ATTENUATION OF THE PRESSOR RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON OF INTRAVENOUS ESMOLOL AND LIDOCAINE.

A DISSERTATION

BY

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DECLARATION
I, AMENAGHAWON ANDREA EHIOZE-OSIFO, here declare that the contents of this dissertation are the results of work done by me at the Lagos University Teaching Hospital, Lagos, Nigeria. The work has not been presented for any publication, examination or fellowship award.

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CERTIFICATION
We certify that this work was carried out by Dr Amenaghawon Andrea Ehioze-Osifo of the Department of Anaesthesia, Lagos University Teaching Hospital, under our supervision.

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DEDICATION

This work is dedicated to my loving family for their support, understanding and prayers which saw me through the residency training.
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I thank the Almighty God for his grace and mercy to start and conclude this work.

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I seize this opportunity to express my appreciation to the other consultants in the Department of Anaesthesia of the Lagos University Teaching Hospital for their immense contribution to my training.

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**LIST OF ABBREVIATIONS**

ANNOVA Analysis of Variance
ASA American Society of Anesthesiologists
BP Blood Pressure
CPB Cardiopulmonary bypass
DBP  Diastolic Blood Pressure
ECG  Electrocardiogram
Fig  Figure
GA  General Anaesthesia
g  gram
HR  Heart Rate
IV  Intravenous
Kg  Kilogram
LUTH  Lagos University Teaching Hospital
MAP  Mean Arterial Pressure
mg  milligram
mgkg\(^{-1}\)  milligram per kilogram body weight
MI  Myocardial Infarction
ml  millilitre
min  minute
mmHg  millimetres of mercury
RPP  Rate Pressure Product
SBP  Systolic Blood Pressure
SD  Standard Deviation
SpO\(_2\)  Arterial oxygen saturation
\(\mu g\)  microgram

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SUMMARY

Laryngoscopy and tracheal intubation often elicit a haemodynamic response which could be deleterious in patients with cardiovascular and intracranial pathology. Lidocaine and esmolol are two of several agents used by anaesthetists to attenuate this response. Lidocaine is the agent commonly used by anaesthetists practicing in most developing countries like Nigeria as it is cheap, while esmolol has been used in parts of North America, Europe and Asia. The effect of esmolol on the pressor response is yet to be evaluated in an African population. The aim of this study was to evaluate and compare the effectiveness of these two drugs in attenuating the haemodynamic changes which accompany laryngoscopy and endotracheal intubation in an adult Nigerian population at the Lagos University Teaching Hospital (LUTH).

Ninety (90) ASA physical status class 1 and 2 adult patients undergoing elective surgical procedures under general anaesthesia were included in this randomised, single-blind, placebo controlled study. The effectiveness of 2mg.kg⁻¹ of esmolol administered two minutes before laryngoscopy was compared with intravenous lidocaine 1.5mg.kg⁻¹ given three minutes before laryngoscopy in attenuating the pressor response to laryngoscopy and endotracheal intubation. The patients were randomly assigned by blind balloting to one of three groups, Esmolol (E), Lidocaine (L), and Control(C). Group E patients had 2mg.kg⁻¹ of intravenous esmolol made up to 20mls, given two minutes before laryngoscopy and intubation. Group L patients had 1.5mg.kg⁻¹ of lidocaine made up to 20mls, administered intravenously 3 minutes before laryngoscopy and intubation, while those in the control group were given a placebo of 20mls of 0.9% saline 3 minutes before laryngoscopy.

Anaesthesia was induced with 4mg.kg⁻¹ of 2.5% thiopentone sodium and tracheal intubation facilitated with 1.5mg.kg⁻¹ suxamethonium chloride in all three groups. Heart
rate (HR), systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Rate pressure product (RPP) were recorded as baseline, immediate post-intubation, 1, 3, 5 and 10 minutes after laryngoscopy and intubation. Readings of HR, SBP, DBP, MAP and RPP were compared with baseline values and among each group.

All patients showed post-intubation increases in haemodynamic variables but to varying degrees. The mean heart rate increased by 19.1%, 25.7% and 41.4% in groups E, L and C respectively. SBP increased by 13.3%, 21.6% and 26.9%, DBP by 16.2%, 34.5% and 46.1%, MAP by 12.2%, 19.1% and 30.2% and RPP by 28.1%, 45.8% and 78.7% in groups E, L and C respectively.

The post-intubation rise in heart rate (HR) was significantly less in both treatment groups (p<0.05) compared to the control group, but more in the esmolol group. There was also a significantly lower increase in SBP post-intubation in the esmolol group (p<0.05), but not in the lidocaine group (p>0.05). The changes in DBP and MAP were significantly less in both treatment groups compared to the control group. Both treatment techniques showed significance in attenuating the post-intubation rise in RPP (P<0.05) but this was more in the esmolol group.

These findings demonstrated that both drugs in the doses used in this study, attenuated the pressor response to laryngoscopy and intubation to varying degrees. As observed in similar studies conducted in non-African patients, intravenous esmolol was statistically superior to intravenous lidocaine for attenuating the haemodynamic response to laryngoscopy and intubation. There were no complications attributable to the use of either drug recorded during the course of the study.
INTRODUCTION

Following the first direct vision examination of the human larynx by Albert Kirstein in 1895\(^1\) and its subsequent modification to involve the insertion of intratracheal tubes by Chevalier Jackson in 1913\(^1,2\) laryngoscopy and tracheal intubation became an integral component of airway management and general anaesthesia.

Physical and direct stimulation of the pharynx and larynx by the laryngoscope blade and the placement of an endotracheal tube elicit a sympathetic nervous system response
with a reflex consisting of a transient increase in blood pressure and heart rate, as well as the occurrence of cardiac dysrhythmias\textsuperscript{3}. These haemodynamic changes were first reported by Reid and Brace in 1940\textsuperscript{4}. King and colleagues\textsuperscript{5} described a similar cardiovascular response to laryngoscopy and intubation in 1951. This reflex has been termed the “pressor response” and has been attributed to the sudden release of plasma catecholamines occurring as a consequence of laryngoscopy and endotracheal intubation\textsuperscript{6}. A 40-50\% increase in mean arterial pressure and a 20\% increase in heart rate may occur if the duration of the stimulus is prolonged\textsuperscript{7}. These haemodynamic changes are greatest one minute after intubation and typically last for about 5-10 minutes before returning to baseline values\textsuperscript{8}. A sudden decrease in blood pressure may be observed as this response ends due to the rapid metabolism of released plasma catecholamines\textsuperscript{6}.

A transient haemodynamic change presents a low risk to healthy individuals. In fact, some researchers have actually questioned the importance attached to the phenomenon\textsuperscript{9-11}. It is however of major clinical significance in patients with pre-existing systemic hypertension, hypertensive heart disease, coronary artery disease, eclampsia, aneurysmal vascular disease and head injury in whom such a change may culminate in perioperative myocardial ischaemia or infarction, cardiac failure, dysrhythmias, cerebrovascular accidents or secondary brain injury\textsuperscript{12}.

With advances in medical care and public health, the number of elderly and high risk patients presenting for elective surgeries has steadily increased. Of particular interest are patients with hypertension and coronary artery disease (CAD). Anaesthetists often encounter hypertensive patients scheduled for elective surgical procedures. Some of these patients are not well controlled or have a background of cardiac, cerebral or renal complications of hypertension. Perioperative hypertension is an important etiological
factor for myocardial ischaemia as a sequel to anaesthesia and surgery\textsuperscript{13}. Recently conducted studies have revealed a high prevalence of essential hypertension amongst Nigerians and research has shown that optimal control of blood pressure is difficult to achieve even with proper medication\textsuperscript{14-16}. Despite the fact that diagnosis and treatment of hypertension are easy, a good number of patients are either not diagnosed or not well controlled. Hypertensive patients have been shown to exhibit an exaggerated haemodynamic response to laryngoscopy and intubation, associated with a high incidence of subendocardial ischaemia.\textsuperscript{17,18} This has been observed to occur even when the patients’ blood pressure appears controlled with anti-hypertensive therapy\textsuperscript{19,20}. Also, under emergency conditions where there is insufficient time for optimisation of the patients’ intercurrent medical problems, achieving optimal blood pressure control may be difficult if not impossible.

