript{156} Ineffective pain control increases patient health risk outcome. Norepinephrine (either parenteral or endogenous) increases blood pressure and has other cardiotoxic effects.\textsuperscript{157,158}

In a randomized, double blind, parallel-group, and cross-over study evaluating the removal of impacted third molars, Knoll Kohler and Fortcsh\textsuperscript{156} demonstrated that systemic norepinephrine levels as a measure of stress were significantly elevated with 4\% articaine with 1:200,000 epinephrine as compared to 4\% articaine with
1:100,000 epinephrine. According to Knoll Kohler et al (also a randomized, double-blind, parallel-group and crossover study), the combination of epinephrine and local anesthetic is especially important in patients suffering from cardiovascular diseases, because only in the combination of epinephrine with the local anesthetic in an appropriate concentration is there a sufficient guarantee of depth and duration of pulpal and surgical anaesthesia and thus the avoidance of patient pain/stress (which increases sympathetic drive) and the ill effects of excess endogenous norepinephrine.\textsuperscript{156}

3.13 CLASSIFICATION OF VASOCONSTRICTORS

AN OVERVIEW OF CLASSIFICATION:

Vasoconstrictors have been classified based on their chemical structure and their mode of action. They are classified as \textit{catecholamines and noncatecholamines} based on the presence or absence of \textit{catechol nucleus}. Felypressin is a synthetic analogue of the polypeptide vasopressin (antidiuretic hormone) and is only used in combination with a prilocaine in concentration of 0.03iu/ml.\textsuperscript{5,22}

Other classification method is based on mode of action whereby the vasoconstrictors are classified as direct acting, indirect acting and mixed acting. The direct acting drugs exert their action directly on the adrenergic receptors whereas the indirect acting drugs act by releasing norepinephrine from the
adrenergic nerve terminals. The mixed acting drugs, act by both direct and indirect pathway.

Vasoconstrictors can be classified in different ways as follows:

1. BASED ON CHEMICAL STRUCTURE
   
   A. CATECHOLAMINES
      
      Epinephrine
      Norepinephrine
      Levonordefrin
      Isoproterenol
      Dopamine
   
   B. NONCATECHOLAMINES
      
      Amphetamine
      Methamphetamine
      Ephedrine
      Mephentermine
      Hydroxyamphetamine
      Metaraminol
      Methoxamine
      Phenylephrine
   
   C. HORMONAL(ANTIDIURETIC) ANALOGUE
      
      Felypressin
2. BASED ON MODE OF ACTION

A. DIRECT ACTING

Epinephrine
Norepinephrine
Levonordefrin
Isoproterenol
Dopamine
Methoxamine
Phenyleprine

B. INDIRECT ACTING

Tyramine
Amphetamine
Methaamphetamine
Hydroxyamphetamine

C. MIXED ACTING

Metaraminol
Ephedrine

3.14 SYSTEMIC EFFECTS/TOXICITY OF VASOCONSTRICTORS

There is a lot of controversy in dentistry over the potential of epinephrine contained in local anaesthesia for causing systemic effects. The intensity of such debates was fueled by the unavailability of vasoconstrictor-free local anaesthetic that can
provide effective pulpal anaesthesia.\textsuperscript{31} It is now an established fact that the epinephrine injected during routine dental anaesthesia significantly elevates the plasma concentration of the hormone. A meta-analysis of various studies has been done, with a conclusion that a single cartridge of 2\% lidocaine with 1:100,000 epinephrine which is equivalent to 18\(\mu\)g of the vasoconstrictor can be expected to double the resting epinephrine concentration.\textsuperscript{158} Concentrations achieved after multiple injections may approximate those associated with such stresses like acute myocardial infarction, strenuous exercise, and insulin induced hypoglycaemia.\textsuperscript{159} Lipp et al,\textsuperscript{160} provided the most direct demonstration that the elevated epinephrine level is as a result of the exogenously administered drug and not to epinephrine released from the adrenal gland through injection of articaine with radio-labeled epinephrine.

Despite the elevated concentrations of epinephrine, cardiovascular responses to injected epinephrine remain modest. Heart rate and mean blood pressure are often not significantly affected which reflects the body’s ability for homeostatic regulation. Cardiac output is increased while peripheral vascular resistance decreases owing to systemic \(\beta_2\)-receptor activation by epinephrine and helps preclude hypertensive responses.\textsuperscript{161} From the above studies, it is obvious that epinephrine contained in local anaesthetics does not usually elicit dramatic systemic cardiovascular responses. However, when given excessively (overdose) some notable side effects may ensue. The clinical manifestations of overdose relate to the CNS stimulation and include increasing fear and anxiety, tension, restlessness, throbbing headache, tremor, weakness, dizzinesss, pallor, respiratory
difficulty, and palpitation. As the blood concentration of epinephrine increases, cardiac dysrhythmias (especially ventricular) become more common; ventricular fibrillation is a rare but possible complication. Dramatic increase in systolic blood pressure (>300mmHg) and diastolic blood pressure (>200mmHg) may be noted which have led to cerebral hemorrhage. Anginal attacks may be precipitated in patients with coronary insufficiency.\textsuperscript{162}

There are several different types of vasoconstrictors available for clinical use. All of them are sympathomimetic amines except for felypressin. The overall summary of systemic actions of sympathomimetic amines can be stated as follows: \textsuperscript{23}

1. EFFECTS ON THE CARDIOVASCULAR SYSTEM

A cardiac excitatory action, which results in an increase in heart rate, force of contraction, and stroke volume occurs.

2. EFFECTS ON THE CENTRAL NERVOUS SYSTEM

There is central nervous system excitation.

3. METABOLIC ACTIONS

There is increase in the rate of glycogenolysis in the liver which may increase blood glucose level, increased oxygen consumption and increase in lactic acid production.\textsuperscript{5,23}
4. EFFECTS ON SMOOTH MUSCLES

There is peripheral excitatory action on smooth muscles including those in blood vessels supplying the mucous membrane and skin. This ultimately provides the vasoconstrictor effect desired in the local anaesthesia.\textsuperscript{23}

5. EFFECTS ON RESPIRATORY SYSTEM

The sympathomimetics may cause a peripheral inhibitory action on certain other types of smooth muscles, such as those in the bronchial tree. This leads to bronchodilatation.

3.15 RECOMMENDED MAXIMUM DOSAGE OF EPINEPHRINE

As a general rule, the minimum concentration that can provide effective anaesthesia should be used. Lignocaine is available with various dilutions of epinephrine (1:50,000, 1:80,000, 1:100,000, 1:200,000, 1:300,000). However, the duration of effective pulpal and soft tissue anaesthesia is similar with all forms.\textsuperscript{163} The American Heart Association has for a very long time stated “the typical concentrations of vasoconstrictors contained in local anaesthetics are not contraindicated in patients with cardiovascular disease so long as preliminary aspiration is practiced, the agent is injected slowly and the smallest effective dose is administered”.\textsuperscript{164} The New York Heart Association in 1954 recommended that the maximal epinephrine doses be limited to 0.2mg in a single appointment.\textsuperscript{165}
Of recent, the Agency for Healthcare Research and Quality reviewed the published literature on the effects of epinephrine in dental patients with high blood pressure. The results suggest that there is statistically insignificant increase in blood pressure and heart rate associated with the use of local anesthetic containing epinephrine.\footnote{166}

<table>
<thead>
<tr>
<th>Table 6:</th>
<th><strong>Recommended maximum dosages of Epinephrine</strong></th>
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<tbody>
<tr>
<td></td>
<td>No. of cartridges</td>
</tr>
<tr>
<td><strong>Epinephrine concentration</strong> (µg/cartridge)</td>
<td>Healthy patients (ASA I)</td>
</tr>
<tr>
<td>1:50,000 (36)</td>
<td>5.5</td>
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<tr>
<td>1:100,000 (18)</td>
<td>11</td>
</tr>
<tr>
<td>1:200,000 (9)</td>
<td>22</td>
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</table>
3.16 DRUG INTERACTIONS OF VASOCONSTRICTORS

The fact that vasoconstrictors affect many systems in the body undoubtedly made them to interact with some drugs that act especially on those systems. The case reports as regards to drug-drug interactions related to epinephrine and local anaesthesia are exceedingly rare.\textsuperscript{24,29,30} The following are the possible drug interactions to vasoconstrictors:

1. INHALATIONAL ANAESTHETICS

Occasionally some dental procedures are performed under general anaesthesia with inhalational agents. In such instances the vasoconstrictor containing local anaesthetics are used to achieve haemostasis rather than anaesthesia. Some of the inhalation general anaesthetics sensitize the myocardium to the direct myocardial effect of the sympathomimetic amines leading to arrythmia. Halothane is the commonly observed culprit as it possesses the lowest arrythmogenic threshold for epinephrine. Enflurane and Isoflurane have a minimal effect on myocardial sensitivity to sympathomimetics.\textsuperscript{31} Controversy exists over the maximum recommended dose of epinephrine for a patient anaesthetized with halothane with a maximum dose ranging from 0.1mg in ten minutes to 0.3mg in sixty minutes.\textsuperscript{32,34,35}

2. ANTIDEPRESSANTS

There are two classes of antidepressant drugs in use – \textit{tricyclic antidepressants(TCA)} and \textit{monoamine oxidase inhibitors(MAOI)}. However, there
is little or no interaction between MAOI and exogenously administered epinephrine as it is inactivated primarily by catechol-o-methyltransferase.\textsuperscript{36} Therefore, inhibiting monoamine oxidase has little effect on the degradation of epinephrine.\textsuperscript{37} Some controversies exist regarding the interaction between tricyclic antidepressants and epinephrine in local anaesthetics for dentistry. Tricyclic antidepressants prevent neuronal uptake of catecholamines at the adrenergic nerve terminals. This results in a higher concentration of catecholamines present at the sympathetic neuroeffector junction. With the use of adrenergic vasoconstrictors in local anaesthetics, one would expect potentiation of vasoconstrictor effects and cardiac stimulation.

