EVALUATION OF EFFECTIVENESS OF INTRACUFF ALKALINIZED LIDOCAINE FOR ATTENUATION OF ENDOTRACHEAL TUBE-INDUCED COUGHING AND HAEMODYNAMIC CHANGES DURING EMERGENCE FROM GENERAL ANAESTHESIA.

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BY

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DEDICATION

THIS WORK IS DEDICATED TO THE ALMIGHTY GOD.

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SUMMARY

Background: Coughing and haemodynamic changes occurs frequently during emergence from general anesthesia with endotracheal intubation. Several methods have been used to attenuate them with various setbacks. Little is known about the use of alkalinized intracuff lidocaine for this purpose in the sub-Saharan region.

Objective: The aim of this study was to determine the effects of alkalinized intracuff lidocaine on ETT induced coughing and haemodynamic changes at emergence from general anaesthesia.

Methodology: Two hundred healthy patients with the American Society of Anaesthesiologist (ASA) physical status I and II scheduled for elective surgery under general anaesthesia with endotracheal intubation were studied. Patients belonged to one of four groups (50 patients/group) depending on whether air, saline, 40mg plain lidocaine or 40mg alkalinized lidocaine was used to inflate their high volume low pressure ETT cuff at intubation. At extubation the incidence of coughing and HR (heart rate), SBP (systolic blood pressure), DBP (diastolic blood pressure), MAP (mean arterial blood pressure) values were recorded over time. Presence of sore throat was assessed at recovery room and 24 hours later in the ward.

RESULT: The incidence of coughing and sore throat assessed in the recovery room was least in the alkalinized lidocaine group, 30% and 16% respectively. Comparison among the 4 groups showed significant difference. $P<0.05$.

Significant changes in HR, SBP, DBP, and MAP from baseline values occurred in all the groups overtime post extubation. However whereas there was an increase in these haemodynamic parameters in the first 4 minutes in air, saline, plain lidocaine groups, in the alkalinized lidocaine group there were either a decrease or no difference in the values.

Conclusion: The use of alkalinized intracuff lidocaine resulted in a decrease in the incidence of coughing, sore throat and haemodynamic changes at emergence from general anaesthesia.

CHAPTER ONE

INTRODUCTION

The respiratory tract is one of the most sensitive part of the human anatomy.[1] In the conscious individual noxious stimulation of the airways elicit vigorous reflex reactions such as gagging, retching or coughing.[1] These reflexes present in varying strength during general anaesthesia depending on the depth of anaesthesia and the drug used to induce anaesthesia.[2]

Laryngoscopy and endotracheal intubation provoke certain reflex physiological response including tachycardia, raised blood pressure and cardiac arrhythmias. This phenomenon has been termed haemodynamic response to laryngoscopy and endotracheal intubation.[1]

Similarly, emergence from general anaesthesia is frequently complicated by endotracheal tube (ETT) - induced coughing, bucking and restlessness, which may lead to hypertension, tachycardia, arrhythmia, myocardial ischemia, surgical bleeding, raised intracranial and intraocular pressure.[3,4,5]

Although, these complication may be transient (lasting 5-15 minutes), and usually tolerated by a lot of patients, certain patients may experience unfavourable or undesirable sequelae.[5]

This is of particular relevance in neurosurgical, ophthalmic and vascular procedure.[3]

Coughing and bucking are recognised complications of endotracheal intubation which may place stress on suture material after ophthalmic surgery with eventual wound breakdown.[4,6]

In neurosurgery, coughing or bucking on the tracheal tube will result in a raised intracranial pressure, which may precipitate intracranial haemorrhage or worsen cerebral oedema.[7]

In parturients with gestational hypertension, tracheal extubation and related haemodynamic changes increase the risk of cerebral haemorrhage and pulmonary oedema.[5]

Significant decrease in ejection fraction and evidence of myocardial ischemia has been demonstrated post extubation in patients with coronary artery disease.[5] Also abdominal wound separation, though rare, is another potential complication associated with increase in intra abdominal pressure secondary to bucking.[5] In all these patients, a smooth emergence from general anaesthesia is desired.[5,6,7,8]

Manoeuvres to achieve smooth emergence include tracheal extubation in the surgical (deep) plane of anaesthesia, administration of intravenous (iv) lidocaine, topical lidocaine (via sprays, or direct instillation into the ETT), 0.05% betamethasone cream applied on ETT, iv narcotics such as Fentanyl, and iv esmolol.[3] However, extubation in a deep plane of anaesthesia may lead to aspiration in the presence of an unprotected airway while use of intravenous lidocaine and intravenous narcotics may lead to delayed emergence from anaesthesia.[3] Furthermore, topical lidocaine is absorbed through the tracheal mucosa which limits its duration and effectiveness.[3]

When lidocaine is injected into the ETT cuff, it spreads through the semipermeable membrane wall and induce anaesthetic action on the trachea.[9,10] This increases airway tolerance of the ETT.[11] The incidence of coughing and haemodynamic changes are also minimised.[3,12-15]

Since lidocaine injected into the ETT cuff have been shown to diffuse through the semipermeable membrane of the ETT cuff,[9,10]. Moreso with an increased diffusion capacity when lidocaine is alkalinized, it will be of benefit carry out a study to see if this can produce sufficient local anaesthetic effect on the trachea and by so

doing increase ETT tolerance by reducing the incidence of cough and haemodynamic changes at emergence from General anaesthesia. It is hypothesied therefore that the use of 40mg alkalinized intracuff lidocaine will result in reduced incidence of coughing and haemodynamic changes than when air, saline, or plain lidocaine is used to inflate the cuff of the endotracheal tube at intubation.

CHAPTER TWO

GENERAL OBJECTIVE

To determine the effects of alkalinized intracuff lidocaine on ETT-induced coughing and haemodynamic changes at emergence from general anaesthesia.

SPECIFIC OBJECTIVES

1. To determine the incidence of ETT-induced coughing during emergence from general anaesthesia.
2. To evaluate the level of haemodynamic changes that occurs during emergence from general anaesthesia.
3. To determine the extent to which ETT-induced coughing and haemodynamic changes are attenuated by alkalinized intracuff lidocaine on emergence from general anaesthesia.
4. To recommend guidelines for attenuating ETT-induced coughing and haemodynamic changes on emergence from general anaesthesia.

CHAPTER THREE

JUSTIFICATION FOR THE STUDY

Despite increasing trend favouring use of regional anaesthesia, some patients will still require general anaesthesia. In these patients complications of tracheal extubation is also of clinical importance as those of tracheal intubation.

The avoidance of bucking and coughing during extubation is seen as an important clinical skill, and one of the clinical hallmarks of the "smooth extubation", which is desirable during emergence from general anaesthesia in many situations. Techniques that were used to achieve this, have their limitations. Hence the need to study the use of alkalinised intracuff lidocaine, which affords airway protection with intact supraglottic reflexes.

The use of alkalinized intracuff lidocaine is a non-invasive, cost effective, relatively easy and safe technique, and will therefore be suitable for a developing country, hence the need for this study in the Nigerian population.

CHAPTER FOUR

LITERATURE REVIEW

The first reported tracheal intubation was by Vesalius in an animal in 1543.[19] Subsequently in the early 1870́s Trendelenburg in Germany performed the first endotracheal anaesthesia in man. Macewen in 1878 reported the first elective endotracheal intubation for anaesthesia. Later, Rosenberg and Kuhn administered cocaine as local anaesthetic to obtund the cough reflex during intubation.[19] Further progress in tracheal intubation was made when in 1913 Jackson invented the first anaesthetic laryngoscope which was subsequently modified by Magill, Miller and Macintosh. With the introduction of curare as a muscle relaxant during general anaesthesia, endotracheal intubation became routine in major abdominal and other surgeries.[19]

Tracheal intubation continues to be a popular means of securing the airways for procedures done under general anaesthesia in developing countries.[4] It is indicated in a wide range of procedures such as head and neck surgeries, surgeries in unusual position(e.g. prone and sitting), and during general anaesthesia with muscle relaxation and intermittent positive pressure ventilation.[20] It also serves to

protect the respiratory tract from inhalation of gastric contents in patients with a full stomach.[20]

Emergence from general anaesthesia with endotracheal intubation is frequently complicated with ETT-induced adverse effects such as bucking, coughing, restlessness and haemodynamic changes. These have been termed ETT-induced emergence phenomena.[3,10,16,18] Coughing and bucking (a more forceful and often protracted cough) are not only unpleasant in sight but can also be harmful.[5] Apart from increase in intrathoracic, intraocular and intracranial pressure, bucking also results in a decrease in Functional residual capacity (FRC.). Bucking, especially in paediatric patients, can rapidly cause hypoxemia, not only due to decrease in minute ventilation but also subsequent to the associated loss in lung volume and resultant atelectasis.[5]

Coughing during emergence from general anaesthesia is a common clinical problem,[8] with incidence ranging from 38% to 98%.[16] Estebe J.P et al,[16] in a randomised controlled study of 60 adult patients, whose ETT cuff was inflated with air(control group) and different concentrations of alkalinized lidocaine(group 2&3), demonstrated a 70% incidence of

coughing in the control group at emergence from general anaesthesia.