The prevalence of coronary artery disease is steadily increasing in sub-Saharan Africa due to trends in urbanisation, changes in life-style and acquisition of technology\textsuperscript{21}. Ischaemic heart disease previously considered rare now ranks 8\textsuperscript{th} among the leading causes of death in men and women in the region\textsuperscript{22,23}. In these patients the tachycardia, hypertension and increase in rate pressure product, concomitant with intubation represent a serious risk and has been shown to result in perioperative myocardial ischaemia and infarction\textsuperscript{22}. Since the presence of coronary artery disease may not always be diagnosed preoperatively, the prevention of these haemodynamic changes and their adverse sequelae is necessary to reduce perioperative morbidity and mortality. Several methods of preventing this response have been recommended\textsuperscript{24-28}. These include the use of alternative guiding devices such as the fibreoptic bronchoscope\textsuperscript{24}, light wand\textsuperscript{25} or airway management with the laryngeal mask airway (LMA)\textsuperscript{26,27}. Recently, the use of the McCoy laryngoscope has been found to reduce the severity of
these haemodynamic changes. Various pharmacological agents have been administered prior to laryngoscopy in an attempt to attenuate this reflex. Of particular interest is the use of intravenous lidocaine which is the agent commonly used by anaesthetists practicing in this environment. The results of studies conducted on its use in this respect have varied. On the other hand, esmolol, an ultra-short acting cardioselective beta-adrenergic blocker has been shown to provide more consistent and reliable protection against the pressor response. There is however a dearth of research on its use in an African population.

This prospective study was undertaken to evaluate the effectiveness of these two agents, namely- esmolol hydrochloride and lidocaine hydrochloride, in attenuating the haemodynamic response to laryngoscopy and tracheal intubation, and to compare their relative effectiveness in a Nigerian population.
AIM AND OBJECTIVES

AIM

To compare the effectiveness of intravenous lidocaine and esmolol in the prevention of the haemodynamic response to laryngoscopy and endotracheal intubation in a Nigerian population at the Lagos University Teaching Hospital.

OBJECTIVES

• To evaluate the effect of an intravenous dose of lidocaine on the haemodynamic response to laryngoscopy and intubation.

• To evaluate the effect of an intravenous dose of esmolol on the haemodynamic response to laryngoscopy and intubation.

• To compare the effects of intravenous lidocaine and esmolol on the pressor response to laryngoscopy and intubation.

• To determine the occurrence of complications with the use of either agent.
A haemodynamic response of increased heart rate and blood pressure to manipulation in the area of the larynx, by means of laryngoscopy and intubation was first reported by Reid and Brace\textsuperscript{4}. Subsequently, Forbes and Dally\textsuperscript{37} reported an average rise in mean arterial pressure of 25mmHg following laryngoscopy and insertion of an endotracheal tube in 22 patients in whom anaesthesia was induced with sodium thiopentone. These haemodynamic changes have been interpreted as being the result of reflex sympatho-adrenal stimulation. In a study conducted by Tomori and Widdicombe using anaesthetised cats, they observed that mechanical stimulation of four areas of the upper respiratory tract i.e. the nose, epipharynx, laryngopharynx and tracheobronchial tree induced reflex cardiovascular responses associated with enhanced neuronal activity in the cervical sympathetic efferent fibres\textsuperscript{38}. These cardiovascular responses, tachycardia and hypertension, as well as the enhanced neuronal activity were most pronounced during stimulation of the epipharynx while those arising from the stimulation of the tracheobronchial tree were least marked\textsuperscript{38}.

Subsequent researchers have confirmed these findings. In a study of 24 patients undergoing elective surgery under general anaesthesia, Shribman et al reported that laryngoscopy alone increased blood pressure and that laryngoscopy and intubation together increased both heart rate and blood pressure\textsuperscript{39}. The study also demonstrated a significant increase in serum catecholamine levels during laryngoscopy with or without concomitant intubation. Similarly, Russel and colleagues\textsuperscript{40} demonstrated a significant increase in mean arterial pressure and plasma norepinephrine levels following endotracheal intubation suggesting a predominantly sympathetic response during intubation. This elevation in blood pressure and heart rate was maximum when the
duration of laryngoscopy exceeded 30 seconds. The authors went on to recommend the need for prophylaxis in high risk patients.

Some authors have questioned the notion that these cardiovascular reflexes are caused solely by increased sympathetic and sympathoadrenal activity. The efferent sympathetic outflow to the heart is T1-T4, while that to the adrenal medulla is from T3-L3. Wathill et al reported that the cardiovascular response to intubation is abolished in patients undergoing thoracolumbar epidural anaesthesia. However, Dohi et al observed that acute sympathectomy induced in part by cervical or lumbar epidural block did not prevent haemodynamic responses to laryngoscopy and intubation.

Anaesthesia literature contains several studies evaluating various pharmacological agents used for attenuating these haemodynamic changes in adults. It has been suggested that the ideal agent for obtunding the pressor response should have a rapid onset of action, be safe, easily administered and have a relatively short duration of action. The following are the various drugs which have been utilised for blunting the haemodynamic response to laryngoscopy and intubation:

**Local anaesthetic agents**

The efficacy of intravenous and topical oropharyngeal local anaesthetic agents for attenuating the pressor response has been extensively studied. The postulated mechanism for inhibiting this sympathetic response is an increased threshold for airway stimulation and central inhibition of sympathetic stimulation. Derbyshire and colleagues investigated the use of topical anaesthesia of the upper airway using 160mg of 4% lidocaine in adult patients. They concluded that it was an ineffective means of ameliorating the pressor and catecholamine response to laryngoscopy and intubation.
Several researchers have recommended 1.5mgkg$^{-1}$ of lidocaine given intravenously 3 minutes before laryngoscopy as optimal for attenuating the response$^{34,35,48}$. Durrani et al$^{46}$ found intravenous chloroprocaine an excellent local anaesthetic for blunting the sympathetic response. A bolus dose of 4.5mgkg$^{-1}$ given 45 seconds before laryngoscopy significantly diminished increases in blood pressure as well as plasma catecholamine concentrations in response to intubation.

**Opioids**

Narcotics have been used for attenuating the haemodynamic as well as catecholamine response to endotracheal intubation$^{49,50}$. The analgesic effects of these agents suppress the nociceptive stimulation caused by laryngoscopy and intubation. There is also a centrally mediated decrease in sympathetic tone associated with their use$^{49}$. Fentanyl in doses ranging between 2µgkg$^{-1}$ and 7µgkg$^{-1}$ given 1 to 2 minutes before laryngoscopy has been found to be effective in attenuating the increase in heart rate, blood pressure and rate-pressure product following laryngoscopy and intubation$^{51,52}$. Crawford et al$^{53}$ reported a significant reduction in post-intubation rise in heart rate, systolic blood pressure and serum epinephrine concentration with the use of 40µgkg$^{-1}$ of alfentanil. However, the doses of opioids required for attenuation of the pressor response often result in hypotension, bradycardia, respiratory depression, skeletal muscle rigidity and delayed recovery$^{51,53}$. Remifentanil, which has a rapid onset and short duration of action, has been used for attenuation of the haemodynamic response. Maguire et al$^{54}$ found that a bolus intravenous dose of 0.5µgkg$^{-1}$ remifentanil followed by a 0.1µgkg$^{-1}$ min$^{-1}$ infusion administered just prior to laryngoscopy, was effective in controlling the response.

**Beta adrenergic blockers**
Selective beta-1 blockade produces a decrease in heart rate and myocardial contractility whereas antagonism of the beta-2 receptor produces bronchial and vascular smooth muscle constriction. Achola et al\textsuperscript{55} studied the use of intravenous practolol 10mg given just before laryngoscopy for attenuation of the pressor response and concluded that it lacked efficacy in this respect. The use of 10mg intravenous propranolol by McCamon and colleagues was associated with excessive myocardial depression (hypotension and bradycardia) and a duration of action which outlasted the transient haemodynamic changes induced by laryngoscopy and intubation\textsuperscript{56}. Of the various beta blockers used for attenuation of the pressor response, esmolol, a beta-1 blocker with an ultra-short duration of action has yielded the most reliable results.\textsuperscript{34,57}

\textbf{Vasodilators}

Sodium nitroprusside and nitroglycerine have been evaluated for the attenuation of the pressor response to laryngoscopy and intubation but their use requires continuous intra-arterial monitoring. Mikawa et al\textsuperscript{30} reported that intravenous nitroglycerine 2.5\textmu gkg\textsuperscript{-1} had no effect on the tachycardia but significantly reduced the mean arterial pressure and rate-pressure product changes associated with tracheal intubation. Similarly, Stoetling\textsuperscript{58} reported that rapid intravenous injection of sodium nitroprusside at a dose of 1-2\textmu gkg attenuated the blood pressure but not the heart rate changes following laryngoscopy and intubation.

\textbf{Calcium channel blockers}

The commonly evaluated calcium channel blocking agents for attenuating the haemodynamic response are verapamil, diltiazem and nicardipine\textsuperscript{59,60}. Yaku et al\textsuperscript{61} found that intravenous verapamil given in a dose of 0.05mgkg\textsuperscript{-1} attenuated the increase in mean arterial pressure and rate pressure product after tracheal intubation. Verapamil failed to prevent the tachycardia despite its negative chronotropic effect. Similarly, both
nicardipine and verapamil at intravenous doses of 0.03mgkg$^{-1}$ and 0.1mgkg$^{-1}$ respectively failed to control the tachycardia despite being effective in attenuating the increase in blood pressure associated with laryngoscopy and intubation$^{62}$.

