Dissertation on

ATTENUATION OF

CARDIOVASCULAR STRESS RESPONSE ACCOMPANYING LARYNGOSCOPY AND INTUBATION : A CLINICAL COMPARISON OF LIGNOCAINE AND DILTIAZEM IN E.N.T. SURGERY

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MD ANAESTHESIOLOGY
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DECLARATION

In the following Pages is presented a consolidated report of Dissertation on "Attenuation of Cardiovascular Stress response accompanying Laryngoscopy and intubation - a Clinical Comparison of Lignocaine and Diltiazem in E.N.T Surgeries".

A clinical study, prepared by me during the last one year in Madras Medical College, and Govt. General Hospital, Chennai. This thesis is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, in partial fulfilment of the rules and regulations for the M.D. Degree examination in Anaesthesiology to be held in February 2006.

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CERTIFICATE

This is to certify that the dissertation entitled "Attenuation of Cardiovascular Stress response accompanying Laryngoscopy and Intubation - A Clinical Comparison of Lignocarine and Diltiazem in E.N.T. Surgeries", is a genuine work done by Dr.S.Ananthappan for the fulfilment of M.D (Anaesthesiology) under my supervision and the guidance of Dr.S.Krishnakumar M.D., Asst. Professor of Anaesthesiology, Department of Anaesthesiology, Madras Medical College, Chennai.

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CERTIFICATE

This is to certify the dissertation entitled "Attenuation of Cardiovascular Stress response accompanying Laryngoscopy and Intubation. A Clinical Comparison of Lignocarine and Diltiazem in E.N.T. Surgeries" is the original work done by Dr.S.Ananthappan for the fulfilment of M.D (Anaesthesiology) under the supervision of Prof. Dr.G.SIVARAJAN M.D., D.A., and the guidance of Dr.S.KRISHNAKUMAR M.D., Asst. Professor of Anaesthesiology, MMC, Chennai.

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CONTENTS

INTRODUCTION

Hypertension and tachycardia have been reported since 1950 during intubation in a light plane of anesthesia. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngo tracheal stimulation, which in turn causes increased plasma norepinephrine concentration. These changes may be fatal in patients with ischeamic heart disease and hypertension.

Tachycardia, hypertension and dysrythymias all occur during laryngoscopy and intubations. The consequent rise in rate/pressure product may result in a myocardial oxygen demand which exceeds the oxygen supply resulting in myocardial ischeamia. This response is sympathetically mediated and can be attenuated by calcium channel blocking drugs. Studies have documented myocardial ischeamic changes due to reflex sympatho adrenal response immediately following laryngoscopy and intubation with a mean increase in systemic pressure of 40mmHg even in normotensive patients.

An increase in heart rate is more likely to produce signs of myocardial ischeamia than hypertension on the ECG. Indeed, in anaesthetized patient, the incidence of myocardial ischeamia on the ECG sharply increases in patients who experience a heart rate greater than 110bpm (ischeamic threshold). A frequent recommendation is to maintain heart rate and blood pressure within 20% of normal awake value for that patient.

Many attempts have been made to attenuate the pressor response to laryngoscopy and intubation.

For eg.

- deep plane of anesthesia
- topical anesthesia
- use of ganglionic blockers
- use of intravenous local anaesthetics
- Sodium nitroprusside infusion
- Magnesium sulphate
- Fentanyl
- Use of beta-blockers
- Calcium channel blockers.

It has been clearly proven by various studies that sympathetic overactivity occurs during laryngoscopy and the importance of suppressing the sympathetic overactivity is well emphasized. The various methods of suppressing the stress response are listed above, and of these, IV Diltiazem appears to be superior to IV Lignocaine. The use of IV diltiazem in suppressing the stress response is compared with IV lignocaine in E.N.T surgical patients, who underwent FESS, Mastoidectomy etc.