3. BETA BLOCKERS

The non-selective beta blocking agents that are commonly used to treat hypertension may interact with epinephrine to enhance its vasopressor effect. The adrenergic receptors are either alpha or beta. Beta receptors are divided into beta-1 and beta-2 receptors. Alpha receptors are present on the peripheral vasculature and produce vasoconstriction on stimulation. On the other hand, the beta-1 receptors are present on the heart and stimulation leads to increase in heart rate, force of contraction, stroke volume and cardiac output. The beta-2 receptors cause vasodilatation on stimulation. The non-selective beta blockers block all the beta receptors and prevent the reflex vasodilatation that may occur as a result of the
vasoconstrictor effect of epinephrine. This leads to significant rise in blood pressure.\textsuperscript{29,154,155}

According to a study by Misutaka et al, it was revealed that cardiac function of dental patients on β-adrenergic blocker therapy can be adversely affected by epinephrine containing local anaesthetics that may cause severe cardiovascular complications. Using an M-mode echocardiography and intraoral injection of 2\% lignocaine with 1:80,000 epinephrine after administration of pindolol on healthy volunteers, the cardiac preload did not alter, whereas the stroke volume has reduced due to an increase in afterload and a decrease in myocardial contractility. Blood pressure was elevated despite the reduced cardiac output as a result of increase in total peripheral vascular resistance.\textsuperscript{167}

4. PHENOTHIAZINES

Phenothiazines have been used for their antiemetic, antipsychotic and tranquilizing effect. There is a report by Alvarez and Frank that phenothiazines have been incriminated in the production of electrocardiographic repolarization abnormalities and sudden death.\textsuperscript{168} Arterial hypotension is a very common phenomenon occurring secondary to phenothiazines administration. This occurs due to blockage of alpha adrenergic receptors in the peripheral vasculature. Treatment of such hypotension with epinephrine may cause disastrous outcome as the vasoconstricting property of the epinephrine is partially blocked by the phenothiazine, but the vasodilating effect remains the same leading to worsening hypotension.\textsuperscript{168} Yagiela et al showed no significant interaction between epinephrine and chlorpromazine. This observation,
and the fact that physicians and dentists have been administering local anaesthetics with vasoconstrictors to patients on phenothiazines without incident for years, seems to indicate that judicious use of vasoconstrictors is unlikely to have deleterious effects in the phenothiazine treated patients.\textsuperscript{169}

3.17 CONTRAINDICATIONS TO VASOCONSTRICTORS IN DENTISTRY

Despite their great benefit when combined with local anaesthetics, the risk may sometimes outweigh the benefit. Depending on the potential risk and morbidity rate of medical complications, the contraindications to the use of vasoconstrictor in dentistry can be classified as either \textit{absolute} or \textit{relative}.

\textbf{ABSOLUTE CONTRAINDICATIONS TO VASOCONSTRICTORS IN DENTISTRY:}

- HEART DISEASES
  a. Unstable angina
  b. Recent myocardial infarction
  c. Recent coronary artery bypass surgery
  d. Refractory arrhythmias
  e. Untreated or uncontrolled severe hypertension
  f. Untreated or uncontrolled congestive heart failure

- UNCONTROLLED HYPERTHYROIDISM
UNCONTROLLED DIABETES

SULFITE SENSITIVITY

PHEOCHROMOCYTOMA

RELATIVE CONTRAINDICATIONS:

-Patients taking tricyclic antidepressants

-Patients taking phenothiazines

-Patients taking monoamine oxidase inhibitors

-Patients taking nonselective beta blockers

-Cocaine abusers

Epinephrine, which is a natural hormone released from the adrenal medulla, has an estimated basal secretion rate ranging from 0.17 to 0.54µg/min in a healthy 70kg adult.\textsuperscript{170,171} There’s about 20 to 40 fold increase in the release of endogenous epinephrine and other catecholamines when persons are subjected to different kind of stress.\textsuperscript{171} The New York Heart Association in 1955 made a recommendation and set a maximal dose for cardiac patients at 0.2mg of epinephrine when used with a local anaesthetic.\textsuperscript{165} Cardiac patients are at higher risk from the massive release of endogenous catecholamines associated with mismanagement of pain control and
anxiety than they are from the small quantities of vasoconstrictors usually used in dental practice.\textsuperscript{165} It is prudent to always obtain a profound and prolonged local anaesthesia with the lowest possible dose of epinephrine when treating a cardiac patient. Controversies still exist as to whether local anaesthetic containing epinephrine can be safely given to patients with heart disease. As a general rule, epinephrine given at a concentration greater than 1:100,000 should be considered hazardous in a patient with heart disease.\textsuperscript{172,173}

As regards to local anaesthetic injection techniques, a considerable vascular penetration of local anaesthetic takes place during intraligamentary injection.\textsuperscript{174} It has also been observed that the haemodynamic changes in blood and heart rate when an intraligamentary injection of local anaesthetic containing 1:100,000 epinephrine is given to be comparable with changes seen with an intravascular injection. Therefore, intraligamentary injection should be considered dangerous and strictly contraindicated in any patient with heart disease, because the haemodynamic effects are likely to be similar to those observed with an intravenous injection.\textsuperscript{175,176}

Unstable angina is characterized by recent worsening of symptoms and poor response to medical treatment. There are four clinical types: de novo angina, crescendo angina, angina at rest, and post-infarction angina.\textsuperscript{177,178} Unstable angina is commonly associated with major pathologic changes of the coronary arteries.\textsuperscript{177} Several investigators have studied the haemodynamic effects of local anaesthetic injection with epinephrine in healthy subjects. Although the injection of 1.8ml of local anaesthetic with epinephrine 1:100,000 was not associated with significant
changes in heart rate and mean arterial blood pressure, injection of a larger quantity of local anaesthetic with epinephrine may not be as safe and may not be without significant haemodynamic changes when administered to patients with severe cardiovascular disease. In normotensive healthy patients, the effect of transient sudden increase in plasma epinephrine level is somewhat minimal, but we must not overlook the serious consequences it could lead to in patients with unstable angina. Several cases of myocardial ischemia and myocardial infarction have been reported after the intravenous and subcutaneous injection of epinephrine for the treatment of allergic reactions. Therefore vasoconstrictors are strictly contraindicated in patients with unstable angina as their chronotrophic and inotrophic properties can cause increase in myocardial oxygen consumption and ultimate increase in the risk of myocardial ischemia.

Currently, it is recommended to postpone dental treatment for a patient that had recent myocardial infarction for a period of at least 3 to 6 months. This principle is widely accepted due to the fact that after a myocardial infarction, higher risk of re-infarction is reported during surgery under general anaesthesia. This delay period is very critical because of the electrical instability of the myocardium which accounts for majority of the sudden deaths reported during the recovery period.

There is evidence which indicates that epinephrine and other catecholamines possess important arrhythmogenic properties which they induce by speeding up the repolarization of the calcium channels that will ultimately lead to arrhythmias and fibrillation. Because of their chronotropic, inotropic, and arrhythmogenic
properties, adrenaline and other vasoconstrictors are strictly contraindicated for patients recovering from myocardial infarction.\textsuperscript{186}

There is paucity of information in the dental literature regarding treatment guidelines for patients who underwent coronary artery bypass surgery. According to a study by Rubin et al, 56\% of 92 patients treated by coronary artery bypass still had complex ventricular arrhythmias at the time of their discharge from the hospital.\textsuperscript{187} Both the injection of local anaesthetic with vasoconstrictor and regular dental treatments could be risky within 3 months after coronary artery bypass surgery.

### 3.18 COMPLICATIONS OF LOCAL ANAESTHESIA

A number of possible complications are attributed to local anaesthetic administration. These complications can either be \textit{local} which occur in the region of the injection or \textit{systemic}. The systemic complications associated with local anaesthetic administration may include over dosage (toxic reactions), allergy, and psychogenic reactions. All of the systemic complications have been discussed in the previous chapters.

This chapter will discuss the local complications and they are listed as follows:

- Needle breakage
- Persistent anesthesia or paresthesia
- Facial nerve paralysis
- Trismus
- Soft tissue injury
Hematoma
Pain on injection
Burning on injection
Infection
Edema
Sloughing of tissues
Post-anesthetic intraoral lesions

NEEDLE BREAKAGE

Breakage and retention of dental needles within tissues has reduced tremendously with the introduction of disposable needles. However, there are still reports of such instances despite the preventable nature of such complications.\(^{188}\)

Stanley FM et al reported involvement in 34 cases of needle breakage within a period of 30 years (1973-2003) in which litigation resulted. In the 33 of these cases the inferior alveolar nerve block was administered at the time of the needle breakage. The remaining incident occurred during a posterior superior alveolar nerve block. The gauge and length of needle used by the dentist in all but one case was a 30-gauge short. A 27-gauge short needle was used in the other instance.