Desalu et al,[4] reported a 34% incidence of coughing on tracheal extubation in a randomised study of 70 patients aged 18-60 years, who had elective non-ophthalmic surgery at Lagos University Teaching Hospital. They also reported a rise in mean heart rate and mean arterial blood pressure. The mean intraocular pressure was increased by 50.3%.[4]

In another prospective controlled study that compared effects of tracheal intubation and extubation on intraocular pressure and haemodynamic parameters in paediatric patients scheduled for ophthalmic procedures, Madan et al also demonstrated increase in intraocular pressure and haemodynamic parameters on tracheal extubation.[21]

Various methods have been used to reduce or eliminate this phenomenon. These include the following;

Deep extubation (removal of the ETT when the patient is in the surgical (deep) plane of anaesthesia), prevents coughing at emergence from anaesthesia.[10] This has been demonstrated in a prospective randomized study involving

100 ASA 1 patients aged 1-4 years who had general anaesthesia for herniotomy and minor urologic procedures. In the study patients were randomized to be extubated either deep or awake after halothane anaesthesia. Result showed higher incidence of respiratory complications in patients extubated awake.[22] However, with deep extubation, the loss of protective airway reflexes and the risk of pulmonary aspiration constitute a major drawback.[10]

Esmolol has been used to attenuate haemodynamic response to tracheal extubation. Fuhrman et al,[23] compared the effects of esmolol and alfentanil on heart rate and Systolic Blood Pressure (SBP) during emergence and extubation in a randomized double-blind investigation of 42 healthy patients having elective surgery. Their patients received either a normal saline bolus followed by a normal saline infusion, a 5mg/kg alfentanil bolus followed by normal saline infusion, or a 500μg/kg esmolol bolus followed by a 300μg/kg/min esmolol infusion when end tidal isoflurane levels were 0.25% or less. Only esmolol bolus dose with subsequent infusion of esmolol significantly controlled the heart rate and SBP response to emergence and extubation.[23] In another study

involving 40 ASA grade 1 and 11 patients scheduled for elective surgery, patients received either esmolo(1.0mg/kg, 1.5mg/kg, or 2mg/kg) or normal saline intravenously in a randomized fashion 2 to 4 minutes prior to extubation. While all doses of esmolol controlled the heart rate response to extubation, 1.0m/kg of esmolol did not attenuate increases in SBP whereas 1.5mg/kg and 2.0mg/kg did. The largest dose of esmolol resulted in significant hypotension and the authors recommended 1.5mg/kg as the best dose to control haemodynamic response to tracheal extubation.[5] For a developing country, cost implication and the availability of esmolol injection and esmolol infusion will be a limiting factor to its use.

Since coughing at emergence resulted, at least in part, from irritation of the tracheal mucosa by the ETT, It seems reasonable to consider topical application of lidocaine to the tracheal mucosa in contact with the ETT as a means of increasing ETT tolerance.[8] Gonzalez et al,[8] in a randomised double-blinded controlled study of 75 adult patients demonstrated a significant reduction in coughing when topical lidocaine was applied on the trachea through a

modified ETT(called “The laryngotracheal instillation of Topical Anaesthesia; LITA”).[8] The decrease in the incidence of coughing was more when compared to the use of iv lidocaine. Also in another double blinded study involving 46 patients requiring elective surgery, who had either 4% lidocaine, saline or nothing instilled through the LITA 30 minutes before extubation, 75% had complete cough suppression in lidocaine group, compared to 14% in saline group and 13% in the control.[24] However cost implication and the availability of the modified ETT is a limitation to this method.[8]

Lidocaine spray and lidocaine jelly application on the surface of the ETT cuff failed to improve ETT tolerance,[18] rather it increased the incidence of coughing and ETT cuff rupture.[18] This is because the pH of lidocaine in the spray and jelly is about 5, which is irritating to the tracheal mucosa.[16] This was demonstrated by Kori et al in a study that evaluated the severity of postoperative sorethroat and the incidence of hoarseness in 60 patients after tracheal intubation, an increase in VAS(visual analogue scale) score was seen when

lidocaine jelly and lidoaine spray are applied on the distal end of the ETT prior to endotracheal intubation.[25]

Another method that has been used to suppress the cough reflex is by the administration of intravenous lidocaine before tracheal extubation.

Intravenous lidocaine in doses of 1-2mg/kg produces a plasma level of 3μg/ml which can suppress coughing and other airway reflexes. In a study carried out by Yukioka et al, 100 patients aged 60 and above received a placebo or either 0.5mg/kg, 1.0mg/kg, 1.5mg/kg or 2.0mg/kg lidocaine intravenously 1 minute before tracheal intubation. The incidence of coughing decreased as the dose of lidocaine increased.[26] Also in a more recent study, 120 patients who had elective surgery were assigned into 3 groups depending on if they received intravenously either saline, 0.5mg/kg, 1mg/kg or 2mg/kg lidocaine 1 minute after beginning of spontaneous respiration, at emergence from general anaesthesia. The incidence of coughing was significantly less in the lidocaine group, while sedation score was highest in the 2mg/kg lidocaine group.[27]

The duration of action of intravenous lidocaine is short (5-20minutes).[10] This narrow antitussive window makes the optimal time of administration during emergence difficult.[10] Intravenous lidocaine as well as intravenous opioids have sedative effect and therefore results in delayed emergence from general anaesthesia.[10] They also depress the swallowing reflex and may permit pulmonary aspiration.[28] To achieve the simultaneous goal of cough suppression and full awakening with intact supraglottic reflexes, better techniques are needed.[10]

The use of intracuff lidocaine have proved to be a better technique. In a randomised study involving 80 patients aged 18 years and above, scheduled for elective surgery lasting between 60-120 minutes, Zamora et al,[29] demonstrated greater reduction in the incidence of coughing at emergence from general anaesthesia in the group that received intracuff lidocaine compared to those that receive intravenous or topical lidocaine.[29]

In another prospective randomised, double blinded study of 63 patients undergoing elective surgery with endotracheal intubation, Fagan et al in Dublin demonstrated a decrease in

the incidence of coughing during extubation when the ETT cuff was inflated with 4% lidocaine when compared to inflation with saline or air.[3]

Also in a study in India, 75 patients with a history of hyperactive airway disease who received general anaesthesia with endotracheal intubation for ophthalmic procedures were divided into 3 groups depending on whether air, saline or alkalinized lidocaine was used to inflate the ETT cuff. Results showed that extubation was smooth in the alkalinized lidocaine group and the incidence of sorethroat was also found to be lower in this group.[30]

Furthermore in 2009, Tanaka et al,[31] conducted a Cochrane systematic review of randomized controlled studies of topical and systemic lidocaine therapy for preventing coughing and postoperative sorethroat after endotracheal intubation, which showed that topical and systemic lidocaine reduced the prevalence and severity of respiratory complications after general anaesthesia with endotracheal intubation. The review involved 12 studies in which a total of 1232 patients participated, with 672 of them allocated to lidocaine therapy and 560 to the control group. The route of administration of

lidocaine in the studies included in the review, include the use of various concentrations of lidocaine in the cuff of the endotracheal tube, intravenous lidocaine, lidocaine spray and gel on the endotracheal tube.[31]

PATHOPHYSIOLOGY OF ETT-INDUCED COUGHING AND HAEMODYNAMIC CHANGES

The exact pathophysiological basis of ETT-induced coughing and haemodynamic changes is yet to be fully elucidated.[32] However, as with the pressor response to laryngoscopy and intubation, it is believed to be a reflex sympathetic and sympatho-adrenal response to airway stimulation or irritation.[1]

Lowrie and colleagues studied 12 patients undergoing major elective surgery and demonstrated increase in heart rate and plasma concentration of adrenaline after tracheal extubation.[33]

Irritation in the upper respiratory tract causes a reflex motor response.[2] The receptors in the upper respiratory tract include slowly adapting (stretch) receptors, and rapidly

adapting (irritant) receptors which are activated briefly by light, dust, chemical stimuli and cold air. It is the rapidly adapting receptors that are responsible for the cough reflex. These receptors are thought to consist of free nerve endings ramifying among epithelial cells.[2] Their afferent impulse run in the vagus nerve via the superior laryngeal branch which carries afferent from within the upper larynx. The central reflex site is in the medulla, and the efferent impulse are carried in the vagus to the laryngeal muscles, and appropriate nerves to the respiratory muscles.[2] Coughing is a complex muscular event. It consist of an initial laryngeal opening, followed by a closure of both the glottis and the supraglottic structures, these structures then open and vibrate moving the epiglottis forcefully backwards and forward.

Increasing age is associated with a reduction in the population of nerve endings of the irritant receptors and this combined with the thickening that occurs in the mucosa of the upper airways causes a reduction in sensitivity to irritant stimulus. Also a decrease in amplitude of electrical potential in superior laryngeal nerve with increasing age(possibly

caused by degenerative changes in sensory neurons of the vagal ganglion) contributes to the reduction in airway sensitivity in the elderly.[34] In a study by Erskine et al involving 102 healthy, non-smoking volunteers, a single measurement of sensitivity was made in each subject using a system delivering small concentration of ammonia vapour for single intermittent breaths to the upper airways and recording glottic closure using an inspiratory pneumotachograph. A decrease in upper airways reflex sensitivity with increasing age was found.[34] The sensitivity of the reflex is also reduced by local anaesthesia of the airways.[34]

Upper airway sensitivity is increased in certain diseases such as asthma, allergic rhinitis, chronic bronchitis and emphysema. This hyperactivity refers to the ease with which the reflexes are elicited and the degree to which it occurs. The reflex response occurs with a lower level of stimulus and in increased magnitude compared to normal individuals. In these disease conditions, damage to epithelium results in removal of epithelial barrier thus allowing greater access to subepithelial receptors by irritant stimulus.[35]

Another pathophysiological mechanism is tracheal mucosal damage. It has been shown that tracheal mucosal damage elicits the cough reflex.[36] Elevated cuff pressure greater than tracheal capillary pressure of 30cmH_2O causes tracheal mucosa ischemia, ciliary loss, inflammation, ulceration and tracheal stenosis.[36] Hence ETT cuff pressure of less than 30cmH_20 have been recommended for safe prolonged intubation.