**Volatile anaesthetic agents**

Inhalational agents like halothane and enflurane in various concentrations have been used during induction to increase depth of anaesthesia as well as control the haemodynamic response$^{63,64}$. High concentrations may prove detrimental in cardiovascular compromised patients. Using halothane 2% with nitrous oxide in oxygen for 2 minutes before laryngoscopy, Kautto et al observed a significant attenuation of the pressor response$^{63}$. However, a higher concentration of halothane produced significant cardiac dysrhythmias. Bedford et al$^{64}$ found 0.7% enflurane a more suitable alternative to 2% halothane for attenuation of the pressor response to laryngoscopy and intubation.

**Intravenous induction agents**

Agents used to induce anaesthesia have been shown to influence the pressor response to laryngoscopy and tracheal intubation. Ebegue$^{65}$ demonstrated that following induction of anaesthesia with 4mgkg$^{-1}$ of sodium thiopentone, the administration of a second dose of thiopentone (4mgkg$^{-1}$) just before laryngoscopy significantly attenuated the heart rate, systolic blood pressure and rate pressure product changes accompanying laryngoscopy and intubation. Similarly, Amadasun$^{66}$ reported that a repeat of an induction dose of sodium thiopentone given just before laryngoscopy was statistically superior to intravenous lidocaine for attenuation of the pressor response.

Sood and colleagues$^{67}$ demonstrated that the administration of a repeat dose (25% of the induction dose) of intravenous propofol just prior to laryngoscopy limits the
duration of the pressor response to one minute. However, 55.5% of their patients complained of pain on injection of propofol.

**Alpha 2-adrenoceptor antagonists**
These agents interact with catecholaminergic neuronal system which modulates tonic and phasic blood pressure control and reduce the release of norepinephrine from nerve endings both centrally and peripherally. Ghignone\(^68\) showed that cardiovascular responses following laryngoscopies of less than 30 seconds duration can be attenuated with 5µg.kg\(^{-1}\)oral clonidine given 45 minutes before laryngoscopy. Scheinin et al\(^69\) found that intravenous dexametomidine at a dose of 0.2-0.7µg.kg\(^{-1}\)attenuates the stress-induced sympathoadrenal responses to laryngoscopy, intubation and surgery and provides increased haemodynamic stability.

**Miscellaneous**
Other drugs that have been used to attenuate the haemodynamic response to laryngoscopy and intubation are; labetalol, magnesium sulphate, gabapentin, captopril, prostaglandin E\(_1\) and adenosine triphosphate.

Amar et al\(^70\) reported that labetalol, a non-selective \(\alpha\) and \(\beta\) adrenergic blocker at a dose of 0.5mgkg\(^{-1}\) significantly attenuated the rise in blood pressure and heart rate, but did not prevent the rise in plasma catecholamines associated with laryngoscopy and intubation. The use of larger doses of labetalol was associated with significant hypotension.

Magnesium sulphate attenuates catecholamine output from adrenal medulla and adrenergic nerve endings and this reduces the severity of the pressor response. Puri and colleagues\(^71\) found intravenous magnesium sulphate 40mgkg\(^{-1}\) effective for attenuation of the pressor response to laryngoscopy and intubation as well as producing less ST segment changes in patients with coronary artery disease undergoing coronary artery
bypass grafting. In patients with gestational hypertension, magnesium was found to be more effective than intravenous lidocaine in attenuating the pressor response. Fassoulaki and colleagues observed that oral gabapentin at a dose of 800-1600mg given at 6 hourly intervals before surgery attenuated the pressor response but not the tachycardia associated with laryngoscopy and endotracheal intubation. Sanir et al evaluated the effect of oral captopril on haemodynamic responses and reported that a dose of 12.5mg administered 45minutes prior to induction of anaesthesia significantly attenuated the hypertensive, but not the tachycardic response to tracheal intubation. In a study by Mikawa and colleagues, prostaglandin E given as an infusion at 0.6ugkg attenuated the hypertension during tracheal intubation but failed to blunt the tachycardia. It also enhanced the increase in plasma noradrenaline concentration following intubation. Adenosine, a potent vasodilator has been successfully used at a dose of 0.05-0.1mgkg to attenuate the haemodynamic response to laryngoscopy and intubation. Its onset of action is fast and its duration of action transient. Although it has a negative chronotropic effect, like other vasodilators it fails to control the tachycardia associated with the response

**INTRAVENOUS LIDOCAINE HYDROCHLORIDE**

Lidocaine is an amide–derived local anaesthetic and class IB anti-dysrhythmic agent. It has found clinical uses in local and regional anaesthesia, treatment of ventricular dysrhythmias, and the attenuation of the haemodynamic response to laryngoscopy and intubation. It acts by stabilising the neuronal membrane by inhibiting the sodium flux required for the initiation and conduction of impulses. Its anti-pressor effect is believed to be via depression of laryngeal reflexes. It also reduces thiopentone requirements by 13.3%.

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The use of intravenous lidocaine for the attenuation of the pressor response has been extensively researched upon with different conclusions.

Abou-Madi et al\textsuperscript{35} compared 1.5 mg kg\textsuperscript{-1} of intravenous lidocaine given 3 minutes before laryngoscopy with placebo in 30 patients; and found that the mean increase in systolic blood pressure was 10.3\% for patients pre-treated with lidocaine and 56\% in patients receiving placebo. The mean increase in heart rate was 16.8\% in the lidocaine group and 38.8\% in the placebo group. Using a similar technique, Tam, Chung and Campbell\textsuperscript{81} observed complete attenuation of the response when this dose of lidocaine was administered 3 minutes before laryngoscopy. Splinter and Cevenko\textsuperscript{82} in a study of 150 geriatric patients, concluded that intravenous lidocaine given 4-4.5 minutes before intubation attenuated the pressor response. They however agreed with Tam et al\textsuperscript{81} that in younger adults, the optimal time to administer intravenous lidocaine is 3 minutes before laryngoscopy.

Lev and Rosen\textsuperscript{34} conducted a review of twenty-five studies pertaining to the use of intravenous lidocaine for attenuation of the pressor response. Sixty per cent (60\%) of the studies reviewed demonstrated that lidocaine produced some benefit in attenuating the cardiovascular response to intubation. A dose of 1.5 mg kg\textsuperscript{-1} administered intravenously 3 minutes before intubation was recommended as optimal. None of the studies documented any harmful effects of prophylactic lidocaine given preintubation.

Amadasun\textsuperscript{48} investigated the effectiveness of intravenous lidocaine in obtunding the pressor response in a sample of Nigerian patients. In a randomised, controlled trial, a total of 80 ASA class 1 and 2 patients were studied in two groups of 40 patients each. Lidocaine was administered at a dose of 1.5 mg kg\textsuperscript{-1} three minutes before laryngoscopy in the study group. He reported that intravenous lidocaine significantly attenuated the
post intubation rise in heart rate and rate-pressure products without significant effect on blood pressure.

Miller and Warren\textsuperscript{83} in a study of 45 Chinese women could not demonstrate any significant benefit of 1.5mg of lidocaine given intravenously 1, 2 or 3 minutes before laryngoscopy. Prior to this, Laurito and colleagues\textsuperscript{84} administered a combination of nebulized lidocaine 4mg.kg\textsuperscript{-1} and an intravenous dose 2mg.kg\textsuperscript{-1}, and reported a lack of effect on the cardiovascular response to laryngoscopy and intubation compared with control. However, in their study they intubated their patients one minute after lidocaine injection. They suggested the abandonment of the use of lidocaine prior to laryngoscopy for the attenuation of the pressor response.

**INTRAVENTOUS ESMOLOL HYDROCHLORIDE**

The use of beta adrenergic blockers for the attenuation of the pressor response was pioneered by Prys-Roberts and colleagues in 1979\textsuperscript{85}. They studied the haemodynamic sequelae to laryngoscopy and intubation in hypertensive patients and demonstrated a significant attenuation of the pressor response in patients pre-treated with intravenous or oral practolol. Subsequently, various workers have demonstrated the utility of beta blockade in attenuation of the pressor response\textsuperscript{56, 86}. Beta-\textsuperscript{adrenoceptor} blockade minimises the increase in heart rate and myocardial contractility (primary determinants of oxygen consumption) by attenuating the positive chronotropic and inotropic effects of increased adrenergic activity\textsuperscript{87}. However, the use of beta-blocking agents for the attenuation is not without risks. Potential negative sequelae related to beta- blockade for attenuation include: excessive myocardial depression, bronchial constriction, and the possibility that the duration of action of these agents may outlast the transient haemodynamic changes induced by laryngoscopy and intubation\textsuperscript{88}. 


Esmolol, methyl-3-{4-3-[isopropyl amino] propoxy phenyl} propionate is a water soluble, cardio-selective, ultra-short acting beta-adrenergic antagonist. It has been shown to be effective in controlling both the heart rate and blood pressure responses to intubation\textsuperscript{89}.