In many of the cases of retained broken dental needles, there is strong clinical and scientific evidence that the needle had been bent (by the doctor) before its insertion into the patient’s mouth.\(^{189}\)
The universal factor that is present in each and every case of retained broken dental needle is the excessive insertion of the needle into the soft tissues to its entire length. Inferior alveolar nerve block (IANB) in the typical adult patient requires soft tissue penetration to a depth of 20 to 25mm. Because the tip-to-hub length of a short dental needle is approximately 20mm, it is evident these needles had to be inserted to their hub to reach the inferior alveolar nerve.\textsuperscript{189}

Another potential cause is sudden unexpected movement by the patient as the needle penetrates muscle or contacts periosteum.\textsuperscript{190}

Retrieval of the fragment is recommended if it is visible using a small hemostat or a Mcgill intubation forceps. However, if the needle is lost (not visible) referral to oral and maxillofacial surgeon is advocated.\textsuperscript{191}

**PERSISTENT ANAESTHESIA OR PARESTHESIA**

Paresthesia is defined as persistent anaesthesia (anesthesia far beyond the expected duration), or altered sensation well beyond the expected duration of anaesthesia. It also includes hyperesthesia and dysesthesia, in which the patient experiences both pain and numbness.\textsuperscript{192}

The patient’s clinical response may include numbness, swelling, itching and tingling. It may also be associated with oral dysfunction, including tongue biting, drooling of saliva, loss of taste, and speech impairment.\textsuperscript{193}

Causes of paresthesia may include trauma to the nerve which may be caused by the needle tip during LA administration, injection of local anaesthetic solution
contaminated by alcohol or sterilizing solution near a nerve produces irritation, resulting in edema and increased pressure in the region of the nerve. Alcohol is neurolytic and can lead to long term trauma to the nerve (paresthesia lasting for months to years).  

Haemorrhage into or around the neural sheath may increase pressure on the nerve, leading to paresthesia.  

The local anaesthetic solution itself may contribute to the development of paresthesia. Haas and Lennon published a retrospective study of paresthesia after the injection of dental local anaesthetics in Canada over a period of 20 years (1973-1993). Only cases where no surgery was performed were considered. One hundred and forty-three cases of paresthesia unrelated to surgery were reported. All reported cases involved either the inferior alveolar or lingual nerve or both. Paresthesia was reported most often after the administration of a 4% local anesthetic, either prilocaine HCL or articaine HCL.  

According to Haas the incidence of permanent paresthesia resulting from all local anaesthetics is approximately 1:785,000; for 0.5%, 2%, and it is approximately 1:1,200,000 for 3% local anaesthetics, and for 4% local anaesthetics it is approximately 1:500,000. It is clear that all local anaesthetics are neurotoxic to some extent. The concentration of the local anaesthetic may have some bearing on the observed incidence of paresthesia.  

FACIAL NERVE PARALYSIS
The seventh cranial nerve supplies motor innervations to the muscles of facial expression. Paralysis of some of its terminal branches occurs whenever an infraorbital nerve block is administered.

Transient facial nerve paralysis is commonly caused by the introduction of local anesthetic into the capsule of the parotid gland, which is located at the posterior border of the mandibular ramus, covered by the medial pterygoid or masseter muscles. Directing the needle posteriorly or inadvertently deflecting it in a posterior direction during an IANB or overinsertion during a Vazirani-Akinosi nerve block, may place the tip of the needle within the body of the parotid gland. Duration of the paralysis is equal to that of the soft tissue anaesthesia usually noted.197

The primary problem that is associated with transient facial nerve paralysis is cosmetic; the person’s face appears lopsided. A secondary problem is that the patient is unable to close one eye voluntarily. There is abolishing of the protective lid reflex, such as winking and blinking become impossible. However, the corneal reflex is intact.189

Transient facial nerve paralysis is preventable during an IANB by ensuring that the needle tip is in contact with the bone of the medial surface of the ramus of mandible before depositing the LA solution. Because there’s no bony contact while administering Vazirani-Akinosi nerve block, the chances of over-insertion is higher, as such greater than 25mm of needle insertion is unacceptable in this technique.189
TRISMUS:

It is defined as a prolonged, tetanic spasm of the jaw muscles by which the normal opening of the mouth is restricted. This term was originally used only in tetanus. However, it is currently used in restricted jaw movement regardless of etiology.\textsuperscript{198}

Trauma to muscles is the most common etiological factor in trismus. Haemorrhage due to injury to the blood vessels in the infratemporal fossa is also one of causative factors of trismus associated with dental injections of local anaesthetics. Large volume of extravasated blood can produce tissue irritation, leading to muscle dysfunction as the blood is resorbed slowly.\textsuperscript{189}

Local anaesthetic solutions containing alcohol or cold sterilizing solutions can produce tissue irritation, and potentially leading to trismus. Local anaesthetics have been documented to have slight myotoxic properties on skeletal muscles. Intramuscular or supramuscular injection of local anaesthetics leads to a rapidly progressive necrosis of the exposed muscle fibers.\textsuperscript{199} A low-grade infection after injection can also cause trismus.\textsuperscript{200}

Multiple needle insertion produces insult to the tissues and consequently trismus. Stacy and Hajjar found that out of 100 needles used for the administration of the IANB, 60\% were barbed on removal from the tissues. The barb occurred when the needle came into contact with the medial aspect of the mandibular ramus.\textsuperscript{201}

Excessive volumes of local anaesthetic solution deposited into a restricted area produce distention of tissues, which may lead to post-injection trismus. This is more common after multiple missed IANBs.\textsuperscript{189}
There is usually a minor limitation of mouth opening secondary to postinjection trismus. However, it is possible for a severe limitation to develop. The average inter-incisal opening in cases of trismus is 13.7mm (range 5 to 23mm). Four cases of severe trismus secondary to multiple inferior alveolar nerve or posterior superior alveolar nerve block were reported by Stone and Kaban, three of which required surgical intervention.

Most cases of trismus resolve with conservative management. Heat therapy, warm saline mouth rinses, analgesics and muscle relaxants are commonly prescribed in the management of trismus. Virtually all cases of trismus related to intraoral injections report improvement within 48 to 72 hours after commencing the above mentioned techniques. However, if pain and dysfunction continued beyond 48 hours, infection should be put into consideration. In such instances antibiotics should be added to the treatment regimen mentioned above. Complete recovery from injection related trismus takes about 6 weeks, with a range of 4 to 20 weeks.

If no improvement is noted within 2 or 3 days without antibiotics or within 5 to 7 days with antibiotics, the patient should be referred to an oral and maxillofacial surgeon for evaluation. In such situations, other more sophisticated treatment options such as ultrasound or appliances may be considered.

**SOFT TISSUE INJURY:**

Self-inflicted trauma to the lips and tongue is caused by the patient inadvertently chewing or biting these tissues while still anaesthetized. It occurs most frequently in younger children and in mentally or physically disabled children or adults;
however, it can occur in patients of all age groups. One major contributing factor leading to soft tissue injury is the fact that soft tissue anaesthesia usually lasts longer than pulpal anaesthesia. As such, dental patients are usually dismissed from the dental clinic with residual soft tissue numbness.\textsuperscript{189} This can be prevented by the use of local anaesthetic of appropriate duration if dental appointment is anticipated to be brief.

A cotton roll can be placed between the lips and teeth and secured with dental floss wrapped around the teeth. Warning the patient and the guardian against eating, drinking hot fluids, and biting on the lips or tongue to test for anaesthesia is recommended. Management of self-inflicted soft tissue injury is symptomatic.\textsuperscript{189}

HAEMATOMA:

Haematoma results from extravasation of blood from the blood vessels to the surrounding soft tissues. It occurs as a result of nicking a blood vessel during an injection. Artery is more prone to cause haematoma due to its higher pressure. The density of the tissue surrounding the injured vessel determines the severity of the case. Certain injections such as IANB, PSANB, INB and MNB are associated with a higher occurrence of haematoma.\textsuperscript{189}

Possible complications of haematoma include trismus and pain. The swelling and discoloration usually subside within 7 to 14 days.\textsuperscript{202}

Immediate management includes pressure and ice application. The ice acts as both analgesic and vasoconstrictor. Heat may be applied to the region the next day.\textsuperscript{189}
PAIN/BURNING ON INJECTION:

Pain on injection is primarily due to careless injection technique. Many other factors can result in pain on injection such as dull needle, rapid deposition of the local anaesthetic solution, and barbed needles (from impaling bone).\textsuperscript{201}

Pain on injection increases patient anxiety and may lead to sudden unexpected movement, increasing the risk of needle breakage.\textsuperscript{189}

The primary cause of burning sensation during local anaesthetic injection is the pH of the solution being deposited into soft tissues. The pH of plain local anaesthetic solution is approximately 5, whereas that of vasoconstrictor containing local anesthetics is usually more acidic (around 3). Wahl and associates after comparing the pain on injection of prilocaine plain to lidocaine with epinephrine (1:100,000) found no statistical difference in patients perception;\textsuperscript{206} however, when bupivacaine with epinephrine (1:200,000) was compared to prilocaine plain, significantly more pain was reported by patients receiving bupivacaine.\textsuperscript{207}

It is extremely difficult if not impossible to eliminate the mild burning sensation that some patients experience during injection of local anaesthetic solution. However, alkalinization of local anaesthetics have been tried in dentistry.\textsuperscript{208}