Lignocaine is the drug that is commonly used in our hospital for controlling intubation response. Diltiazem, a calcium channel blocker has been found in various studies to attenuate intubation response, hence we made a study by comparing Diltiazem and Lignocaine for obtunding intubation response, in the Department of Anaesthesiology at Govt. General Hospital, Chennai-600 003.

AIM OF STUDY

To compare the efficacy of IV lignocaine and IV Diltiazem in attenuating the cardiovascular stress response during laryngoscopy and intubation in E.N.T Surgeries.

ANATOMY - NERVE SUPPLY OF LARYNX

Nerve supply of larynx is from Superior laryngeal nerve and Recurrent laryngeal nerve, which are branches of vagus nerve.

Superior laryngeal nerve arises from the middle of the inferior ganglion of the vagus, runs downwards and forwards on the superior constrictor muscle deep to internal carotid artery and reaches the middle constrictor muscle where it divides into external laryngeal nerve and internal laryngeal nerve. External laryngeal nerve is thin, accompanies superior thyroid artery, pierces deep constrictor and ends by supplying the cricothyroid muscle.

Right recurrent laryngeal nerve arises from vagus in front of right subclavian artery, winds backwards below the artery to reach the tracheo-oesophageal groove. It is related to the inferior thyroid artery in its upper part. The nerve then passes deep to lower border of inferior constrictor muscle, and enters the larynx behind the cricothyroid joint. It supplies all the intrinsic muscles of the larynx except the crico thyroid and carries sensory fibres to the larynx below the level of vocal cord.

The left recurrent laryngeal nerve arises from the vagus in the thorax. It curves around the aortic arch and soon gains entry into the tracheo-oesophageal groove. Thereafter its course is similar to that of the right recurrent laryngeal nerve.

PHYSIOLOGY -REFLEX CIRCULATORY RESPONSE TO LARYNGOSCOPY AND INTUBATION

Hypertension and tachycardia frequently accompany laryngoscopy and endotracheal intubation. These circulatory changes are transient and of little significance in patients with normal heart. Hypertension and tachycardia following laryngoscopy and intubation is due to increase in plasma catecholamine concentration, which is more pronounced in ischeamic heart disease patients leading to deleterious effect. These reflex circulatory changes occur due to stimulation of sympatho adrenal response to noxious stimuli. Cardiac arrhythmias occur in 5% to 15% of patients during endotracheal intubation under light plane of anaesthesia. Sudden death, presumably from ventricular fibrillation, has also been reported to result reflexly from intubation.

METHODS TO ATTENUATE CIRCULATORY RESPONSE TO LARYNGOSCOPY AND INTUBATION

Hypertension and tachycardia have been reported since 1950 during intubation in a light plane of anaesthesia. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation which in turn leads to increased plasma norepinephrine concentration, which may be fatal in patients with heart disease and hypertension.

Many attempts have been made to attenuate the pressor response.

They are :

- Deepening the plane of anaesthesia with volatile inhalation agent
- Topical anaesthesia with xylocaine spray
- Use of ganglionic blockers
- Use of beta blockers
- Sodium nitroprusside infusion
- Nitroglycerine infusion
- Calcium channel blockers - Diltiazem
- Magnesium sulphate
- Opioids like fentanyl
- Anti-hypertensive like phentolamine
- use of IV lignocaine
- Alpha-agonist like Clonidine.

Sodium nitroprusside and nitroglycerine are effective but requires continuous intra arterial blood pressure monitoring.

Calcium channel blockers are effective because myocardial depression produced by it is minimised by reduction in afterload, so that cardiac output remains unchanged.

Magnesium sulphate can also be used to control the hypertensive response by reducing the plasma norepinephrine concentration.

Addition of a potent analgesic such as fentanly also attenuates the intubation response.

PHARMACOLOGY CALCIUM CHANNEL BLOCKERS

Calcium channel blockers are a diverse group of structurally unrelated compounds that selectively interfere with inward calcium ion movement across myocardial and vascular smooth muscle cells (Durand, et al., 1991, Kaplan, 1989) Calcium ions play a key role in the electrical excitation of cardiac cells and vascular smooth muscle cells.