Digital palpation of the ETT pilot balloon as a means of estimating cuff pressure is unreliable. This was demonstrated by Sathiskumar et al in Northwest England in an audit involving 30 anaesthesized and 30 critically ill patients, in whom adequacy of cuff inflation was by palpation of their pilot balloon. They recorded a mean cuff pressure of 62cmH_20 in the anaesthesized group and 43cmH_20 in the critically ill group. ETT cuff pressure was above 100cmH_20 in 27% of the patients. They recommended routine measurement of cuff pressure in anaesthesized and critically ill patients.[37] Other methods used to avoid over inflation of the ETT cuff include minimal occlusive volume and minimal

leak volume. However minimal leak volume has been associated with some degree of pulmonary aspiration.[38]

During general anaesthesia with nitrous oxide, it easily diffuses into the ETT cuff thereby causing a rise in intracuff pressure, mucosal damage and coughing on emergence from general anaesthesia.[32,36] Filling the ETT cuff with saline prevented this process thus leading to a decrease in the incidence of emergence complications.[32]

This was demonstrated in a study by Combes et at, in which 50 patients who received general anaesthesia maintained with nitrous oxide had the cuff of their ETT inflated with either saline or air.[32] Furthermore when nitrous oxide was used to inflate the cuff, cuff pressure did not rise and there was a reduction in the incidence of coughing and sorethroat after extubation, as demonstrated by Kasarawa et al in a prospective randomised study of 125 patient whose ETT cuff was inflated with various concentration nitrous oxide and air as control group.[39]

Also, the quality of tracheal intubation contributes to laryngeal morbidity. Excellent intubation conditions are less frequently associated with postoperative airway sequelae. In

a randomised study of 80 patients who received propofol/fentanyl induction, 40 of them were intubated with atracurium while the remaining 40 were intubated without atracurium, Mencke et al showed that postoperative hoarseness and vocal cord sequelae were higher when atracurium was omitted.[40]

Obesity is another condition which may predispose patients to laryngeal morbidity during endotracheal intubation and later cause coughing and sore throat postextubation. Obesity has a direct effect on the mechanical behaviour of the respiratory system by altering lung volume and airway calibre. Schachter et al in Australia, in an epidermiological study involving 1971 white adults aged 18-73 years demonstrated a high occurance of wheezing and shortness of breath in the severely obese.[41]

Also, Juvin et al using the IDS (Intubation difficulty scale) in a study involving 134 lean and 129 obese patients showed that intubation difficulty was more common in the obese patient (15.5%) than in the lean patients (2.2%).[42]

Other disease conditions that have been shown to affect haemodynamic response to tracheal intubation and extubation include diabetes mellitus and hypertension. In a study involving 10 non-diabetic and 10 diabetic patient who

had abnormal autonomic function when tested on the day before surgery, Vohr et al,[43] demonstrated an exaggerated pressor response to tracheal intubation. They found a greater increase in heart rate, mean arterial pressure and vascular resistance in the diabetic group, which may reflect the autonomic dysfunction.[43]

In another study, involving 16 patients with untreated and 20 patients receiving antihypertensive therapy up to the day of surgery, Greene et al, demonstrated an increase in the haemodynamic response to intubation and extubation in the untreated group.[44]

It has also been shown that anterior neck, cervical spine and maxillofacial surgeries may cause a disruption of venous and lymphatic drainage leading to the development of pharyngolaryngeal edema or cervical haematoma which will predispose patients to respiratory complications at extubation.[5]

MECHANISM OF ACTION OF ALKALINIZED INTRACUFF LIDOCAINE ON ETT-INDUCED COUGHING AND HAEMODYNAMIC CHANGES

Lidocaine the first amino amide – type local anaesthetic, was first synthesied under the name xylocaine by Swedish chemist Nils Lofgren in 1943.[45] It was first introduced as a local anaesthetic in 1947.[46] It revolutionized regional anaesthesia because of its superior safety margin to previous agents used as local anaesthetic. Lidocaine became the standard drug against which other local anaesthetic are compared.[46] Its kpa is 7.9, and it is 65% protein bound. Its maximal recommended dose is 3mg/kg without adrenaline and 7mg/kg with adrenaline.[46] Its toxic plasma level is above 10µg/ml.[46]

Lidocaine produces reversible blockade of neural transmission in autonomic, sensory and motor nerve fibres.[46] It binds to fast sodium channels in the axon membrane from within, preventing sodium entry during depolarization. The threshold potential is thus not reached and the action potential of the nerve not propagated.[46]

Endotracheal tubes are constructed from polyvinyl chloride membrane, which is primarily a hydrophobic plastic.[3] The thin polyvinyl chloride membrane which constitute the tubes cuff, allows simple diffusion of lidocaine across it.[3] Because

the coefficient of diffusion and the thickness of the material can be assumed to be standard across a specific range of ETTs, the limiting factor in the diffusion process are lidocaine concentration and time.[3]

The diffusion mechanism through the cuff membrane can be compared to the mechanism of diffusion in the epidural space.[10,21] Local anaesthetic applied to the nerve membrane exist in two forms; non-ionized free base and ionized cation.[10] An increase in the non-ionized fraction of the local anaesthetic results in improved nerve penetration and more rapid onset of blockade.[10] It is therefore reasonable to speculate that an increase in the non-ionized fraction may prompt local anaesthesia to diffuse more rapidly across an ETT cuff.[10] The proportion of the drug that is uncharged also depends on the pka, i.e. its dissociation constant, which is temperature dependent.[10] As a local anaesthetic is warmed, the pka decreases and the proportion of uncharged drug available for action increases.[10] Therefore alkalinisation and warming are two techniques frequently used to increase the proportion of uncharged drug.[10]

In an in vitro and in vivo study Estebe et al,[16,18] demonstrated diffusion of lidocaine across ETT cuff. In the in vitro study, 2ml of 2% lidocaine with 8, 12 and 15ml of 8.4% $NaHCO_3$ was placed inside a high volume low pressure cuff. Release of lidocaine from the ETT cuffs was measured by means of a spectrophotometer.

In another in vitro study, Huang et al,[10] demonstrated by the use of gas chromatography that lidocaine diffuses across the wall of ETT cuffs. They also showed that alkalinisation with or without warming, but not warming alone, promotes lidocaine diffusion from ETT cuffs.[10] These studies also showed that lidocaine alone has a low diffusion rate across an ETT cuff.(1% released during a 6-hour period). Addition $NaHCO_3$ resulted in a 63-fold increase in the diffusion of lidocaine across the ETT cuff.[47] Without alkalinization, high doses of lidocaine (about 500mg) intracuff, will be needed to produced clinical effects(reduction in ETT induced coughing and haemodynamic changes), but this could be dangerous if the cuff ruptures.[18] Cuff rupture in this instance, will lead to absorption of greater than maximal safe dose of lidocaine(3mg/kg), which may predispose to systemic toxicity. Also

there will be air leakage from the trachea during intermitent positive presure ventilation.

Alkalinization of lidocaine allows the diffusion of 65% (in a 6 hour period) of the neutral base form of lidocaine through the hydrophobic structure of the ETT cuff. This makes it possible to use a low dose of lidocaine (40mg) intracuff to produce the desired clinical effect.[18]

In another in vitro study by Jaichandran et al, using high performance liquid chromatography, it was found that the time interval needed for the releases of the minimum concentration of lidocaine required to block the cough receptors (using a mixture of 6mls 2% lidocaine and 0.5% $NaHCO_3$) was around 90minutes.[48]

The toxicity of a local anaesthetic must be considered regardless of the route of administration.[3] In this regard, concerns with use of alkalinized intracuff lidocaine are two folds; the risk of systemic absorption and the consequence of ETT cuff rupture.[3] Estebe et al,[16] reported that in a pharmacokinetic study, lidocaine diffusion via an ETT cuff with alkalinized 40mg lidocaine gave a very small plasma concentration of lidocaine (Cmax < 0.08µg/ml).[16] This

concentration is smaller than with topical lidocaine(0.43-1.5μg/ml) or with iv lidocaine (2-3μg/ml).[16]

Also lidocaine diffusion via the ETT cuff is time-dependent and thus it is presumed that plasma levels will rise more slowly than after direct topical application, thus reducing the risk of systemic toxicity.[3] Systemic toxicity under general anaesthesia will manifest as bradycardia, hypotention, arrhythmias, seizures, respiratory depression or cardiac arrest. With the airways secured by endotracheal intubation, treatment of this condition will include increase in fractional inspired oxygen concentration, mechanical ventilation, use of intravenous fluids and vasopressors to correct circulatory failure. Chest compression is commenced if cardiac arrest occurs, while seizures is aborted with intravenous thiopentone.