INFECTION:
Infection following local anaesthetic administration rarely occurs since the introduction of sterile disposable needles and glass cartridges. However, the main cause of post-injection infection is contamination of the needle before administration of the anaesthetic. This occurs when the needle touches mucous membrane in the oral cavity. Another factor that may lead to possible infection is improper technique in the handling of the local anaesthetic equipment and improper tissue preparation for injection.¹⁸⁹

EDEMA:

Swelling of the tissues may be caused by trauma, infection, haemorrhage, and allergy. Edema related to local anaesthetic administration is seldom intense enough to produce significant problems such as airway obstruction. Angioneurotic edema occurs in an individual allergic to some components of the local anaesthetic and can compromise airway.²⁰⁹

Hereditary angioedema is a condition characterized by sudden onset of brawny non-pitting edema affecting the face, extremities, and mucosal surfaces of the intestine and respiratory tract often without obvious precipitating factor. Manipulation within the oral cavity, including local anaesthetic administration, may precipitate an attack. Karlis and associates noted that 15% to 33% of untreated angioedema patients died from acute airway obstruction secondary to laryngeal edema.²¹⁰

Allergy-induced edema is potentially life threatening. Its severity and location are significant in determining the appropriate treatment option. If the swelling develops in buccal soft tissues and there is absolutely no airway involvement, treatment
consists of intramuscular (IM) and oral histamine-blocker administration. Whereas if the edema occurs in any area where it compromises airway, treatment is more aggressive and involves basic life support, intravenous (IV) or IM epinephrine administration, IV or IM histamine-blocker, IV or IM corticosteroid, cricothyrotomy if total airway obstruction is developing.  

SLOUGHING OF TISSUES:

Epithelial desquamation and sterile abscess are complications that may arise secondary to local anaesthetic application. Epithelial desquamation may occur as a result of application of a topical anaesthetic to the gingival tissues for a prolonged period. Sterile abscess develops as a result of ischemia, secondary to the use of vasoconstrictor containing local anaesthetics. It usually develops on the hard palate. Usually no formal management is necessary for either epithelial desquamation or sterile abscess. However, analgesics can be applied topically to minimize irritation to the area.

POSTANESTHETIC INTRAORAL LESIONS:

Recurrent apthous stomatitis or herpes simplex can occur intra-orally after local anaesthetic injection or after any trauma to the intraoral tissues.

Recurrent apthous stomatitis is the most common oral mucosal disease in human beings. Recurrent apthous stomatitis is more frequently observed than herpes simplex, typically developing on movable tissues such as the buccal vestibule.
Herpes simplex can develop intraorally, although it is more commonly seen extraorally. It is of viral origin and develops more on the attached mucosa such as the hard palate. The virus is latent and can be reactivated by trauma to the tissues from needle, local anaesthetics e.t.c.\(^{189}\)

Management is symptomatic and may include the use of topical anaesthetic solutions, orabase without kenalog, tannic acid preparation (zilactin), mixture of equal amounts of diphenhydramine (Benadryl) and milk of magnesia rinsed in the mouth effectively coat the ulcerations and provide pain relief.\(^{212}\)

3.19 EFFECT OF ANXIETY ON BLOOD PRESSURE

Anxiety is one of the most common psychological factors that have been attributed to increase blood pressure for a very long time.\(^{213}\) It has also been shown to be related to worse cardiovascular outcomes in patients with cardiovascular disease.\(^{214}\) However, the interaction between mood disorders and cardiovascular disease is a chicken and egg phenomenon; the causal relationship between the two entities is not so clear.\(^{215}\) There is relatively strong evidence that short term anxiety is capable of elevating blood pressure in an acute fashion. However, these evidences are not strong enough when anxiety is related to sustained hypertension.\(^{215}\)

Anxiety is a known potential factor that contributes to the development of white-coat hypertension, masked hypertension and pseudo-pheochromocytoma. It also plays a role in the development of resistant hypertension, majorly due to resistance of patients to lifestyle changes and drug adherence.\(^{213}\)
PATHOMECHANISM OF ANXIETY IN ELEVATING BLOOD PRESSURE

The pathomechanism of depressive and anxiety disorders in elevating BP and subsequent development of CVD remains unclear. Several hypotheses have been developed to explain this association. Psychosocial stressors associated with anxiety disorders raise autonomic arousal via the hypothalamic-pituitary-adrenal axis, which increases circulating catecholamines. One study showed that trait anxiety was associated with higher plasma norepinephrine in patients with essential HT, suggesting a chronic increase of sympathetic activity. The increased adrenergic discharge observed in patients with panic disorder may also eventually cause irreversible peripheral vasoconstriction, resulting in chronic HT. Hypertensive patients with anxiety also have been found to have reduced sinus vagal modulation compared to hypertensive patients without anxiety symptoms. Other potential mechanisms include an increase in adverse behaviors due to stress and anxiety that impact health such as increased eating, smoking, alcohol use, and decreased exercise.

ANXIOLYTIC DRUGS AND THEIR ROLE IN ALLAYING ANXIETY

Several groups of drugs have been used to reduce anxiety in anxious patients undergoing dental procedures such as benzodiazepines, beta adrenergic blockers, and nitrous oxide. However, the most commonly administered drugs are benzodiazepines. Both oral and intravenous routes have been satisfactory. Propranolol, a prototype non-selective beta adrenergic antagonist, competes at the receptor level with catecholamines, thereby blocking their orthosympathetic...
Propranolol is widely used clinically to block the peripheral sites of noradrenergic system to treat hypertension, coronary artery disease, and tachyarrhythmias. However, propranolol can also be used to block beta adrenoreceptors in the CNS due their lipophilic property; hence they can readily cross blood-brain-barrier. Evidence suggests that propranolol positively influences dental state anxiety.

Other commonly used drugs in reducing dental anxiety are benzodiazepines such as diazepam, alprazolam, midazolam etc. Benzodiazepines act by increasing the efficiency of a neurotransmitter gamma-aminobutyric acid (GABA) at the GABA<sub>A</sub> receptor to decrease the excitability of neurons. This diminishes the communication between neurons which ultimately leads to calming effect. All GABA<sub>A</sub> receptors contain an ion channel that conducts chloride ions across neuronal cell membrane. Binding of benzodiazepines to this receptor will increase the chloride conduction across the neuronal cell membrane. This increased chloride influx hyperpolarizes the neuron’s membrane potential. As a result, the difference between resting potential and threshold potential is increased and firing is less likely.

Benzodiazepines can be classified as short acting, long acting and intermediate acting based on their half-life. The long acting benzodiazepines such as diazepam and chlordiazepoxide have metabolites which can be active for a very long time. They have a half-life of about 40-250 hours. The short acting benzodiazepines such as midazolam and triazolam have half-life of about 1-12 hours. The intermediate acting compounds such as alprazolam, nitrazepam and clonazepam have a median half life of 12-40 hours.
3.20 STUDIES BY OTHER RESEARCHERS ON THE TOPIC.

Only a handful of studies were published both locally and internationally on this topic. Some of which are as follows:

1. THE EVALUATION OF THE CHANGES IN BLOOD PRESSURE AND PULSE RATE OF HYPERTENSIVE PATIENTS DURING TOOTH EXTRACTION.

   Analysis of the data after administration of LA with vasopressor (Articain HCl with 0.0012mg epinephrine hydrochloride) indicated no statistically significant changes in the systolic and diastolic blood pressures and pulse rate for all interval measurements in both normotensive and hypertensive patients\textsuperscript{222}.

2. EFFECT ON BLOOD PRESSURE AND PULSE RATE AFTER ADMINISTRATION OF AN EPINEPHRINE CONTAINING DENTAL LOCAL ANAESTHETIC IN HYPERTENSIVE PATIENTS.

   The conclusion of this study is that epinephrine containing dental local anaesthesia decreased systolic blood pressure in stage 2 hypertension patients\textsuperscript{223}.

3. EVALUATION OF HEMODYNAMIC CHANGES IN HYPERTENSIVE PATIENTS DURING TOOTH EXTRACTION UNDER LOCAL ANAESTHESIA.

   This study concluded that there was no statistically significant difference in blood pressure and pulse rate in the two groups (patients treated with plain and patients treated using vasoconstrictor containing LA). However, the highest alteration in parameters was observed during tooth extraction in the two groups.
They opined that the hemodynamic changes induced by injecting 2% lignocaine with adrenaline in patients with controlled hypertension during tooth extraction is within normal range and is not different from that induced by 2% lignocaine without adrenaline\(^{224}\).

4. **INFLUENCE OF LOCAL ANAESTHETICS WITH ADRENALINE 1:100,000 IN BASIC VITAL CONSTANTS DURING THIRD MOLAR SURGERY.**

The findings of this study are that there was increase in systolic blood pressure with mepivacaine and articaine; decrease in diastolic blood pressure with lidocaine; increase in heart rate with all anaesthetics, but with no statistical significance in case of prilocaine. The variations in mean blood pressure and oxygen saturation were not statistically significant\(^{225}\).

5. **EFFECT OF LOCAL ANAESTHETICS WITH AND WITHOUT VASOCONSTRICTOR AGENT IN PATIENTS WITH VENTRICULAR ARRHYTHMIAS.**

The objective of this study was to evaluate and compare the hemodynamic effects of the use of local anaesthetics with a non-adrenergic vasoconstrictor in patients with ventricular arrhythmia, when compared to the use of anaesthetics without vasoconstrictor.
No haemodynamic alterations or increase in the number and complexity of the ventricular arrhythmia related to the anaesthetic used in the dental procedure were observed in either group⁸.
CHAPTER FOUR

MATERIALS AND METHODS

4.1 STUDY DESIGN:

The study was a prospective randomized comparative design involving the assessment of blood pressure and pulse rate changes that may occur as a result of administration of local anaesthetic agent containing vasoconstrictor (epinephrine) during forcep extractions of teeth at the AKTH Kano over a period of one year. The study group was treated using 2% lignocaine with 1:80,000 epinephrine, while the control was treated using 2% plain lignocaine (without epinephrine). There was a random enrollment of subjects who presented for forcep extractions of teeth, met the inclusion criteria and consented to participating in the study.