CLASSIFICATION

Commercially available calcium channel blockers are classified on the basis of chemical structure as

a. Phenyl alkylamines
b. 1,4 dihydropyridines
c. Benzothiazepines

These drugs block calcium entry into cardiac and vascular smooth muscle cells at the alpha, sub unit, 1,4 dihydropyrimidines are selective for the arteriolar beds where as the phenyl alkalamines and benzothiazipines are selective for the atrioventricular node.

MECHANISM OF ACTION

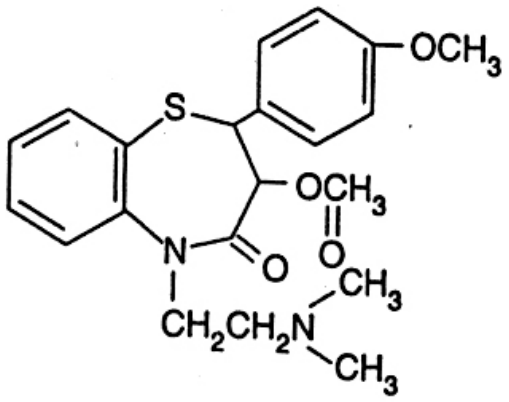
Voltage gated calcium ion channels are present in the cell membranes of skeletal muscle, vascular smooth muscle, cardiac muscle, mesentric muscle, glandular cells and neurons. Of the two types T and L of voltage gated channels present in the cardiovascular system, the L-type is the main channels

for slow and sustained calcium ions entry into vascular smooth muscle cells. Even though the T-type channels are also present on vascular smooth muscle cell membranes, insignificant amounts of calcium ions enter cells through them, and they are not influenced significantly by calcium channel blockers.

The L-type channel has five sub units alpha, alpha 2, beta, gamma and delta. The alpha, sub unit forms the central part of the channel and provides the main pathway for calcium ions entry into cells.

Direct activation of the vascular smooth muscle cell voltage-gated channels by nervous stimuli initiates an action potential, calcium ion influx, and myofilament contraction. This process is known as excitation contraction coupling. The intracellular calcium combines with calmodulin, the calcium binding protein, to form the calcium - calmodulin complex. This complex activates myosin and causes the formation of cross bridges with actin. These cross bridges begin the process of muscular contraction.

PHARMACOLOGY OF DILTIAZEM



Chemical

A benzothiazipine, a calcium channel blocker

Main actions

It increases myocardial oxygen supply and decreases myocardial oxygen demand by coronary artery dilation, possibly aided by direct and indirect haemodynamic alterations.

Mode of Action

Diltiazem acts dose dependent inhibition of the slow inward calcium current in normal cardiac tissue.

Route of Administration / Doses

The adult oral dose is 30-120 mg 6-8th hrly.

Effects

CVS : Diltizem is a potent peripheral and coronary arterial vasodilator, leading to a decrease in the systemic and pulmonary vascular resistances; the cardiac output increases due to a reduction in after load. Little effect on the heart rate occurs in man, bradycardia tends to occur with chronic use. A-V nodal conduction is decreased by the drug, diltiazem is thus of use in the treatment of supra ventricular tachycardia.

RS : Inhibits bronchoconstriction due to inhaled histamine in man.

AS : A significant reduction in lower oesophageal pressure is produced in patients with achalasia, although no effect is seen in normal patients.

GU : Renal artery dilation leading to an increased renal plasma flow and subsequent diuresis occurs after the administration of diltiazem. Uterine activity is decreased invitro.

Metabolic

Platelet aggregation is decreased by diltiazem invitro, although no significant effect on haemostasis can be demonstrated invivo.

Side effects

Occur in 2-10% and include headache, flushing, peripheral oedema and bradycardia.

Kinetics

Absorption : 90% of an oral dose is absorbed, the bioavailability by this route is 33-40% due to significant first effect.

Distribution : 78-87% protein bound in the plasma.