Esmolol blocks the agonist effect of sympathetic neurotransmitters by competing for beta 1 receptor sites. At therapeutic doses it lacks intrinsic sympathomimetic or membrane stabilizing properties. Its anti-arrhythmic activity is due to blockade of adrenergic stimulation of pacemaker potential. It is a class II antiarrhythmic agent\textsuperscript{90}.

Esmolol undergoes rapid hydrolysis by esterases in red blood cells to a free acid metabolite and methanol culminating in a short elimination half-life of 9.2 \pm 2.0 minutes. The short duration of action has led to its use in a number of situations requiring beta receptor antagonism of limited duration e.g. treatment of supraventricular dysrhythmias, perioperative hypertension and phaeochromocytoma\textsuperscript{64}.

A total body clearance of 285 ml/min ensures a rapid offset of action and it is eliminated via the kidneys almost entirely as its metabolite\textsuperscript{91}. It achieves peak effect on heart rate within one minute and on blood pressure within two minutes of intravenous injection\textsuperscript{92}.

These unique pharmacokinetic and pharmacodynamic properties make esmolol suitable for administration by either continuous infusion or bolus injection. It has been used in different doses either as a bolus or in an infusion form to attenuate the haemodynamic response to laryngoscopy and endotracheal intubation.

The first study conducted on the subject was published by Gold et al\textsuperscript{93} who found that peak heart rates and systolic pressures following intubation after ketamine induction were significantly attenuated by esmolol. Several researchers have established the effectiveness of esmolol infusions in the prevention of haemodynamic alterations following tracheal intubation. Ghaus et al\textsuperscript{94} reported that a bolus infusion of esmolol
administered at a dose of 300µg.kg\(^{-1}\).minute\(^{-1}\) for 4 minutes, followed by a maintenance infusion of 200µg.kg\(^{-1}\).minute\(^{-1}\) for 12 minutes offered significant control of all the haemodynamic variables. Figueredo and Fuentes\(^{95}\) conducted a meta-analysis of 38 randomised controlled trials on the effect of esmolol on the adrenergic stress response. Eleven different regimens demonstrated effectiveness in the attenuation of heart rate and blood pressure after laryngoscopy and intubation, the most effective of which was a loading dose of 500µg.kg\(^{-1}\).minute\(^{-1}\) over 6 minutes followed by a continuous infusion of 200-300µg.kg\(^{-1}\).minute\(^{-1}\) for 9 minutes.

Some authors have argued that while infusions are easy to set up, they require additional equipment and time which may not be readily available\(^{96,97}\). In addition, the dosing regimen and time required for preparation of an infusion may add a degree of complexity to the induction process which is often unnecessary. Miller et al\(^{97}\) advocated that since esmolol has a rapid onset and short duration of action, bolus injection might be a simple and effective alternative to infusion in situations involving transient hyperdynamic cardiovascular events such as laryngoscopy and intubation.

The use of bolus dosing of esmolol for the control of the pressor response to laryngoscopy and intubation has produced different results.\(^{97,86}\) The optimal bolus dose of esmolol required to attenuate the haemodynamic response to laryngoscopy and endotracheal intubation has been a subject of debate. Various researchers have administered esmolol as either fixed doses or on a weight basis. Tariq et al\(^{98}\) used esmolol at a dose of 1mg/kg 2 minutes before laryngoscopy and concluded that it only partially attenuated the haemodynamic response but did not abolish it completely. Miller and Martineau\(^{99}\) demonstrated that bolus doses of esmolol, approximately 1.5mg.kg\(^{-1}\), administered to patients with known or suspected coronary artery diseases 2 minutes before laryngoscopy and intubation, could effectively control post induction
increases in heart rate. Hussein and Sultan\textsuperscript{100} evaluated the efficacy of esmolol at 2mg.kg\(^{-1}\) bolus given 2 minutes before intubation and reported an attenuation of the increase in heart rate but not arterial pressure. However, following the administration of an even larger dose of 4mg.kg\(^{-1}\) 2 minutes before laryngoscopy in 100 elderly patients scheduled for cataract surgery, Van den Berg and Honjol reported that esmolol prevented the rise in heart rate and rate-pressure product only\textsuperscript{101}. Their findings were similar to those of Cucchiara et al\textsuperscript{102} who concluded that although the increase in heart rate and blood pressure associated with laryngoscopy and endotracheal intubation were significantly lower when compared with placebo; the incidence of raised blood pressure was about 60% even with large doses of esmolol.

Oxorn and Knox\textsuperscript{103} evaluated the effectiveness of esmolol administered in fixed doses of 100mg and 200mg 90 seconds before laryngoscopy, in 48 patients undergoing elective hysterectomy. They reported an attenuation of the rise in heart rate for 2.5 minutes following intubation after which it became indistinguishable from placebo. The rise in blood pressure however, was not mitigated by either dose of esmolol when compared with placebo. Rathore et al\textsuperscript{104} went further to compare three bolus doses of esmolol for attenuation of the pressor response in 100 patients scheduled for elective surgery under general anaesthesia. The patients were administered 50mg, 100mg or 150mg of esmolol 2 minutes before laryngoscopy and intubation. All the doses were effective in blunting the pulse rate response but only the 150mg dose proved effective in blunting the blood pressure response.

However, Bernstein\textsuperscript{105} used similar doses of esmolol in a bolus fashion 2 minutes before laryngoscopy and intubation, and found that hypertension and tachycardia were both prevented following rapid sequence induction. He also reported a significantly lower incidence of post-intubation ventricular tachyarrhythmias in the esmolol group. His
findings were attributed to a slightly larger dose of thiopentone (5mg.kg\(^{-1}\) versus 4.6mg.kg\(^{-1}\)) given in closer proximity to the time of laryngoscopy and intubation than was done by Oxorn and colleagues. There were no significant side effects attributable to the use of esmolol in any of the studies.

**ESMOLOL VERSUS LIDOCAINE**

Helfman and colleagues\(^{106}\) compared the efficacies of intravenous esmolol and lidocaine in attenuating the pressor response. In a double-blind, placebo-controlled trial involving 80 patients undergoing non-cardiac surgery, they compared lidocaine 200mg, fentanyl 200µg and esmolol 150mg, to determine which best prevented tachycardia and hypertension due to tracheal intubation. Mean percentage increases in heart rate during and after intubation were lowest in the esmolol group (12%) compared to the lidocaine (51%), fentanyl (18%) and placebo (44%) groups; while the mean systolic blood pressure increases were lowest in the fentanyl group (12%) compared to the esmolol (19%) and lidocaine (20%) groups. Only esmolol provided consistent and reliable protection against increases in both heart rate and blood pressure accompanying laryngoscopy and intubation. Feng et al\(^{107}\) conducted a similar study but the test drugs were administered on a weight basis as against the fixed doses used by Helfman and colleagues. The incidence of tachycardia (heart rate more than 100/min) was 15% in the esmolol group, significantly lower than the lidocaine (75%), fentanyl (55%) and control (85%) groups. The incidence of hypertension (systolic blood pressure > 180mmHg) was also lower (20%) in the esmolol group compared to the lidocaine (70%), fentanyl (40%) and control (80%) groups. They concluded that only esmolol reliably offered protection against increases in both heart rate and systolic blood pressure.
Questions have been raised with regards to the methodology deployed by these groups of researchers which may have inadvertently introduced a bias in favour of esmolol\textsuperscript{108}. In both studies, laryngoscopy and intubation were performed 2 minutes after induction. This might be expected to favour the effectiveness of esmolol which has a peak effect on heart rate and blood pressure at 1 to 2 minutes as against that of lidocaine which is at 2 to 3 minutes thus explaining why the principal benefits of lidocaine administered within this time frame were not achieved.

Levitt and Dresden\textsuperscript{109} compared the effects of esmolol and lidocaine on the pressor response during intubation of patients with intracranial hypertension following isolated head trauma. Esmolol 2mg.kg$^{-1}$ or lidocaine at 2mg.kg$^{-1}$ was administered intravenously just prior to intubation. The study did not reveal any significant difference as neither drug effectively attenuated the haemodynamic response to intubation.