Alkalinization increases the pH of lidocaine close to physiological pH hence the risk of mucosal irritation is reduced in the event of ETT cuff rupture.[16] Interestingly, the incidence of ETT cuff rupture is rare.[16]

CHAPTER FIVE

PATIENTS AND METHODS

STUDY LOCATION

The study was carried out on adult patients who had general anaesthesia with endotracheal intubation at University of Nigeria Teaching Hospital, Enugu. It is a 700 bedded tertiary hospital located in south east Nigeria.

ETHICAL APPROVAL

Ethical clearance for the study was obtained from the hospital Ethics Committee.

SAMPLE SIZE

Sample size calculation was based on previous studies. The incidence of coughing in the study by Estebe et al,[16] (Alkalinization of intracuff lidocaine and gel lubrication protect against tracheal tube-induced emergence phenomena) was 70%.

Under the null hypothesis of no difference in the incidence of coughing between two groups, the null proportion will be 50%.[49]

To calculate the sample size with a significance level of 5% and power of study of 80%, the following formula was used.[49]

$$N > \frac{[u\sqrt{\pi(1-\pi)} + v\sqrt{\pi_o(1-\pi_o)}]^2}{(\pi-\pi_o)^2}$$

Where n= required minimum sample size

π = proportion of interest =70% (0.7)

π_o = null hypothesis proportion = 50% (0.5)

u = power of study, 80% = 0.84

v = significant level of 5% = 1.96

$$n > \frac{[\ 0.84 \times \sqrt{0.7(\ 1-0.7)} + 1.96 \times \sqrt{0.5(\ 1-\ 0.5)}]^2}{(0.7-\ 0.5)^2}$$

$n > 1.860/\ 0.04 = 46.5$

About 46 patients were required in each group.

PATIENT SELECTION

After obtaining approval of the hospital ethics committee, and written informed consent, about 200 American Society of Anaesthesiology (ASA) physical status 1 or 11 adult patients were enrolled in a prospective double blinded randomized study.

Inclusion criteria :

A. Type of procedure; Elective gynaecological, orthopaedic, urological, plastic, and general surgical procedures.

B. Age range; 18 – 60 years.

C. BMI Status; less than 30.

D. ASA Status; 1 or 2.

E. Mallampati Status; 1 or 2.

Exclusion criteria :

A. History of allergy, asthma and smoking.

B. History of previous laryngeal or tracheal surgery or pathology.

C. Patients with predicted difficult intubation.

D. Patients with raised intracranial pressure.

E. Patients with active upper respiratory infection.

F. Patients with hypertension and diabetes mellitus.

G. More than 1 attempt at endotracheal intubation.

H. Surgery lasting less than 1 hour.

I. Procedures requiring insertion of nasogastric tube.

J. Anterior neck, cervical spine, oral and maxillofacial surgeries.

Randomization

Patients belonged to one of 4 groups; air, saline, plain lidocaine or alkalinized lidocaine. These substances were used to inflate the ETT cuff. Equal number of cards marked A, B, C, D representing each of the 4 groups, placed in sealed brown envelopes was put into a box and shuffled. The total number of sealed envelopes was equal the sample size plus attrition (200). Patients belonged to the group they picked from the box of sealed brown envelopes.

Blinding

The assistance of colleagues (fellow anaesthetists) was obtained. The set of anaesthetists who intubated and extubated the patients were different from those who collected the patients data. Both those who collected data and the patients enrolled for the study were unaware of the agent used to inflate the cuff of the endotracheal tube.

PREOPERATIVE MANAGEMENT AND ANAESTHESIA

All patients were seen and reviewed the evening before surgery. Demographic data was obtained and history taken to determine those that will be included or excluded. General and systemic examination was carried out and BMI calculated from patient́s height and weight. Airway assessment and Mallampati scoring was done to exclude the likelihood of a difficult intubation. Those who qualified to be included in the study were then subjected to sampling. Routine preoperative fasting was instituted, and all patients were premedicated with 10mg oral diazepam 1-2 hours before surgery to allay their anxiety. In the theatre, monitoring of heart rate (HR), non-invasive blood pressure (NIBP),Mean arterial pressure (MAP),Electrocardiograph (ECG) and Oxygen saturation ($Sp0_2$) was obtained using DAS 4000 Multi-parameter Monitor

(G.E. Medical Systems Information Technologies, Inc, Wisconsin, U.S.A).

The above mentioned vital signs were monitored at 5 minutes interval and recorded on the patient´s anaesthetic chart. Intravenous access was established with a wide bore cannula and maintained with normal saline. Antisialogogue (atropine 0.02mg/kg) and antiemetic (metoclopramide 10mg) was administered intravenously as a prophylactic against excessive secretions and post operative nausea and vomiting respectively. Patients were pre-oxygenated with 100% oxygen via face mask. Anaesthesia was induced with a sleep dose of sodium thiopentone, 5mg/kg and end point determined by lack of response to verbal contact. Succinylcholine 1.5mg/kg was administered to facilitate direct laryngoscopy and the trachea intubated with the appropriate size low pressure high volume ETT, whose cuff integrity has been assessed prior to use. Correct placement was confirmed by chest auscultation for equal breath sounds on both lung fields, and by capnography.

For the air group, ETT cuff was inflated with air up to the minimal occlusive volume (i.e. no air leaks detected under controlled

ventilation). While for the normal saline group, normal saline was used to inflate the ETT cuff up to the minimal occlusive volume.

For the plain lidocaine group, ETT cuff was inflated with 2ml of 2% lidocaine (40mg) and sterile water added up to the minimal occlusive volume. While for the alkalinized lidocaine group, ETT cuff was inflated with 2ml of 2% lidocaine(40mg) and 8.4% sodium bicarbonate added up to the minimal occlusive volume. The volume used to inflate the cuff was recorded.

Anaesthesia was maintained with isoflurane in oxygen via a circle breathing system and intermittent positive pressure ventilation commenced after muscle relaxation had been instituted with pancuronium 0.08mg/kg. Ventilation was adjusted to maintain normocapnia. Analgesia was maintained with intravenous morphine 0.1mg/kg. Intravenous fluid (crystalliods) was given to take care of fluid deficit, maintanance, ongoing loss and third space loss. Fluid deficit and maintanance was calculated based on 4,2,1 (ml/kg/hour) rule.

At the end of surgery, isoflurane was discontinued and residual neuromuscular blockade reversed with neostigmine 0.04mg/kg and glycopyrrolate 0.2-0.4mg, when spontaneous respiration began. Baseline pre-extubation HR, NIBP, $Sp0_2$ were recorded.

Gentle pharyngeal toileting was performed and ETT removed when the following criteria are met; Spontaneous ventilation with tidal volume greater than 300ml (which was displayed on the ventilator monitor." Drager Fabius"), the ability to respond to verbal command or demonstration of purposeful movement. After extubation, HR, SBP, DBP, MAP and SpO_2 values were recorded at 1, 2 ,4 ,6, 8 and 10 minutes respectively. The volume of air or fluid aspirated from the ETT cuff during extubation was recorded. The number of episodes of coughing from the time spontaneous ventilation began, to 30 minutes post extubation was recorded.

Coughing was taken to include bucking (defined as a more forceful and protracted cough), and a true cough. The patient was then transferred to the recovery room.

Sore throat was evaluated at the time of discharge from recovery room and 24hours post extubation using visual analogue scale (0-100 mm).

The data collection form was used to document patients characteristics.

The primary outcome measure was the incidence of coughing. Secondary outcome measures were the incidence of sore throat and haemodynamic changes.

STATISTICAL ANALYSIS

Data collected was presented as tables and graphs. They were analysed with the aid of a computer analytical package; Statistical package for social sciences (SPSS®15 Inc Chicago Illinois).The sampled population's gender, ASA Physical status, Mallampati score, occurance of cough and sore throat was presented as frequencies and percentages and were analysed using chi squared test. Patient's Age, Weight, Height, Haemodynamic parameters and duration of anaesthesia was reported as mean ± standard deviation. They were analysed using ANOVA test. The volume of substance used to inflate the ETT cuff and volume aspirated at extubation were analysed using Mann-Whitney test and Wilcoxon test. A p value of less than 0.05 was accepted as statistically significant.

CHAPTER SIX

RESULTS

Fifty patients were recruited and completed the study in each of the 4 groups. Table 1 shows Age, Weight and Height distribution of the patients. There was a significant difference in age and weight distribution among the groups.($P<0.05$), while there were no difference in the height distribution.($P>0.05$).

The mean duration of anaesthesia in the air, saline, plain lidocaine and alkalinized lidocaine groups were 121±48, 128±55, 111±59 and 124±43 minutes respectively showing no significant difference among the four groups ($P>0.05$).

The mean volume of substance used to inflate the ETT-cuff were 6.15 ± 0.70ml, 6.46 ± 0.48ml, 6.20 ± 0.78ml and 6.60 ± 0.56ml in the control, saline, plain lidocaine and alkalinized lidocaine groups respectively. While the mean volume aspirated were 6.11 ± 0.74ml, 6.38 ± 0.50ml, 6.06 ± 0.72ml and 6.04 ± 0.60ml in the air, saline, plain lidocaine and alkalinized lidocaine groups respectively. There were no significant difference between the volume used to inflate the cuff and the volume aspirated among the groups. ($P>0.05$).