4.2 STUDY AREA

This study was conducted in Aminu Kano Teaching Hospital, Kano state, located in the North-West geopolitical zone of Nigeria. Kano state is situated in the tropical wet-and-dry climatic zone, with four (4) seasons namely; the hot and dry season, the wet and warm season, the warm and dry season and the cool and dry season (also called the harmattan season). The harmattan season spans between December and February and sometimes can extend between November and March.226
Kano has a land area of 20,790 square kilometers with a population size of about 9,401,288. from 2006 National Censors. The state is made up of forty-four (44) Local Government Areas (L.G.A.), divided into three (3) senatorial districts viz; Kano metropolis, Southern Kano and Northern Kano.

Kano metropolis has the largest population of the three divisions with an estimated population of 3.5 million. It consists of Eight L.G.A viz; Dala, Fagge, Gwale, Kano municipal, Tarauni, Nassarawa, Kumbotso and Ungogo. The metropolis is predominantly populated by the Hausa and Fulani ethnic groups.

Other ethnic groups of significant proportion in the metropolis include Nupe, Kanuri, Yoruba, Igbo, Tiv, Idoma and Igala. There is also a small population of foreigners from the neighbouring African countries, like Niger republic, Ghana, Chad and Cameroon.

4.3 STUDY CENTRE

The study was conducted in Oral and Maxillofacial Surgery department of Aminu Kano Teaching Hospital (AKTH), Kano. AKTH serves as a major referral center for dental and maxillofacial surgery patients in the Northwest geopolitical zone of Nigeria. The hospital was founded in August 1988 and has a bed capacity of about 500. The Oral and Maxillofacial Surgery department of Aminu Kano Teaching Hospital frequently attends to patients who require minor oral surgical procedures which include simple exodontias, surgical disimpaction of third molars, tissue biopsies, among others.
4.4 STUDY POPULATION

This study was conducted amongst consenting patients aged 18 to 55yrs who were either normotensive or known controlled hypertensive who presented for forcep extraction of teeth.

4.5 INCLUSION CRITERIA

a. All normotensive patients between the age of 18 to 55yrs who presented in oral surgery clinic for minor oral surgical procedures and consented to participate in the study.

b. All patients with a known history of hypertension but on medications.

4.6 EXCLUSION CRITERIA

a. Patients who met the inclusion criteria for minor oral surgical procedures but does not consented to participating in the study.

b. Patients with blood pressure > 140/90mmHg.

c. Patients whose anxiety scores were high or very high.

d. Patients with systemic illness (e.g. thyrotoxicosis, uncontrolled diabetes mellitus).

e. Patients on medications like non-selective beta blockers, tricyclic antidepressants and phenothiazines.

f. Patients who were receiving treatment for psychiatric illness or suffering from any form of mental retardation.
4.7 SAMPLING TECHNIQUE

Simple random sampling method was adopted for the study to allocate the patients into either the study group or control group using balloting. Equal number of pieces of paper with “yes” or “no” written was squeezed and put in an envelope. Consecutive patients were asked to pick one. Depending on the writing on the paper, they were enrolled into the study group or control group. If the writing on the paper was “yes”, the patient was enrolled into the study group while if the writing on the paper was “no”, the patient was enrolled into the control group.

4.8 SAMPLE SIZE CALCULATION

As the study carried out was a comparative study with quantitative variables, the following formula was used to calculate the sample size:

\[ \text{Sample size (n)} = \frac{(Z_\alpha + Z_\beta)^2 \cdot \left(\sigma_1^2 + \sigma_2^2\right)}{(M_1 - M_2)^2} \]

Where \( n \) = minimum sample size in each group.

\( Z_\alpha \) is the standard normal deviate corresponding to 95% level of significance. The value obtained from the normal distribution table was 1.96.

\( Z_\beta \) = the standard normal deviate corresponding to the power of the test to detect differences, set at 95%. The value obtained from the normal distribution table was 1.64

\( \sigma_1 \) = standard deviation in group 1, which corresponded to the standard deviation of the systolic blood pressure after local anesthetic injection with epinephrine = 8.91
\( \sigma^2 \) = standard deviation in group 2, which corresponded to the standard deviation of the systolic blood pressure after the local anesthetic administration without epinephrine = 8.11

\( m_1 \) = mean systolic blood pressure of group 1, which corresponded to mean systolic blood pressure after local anesthetic injection with epinephrine = 125.66

\( m_2 \) = mean systolic blood pressure of group 2, which corresponded to mean systolic blood pressure after local anesthetic administration without adrenaline = 117.32

Using the above values, the minimum sample size was calculated as follows:

\[
n = \frac{(1.96 + 1.64)^2 \left(8.91^2 + 8.11^2\right)}{(125.66 - 117.32)^2} \]

\[
= \frac{(3.6)^2 (79.38 + 65.77)}{(8.34)^2}
\]

\[
= (12.96) (145.15)
\]

\[
69.55
\]

\[
= 1881.14
\]

\[
69.55
\]

\[
= 27.04
\]

Therefore the minimum sample size is 27 per group. However, sample size of 100 (50 per group) was used in this study to increase precision.
Note: The standard deviations as well as the mean blood pressure were obtained from a previous study.229

4.9 INSTRUMENTS OF MEASUREMENT

STUDY QUESTIONNAIRE

The questionnaire consisted of five sections. Section A was about the demographic data of the patient which included serial no., hospital no., phone no., age, sex, occupation, ethnicity, nationality, level of formal education. Section B was designed to record the medical history of the patient; whether the patient had a history of hypertension or not and the time of diagnosis. Section C was designed to record the anxiety level of the patient on a scale of zero to hundred. In section D, the type of anaesthesia administered was recorded which was either plain 2% lignocaine without epinephrine or 2% lignocaine with epinephrine 1:80,000, also the number of cartridges used and the injection technique were recorded in this section. Section E was where the blood pressure and pulse rate readings obtained were recorded. The blood pressure and pulse rate were recorded 5 minutes before LA injection, 5 minutes after LA injection, 2 minutes into the procedure, 15 and 30 minutes after the procedure.

THE ANXIETY SCALE
This is a numerical scale which was used to subjectively score the patient’s anxiety level. It is a linear scale with zero being the lowest (no anxiety at all) and hundred being the highest score (the worst possible anxiety). Zero to twenty was translated as “low”, twenty one to forty as “medium”, forty-one to sixty as “moderate”, sixty-one to eighty as “high”, and eighty-one to hundred as “very high”. Patients were asked to observe and indicate a number that best described their anxiety for the dental extraction.

Patients with high and very high anxiety score were excluded from the study.

**BLOOD PRESSURE MEASURING DEVICE**

A pre-calibrated non-invasive electronic digital blood pressure measuring device (EchoMax Plus manufactured by Hubdic Co. Ltd Korea) was used in the study to record both the blood pressure and pulse rate of the patients.

### 4.10 STUDY PROTOCOL

Subjects were recruited into the study via the oral surgery clinic of the hospital. Only forcep extractions of upper and lower molar teeth were included in the study giving due consideration to ethical issues that might come up when more invasive procedures such as surgical extractions, and biopsies are included in the study and performed with plain local anaesthesia in the control group. All patients, both male and female aged 18 to 55yrs who met the inclusion criteria were recruited into the study.

Firstly, the aim and objectives of the study were explained to the patients in very simple terms by the researcher and their permission sought for recruitment into the
study. Once permission had been obtained, the patients were made to sign the informed consent form.

Then anxiety level was scored using a numerical scale with a score of zero to hundred. Patients with high and very high anxiety score were excluded from the study.

Patients were then randomly distributed into either study or control group using simple random sampling (ballot method).

Baseline blood pressure and pulse rate of patients were measured 5 minutes before the local anaesthetic injection. A maximum of two cartridges of the local anaesthetic (2% lignocaine with 1:80,000 epinephrine) was given for each patient in the study group. Same quantity of 2% plain lignocaine was also given to the control group. Aspirating dental syringe was used in both the study and control groups to avoid intravascular injection. Patients requiring more than two cartridges for the procedure were dropped out of the study. The injection technique was dependent on the type of procedure to be performed and site.

Blood pressure and pulse rate were checked 5 minutes after the local anaesthetic injection but before the onset of procedure, then another measurement was taken 2 minutes after commencing the procedure. Final check of blood pressure and pulse rate was done 15 and 30 minutes after the procedure using a pre-calibrated digital blood pressure monitor. Blood pressure and pulse rate were measured twice at each instance and average was recorded. Emergency medical kit was made available to manage emergencies that might arise.
Patients were discharged after the procedure. Measurements of the vital signs as well as the procedure were done by the researcher only.

4.11 ETHICAL CONSIDERATION

Ethical approval was obtained from Aminu Kano Teaching Hospital Ethical review committee before the commencement of the study.

A detailed explanation of the study was conveyed by the researcher to all participants who consented to participating in the study. They appended their signatures or thumb prints (depending on literacy status) on the informed consent form before the commencement of the study.