A few researchers have recommended the use of a combination of both drugs for obtunding the pressor response to laryngoscopy and intubation. In a study conducted by Kindler et al in 1996\textsuperscript{110}, they compared esmolol, lidocaine and a combination of both drugs administered 2 minutes prior to laryngoscopy. Esmolol 1 to 2 mg.kg$^{-1}$ was found to be reliably effective in attenuating the heart rate response to intubation while the combination of esmolol 2mg.kg$^{-1}$ and lidocaine 1.5mg.kg$^{-1}$ attenuated both the heart rate and blood pressure responses to intubation. Neither esmolol nor lidocaine administered alone affected the blood pressure response. Bansal and Pawar\textsuperscript{111} compared the efficacy of two bolus doses of esmolol with or without lidocaine in 80 patients with pregnancy induced hypertension scheduled to undergo lower segment caesarean section. The patients were allocated to four groups of 20 patients each and were administered esmolol 1mg.kg$^{-1}$ alone, esmolol 2mg.kg$^{-1}$ alone, esmolol 1mg.kg$^{-1}$ and lidocaine 1.5mg.kg$^{-1}$, or esmolol 2mg.kg$^{-1}$ and lidocaine 1.5mg.kg$^{-1}$ 2 minutes before
laryngoscopy and intubation. The combinations of esmolol and lidocaine were effective in attenuating the adrenergic responses to laryngoscopy and intubation. There were no adverse effects in the mothers or their babies.

MATERIALS AND METHODS

This was a prospective study conducted over a period of six months among adult
elective surgical patients at the Lagos University Teaching Hospital. The approval of the Research and Ethics Committee of the hospital (Appendix III) and informed consent (Appendix II) of each patient were obtained. Ninety (90) patients with the American Society of Anesthesiologists (ASA) physical status 1 or 2, between the ages of 18 and 60 years were included in the study. There were 50 males and 40 females. Exclusion criteria included: known allergies to beta-adrenergic antagonists or local anaesthetic agents; compensatory tachycardia (anaemia, infection, and hypovolaemia); cardiac diseases (heart block of any degree, myocardial infarction, congestive cardiac failure, and cardiac dysrhythmias); bronchospastic disease and chronic obstructive airway disease. Also excluded were those on cardioactive drugs, antihypertensive agents, theophylline, beta-agonist, and ipatropium bromide or inhaled steroid therapy. All the patients were seen in the ward at least a day before surgery for pre-operative assessment. This entailed obtaining a history, conducting physical examination and requesting relevant investigations. The patients were weighed and their weights were documented in their case notes. Anaesthetic premedication was prescribed consisting of 10mg oral diazepam given with a sip of water the night before surgery and one hour before induction of anaesthesia. Preoperative fasting guidelines of 6 hours to solids and 2 hours to clear fluids were observed.

On arrival at the operating theatre, the patients who required endotracheal intubation were randomly assigned by blind balloting to one of three groups, L (Lidocaine), E (Esmolol) and C (Control). The anaesthetic drugs were drawn in appropriate doses and an equipment check was performed. A multiparameter Siemens™ monitor incorporated with a blood pressure cuff and pulse oximetry probe was attached to the patients. Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and arterial oxygen saturation (SpO2) were obtained in
the supine position and recorded by an anaesthetist registrar (person A). Intravenous access was established using a size 18G cannula and an infusion commenced with a 0.9% saline solution. Based on the designated study group, the drugs were drawn in sterile unlabelled 20ml syringes and made up to equal volumes of 20mls with normal saline by the primary researcher (person B). This was done in the preanaesthetic room after which the drug was handed over to an anaesthetist registrar for administration to the patient (person C). All test drugs were colourless.

The patients were pre-oxygenated for five minutes by the primary researcher. During preoxygenation, the group L patients were given 1.5mg.kg\(^{-1}\) of Lidocaine hydrochloride while the group E patients received 2mg.kg\(^{-1}\) Esmolol hydrochloride by slow intravenous injection over 30 seconds. Patients in the control group (C) received 20mls of 0.9% saline solution. Following the administration of the test drugs, the haemodynamic variables were measured and recorded (pre-induction values) by the anaesthetist registrar (Person A) who was blinded to the designated agent.

Anaesthesia was then induced in all the groups with 5mg.kg\(^{-1}\) thiopentone sodium by slow intravenous injection followed with 1.5mg.kg\(^{-1}\) suxamethonium chloride given intravenously. Prior to and during the induction period, verbal contact was maintained with the patients to detect any adverse reactions to the test drugs such as tinnitus, circumoral numbness, pain at the injection site or tightness in the chest.

After adequate muscle relaxation as judged by jaw relaxation or disappearance of fasciculations, laryngoscopy was undertaken by the primary researcher with a size 4 curved Macintosh blade at 3 minutes in the Lidocaine and Control groups and 2 minutes in the Esmolol group, and then endotracheal intubation with an appropriate sized polyvinyl chloride (PVC) tube was done in each case. Following successful passage of the tracheal tube and immediately after removal of the laryngoscope, HR, SBP, DBP
and MAP were recorded from the automatic oscillometer while the Rate Pressure Product (RPP) was calculated and recorded. Surgical stimulation as well as the administration of analgesic supplements and muscle relaxants were avoided during the study period i.e. start of induction to 10 minutes later. Anaesthesia was maintained with an inspired halothane concentration of 1.5-1.8% in 100 per cent oxygen.

HR, SBP, DBP and MAP readings were obtained at 1, 3, 5 and 10 minutes after tracheal intubation and at 10 minute intervals thereafter till the end of surgery.

The Rate Pressure Product (RPP) was calculated thus;

\[ \text{Rate Pressure Product} = \text{Heart Rate} \times \text{Systolic Blood Pressure} \]

The duration of laryngoscopy and intubation was determined by stop watch measurement and recorded. This was taken as the time from oral passage of the laryngoscope to successful placement of the endotracheal tube. Patients with difficult and/or repeated laryngoscopy and/or intubation that lasted for over 30 seconds were excluded from the study. Laryngoscopy was performed by the primary researcher in all the patients.

The following parameters were defined for the study: 1) Hypotension was defined as SBP < 25% of baseline value or 90 mm Hg; 2) Hypertension was defined as SBP > 25% of baseline value or 150 mm Hg; 3) Tachycardia was defined as HR > 25% of baseline value; 4) Bradycardia was defined as HR < 60 beats.min⁻¹.

Data collected was entered into a proforma (Appendix I) and analysed with computer analytical package Epi 6 info, version 6.4.

Data was reported as mean± SD and percentage changes. Repeated measures of ANOVA were used to compare values for heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product, to baseline values in each group. Repeated measures of ANOVA were also used to compare the
haemodynamic variables between the three groups. Differences were deemed significant at a p value<0.05.

Microsoft excel™ software was used for graphical presentation.

**RESULTS**

Patients were selected from the different surgical specialties. Patients presenting for general surgical procedures constituted the largest number of 28 (31.1%), while the ear, nose and throat (ENT) surgery patients were the least (2.2%). Figure 1 shows the distribution of the sample population according to surgical specialty.

The demographic data was compared among the three groups. There was no significant difference between the groups with respect to age, gender, weight, ASA score or
duration of laryngoscopy (Table 1).

A. **HEART RATE**

Compared with the baseline readings, the mean heart rate was increased after laryngoscopy and tracheal intubation in all three groups as depicted in figure 2. This was highest in the control group where laryngoscopy and intubation caused a rise in the heart rate from a mean baseline value of 80.6 to 114.0, an increase of 41.4% which was statistically significant (p=0.000). In the lidocaine group, the heart rate rose from 82.2 to 108.4, an increase of 25.7%. This was significantly less than the rise observed in the control group (p=0.012). There was an initial decrease in heart rate after the administration of esmolol which was significant (p=0.04) but this was followed by a rise following laryngoscopy and intubation. In the esmolol group, mean heart rate increased from 86.8 to 103.4, an insignificant increase of 19.1%. This differed significantly from the control group (P=0.001) but not the lidocaine group (p=0.275). At 1, 3 and 5 minutes after laryngoscopy and endotracheal intubation, there was a decrease in heart rate in all the three groups but the changes were not statistically significant (P>0.05) and at 10 minutes post-intubation, this parameter closely approached baseline values in the esmolol and lidocaine groups (figure 3)

B. **MEAN SYSTOLIC BLOOD PRESSURE**

Compared to the baseline values, the systolic blood pressure (SBP) increased in all three groups following laryngoscopy and intubation (figure 4). The increase was highest in the control group where it rose significantly from a mean baseline value of 128.7 to 163.3 (26.9%) post-intubation (p=0.002), and least in the esmolol group, which increased from 135.1 to 153.1 (13.3%) (p=0.056). There was a significant difference between the esmolol and control groups (p=0.002). In the lidocaine group there was a
significant rise in SBP of 21.6% post laryngoscopy and intubation, but this did not differ significantly from the esmolol (p=0.066) or control (p=0.055) groups.

Systolic blood pressure gradually declined in all the three groups and decreased below baseline values after 5 minutes in all the three groups. The decrease was significant in both treatment groups (p=0.02) but not in the control group (p=0.062). Despite this drop, systolic blood pressure remained above 110 mmHg in all three groups. Figure 5 shows the mean systolic blood pressure changes in all three groups.