Table 2 shows gender distribution of patients. There were no significant difference in the gender distribution.(P>0.05). Similarly, there were no significant difference in ASA Physical status and Mallampati score of the sampled population as shown in tables 3 and 4 respectively.(P>0.05).

Coughing occurred least in the alkalinized lidocaine group. Only 15 patients (30%) had cough in this group. In the air and plain lidocaine groups coughing occurred in 29 (58%) patients each, while in the saline group it occurred in 30 patients (60%). Overall there was a significant difference in the incidence of coughing among the 4 groups (P<0.05). Table 5.

The incidence of sore throat recorded at the recovery room followed a similar pattern to that of coughing. It occurred in 8 patients (16%) in the alkalinized lidocaine group while in the air, saline and plain lidocaine groups it occurred in 18 patients(36%), 21 patients(42%) and 20 patients(40%) respectively. This showed a significant difference among the 4 groups.(P<0.05) Table 6.

After 24 hours sore throat occurred in 16 patients (32%) in the air group, 14 patients (28%), 18 patients (36%) and 13 patients (26%) in the saline, plain lidocaine and alkalinized lidocaine groups

respectively. Compared among the 4 groups there were no significant difference.(P>0.05) Table 7.

Tables 8 – 11 shows Post Hoc test of ANOVA, of mean HR, SBP, DBP, and MAP changes from baseline(time 00) to 1st, 2nd, 4th,6th,8th, and 10th minute respectively. Mean values in each time category are grouped and the different groups given superscript ($^{a-d}$) in descending order from the largest mean to the smallest mean. Significant difference occurs between values with different superscript while values sharing similar superscript have no significant difference.

Table 8 shows mean HR changes. In the air group, it changed from 98.38±15.21^{c} to 107.00±20.52^{ab} in the 1st minute, a significant increase. In the 2nd minute it was 110.40±19.14^{a} which is not a significant increase from 107.00±20.52^{ab}. At the 6th minute mean HR dropped to 90.50±13.62^{c} which is similar to baseline level of 96.38±15.21^{c}. In saline group mean HR increase from 89.20±11.73^{b} to 96.16±13.10^{a} and 97.34±15.93^{a} in the 1st and 2nd minute and then declined in the 4th minute to 86.86±13.23^{bc} which is similar to baseline value of 89.20±11.73^{b}. In the plain lidocaine group mean HR did not show significant changes in the 1st, 2nd and 4th minute. Baseline value of 107.86±21.68^{bc} was similar to 1st minute value of

115.70±18.44^{ab} which was also not different from 4th minute value of 112.92±20.50^{abc}. Similarly, in the alkalinized lidocaine group, baseline mean HR of 102.38±16.92^{a} was not different from 1st minute value of 100.00±15^{ab}. At the 2nd minute there was a significant decline in mean HR to 97.36±14.28^{cd}. Overall the changes in mean HR was significant in all groups.($P<0.05$).

Similarly, blood pressure changes accompanied tracheal extubation in all the groups. Table 9 shows mean SBP changes overtime post extubation. In the air, saline, and plain lidocaine groups there were significant increases in mean SBP which peaked in the 4th minute post extubation unlike in the alkalinized lidocaine group were baseline mean SBP of 131.46±10.11^{a} was not different from 130.16±10.61^{ab} seen in the 1st minute. Thereafter in the 2nd to 10th minute, there was a significant decline in mean SBP. Overall, changes in mean SBP overtime was significant in all the groups. ($P<0.05$).

Tracheal extubation also affected the diastolic blood pressure in all the groups, and as with systolic blood pressure, the changes peaked in the 2nd minute Post extubation in air, saline and plain lidocaine groups before declining to baseline values. Table 10 (Fig 3).

In air group it increased from 81.94±11.43^{cd} to 90.46±15.38^{b} in the 1st minute and further to 98.96±12.45^{a} in the 2nd minute before declining to 83.54±11.31^{c} in the 6th minute. In saline group the increase in the 1st and 2nd minute (88.82±12.86^{a} and 86.66±13.27^{ab}) were similar. Again in plain lidocaine group it moved and peaked in the 2nd minute from 82.92±10.77^{c} to 94.66±13.12^{a}, but in the alkalinized group, 1st and 2nd minute values of 82.82±10.02^{ab} and 82.80±8.71^{ab} was no different from the baseline value of 83.70±9.30^{a}. Overall the mean DBP changes overtime was significant in all group (P<0.05).

Similarly, changes were recorded in the means of MAP in all the groups over time. Table11 (Fig 4). The mean values of MAP showed significant increase in the 1st and 2nd minutes post extubation, in the air, saline and plain lidocaine groups, while in the alkalinized lidocaine group,1st and 2nd minute values were similar to baseline value with a decline recorded after the 6th minute post extubation. Significant changes occurred in all the 4 groups up to the 10th minutes post extubation (P<0.05).

Mild laryngospasm with oxygen saturation less than 94% occurred in 3 patients in the saline group and 1 in the control (air) group. The all resolved with the administration of 100% oxygen. Except

for Sinus tachycardia, no abnormal ECG tracing was reported in any of the groups.

Table 1. Demographic Data of patients in the 4 groups and the P- values when compared to the control group

Demographic Variables	Air Group (n=50).	Saline Group (n=50)	Plain lidocaine (n=50)	Alkalinized lidocaine (n= 50)	P.values
Age(years)	40±13	34±9	35±11	*42±12	0.001
Weight(Kg)	64±6	*67±6	64±5	64±6	0.019
Height(m)	1.69±.04	1.69± 0.06	1.67± 0.051	1.67± 0.06	0.073
Duration of Anaesthesia	121±48	128±55	111±59	124±43	0.399

(minutes)

Table 2: Crosstabulation for Gender

GROUPS	MALE	FEMALE	TOTAL
Air group	23 (46%)	27(54%	50(100%)
Saline Group	21(42%)	29(58%)	50(100%)
Plain Lidocaine Group	23(46%)	27(54%)	50(100%)

Alkalinized Lidocaine Group	23(46%)	27(54%)	50(100%)
Total	90(45%)	110(55%)	200(100%)

P value = 0.970

Table 3: Crosstabulation for ASA Physical Status

GROUPS	ASA 1	ASA 2	TOTAL
Air group	26(52%)	24(48%)	50(100%)
Saline Group	26(52%)	24(48%)	50(100%)
Plain Lidocaine Group	24(48%)	26(52%)	50(100%)
Alkalinized Lidocaine Group	23(46%)	27(54%)	50(100%)

Total	99(49.5%)	101(50.5%)	200(100%)

P value = 0.910

Table 4: Crosstabulation for Mallampati Score

GROUPS	MAL.1	MAL.2	TOTAL
Air group	28(56%)	22(44%)	50(100%)
Saline Group	25(50%)	25(50%)	50(100%)
Plain Lidocaine Group	30(60%)	20(40%)	50(100%)
Alkalinized Lidocaine Group	26(52%)	24(48%)	50(100%)

Total	109(54.5%)	91(45.5%)	200(100%)

P value = 0.755

Table 5: Crosstabulation for Presence of Cough

GROUPS	YES	NO	TOTAL
Air group	29(58%)	21(42%)	50 (100%)
Saline Group	30(60%)	20(40%)	50(100%)
Plain Lidocaine Group	29(58%)	21(42%)	50(100%)
Alkalinized Lidocaine Group	*15(30%)	35(70%)	50(100%)

Total	103(51.5%)	97(48.5%)	200(100%)

P value = 0.006

Table 6: Crosstabulation for Presence of Sorethroat at recovery room

GROUPS	YES	NO	TOTAL
Air group	18(36%)	32(64%)	50 (100%)
Saline Group	21(42%)	29(58%)	50(100%)
Plain Lidocaine Group	20(40%	30(60%)	50(100%)
Alkalinized			

Lidocaine Group	*8(16%)	42(84%)	50(100%)
Total	67(33.5%)	133(66.5%)	200(100%)

P value = 0.022

Table 7: Crosstabulation for Presence of Sorethroat after 24hours

GROUPS	YES	NO	TOTAL
Air group	16(32%)	34(68%)	50 (100%)
Saline Group	14(28%)	36(72%)	50(100%)
Plain Lidocaine Group	18(36%)	32(64%)	50(100%)
Alkalinized Lidocaine Group	13(26%)	37(74%)	50(100%)

Total	61(30.5%)	139(69.5%)	200(100%)

P value = 0.707

Fig 1 Comparison of trends in mean heart rate response to extubation.