4.12 DATA COLLECTION PROCESS

Data collection was done by means of interviewer-administered structured questionnaire. It was obtained with the aid of one (1) questionnaire designed for this study (Appendix I). Information collected from the questionnaire (Appendix I) included subject’s demographics, procedure done, blood pressure readings before anaesthesia, after anaesthesia, during the procedure and after the procedure, and patient’s anxiety level. The recording was done by the examiner with the help of the assistant (Dentist), who could pass instructions and interpret result to the researcher for proper documentation.

4.13 DATA ANALYSIS
The data was recorded on a proforma designed for the purpose of this study (Appendix I). All data collected was entered into a personal computer. Data was presented using tables, charts and graphs. Quantitative data was summarized using means and standard deviations, while qualitative aspect was described using frequencies and percentages.

Data analysis was performed using Statistical Package for Social Sciences Version 17.0 (SPSS Inc. Chicago, Il, USA). The level of significance was determined using paired t-test. Multivariate logistic regression was done to determine the influence of socio-demographic variables, anxiety level, number of cartridges used and injection technique on the outcome of the study. A confidence interval of 95% was used in this study and a p-value of less than 0.05 was considered significant.

CHAPTER FIVE

RESULTS
This chapter presents results of the study findings as outlined in the objectives and questionnaire. All the selected patients agreed and consented to participate in the study, giving a response rate of 100%.

**Socio-demographic data**

A total of 100 subjects aged between 18 and 55 years participated in the study. The mean age and standard deviation of all the participants was 34.66±10.3. There was no statistically significant difference in the mean age of respondents in the two study groups, with the vasoconstrictor group having 33.72±9.8 years and the group without vasoconstrictor having 35.60±10.9 years (p=0.367). **Table 1**

The participants consisted of 39(39%) males and 61(61%) females. There were 20(40%) males and 30(60%) females in the study group. While the control group, consisted of 19 (38%) males and 31(62%) females. **Table 2**

Occupation of the participants was also fairly balanced as there were 19(38%) civil servants in the study group and 17(34%) in the control group making up the largest percentage. This is followed by traders in which there were 10(20%) of them in the study group and 11(22%) in the control group. There were 9(18%) dependents in the study group and 8(16%) in the control group. The students followed with 4(8%) in the study group and 11 (22%) in the control group. Those with the least representation included professionals, motorcyclists/drivers and artisans. **Table 2**

The major ethnic group among the participants were Hausa with 36(72%) participants in the study group and 40 (80%) in the control group. Other ethnic groups that participated in the study in order of decreasing frequency included Yoruba, Fulani and Ibo. **Fig. 1&2**
Almost all the participants in the study were Nigerians in Nationality making up 99(99%) of both the study and control group with just 1(1%) non-Nigerian.

The participants comprised of high percentage of people with tertiary level of education with 31(62%) participants in the study group and 34 (68%) in the control group.

The two groups were therefore matched for gender, occupation, ethnicity (figure 1&2), nationality and level of education as no statistically significant difference was found amongst these variables with a p-value of (0.838, 0.217, 0.157, 1.000,0.891) respectively. Table2

Table 1: Showing the mean age of the participants.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Age</th>
<th>Number</th>
<th>Std. Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>33.72</td>
<td>50</td>
<td>9.76</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>35.6</td>
<td>50</td>
<td>10.967</td>
<td>0.367</td>
</tr>
<tr>
<td>Total (All participants)</td>
<td>34.66</td>
<td>100</td>
<td>10.372</td>
<td></td>
</tr>
</tbody>
</table>

The above table shows the mean age of the participants in the study and control group was not statistically significant.

Table 2: Socio-demographic characteristics of Respondents

<table>
<thead>
<tr>
<th>Socio-demographic Variable</th>
<th>Group</th>
<th>Vasoconstrictor n (%)</th>
<th>No Vasoconstrictor n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>20 (40.0)</td>
<td>19 (38.0)</td>
<td>0.838</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>30 (60.0)</td>
<td>31 (62.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>50 (100)</td>
<td>50 (100)</td>
<td></td>
</tr>
</tbody>
</table>
The above table shows that there was no statistically significant difference between the two groups in all the socio-demographic variables.

**Fig.1**: A pie chart showing the ethnic distribution in the study group
The pie chart above shows that Hausas were the predominant participants in the study group, whereas Fulani had the least participants.

Fig.2: A pie chart showing the ethnic distribution among the control group.
This pie chart illustrates that Hausas were the predominant ethnic group in the control group and other languages representing the minority among the participants in the control group.

**Pre-anesthetic data**

The two groups were homogenous in terms of history of hypertension with 12 (24%) of participants in the study group and 13 (26%) of participants in the control group giving history of hypertension. No statistically significant difference was found (p-value = 0.817).

The number of local anaesthetic cartridges used, and injection techniques were not statistically significant amongst the two groups with p-values of (0.155, and 0.305) respectively. However, there was statistically significant difference in terms of the level of anxiety between the two groups with a higher percentage of participants in the control group scoring medium and moderate levels of anxiety (p-value = 0.004). Table 3

**Table 3: Pre-A anaesthetic Evaluation of Participants**
<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>n (%)</th>
<th>n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vasoconstrictor</td>
<td></td>
<td>No Vasoconstrictor</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (24.0)</td>
<td>13 (26.0)</td>
<td></td>
<td>0.817</td>
</tr>
<tr>
<td>No</td>
<td>38 (76.0)</td>
<td>37 (74.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50 (100)</td>
<td>50 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low/low</td>
<td>10 (20.0)</td>
<td>0 (0.0)</td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Medium</td>
<td>16 (32.0)</td>
<td>21 (42.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>24 (48.0)</td>
<td>29 (58.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50 (100)</td>
<td>50 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Cartridges</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>33 (66.0)</td>
<td>26 (52.0)</td>
<td></td>
<td>0.155</td>
</tr>
<tr>
<td>2</td>
<td>17 (34.0)</td>
<td>24 (48.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50 (100)</td>
<td>50 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection technique</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve block</td>
<td>28 (56.0)</td>
<td>33 (66.0)</td>
<td></td>
<td>0.305</td>
</tr>
<tr>
<td>Infiltration</td>
<td>22 (44.0)</td>
<td>17 (34.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50 (100)</td>
<td>50 (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The above table shows that there was statistically significant difference in the anxiety level between the two groups.
Baseline haemodynamic data

The mean systolic blood pressure before LA in all the participants was 126.19±10.9 mmHg, with a mean of 126.80±11.4 mmHg in the study group and 125.58±10.5 in the control group. The mean diastolic blood pressure of all participants before LA was 73.87±10.9 mmHg with a mean of 74.32±10.9 mmHg in the study group and 73.42±11.0 mmHg in the control group. The mean pulse rate of all the participants before LA was 88.11±16.5bpm with a mean value of 89.86±17.7bpm in the study group and 86.36±15.2bpm in the control group. Table 4

Haemodynamic relationships of the study and control group

The haemodynamic relationship between the study and control group at different time intervals is detailed in Tables 4, 5, 6, 7 and 8. There was no statistically significant difference between the two groups at all intervals. However, the highest alteration found in the blood pressure was during the procedure in which there was increase in both the mean systolic and diastolic blood pressure in the control group. Table 6

The different alteration pattern in mean systolic blood pressure in the two groups is better depicted in Fig.3. There was a slight decrease in the mean SBP from the baseline value of 126.80mmHg to 125.36mmHg in the study group, and from 125.58mmHg to 122.98mmHg in the control group, 5 minutes after LA injection. After this decrease, there was an increase in the mean SBP to about 126.78mmHg and 130.88mmHg in the study and control groups respectively. It is noteworthy that the rise was sharper in the control group than in the study group. The mean SBP dropped down to near pre-LA level in both groups after about 30 minutes.
Fig.3: Comparison of mean systolic blood pressure between study and control groups.

Line graph showing there was decrease in SBP in both groups after LA administration and marked increase in SBP in the control group during the procedure.

The mean diastolic blood pressure also followed the same pattern of fluctuation. It decreased from the baseline value of 74.32mmHg to 71.36mmHg in the study group, and from 73.42mmHg to 69.90mmHg in the control group. There was a remarkable upsurge from the post-anaesthetic value to about 78.12mmHg in the control group. The values in both groups also came to near pre-anaesthetic reading in about 30 minutes. Fig.4
Fig. 4: Comparison of mean diastolic blood pressure between study and control groups.

Line graph showing there was slight decrease in the DBP in both groups after LA administration and remarkable increase in DBP during the procedure.

The pulse rate also showed a constant pattern of higher value in the study group as compared to the control group at all intervals. Furthermore, there was clear depiction of physiological response to decrease in pulse rate by increase in blood pressure. Fig. 5
In this graph, both the study and control group showed more or less similar pattern of pulse rate fluctuation.