C. MEAN DIASTOLIC PRESSURE
The control group (C) and both study groups (L and E) all registered a rise in the mean diastolic pressure (DBP) immediately after laryngoscopy and intubation. In the esmolol group there was an initial insignificant fall in diastolic blood pressure following the administration of the drug (p=0.506). The mean diastolic pressure in the control group rose from 78.0 mmHg to 114.0 mmHg (46.1%) at laryngoscopy and intubation, whereas in the lidocaine and esmolol groups, the values rose from 79.1 and 85.6 mmHg to 106.3 (34.5%) and 99.5 mmHg (16.2%) respectively. The difference between both treatment groups and the control group was significant following intubation but this was more significant in the esmolol group (p=0.000) compared to the lidocaine group (P=0.001) (figure 6)

By 5 minutes the mean diastolic blood pressure decreased below baseline values but remained above 70 mmHg in all three groups (figure7).

D. MEAN ARTERIAL PRESSURE
There was an initial decrease in mean arterial pressure (MAP) in the esmolol and Lidocaine groups following the administration of the study drugs which was not statistically significant (p=0.06 and p=0.08 respectively). This increased in all groups
following laryngoscopy and intubation. In the control group, there was a significant 30.2% increase from mean baseline value of 97.1 to 126.4 (p=0.001). In the lidocaine group, the mean baseline MAP of 109.3 rose to 130.2 post intubation, an increase of 19.1%. The increase was least in the esmolol group where it rose from 103.8 to 116.5 (12.2%). These changes were significantly less in both groups compared to the control group, but more so in the esmolol group (p=0.000) than the lidocaine group (p=0.02). (Figure 8). There was no significant difference between both treatment groups (p=0.08).

By 3 minutes post-intubation, there was a progressive decrease in MAP and by 5 minutes the values had dropped to less than the baseline values (figure 9). This drop was most in the lidocaine group (19.5%) and least in the control group (10%).

E. THE MEAN RATE PESSURE PRODUCT (RPP)

The mean rate pressure product values in the control group showed a significant increase at intubation from 10381.3 to 18549.9 (78.7%) p=0.000. The values in the lidocaine and esmolol groups also showed an increase from 11438.6, 12550.9 to 16681.4 (45.8%) and 16072.7 (28.1%) respectively (figure 10). The difference was highly statistically significant compared to control group in both lidocaine and esmolol groups following intubation, p=0.000 and p=0.000 respectively. At 3 minutes post-intubation, a decrease in the mean rate pressure product below the baseline value was observed in the esmolol group and was sustained till 10 minutes post intubation (figure 11).

There were no complications attributable to the use of either study drug recorded during the course of the study.
FIGURE 1. THE DISTRIBUTION OF PATIENTS ACCORDING TO SURGICAL SPECIALTY
<table>
<thead>
<tr>
<th></th>
<th>Control n=30</th>
<th>Lidocaine n=30</th>
<th>Esmolol n=30</th>
<th>P value</th>
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<tr>
<td>Age/years mean± SD</td>
<td>35.0±13.35</td>
<td>38.8±10.99</td>
<td>36.0±11.72</td>
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<tr>
<td>Weight/ kg mean± SD</td>
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<td>70.5±11.97</td>
<td>60.7±9.79</td>
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<td>Gender ratio (M:F)</td>
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<td>15:15</td>
<td>18:12</td>
<td>0.302</td>
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<tr>
<td>ASA classification ratio ( I:II)</td>
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<td>16:14</td>
<td>17:13</td>
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<tr>
<td>Duration of laryngoscopy and Tracheal intubation/ seconds (mean ± SD)</td>
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<td>19.77±3.76</td>
<td>21.3±5.90</td>
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</table>
FIGURE 2. MEAN HEART RATE

![Mean Heart Rate Graph]

Mean Heart Rate (beats/minute)

- Baseline
- Immed post-intubation
- 3 Min
- 10 Min

Control
Esmolol
Lidocaine
FIGURE 3. PERCENTAGE CHANGE FROM BASELINE
IN MEAN HEART RATE

![Graph showing the percentage change from baseline in mean heart rate for different time points and interventions. The graph compares baseline, pre-induction, immediately post-intubation, and time points at 1 Min, 2 Min, 5 Min, and 10 Min for Control, Esmolol, and Lidocaine.]
FIGURE 4. MEAN SYSTOLIC BLOOD PRESSURE

Mean Systolic Blood Pressure (mmHg)

Time

Baseline, Pre-induction, Immed post Intubation, 1 Min, 3 Min, 5 Min, 10 Min

- Control
- Esmolol
- Lidocaine
FIGURE 5.  PERCENTAGE CHANGE FROM BASELINE IN MEAN SYSTOLIC BLOOD PRESSURE

<table>
<thead>
<tr>
<th>Time</th>
<th>Baseline</th>
<th>Pre-induction</th>
<th>Immed post Intubation</th>
<th>1 Min</th>
<th>3 Min</th>
<th>5 Min</th>
<th>10 Min</th>
</tr>
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<tbody>
<tr>
<td>% Change from baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Esmolol</td>
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<td></td>
</tr>
<tr>
<td>Lidocaine</td>
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</tbody>
</table>
FIGURE 6. MEAN DIASTOLIC BLOOD PRESSURE

Mean Diastolic Blood pressure (mmHg)

Time

Baseline, Pre-induction, Immed post intubation, 1 Min, 3 Min, 5 Min, 10 Min

Control, Esmolol, Lidocaine
FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time

FIGURE 7. PERCENTAGE CHANGE IN MEAN DIASTOLIC PRESSURE

% change in Diastolic blood pressure

Baseline  Pre-induction  Immed post intubation  1 Min  3 Min  5 Min  10 Min

Time
FIGURE 8. MEAN ARTERIAL PRESSURE

Mean Arterial pressure (mmHg)
FIGURE 9. PERCENTAGE CHANGE FROM BASELINE IN MEAN ARTERIAL PRESSURE

![Graph showing percentage change from baseline in mean arterial pressure over time for different treatment groups.](image-url)
FIGURE 10. MEAN RATE-PRESSURE PRODUCT
FIGURE 11. PERCENTAGE CHANGE FROM BASELINE IN MEAN RATE-PRESSURE PRODUCT

![Graph showing percentage change from baseline in mean rate-pressure product for various time points and interventions.]
DISCUSSION

Laryngoscopy and intubation are associated with a cardiovascular response of elevated blood pressure and pulse rate as well as occasional dysrhythmias. Lidocaine and esmolol are two drugs which have been used by anaesthetists in an attempt to attenuate this response.

In this study, treatment with intravenous lidocaine three minutes before laryngoscopy and intubation significantly attenuated the post-intubation increases in heart rate and rate pressure product. A dose of 1.5mg.kg$^{-1}$ was chosen based on work by Tam, Chung and Campbell who observed complete attenuation of the response when this dose of lidocaine (1.5mg.kg$^{-1}$) was given three minutes before laryngoscopy and intubation$^{65}$. Similarly, a review of 25 studies by Lev and Rosen on the preintubation use of lidocaine revealed that a dose of 1.5mg.kg$^{-1}$ given intravenously three minutes before intubation was optimal$^{34}$. In the present study, the heart rate increased by 25.7% in patients who received lidocaine compared to the control value of 33.4%. This shows that lidocaine as used in this study attenuates but does not abolish the post intubation rise in heart rate. This correlates with
the findings of Wilson et al\textsuperscript{112} who reported that irrespective of the timing of administration of intravenous lidocaine, 2, 3 or 4 minutes before tracheal intubation, there was an increase in heart rate of 21-26 % in all groups studied. In this study, intravenous lidocaine had an insignificant effect on the systolic blood pressure; 21.6\% rise compared to the control value of 26.9\%. The effects of intravenous lidocaine on diastolic blood pressure and mean arterial pressure were also not significant.
Several authors have emphasized the importance of timing of administration of lidocaine on its ability to attenuate the pressor response to laryngoscopy and endotracheal intubation. Tam et al\(^8\) showed that when administered intravenously three minutes before intubation, 1.5mg.kg\(^{-1}\) lidocaine significantly attenuated haemodynamic changes secondary to emergency intubation in patients with raised intracranial pressure following blunt head injury. Wang et al\(^1\) reported that the values of systolic and diastolic pressures one minute after intubation were significantly less in groups where 1.5mgkg\(^{-1}\) lidocaine was given either 3 or 5 minutes before intubation.

In Miller and Warren’s study of a group of 45 Chinese women, intravenous lidocaine 1.5mg.kg\(^{-1}\) failed to attenuate the cardiovascular response to laryngoscopy and tracheal intubation irrespective of the timing of administration i.e. 1, 2 or 3 minutes before laryngoscopy\(^8\). In the same vein, Chraemmer-Jorgensen and colleagues\(^1\) reported a total lack of effect of intravenous lidocaine given 2 minutes prior to laryngoscopy and intubation, on the haemodynamic responses. Despite pre-treatment of their patients with intravenous lidocaine, the rate-pressure products were observed to approach levels considered potentially dangerous to patients with ischaemic heart disease. Differences in study protocol, patient population, premedication, depth of anaesthesia, duration of laryngoscopy and interval between lidocaine administration and laryngoscopy may account for these apparently varied results among the different studies.