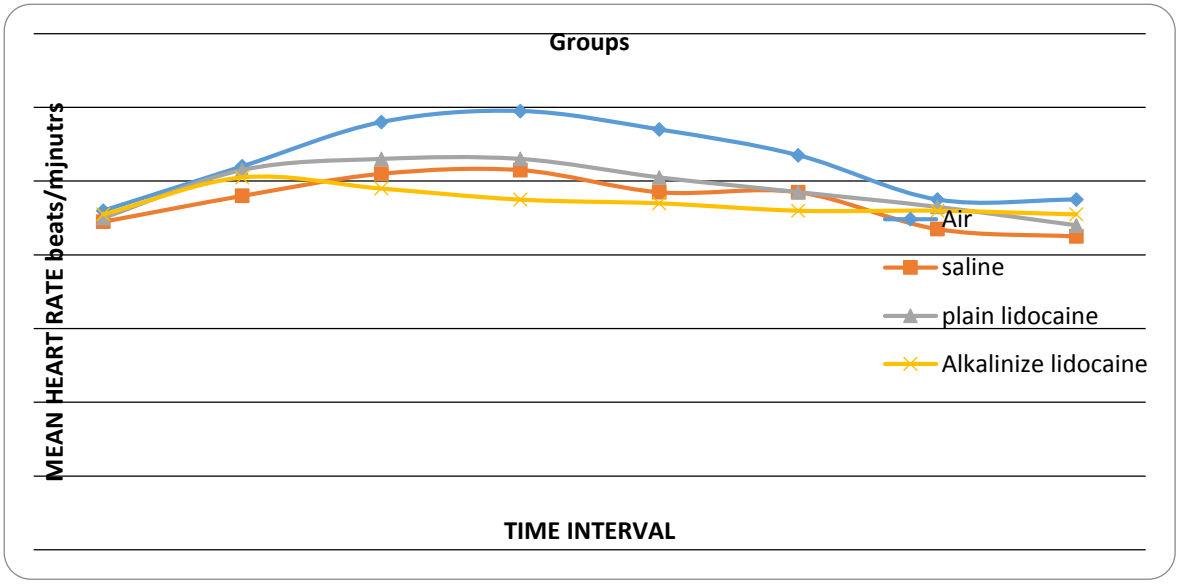


Fig 2. Comparison of trends in mean SBP response to extubation.

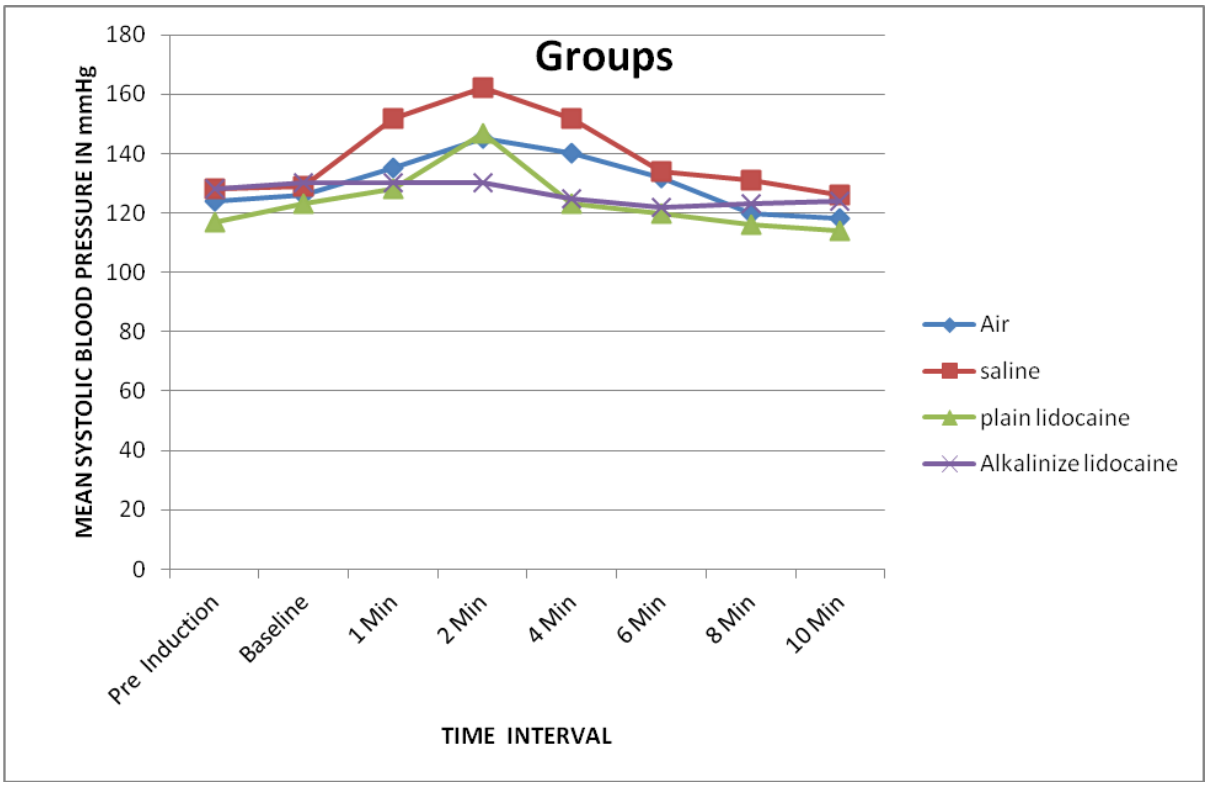


Fig 3. Comparison of trends in mean DBP response to extubation.

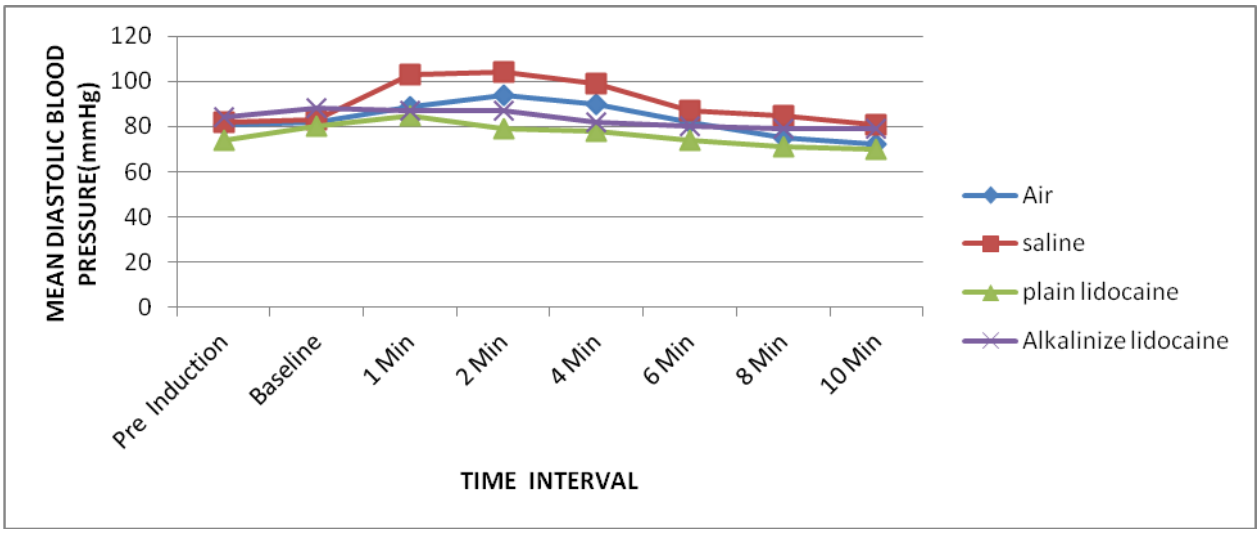
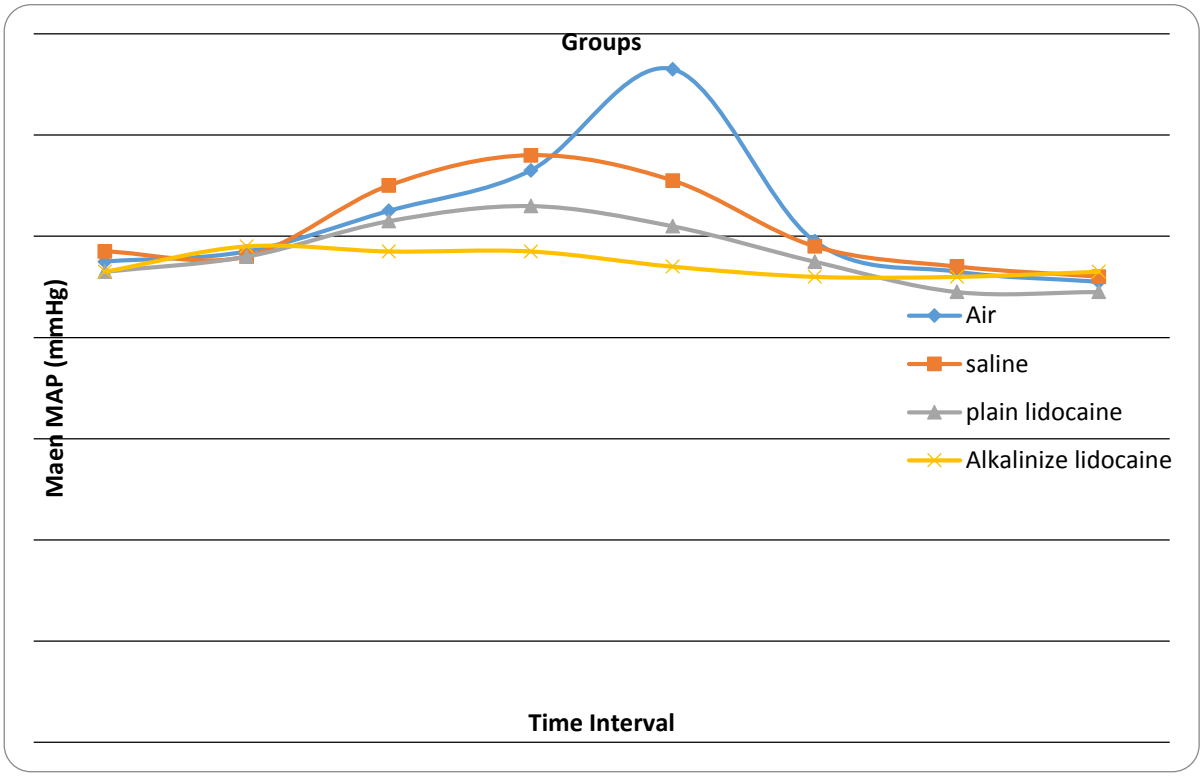


Fig 4 Comparison of trends in mean MAP response to extubation.