Table 4: Blood Pressure and Pulse Rate 5 minutes Before Local Anaesthetic Injection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>126.80</td>
<td>11.452</td>
<td>0.580</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>125.58</td>
<td>10.510</td>
<td></td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>74.32</td>
<td>10.927</td>
<td>0.683</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>73.42</td>
<td>11.073</td>
<td></td>
</tr>
<tr>
<td>Pulse Rate</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>89.86</td>
<td>17.757</td>
<td>0.293</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>86.36</td>
<td>15.275</td>
<td></td>
</tr>
</tbody>
</table>

The above table shows that there was no statistically significant difference in SBP, DBP & PR between the two groups before LA administration.
### Table 5: Blood Pressure and Pulse Rate 5 Minutes after the Local Anaesthetic Injection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic Blood Pressure</strong></td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>125.36</td>
<td>13.953</td>
<td>0.408</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>122.98</td>
<td>14.667</td>
<td></td>
</tr>
<tr>
<td><strong>Diastolic Blood Pressure</strong></td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>71.36</td>
<td>11.602</td>
<td>0.502</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>69.90</td>
<td>9.988</td>
<td></td>
</tr>
<tr>
<td><strong>Pulse Rate</strong></td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>92.44</td>
<td>18.495</td>
<td>0.248</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>88.52</td>
<td>15.096</td>
<td></td>
</tr>
</tbody>
</table>

The above table shows no statistically significant difference in SBP, DBP & PR 5 minutes after LA administration.

### Table 6: Blood Pressure and Pulse Rate during the Procedure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic Blood Pressure</strong></td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>126.78</td>
<td>15.700</td>
<td>0.195</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>130.88</td>
<td>15.733</td>
<td></td>
</tr>
<tr>
<td><strong>Diastolic Blood Pressure</strong></td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>73.34</td>
<td>12.328</td>
<td>0.060</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>78.12</td>
<td>12.758</td>
<td></td>
</tr>
<tr>
<td><strong>Pulse Rate</strong></td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>91.26</td>
<td>19.624</td>
<td>0.134</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>85.86</td>
<td>15.869</td>
<td></td>
</tr>
</tbody>
</table>

This table shows that there was no statistically significant difference in SBP, DBP & PR between the two groups during procedure.
Table 7: Blood Pressure and Pulse Rate 15 Minutes after the Procedure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Pressure</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>122.40</td>
<td>14.737</td>
<td>0.098</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>127.04</td>
<td>12.965</td>
<td></td>
</tr>
<tr>
<td>Diastolic Pressure</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>73.38</td>
<td>12.763</td>
<td>0.303</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>75.94</td>
<td>11.965</td>
<td></td>
</tr>
<tr>
<td>Pulse Rate</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>85.06</td>
<td>15.990</td>
<td>0.377</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>82.34</td>
<td>14.649</td>
<td></td>
</tr>
</tbody>
</table>

This table shows that there was no statistically significant difference in SBP, DBP & PR between the two groups 15 minutes after the procedure.

Table 8: Blood Pressure and Pulse Rate 30 Minutes after the Procedure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Pressure</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>124.52</td>
<td>12.453</td>
<td>0.545</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>125.96</td>
<td>11.234</td>
<td></td>
</tr>
<tr>
<td>Diastolic Pressure</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>74.58</td>
<td>10.218</td>
<td>0.985</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>74.62</td>
<td>10.616</td>
<td></td>
</tr>
<tr>
<td>Pulse Rate</td>
<td>Vasoconstrictor</td>
<td>50</td>
<td>85.58</td>
<td>15.786</td>
<td>0.800</td>
</tr>
<tr>
<td></td>
<td>No Vasoconstrictor</td>
<td>50</td>
<td>84.82</td>
<td>14.095</td>
<td></td>
</tr>
</tbody>
</table>
This table shows that there was no statistically significant difference in SBP, DBP & PR between the two groups 30 minutes after the procedure.

**Table 9: Multivariate Logistic Regression Model**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>B</th>
<th>p-value</th>
<th>Adjusted Odds Ratio</th>
<th>95% CI of Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Sex</td>
<td>0.647</td>
<td>0.340</td>
<td>1.910</td>
<td>0.51</td>
</tr>
<tr>
<td>Occupation</td>
<td>1.666</td>
<td>0.327</td>
<td>5.289</td>
<td>0.19</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>0.407</td>
<td>0.838</td>
<td>1.503</td>
<td>0.03</td>
</tr>
<tr>
<td>Highest Educational Level</td>
<td>0.113</td>
<td>0.959</td>
<td>1.119</td>
<td>0.02</td>
</tr>
<tr>
<td>Anxiety Level</td>
<td>-0.488</td>
<td>0.444</td>
<td>0.614</td>
<td>0.18</td>
</tr>
<tr>
<td>No of Cartridge</td>
<td>-0.691</td>
<td>0.198</td>
<td>0.501</td>
<td>0.17</td>
</tr>
<tr>
<td>Injection Technique</td>
<td>0.260</td>
<td>0.636</td>
<td>1.297</td>
<td>0.44</td>
</tr>
<tr>
<td>Constant</td>
<td>-1.239</td>
<td>1.000</td>
<td>0.290</td>
<td></td>
</tr>
</tbody>
</table>

B = Coefficient of Regression, CI = Confidence Interval
Upon analysis using multivariate logistic regression model, none of the parameters was found to be an independent predictor of difference in the BP and PR between the study and control groups.

The variable of reference used for sex is male, and for occupation is student, for ethnicity is Ibo, for highest educational level is uneducated, for anxiety level low, for number of cartridge one and for injection technique is nerve block.

**CHAPTER SIX**

6.1 **DISCUSSION**

Majority of minor oral surgical procedures required the use of local anaesthetics.\(^5,6\) The currently used local anaesthetic agents consist of a vasoconstrictor as part of the composition to improve the biological properties of the solution which may be either adrenergic agonist or felypressin.\(^3\) Of these vasoconstrictors, adrenaline is the most frequently used vasoconstrictor in daily dental practice to achieve the desired properties.\(^4\)-\(^6\) Such properties include haemostasis, increased depth and duration of anaesthesia, decreased systemic absorption, decreased dose of anesthetic agent required and subsequently reduced toxicity.\(^4\)-\(^7\) These vasoconstrictors cause some haemodynamic changes which may be either by direct action on the cardiac muscle or by stimulation of the autonomic innervations of the heart.\(^8\) All of these effects may cause, depending on the concentration of the vasoconstrictor, an increased heart rate, increased force of cardiac contraction and ultimately increased blood pressure.\(^8\) However, the occurrence of most adverse reactions is due to inappropriate high dose injection and accidental injection into the vasculature.\(^9,10\) Many authors concluded that adrenaline has a safety range,\(^21,22\) its threshold in cardiovascular patients is not yet clear.\(^23,24\) However, controversies still exist
as regards to the concentration of adrenaline in local anaesthetic solutions and its mode of usage.\textsuperscript{27} Furthermore, the fact that adrenaline is a vasopressor agent has made many authors to implicate it as the causative agent in certain clinical situations of hypertension encountered in the dental office.\textsuperscript{26,27} Hypertensive patients represent an important risk group among patients visiting the dental clinic as many of them give a history of high blood pressure.\textsuperscript{26}

The age of the patients that participated in this study differed from those that participated in the study conducted by Ogunlewe et al.\textsuperscript{224} The age range of patients in their study was 24 to 75 years with mean ± standard deviation of 50.1±11.7, but almost similar age group was found in a study conducted by Mohammed et al\textsuperscript{229} in which the mean age was 36.67±8.42 and 35.45±7.99 which were within the range of 25 to 50 years old. This wide variation in the mean age of the patients between this study and that of Ogunlewe et al\textsuperscript{224} could be simply explained due to the fact that in their study only hypertensive patients were included and there is likelihood of having more hypertensive patients among the middle age and elderly group.

The gender of the participants in this study had some similarities and differences to the previously conducted studies. In this study there was a slightly higher female to male ratio of about 1.5:1 which is consistent with the study by Ogunlewe et al\textsuperscript{224} with a similar ratio of about 1.5:1. A higher female to male ratio was reported by Gungormus et al\textsuperscript{4} with a female to male ratio of about 2:1. However, different findings were reported by Mohammed et al\textsuperscript{229} and Marcelo et al\textsuperscript{230} with a female to male ratio of about 1:1. The reasons for this higher female to male ratio in this our study and others that are consistent
with it could be attributed to low pain threshold that exists in females compared to males which could explain why they sought medical attention faster than their male counterpart.

It can be deduced from this study that there were no statistically significant changes in the SBP, DBP, and PR following administration of 2% lignocaine with 1:80,000 epinephrine (Fig. 3-5). Similar result was reported by Gungormus et al., Chaudary et al., Ogunlewe et al., and de Morais et al. These findings are contrary to what Mohammad et al. reported. They reported a statistically significant difference in all the three hemodynamic parameters (SBP, DBP & PR) after administration of one cartridge of 2% lignocaine with 1:80,000 adrenaline. However, in their study the following have been noted: First, they used different anaesthetic agents for study and control group (2% lignocaine + 1:80,000 adrenaline and 3% mepivacaine respectively) which is enough to bring about bias. Second, in their methodology they did not mention whether confounders like anxiety was taken care of or not. And lastly, mercury barometer was used to monitor the blood pressure before and after local anaesthetic administration which may cause inconsistencies in the readings.