The pharmacokinetic properties of intravenous lidocaine may explain its ability to attenuate the pressor response within a tightly specific time frame. Following intravenous injection, the onset of action is between 45-90 seconds with a peak effect at 1-3 minutes\(^7\). Its optimum effect on the haemodynamic response to laryngoscopy and intubation is most
likely exerted at about its peak effect. It also obtunds laryngeal reflexes and reduces thiopentone requirement by 13.3%\textsuperscript{79,80}. Abou-madi et al\textsuperscript{35} suggested other possible mechanisms to explain the anti-pressor effects of lidocaine. These include a direct myocardial depressant effect, a peripheral vasodilating effect and a possible effect on synaptic transmission.

There were no complications recorded following the administration of intravenous lidocaine in this study. However, in their study evaluating the haemodynamic response to laryngoscopy and intubation in geriatric patients, Splinter and Cervenko reported that 34% of their patients who were given intravenous lidocaine developed tinnitus\textsuperscript{82}.

In this study, the administration of intravenous esmolol resulted in a 19.1% increase in post-intubation heart rate compared to 41.4% in the control group and 25.7% in the intravenous lidocaine group. The esmolol group showed a rise in systolic blood pressure (13.3%) but this was significantly less than those observed in the lidocaine (21.6%) and control (26.9%) groups. The response to the dose of esmolol used in this study was similar to that obtained by Helfman et al\textsuperscript{106} who compared lidocaine and esmolol for attenuation of the pressor response and reported mean percent increases in heart rate of 44% lidocaine, 51% placebo and 18% in esmolol group. Mean systolic blood pressure percent increases were 20% in the lidocaine, 36% in the placebo and 19% in the esmolol groups. Only esmolol provided consistent and reliable protection against increases in both heart rate and systolic blood pressure accompanying laryngoscopy and intubation.

The rationale for the administration of esmolol as a bolus rather than as an infusion in this study was twofold; the desire for a rapid onset and short duration of action in order to promptly treat a transient haemodynamic event as well as the convenience of bolus
administration compared with the preparation and administration of an infusion. A dose of 2mg.kg\(^{-1}\) administered two minutes prior to laryngoscopy and intubation was chosen for this study based on results of several published trials evaluating the use of esmolol for attenuation of the pressor response\(^{92,99,105}\). Sintetos et al\(^{92}\) recommended that esmolol be given 2 minutes before intubation for effective results because its maximum effects on heart rate and blood pressure occurred in the first and second minutes respectively.

At 5 minutes, both treatment groups showed significant decreases in mean SBP compared to baseline which persisted even until 10 minutes after intubation. This could be attributed to the rapid metabolism of released catecholamines, myocardial depressant effect of the volatile agent (halothane) and the absence of surgical stimulation\(^{6,10,63}\). Although none of the patients in the study had hypotension, by definition, the 14.5% and 13.8% mean reduction in SBP observed in the esmolol and lidocaine groups respectively, suggest their potential for hypotension especially in haemodynamically unstable patients.

The rate-pressure product (RPP) increased post intubation in all the groups. Esmolol showed significantly greater effects than lidocaine in attenuating the post-intubation rise in RPP. The rate-pressure product (a product of the systolic blood pressure and heart rate) is a good index of myocardial oxygen consumption and a threshold of RPP has been correlated with the onset of angina in patients with known coronary artery diseases or those who have risk factors for coronary artery disease\(^{115}\). Increased blood pressure and heart rate lead to elevated myocardial oxygen demand and the haemodynamic changes at intubation may precipitate myocardial ischaemia and infarction. Tachycardia increases myocardial oxygen demand, decreases diastolic filling time, and hence coronary blood
flow. A moderate increase in heart rate (15%) has been shown to be accompanied by a 17% decrease in coronary perfusion pressure\textsuperscript{116}.

Raised blood pressure, on the other hand, increases both oxygen demand and supply and thus has a less predictable effect on myocardial oxygen balance. Furthermore, the increase in blood pressure accompanying laryngoscopy and intubation has been attributed to an increase in cardiac output rather than increased systemic resistance\textsuperscript{117}. Hence, by its predominant attenuation of increases in heart rate, esmolol is more likely to optimize the myocardial oxygen supply/demand relationship. Recommendations of maximum permitted RPP range from 12,000 to 23,000 mmHg beats.min\textsuperscript{-1} and values exceeding this are commonly associated with myocardial ischaemia and angina\textsuperscript{118}. The patient’s preoperative level should however serve as a guide. Rao et al\textsuperscript{119} recommended that in the anaesthetic management of patients with cardiac morbidity presenting for non-cardiac surgery, the heart rate and systolic blood pressure and thus the RPP should not fluctuate beyond 20% of the baseline value. Although RPP does not predict regional myocardial supply-demand relationships, examination of the individual components (heart rate and systolic blood pressure) is a useful guide in the management of ischaemic heart disease. Of the two treatment techniques used in this study, esmolol was superior as it significantly attenuated the heart rate, systolic blood pressure and rate-pressure product changes. However, the 28.06% rise in RPP recorded in the esmolol group still exceeds Rao’s 20% recommendation. This is however significantly superior to the 45.8% of the lidocaine group and the 78.7% of the control group.

The transient decrease in RPP observed in the esmolol group following the administration of the drug, correlate with those of Liu and colleagues who using esmolol to control
haemodynamic responses associated with tracheal intubation, reported a decrease in RPP prior to induction of anaesthesia. As observed in the present study, Liu et al reported a post intubation increase in RPP which was 50% less in the esmolol-treated patients compared to the placebo group. However, Buffington was of the opinion that during anaesthesia, myocardial ischaemia is poorly correlated with RPP. His advocacy of the Pressure Rate Quotient (PRQ) as a more reliable index of myocardial ischaemia is disputed by other workers.

Apart from causing a transient decrease in heart rate and blood pressure following its administration at induction, there were no adverse effects attributable to the use of esmolol in this study. Miller et al showed that esmolol in doses of 1.5-3.0mg.kg did not alter stroke volume or depress left ventricular function in patients with preserved cardiac function.

In this study, the adoption of different time intervals for administration of esmolol and lidocaine i.e. 2 and 3 minutes respectively, may have introduced a possible source of bias with respect to blinding. Review of available literature revealed that these doses and time intervals were safe and produced consistent results with respect to attenuation of the pressor response. This bias was reduced by the use of an impartial observer (anaesthetist registrar) who measured and recorded the haemodynamic data.

Thomson and Hung have questioned the clinical significance of the haemodynamic responses associated with laryngoscopy and intubation and argue that the subject does not deserve the attention it attracts. They are quick to point out that a transient increase in arterial blood pressure and heart rate occurs in most of our daily activities and may not be of any clinical importance. Hung argued that the interpretation of cardiovascular
responses to anaesthetic drugs is difficult when a noxious intervention such as laryngoscopic intubation introduces confounding variables such as magnitude and duration of the noxious intervention as well as variables introduced by various medical conditions such as cardiovascular diseases and diabetes mellitus. These he postulated, may explain the inconsistent results reported in previous studies. In his experiment in which 21 healthy volunteers were subjected to stress tests with continuous haemodynamic monitoring (intra-arterial blood pressure and heart rate), he was able to demonstrate that haemodynamic responses occur with normal daily activities and these responses are generally well tolerated, provided they are short lived.

The clinical significance of the pressor response to laryngoscopy and intubation is most important in the perioperative management of patients with cardiovascular diseases and intracranial hypertension. Prys-Roberts et al\textsuperscript{17} found that hypertensive patients, whether treated or untreated, are prone to much greater changes in arterial pressure (and thus RPP), than normotensive patients of the same age group. They found that the excessive swings in blood pressure observed in their patients, were accompanied by electrocardiograph (ECG) evidence of myocardial ischaemia. In the hypertensive patient with normal left ventricular function, the blood pressure falls at induction without a significant fall in heart rate; thus maintaining left ventricular filling pressure and blood supply. Hence the incidence of myocardial ischaemic changes in these patients is less than 6%. However, in the patient with hypertensive heart disease and poor left ventricular function, the heart rate increases following induction of anaesthesia, with a decrease in filling pressure and left ventricular blood flow. The risk of ischaemic changes in these patients is almost as high as 33%\textsuperscript{103}. Urban et al\textsuperscript{18} examined the relationship between several intraoperative haemodynamic
variables, fixed cardiac risk factors, intraoperative myocardial ischaemia and postoperative myocardial infarction (PMI) in a group of patients undergoing coronary by-pass graft (CABG) surgery. They found that RPP > 12,000(beats.min\(^{-1}\).mmHg\(^{-1}\)) was significantly associated with pre-cardiopulmonary bypass (pre-CPB) myocardial ischaemia. In addition, a pre-CPB electrocardiography ischaemia was significantly associated with a postoperative myocardial infarction.