CHAPTER SEVEN

DISCUSSION

The main findings in this study were a decrease in the incidence of coughing, sorethroat and changes in haemodynamics at emergence from general anaesthesia when 40mg alkalinized lidocaine was used to inflate the ETT-cuff. This finding is similar to those in other studies conducted in other parts of the world,[15],[16,18] although a few variations in the intensity and duration of responses existed. This could be attributed to various type of anaesthetic agent and adjunts used. In one of their studies, Estebe et al,[18] in addition to the use of alkalinized intracuff lidocaine, applied a water soluble lidocaine gel to the ETT in the lidocaine groups prior to intubation and then compared the occurrence of sorethroat and haemodynamic changes with a control(air) group. Though the incidence of sorethroat was decrease in the alkalinized lidocaine group, there were no significant differences in heart rate and blood pressure among the groups. This may be as a result of the addition of lidocaine gel, as they have been shown to irritate the airways leading to coughing and haemodynamic changes.

In other to exclude as much as possible other factors that might predispose patients to coughing, sorethroat and haemodynamic changes at extubation other than airway manipulation, patients with history of smoking, allergy, respiratory tract infection, laryngeal pathology or surgery, which predisposes to airway hyperactivity,[35] were excluded from the study. This is due to the fact that in these patients, airway reflex responses occurs with a lower level of stimulus and in an increased magnitude compared to normal individuals. Also hypertensive patients were excluded as they are prone to increase in haemodynamic response to tracheal extubation.[44] Patients on nasogastric tube were also excluded, as its use during and after surgeries has been associated with an increased incidence of sorethroat.[36] Minute ventilation was adjusted to achieve normocapnia, while heart rate and blood pressure measurements were made with patients in supine position to prevent hydrostatic changes which might affect haemodynamics.

Despite the random assignment of patients used in this study, there turned out to be a difference in the mean age and weight of patients in the 4 groups. Whether these differences are of any clinical significance is unknown since the effect if any in patients

of the same age and physical status range, on ETT- induced coughing is unknown[8]

There was no significant difference in the mean duration of anaesthesia in all groups and this was well above the 60 minutes period required for sufficient amount of 40mg alkalinized lidocaine to diffuse through the ETT-cuff.[3]

The incidence of cough in the control (air) group was 58% which is within the range of 38 -96% reported in earlier studies.[8,16] This is however lower than the 70% demonstrated by Estebe J.P. et al.[16] This may be because of the difference in the type of cuff in the endotracheal tube used in their study. They used the high pressure, low volume cuff in contrast to low pressure high volume used in this study. With the high pressure low volume, the surface area available for diffusion of alkalinized lidocaine will be reduced. Also the pressure transmitted from the ETT – cuff to the tracheal mucosa will be more, resulting in a more likelihood of tracheal mucosal damage. The use of alkalinized lidocaine resulted in 28% reduction in the incidence of cough in this study. This is lower than the result obtained by Lais H.C. et al,[36] in which the incidence of cough was 44% in the control(air) group and 8% in the alkalinized lidocaine group, a 36% reduction[36]. The increase

could be due to the fact that N_20 was used in their study to maintain anaesthesia. N_20 is known to diffuse into the ETT-cuff when air is used to inflate the cuff resulting in increase in cuff pressure and thereby predisposing to an increase in Post extubation laryngeal morbidity .[32,36]

The result showed significant difference in the incidence of cough and sorethroat recorded in the recovery room between the 4 groups. ($P<0.05$). Similar result was also noted when alkalinized lidocaine group was compared with either the saline or the plain lidocaine groups. This showed that 40mg plain lidocaine did not permit enough diffusion of lidocaine through the ETT-cuff membrane to anaesthesize the trachea. The addition of 8.4% $NaHCO_3$ greatly enhanced the diffusion of 40mg lidocaine through the membrane of the ETT-cuff. This is in conformity with previous studies.[15] Estebe et al,[15] compared the incidence of sore throat among three group who received 40mg plain lidocaine, 40mg alkalinized lidocaine, with air as control group, and showed that there was a reduction in the incidence of sorethroat in the plain lidocaine group compared to the control and an even a further reduction in the alkalinized lidocaine group[15]. Hence the amount of plain lidocaine diffusing through the ETT-cuff was relatively less

compared to the alkalinized lidocaine. In this study, a significant difference in the incidence of sore throat recorded in the recovery room which was noted among the 4 groups, did not occur when sorethroat was assessed 24 hours later. This may be as a result of the duration of action of topical lidocaine on the trachea being less than 24 hours.

As in previous studies,[4,32,36] heart rate and blood pressure changes accompanied tracheal extubation, however the rise in mean heart rate, mean systolic blood pressure and mean diastolic blood pressure seen in the air, saline and plain lidocaine group peaked in the 2nd minute post extubation and thereafter declined to pre induction values, unlike in the study by Desalu et al[4] in Lagos where it peaked immediately after tracheal extubation. This may be as a result of difference in anaesthetic agents and adjuncts used, as in their study anaesthesia was maintained with halothane in 70% nitrous oxide and 30% oxygen. The residual effect of these agent in the emergence period may have resulted in more cardiovascular depression and analgesia and hence less haemodynamic changes than in this study where anaesthesia was maintained with isoflurane in oxygen.

Several studies,[32,36] have shown lower incidence of coughing and sorethroat when the cuff pressure is maintained below 30 cmH_20. This is because cuff pressure greater than 30 cmH_20 can cause tracheal mucosal congestion and oedema. Apart from measuring cuff pressure with a manometer, other techniques used to prevent cuff overinflation include the minimal occlusive volume and minimal leak volume. In this study, the minimal occlusive volume technique was used. Since the results of this study is similar to other studies were ETT-cuff overinflation was prevented by use of manometer.[18,32,36] It shows that minimal occlusive volume technique is also effective in preventing ETT-cuff overinflation.

As with the sympathoadrenal response to laryngoscopy and intubation haemodynamic changes accompanied endotracheal extubation[4,32,36] In this study, changes in HR, SBP, DBP and MAP were observed in all groups, however increases in these parameters over time post extubation were more marked in the air and saline groups than in the plain lidocaine group. This is due to the fact that with plain lidocaine, some diffusion of lidocaine from the ETT- cuff occurred though to a lesser extent than with alkalinized lidocaine.[15] While for the alkalinized lidocaine group HR, SBP, DBP and MAP tended towards immediate decline

towards pre induction values as a result of much more lidocaine diffusion from the ETT-cuff producing greater ETT tolerance.

The greatest increase in HR, SBP, DBP and MAP occurred in the 2nd minute post extubation in the air, saline and plain lidocaine groups, and was maintained above baseline values for 4 minutes. This is similar to the result obtained in the study by Desalu et al[4] in Lagos were the rise in heart rate was maintained for 5 minutes. In about the 6th minute post extubation, there were no significant difference with baseline values. No cuff rupture was recorded in this study as in previous studies.[16,36] This confirms that introduction of 40mg 2% plain lidocaine, or 40mg 2% alkalinized lidocaine is not deleterious to the ETT-cuff. Abnormalities in ECG tracing such as arrhythmias and bradycardia was not seen in any of the patients in this study. This shows that the risk of local anaesthetic toxicity with the use of 40mg intrcuff lidocaine is very low. This is due to the fact that lidocaine diffusion from the ETT-cuff with alkalinized 40mg lidocaine, results in a very small plasma lidocaine concentration.

CONCLUSION

Coughing and haemodynamic changes have been shown to complicate endotracheal extubation. Although these changes are transient and can be tolerated by majority of patients, however those who underwent neurosurgical, ophthalmic and vascular procedures may experience unfavourable sequelae such as raised intracranial pressure, intracranial haemorrhages, wound breakdown and myocardial ischemia. Several methods have been used to obtund these response, however with various setbacks.

The use of 40mg intra cuff alkalinized lidocaine is being advocated as a non-invasive, cost effective, relatively easy and safe technique. This study has confirmed the effectiveness of 40mg alkalinized intracuff lidocaine in reducing the incidence of coughing and haemodynamic changes at emergence from general anaesthesia. Bucking on the ETT and coughing post extubation results in an increase in heart rate and blood pressure. When 40mg alkalinized lidocaine is used to inflate the ETT cuff, it diffuses from the cuff and anaesthesize the trachea resulting in less bucking and coughing and subsequently less increase in heart rate and blood pressure.

LIMITATIONS

In this study, the exact pressure of the ETT-cuff after inflation was not measured due to unavailability of appropriate manometers to measure cuff pressure after inflation with air or liquid substances in the study centre. ETT-cuff overinflation was prevented by the use of minimal occlusive volume technique. Nevertheless, if there is rupture, there will be airway soilage.

Also serum levels of lidocaine was not measured in patients whose ETT-cuff was inflated with either plain lidocaine or alkalinized

lidocaine due to unavailability of High performance liquid chromatography in the study centre.