A slight decrease in mean SBP was observed in this study after local anaesthetic administration. The decrease was more in the control group than in the study group (Fig. 3). Similar finding was observed by Chaudary et al. They reported a decrease in systolic blood pressure after local anaesthesia with adrenaline was injected in patients with stage 2 hypertension undergoing exodontia. This is however, contrary to what Akinmoladun et al., Nedal et al., and Ogunlewe et al. found. The latter reported slight increase in the mean SBP after LA with adrenaline administration though not statistically significant. Nedal et al. conducted their study using three local anesthetic agents with different concentrations of adrenaline (2% lignocaine with 1:80,000 epinephrine, 4% articaine with
1:100,000 epinephrine and 4% articaine with 1:200,000 epinephrine). Haemodynamic parameters were measured 3 minutes before LA, 3 minutes after LA and 3 minutes after extraction. They reported a significant increase in SBP 3 minutes after LA administration in study group treated using 2% lignocaine with 1:80,000 epinephrine. My finding (decrease in SBP after LA administration) could be explained in two ways: First, it is a known fact that lignocaine is a potent vasodilator; as such its vasodilator effect may take precedence over the vasoconstrictor effect of the adrenaline which further explains why the reduction is more marked in those patients treated with plain lignocaine. Secondly, the anxiety of having an intra-oral injection that may have slightly elevated the baseline blood pressure is nullified as soon as the injection is given, which consequently may reduce the blood pressure. Lastly, the pain that might have been the indication for the extraction which could also trigger endogenous catecholamine release was abated as soon as the LA starts working.

This study also found that there was an increase in mean SBP from the baseline during the procedure in both the study and control groups (Fig.3). This finding was more pronounced in those patients whose procedure was done using plain lignocaine which can be explained partly due to the fact that the plain lignocaine was less potent, had lesser depth and duration of action as compared to the one containing adrenaline. This in turn may result in poor pain control with attendant consequences such as pain induced release of endogenous catecholamines which may ultimately elevated the blood pressure. On the other hand, the vasoconstrictor group (study group) did not exhibit remarkable change in blood pressure possibly due to profound anaesthesia which eliminates the physiological response of releasing the endogenous catecholamines to pain and stress. This finding may also be
attributed to factors like psychological stress and anxiety which is consistent to what Ogunlewe et al.\textsuperscript{224} reported because there was significantly higher percentage of patients with medium and moderate anxiety scores in the control group than in the study group in this study (p-value = 0.004) Table-3. Because of the statistically significant difference in the anxiety level between the study and control group, multivariate logistic regression was done and it suggests that neither the anxiety level nor the socio-demographic variables was an independent predictor of difference in BP and PR between the two groups. (Table 9)

Similar finding was also observed in the mean DBP where it fell after the local anaesthetic administration in both groups; it then gradually increased during the procedure although the magnitude was higher in the control group.

The pulse rate slightly increased in both study and control groups after the local anaesthetic administration, it then continued to decrease during the procedure till it reached a value below the pre-anaesthetic level 15 minutes after the procedure, it then rose to almost pre-anaesthetic value 30 minutes after the procedure. This is not surprising as it depicted the typical physiological response that occured; it is generally accepted that the pulse rate increases when there is a decrease in blood pressure and vice versa. This study showed a similar pattern, as there was an increase in pulse rate 5 minutes after the LA administration which corresponded to the time when both the SBP and DBP had decreased and there was decrease in pulse rate during the procedure which also corresponded to when both the SBP and DBP had increased. Fig.3, 4, & 5.

All the haemodynamic parameters studied returned to almost pre-anaesthetic value after the procedure.
At this juncture, it can be deduced that the use of adrenaline containing local anaesthetics was more favorable to the haemodynamic variables both in controlled hypertensive and normotensive patients than the plain local anaesthetics due to their lack of adverse effects on blood pressure and pulse rate as well as more effective pain control during the procedure.

6.2 TEST OF HYPOSTHESIS:

This study supports the null hypothesis which states that administration of optimal dose of adrenaline containing local anaesthetic agents does not significantly affect the blood pressure of healthy (non-hypertensive) and controlled hypertensive patients and it also rejects the alternative hypothesis which states that administration of adrenaline containing local anesthetic agents can significantly affect the blood pressure of healthy (non-hypertensive patients) and controlled hypertensive patients.
CHAPTER SEVEN

7.1 CONCLUSION:
The result of this study has demonstrated that the use of optimal dose of adrenaline contained in local anaesthetics did not lead to a significant increase in blood pressure in both normotensive and controlled hypertensive patients.

7.2 RECOMMENDATIONS:
Based on the findings from this study, the following are recommended

1. Routine use of adrenaline containing local anaesthetics for dental procedures due to its added advantages over plain local anaesthesia such as increased depth and duration of anaesthesia, decreased bleeding in the operating field, decreased systemic absorption of the local anesthetic agent; and lack of adverse effects on the cardiovascular system.

2. Proper pre-operative non pharmacologic management of anxiety as this will go a long way in reducing the patient’s fear to the dental procedure. This will indeed prevent anxiety from building up unnecessarily with its attendant effect on blood pressure.
3. Further research on patients with uncontrolled hypertension to determine the safety of using adrenaline containing local anaesthetic in that group of patients.

7.3 **LIMITATIONS OF THE STUDY:**

1. This research was only limited to normotensive and controlled hypertensive patients and could not be extrapolated to uncontrolled hypertensive patients.

2. The influence of anxiety on blood pressure cannot be completely ruled out even with the anxiolytic drugs.

3. The digital blood pressure measuring device can develop unnoticed fault usually from low battery power. Although this is a known fact, the use of the analog measuring device (sphygmomanometer) is not advisable due to the inconsistencies of readings between different assessors and the possibility of mercury toxicity. However, this was taken care of by frequently changing the battery.

4. The extractions done may vary in their difficulty amongst different patients which may increase the patient’s pain and anxiety. These two factors may invariably increase the blood pressure.
APPENDIX I

Dear Respondent,

My name is Dr Abubakar Mohammad Kaura, a resident in the department of Family Dentistry of Aminu kano Teaching Hospital. I am conducting a research titled **effects of vasoconstrictor on arterial blood pressure during minor oral surgical procedures in Aminu Kano Teaching Hospital**, Kano state of Nigeria. The questionnaire will be administered with assistance from the researcher. All information obtained will be treated as confidential. You will be required to sign an informed consent form, if you agree to participate in the study. Thank you.

**SECTION A – DEMOGRAPHIC DATA**

SERIAL NO: ---------  HOSPITAL NO: ---------

PHONE NO: --------------

EMAIL ADDRESS: -------------------------------

1. **AGE** (in years):

2. **SEX**: Male □ Female □

3. **OCCUPATION**: Student □ Dependent □ Artisan □ Trader □ Motorcyclist/Drivers □ Civil/Public Servant □ Professional □

4. **ETHNICITY**: Ibo □ Yoruba □ Hausa □ Fulani □ Others □

5. **NATIONALITY**: Nigerian □ Non-Nigerian □
6. **LEVEL OF FORMAL EDUCATION:** Uneducated [ ] Primary [ ] Secondary [ ]
   Tertiary [ ] Islamic/Arabic [ ]

**SECTION B - MEDICAL HISTORY:**

(a) Hypertension: Yes [ ] No [ ]

If yes, when was the first diagnosis?........

Which medications are you currently on?

  i.  
  ii.  
  iii.  
  iv.  

**SECTION C - ANXIETY LEVEL**

![Anxiety Scale](image)

Please, observe and indicate a number that better describes your anxiety for your today dental treatment. The number 0 (zero) means that you don’t feel any anxiety and the number 100 means the worst possible anxiety.

**SECTION D - TYPE OF ANESTHESIA**

Plain [ ] With epinephrine [ ]

No. of cartridges: ______

Injection technique: Nerve Block [ ] Infiltration [ ]

**SECTION E - BLOOD PRESSURE AND PULSE RATE READINGS**

(1) 5 minutes before LA injection [ ] [ ]
(2) 5 minutes after LA injection [ ] [ ]
(3) During the procedure (2 minutes) [ ] [ ]
(4) 15 minutes after the procedure [ ] [ ]
APPENDIX II

INFORMED CONSENT

My name is Dr. Abubakar Mohammad Kaura, a resident in the department of Family Dentistry, Aminu Kano Teaching Hospital Kano. I am conducting a study with the details below. I am seeking your consent to be included in the study.

Title of investigation: Effect of vasoconstrictor on arterial blood pressure during minor oral surgical procedures.

Purpose of study: To find out the effect of adrenaline contained in local anesthetic on blood pressure.

Procedure: Minor oral surgery.

Discomfort and Risk: Numbness and burning sensation.

Potential benefit: Effective pain control.

Contact person: Dr. Abubakar Mohammad Kaura.

This to certify that I ................................................................. here by agree to participate in this scientific investigation that is an authorized part of education and research programs for residency training at Aminu Kano Teaching Hospital, Nigeria under the supervision of Dr Tunde Bamgbose.
The investigation and my role in the investigation have been clearly defined and fully explained to me.

I have been given an opportunity to ask whatever question(s) I may have and I have had such questions answered to my satisfaction.

I understand that any data or answers to questions with regard to my identity will be kept strictly confidential and will not be released for any purpose without my written consent.

I certify that to the best of my knowledge I have disclosed all relevant information correctly.

I further understand that I am free to withdraw my participation at any time

I hereby consent to the participation of this study.

………………………………………………………………………………………………………………………………………………………………………………
………………………………………………………………………………………………………………………………………………………………………………

Name of patient/signature/date

I, the undersigned, have fully defined and explained the investigation to the above subject,

………………………………………………………………………………………………………………………………………………………………………………
………………………………………………………………………………………………………………………………………………………………………………

Name of investigator/signature/date

I was present when the study was explained to the patient and to the best of my knowledge convinced that, the patient will not be denied treatment or disenfranchised if he/she declines to participate in the research.

………………………………………………………………………………………………………………………………………………………………………………
………………………………………………………………………………………………………………………………………………………………………………

Name of witness/signature/date
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