In an earlier editorial on the subject by Thomson\(^9\), several observations were made. He noted that although researchers documented the haemodynamic changes accompanying laryngoscopy and intubation, they gave no information on outcome. Thus, the influence of their interventions on the incidence of perioperative cardiovascular morbidity and mortality were unknown. Although he admitted that certain subgroups of patients (i.e. those with symptomatic aortic aneurysm, recent myocardial infarction, cerebral aneurysm or intracranial hypertension) required careful haemodynamic control during intubation of the trachea, he noted that such patients were never included in the control group of studies examining the efficacy of haemodynamic control during laryngoscopy and intubation. He advocated that since myocardial infarction accompanying perioperative myocardial ischaemia occurred between the second and fifth postoperative day, greater benefits will be achieved if haemodynamic control is extended to cover the entire perioperative period, rather than limited to two minutes following intubation\(^9\).

While making pertinent observations, Thompson appears to have ignored the ethical aspects of such research. Withholding therapy from patients at risk in order to determine outcome would raise a lot of questions with regards to ethics. Nonetheless, search of the literature revealed a number of studies performed on patient populations at risk of
developing perioperative complications such as the elderly, those with documented coronary artery disease, vascular disease, hypertension, diabetes and obesity\textsuperscript{66,95,97}. In these studies, the duration of laryngoscopy and intubation was limited to 30 seconds to avoid unduly endangering the patients in the control groups. Although the various researchers did not advocate the routine use of these agents for all patients undergoing general anaesthesia, they were recommended as useful adjuncts in patients at risk when it is imperative to control haemodynamic responses to transient perioperative stimuli.

In this study, the unit costs of esmolol and lidocaine per patient were averagely N1, 700 ($14.20) and N200 ($1.70) respectively which makes lidocaine more cost-effective to use for attenuation of pressor responses to laryngoscopy and endotracheal intubation\textsuperscript{5}. This is particularly of significance in the face of dwindling health care resources and poor funding. However, the use of more expensive drugs may be justified in susceptible groups of patients if it will result in better perioperative management, reduced morbidity or an overall reduction in length of hospital stay. Although esmolol is currently more expensive than lidocaine, the observation in the past is that as patent rights expire, regularly used drugs become cheaper and more readily available for use in Nigeria.

**CONCLUSION**

This study has confirmed that significant increases in haemodynamic variables accompany laryngoscopy and endotracheal intubation following the widely utilized technique of induction of anaesthesia with sodium thiopentone followed by suxamethonium for tracheal intubation. These changes are maximal immediately after intubation, but return to baseline values by 5 -10 minutes.

Neither drug deployed in this study completely abolished this response but it was
attenuated to varying degrees. Intravenous lidocaine 1.5mg.kg\(^{-1}\) administered 3 minutes before laryngoscopy significantly attenuated the heart rate and rate-pressure product changes following laryngoscopy and intubation. Intravenous esmolol 2mg.kg\(^{-1}\) given 2 minutes prior to laryngoscopy was statistically superior to lidocaine as it significantly attenuated all the cardiovascular changes. Comparing the results obtained in this study with those conducted in Europe, North America and Asia in other patient groups, intravenous esmolol had a significant effect in this African population as it significantly attenuated every measured haemodynamic variable.

The use of these two agents in the doses deployed in this study was not associated with any untoward effects.
RECOMMENDATIONS

Based on the findings of this study, it is recommended that;

- Greater efforts should be made by hospitals and relevant regulatory agencies to make esmolol hydrochloride readily and cheaply available to anaesthetists practicing in Nigeria for the control of periods of intense sympathetic stimulation such as laryngoscopy and intubation. This would enhance perioperative patient management and add on to the safety of anaesthetic practice.

- Although not recommended for routine administration in all patients, esmolol is a useful adjunct for use by anaesthetists involved in perioperative management of patients with identifiable risk factors for coronary artery disease, hypertension or hypertensive heart disease with preserved cardiac function as these patients are at high risk for development of myocardial ischaemia and infarction following laryngoscopy and intubation.

- A dose of 2mgkg\(^{-1}\) esmolol administered 2 minutes before laryngoscopy is optimal for attenuation of the pressor response.

- The use of intravenous lidocaine at a dose of 1.5mgkg\(^{-1}\) given 3 minutes before laryngoscopy should not be abandoned. However it should be reserved for use in patients in whom beta blockers are contraindicated (reactive airway disease,
diabetes mellitus, heart block, congestive cardiac failure and bradyarrhythmias i.e. HR<60beats.minute\(^{-1}\)) or where more effective agents are unavailable for use.

- A combination of lower doses of esmolol and lidocaine may offer better control of the pressor response in Nigerians and is worth evaluating in the future.

**LIMITATIONS**

This study had the following limitations.

1. All the patients received the same dose of oral diazepam premedication irrespective of weight due to the available formulation of diazepam tablets. This may have modified the observed pressor response as benzodiazepines are known to have a moderating effect on intraoperative cardiovascular responses\(^{103}\).

2. Cardiac dysrhythmias and myocardial ischaemia are two well documented consequences of the haemodynamic response to laryngoscopy\(^4\). Thus continuous electrocardiogram (ECG) monitoring of leads II and V5 is highly desirable in a study like this. The available continuous ECG monitors in this centre were malfunctional at the time of data collection for this study.

3. Direct intra-arterial measurements which give continuous, beat-to-beat blood pressure readings would have provided more precise information on the haemodynamic changes and the effectiveness of the studied drugs in attenuating the pressor response. Facilities for such monitoring are not available in this centre.

4. Several studies have established that the haemodynamic changes observed during laryngoscopy and intubation are associated with corresponding increases in serum adrenaline and noradrenaline levels\(^{6,39,40}\). It would have been worth determining if
any of the treatment techniques used in this study had an effect on the plasma catecholamine levels. However, the unavailability of facilities for conducting such biochemical assays in this centre as well as the cost implications of external analysis precluded this.

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APPENDIX I

PROFORMA

ATTENUATION OF THE PRESSOR RESPONSE TO
LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A
COMPARISON OF ESMOLOL AND LIDOCAINE

Name: Hospital No: Date:
Age: Sex: Weight:

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Height: Drug history: Diagnosis: Surgical procedure: ASA score: Premedication:

Study Group: Group L ( )

Group E ( )

Group C ( )

Duration of laryngoscopy and intubation:

<table>
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<th>Immediate Post intubation</th>
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HR = Heart rate, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Arterial Pressure, RPP = Rate Pressure Product.

**Complications**

- Bradycardia
- Bronchospasm
- Hypotension
- Tinnitus
- Circumoral numbness
- Pain on injection
- Others (specify)
APPENDIX II

PATIENT INFORMED CONSENT

TITLE OF THE STUDY: Attenuation of the pressor response to laryngoscopy and endotracheal intubation: A Comparison of intravenous esmolol and lidocaine.
INTRODUCTION
You are being approached because you are going to have elective surgery under general anaesthesia. Laryngoscopy and endotracheal intubation are an integral component of airway management during general anaesthesia. They have been shown to result in a rise in heart rate, blood pressure and the occurrence of arrhythmias. This may have detrimental effects in susceptible patients e.g. patients with ischaemic heart diseases, hypertension and head injuries. Various drugs have been suggested to prevent these haemodynamic changes. Esmolol and Lidocaine are two of such drugs.

PURPOSE AND DESCRIPTION OF STUDY
The aim of this study is to evaluate the effects of each drug and compare their effects in preventing these haemodynamic changes. During the preoperative anaesthetic visit on the ward, an anaesthetist will explain the study protocol, answer any questions you may have and ask for a written informed consent.
In the operating theatre, according to our routine management, an intravenous infusion will be set up in order to give you appropriate anaesthetic drugs. We will monitor your blood pressure, heart rate and oxygen level as part of standard practice.
You will be assigned to one of three groups by balloting. The groups would be named according to the study drug that will be used. The same drugs will be given to every patient for induction of anaesthesia and maintenance of anaesthesia will be standard for every patient.

POTENTIAL RISKS
Since the study drugs will be administered on a weight basis, with adequate consideration given to maximum safe doses and contraindications to their use, the risk s involved in participating in this study are minimal.

CONFIDENTIALITY
All information obtained during the study will be held in strict confidence
CONSENT FORM

Signing this consent form does not wave your legal rights nor does it relieve the investigators or this institution from legal and professional responsibilities.

CONSENT

I have had an opportunity to ask all necessary questions regarding the information of my participation in this study and have received satisfactory answers. I understand that my participation in this study is entirely voluntary. I, the undersigned, accept to participate freely in this research project.

------------------------------------------------------------------
Patient’s name                                                     signature and date
------------------------------------------------------------------

------------------------------------------------------------------
Witness name                                                      signature and date
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ATTENUATION OF THE PRESSOR RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON OF INTRAVENOUS ESMOLOL AND LIDOCAINE