RECOMMENDATIONS

In patients who will undergo general anaesthesia with endotracheal intubation, the prevention of ETT induced coughing and haemodynamic changes following extubation should be given adequate attention in the practice of anaesthesia, especially in those patients at risk of severe adverse effects, i.e parturients with gestational hypertension, coronary artery disease, neurosurgical and ophthalmic surgery patients.

From this study the following are recommended

- In the absence of appropriate manometer to measure ETT-cuff pressure, minimal occlusive volume technique can be applied.

- Sodium Bicarbonate (Alkaline) and lidocaine should be readily available in the theatre for inflating the ETT-cuff in patients at risk of severe adverse effects.

- Adequate monitoring of heart rate, blood pressure and ECG should be continued even after patients have been extubated.

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APPENDIX 2

Data Collection Form

Study Title: **Evaluation of Effectiveness of Intracuff Alkalinized Lidocaine for attenuation of Endotracheal tube- induced coughing and haemodynamic changes during emergence from General Anaesthesia**

Date…… Patient's Group……

(A) <u>Patients Demographic Data</u>

1.Hospital number…… Type of surgery……

2. Gender ……

3. Age (in years)……

4. Weight(Kg)……

5. Height(Metres)……

6. BMI(Kg/m^2)……

(B) <u>Pre-anaesthetic information</u>

1. ASA physical status…… 2. Mallampati score……

3.Pre operative Vital signs. HR…… SBP…….DBP….. MAP……SpO_2…

(C)<u>Intra operative information</u>

Vital signs	Baesline	1 Minute	2 Minutes	4 Minutes	6 Minutes	8 Minutes	10 Minutes
HR							
SBP							
DBP							
MAP							

SpO_2							

Duration of Anaesthesia.....

Number of coughs from time spontaneous ventilation begins to 30 minutes post extubation.....

Volume of agent used to inflate ETT cuff..... Volume aspirated.....

Sorethroat at Discharge from recovery room.....24Hrs post extubation.....

Comment(s).....

APPENDIX 3

PATIENT INFORMED CONSENT

To the patient,

You have been selected to take part in a research which is proposed to study the use of alkalinized intrcuff lidocaine in attenuating endotracheal tube-induce coughing and haemodynamic changes.

Approval for this study has been obtained from the ethical committee of the hospital.

Information/Voluntary nature of participation:

In order to decide whether to be part of the study or not, you have to understand about the study and give an informed consent. Participation is completely voluntary, and you are free to withdraw from it at any stage of the study without any consequences. There will be no additional cost to you for being part of the study.

Purpose of the study

The purpose of the study is to see to what extent alkalinized lidocaine attenuates coughing and haemodynamic changes at emergence from general anaesthesia.

Description of study procedure:

To enable the surgeons carry out the surgical operation on you, we (anaesthetist) will give you drugs that will make you unconscious, remove your pains and make you unable to move any of your muscles. In this state, you will be unable to breath on your own,

therefore a machine (ventilator) will breath for you throughout the duration of the operation. To enable us connect you to the ventilator, a tube,(endotracheal tube) will be passed from your mouth into your wind pipe. Through this tube, oxygen and some gases will be passed into your lungs to enable you stay alive and unconscious. The tube has a ballon at its tail end that is usually blown up with air to ensure that secretions do not enter your lungs.

Sometimes, after surgery, when patients are waking up, the presence of the tube in their wind pipe makes them to cough. In this study we will use either air, saline, or a drug (Lidocaine or alkalinized lidocaine), depending on the group you will belong, to blow up the ballon instead of air. This drug will gradually seep out of the ballon into your wind pipe and help to prevent you from coughing.

Confidentiality

The information you give and your participation in the study will be kept confidential. If the study is published no data will reveal the individual participants.

Benefits from the study

1. Results from the study will help enhance knowledge about the subject matter. This will help advance patient care which you may benefit from.
2. You will get treatment services at no additional cost to you during the study.
3. Every effort will be made to give you the best expert attention during the study.

Risk during the study

During the research, you will not be exposed to any drugs or procedure that is not indicated. You will not be exposed to any additional risk.

Feedback

In case you have any enquiries or concern regarding the research, you can contact; Dr Madu I.C., Department of Anaesthesia UNTH, Enugu, Nigeria. Tel; +(234)-8062617737.

Response from the patient

I have read the above information. I have fully understood the procedure, the benefits and the risks have been well explained to me. All my doubts and worries have been clarified. I hereby give consent freely to participate in the research.

.....	.....
Name and signature of subject	Name and signature of researcher
Date.....	Date.....

.....

Name and signature of witness

Table 8. Mean Heart Rate (Beats/min) values of the four groups over time

GROUPS	Baseline (00)	1 minute	2 minutes	4 minutes	6 minutes	8 minutes	10 minutes	P-value
Air	96.38±15.21^{C}	107.00±20.52^{ab}	110.40±19.14^{a}	103.20±18.93^{b}	95.50±13.62^{c}	89.89±14.28^{cd}	86.62±13.58^{d}	0.000
Saline	89.20±11.73^{b}	96.16±13.10^{a}	97.34±15.93^{a}	86.86±13.23^{bc}	84.16±11.35^{cd}	82.44±11.25^{cd}	80.16±8.42^{d}	0.000
Plain Lidocaine	107.86±21.68^{bc}	115.70±18.44^{ab}	119.12±19.91^{a}	112.92±20.50^{abc}	106.22±21.47^{c}	97.98±21.05^{d}	93.34±16.58^{d}	0.000
Alkalinized Lidocaine	102.38±16.92^{a}	100.00±15.58^{ab}	97.36±14.28^{cd}	96.04±13.82^{cd}	93.48±13.60^{cd}	92.52±13.09^{cd}	90.94±11.75^{d}	0.000

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Table 9. Mean Systolic Blood Pressure (mmHg) of the 4 groups over Time

GROUPS	Baseline (00)	1 minute	2 minutes	4 minutes	6 minutes	8 minutes	10 minutes	P-value
Air	130.190± 10.68^{d}	147.60± 13.26^{b}	161.84± 17.62^{b}	148.28± 23.85^{b}	132.96± 13.38^{c}	128.58± 11.15^{d}	125.56± 10.91^{d}	0.000
Saline	128.82±18.52^{b}	135.34± 15.79^{a}	135.34± 15.03^{a}	129.24± 9.60^{b}	125.12± 10.43^{c}	121.54± 10.67^{c}	119.94± 11.06^{c}	0.000
Plain Lidocaine	128.68±14.76^{cd}	137.66± 13.97^{b}	145.60± 15.12^{b}	138.06± 18.65^{b}	132.68± 19.15^{bc}	125.28± 13.00^{d}	123.42± 13.65^{d}	0.000
Alkalinized Lidocaine	131.46±10.11^{a}	130.16± 10.61^{ab}	129.98± 8.35^{b}	126.60± 10.08^{bc}	124.08± 9.21^{c}	124.36± 8.99^{c}	124.44± 7.95^{c}	0.000

Table 10. Mean Diastolic Blood Pressure (mmHg) of the 4 groups over Time

	Baseline (00)	1 minute	2 minutes	4 minutes	6 minutes	8 minutes	10 minutes	P-value
Air	**81.94±11.43^{cd}**	**90.46±15.38^{b}**	**98.96±12.45^{a}**	**93.62±17.47^{b}**	**83.54±11.31^{c}**	**80.48±9.31^{cd}**	**77.62±9.72^{d}**	**0.000**
Saline	**84.68±12.47^{b}**	**88.82±12.86^{a}**	**86.66±13.27^{ab}**	**83.26±8.28^{c}**	**79.50±8.40^{c}**	**78.36±14.55^{c}**	**76.22±9.43^{c}**	**0.000**
Plain Lidocaine	**82.92±10.77^{c}**	**89.04±12.46^{b}**	**94.66±13.12^{a}**	**90.50±17.10^{ab}**	**83.72±15.23^{c}**	**78.92±10.01^{cd}**	**77.26±9.41^{d}**	**0.001**
Alkalinized Lidocaine	**83.70±9.30^{a}**	**82.82±10.02^{ab}**	**82.80±8.71^{ab}**	**79.50±8.58^{c}**	**77.98±8.29^{c}**	**77.84±7.85^{c}**	**78.24±7.44^{c}**	**0.000**

Table 11. Mean of Mean Arterial Pressure (mmHg) of the 4 groups over Time

GROUPS	Baseline (00)	1 minute	2 minutes	4 minutes	6 minutes	8 minutes	10 minutes	P-value
Air	97.12±11.95^{d}	108.12±17.06^{b}	120.82±12.67^{a}	111.58±13.32^{b}	98.74±9.50^{c}	95.40±9.23^{d}	93.06±9.16^{d}	0.000
Saline	97.82±12.47^{b}	102.78±12.85^{a}	101.74±13.27^{b}	97.56±8.28^{c}	93.72±8.40^{c}	93.72±8.40^{c}	91.34±9.43^{a}	0.000
Plain Lidocaine	97.06±10.77^{c}	103.96±12.46^{bc}	111.18±13.12^{a}	105.26±17.10^{b}	98.92±15.23^{c}	98.92±15.23^{cd}	91.54±9.41^{f}	0.000
Alkalinized Lidocaine	99.00±9.30^{a}	98.04±10.02^{ab}	98.04±8.71^{ab}	94.88±8.58^{bc}	92.94±8.29^{c}	92.94±8.29^{c}	93.28±7.44^{c}	0.000