Metabolism : By deacetylation and demethylation in the liver with subsequent conjugation to glucuronide and sulphates - the metabolites are active.

Excretion: 1-4% excreted unchanged in the urine. The clearance is 11.5 - 21.3 ml / Kg/min and the elemination half life is 2-7 hrs. Renal failure has no effect.

Uses

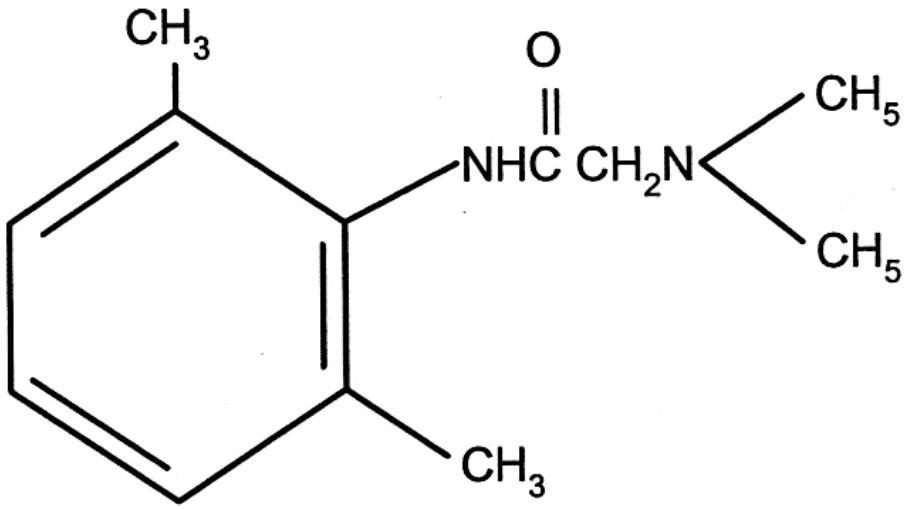
In the treatment of

1. Stable and variant angina
2. Hypertension
3. Supraventricular tachycardia
4. Raynand's phenomenon
5. Migraine
6. Oesophageal disorders
7. Attenuation of stress response to intubation

Presentation

As 60, 90, 120, 180 mg tablets and Inj 5 ml vial containing 5 mg/ml.

PHARMACOLOGY OF LIGNOCAINE



Lignocaine was synthesized in 1943 in Sweedan by Lofgren and was introduced into clinical practice in 1948.

DESCRIPTION

Lignocaine hydrochloride is 2-diethylamino-aceto-2'6xylilide hydrochloride monohydrate. It appears as a white crystalline powder which is odourless. It is very soluble in water, freely soluble in chloroform and in ethanol and is practically insoluble in ether.

Molecular formula - C14H22 N20 Hcl.H20

Molecular weight - 288.8

Lignocaine hydrochloride injection is a sterile, isotonic solution containing lignocaine hydrochloride B.P., 1% or 2%, and sodium chloride, B.P., in water for injection.

Lignocaine is a week base with amphiphillic property. A hydrophilic amine on one side and a lipophillic aromatic residue on the other side and are joined through an amide linkage.

MECHANISM OF ACTION:

Local anaesthetics block the nerve conduction by decreasing the entry of sodium ions during upstroke of action potential. As the concentration of local anaesthetic is increased the rate of rise of action potential and maximum depolarization decreases causing slowing of conduction. Finally local depolarization fails to reach the threshold potential and condition block ensues. The local anesthetics interact with a receptor situated within the voltage sensitive sodium channel and raise the threshold of channel opening.

Sodium channel has an activation gate(A) near its extracellular mouth and an inactivation gate(I) at the intracellular mouth. In the resting state, the activation gate is closed. Threshold depolarization of the membrane opens the activation gate allowing sodium ions to flow in along the concentration

gradient. Within a few milliseconds inactivation gate closes and ion flow ceases.

The local anaesthetic recepter is located within the channel in its intracellular half. Local anaesthetic traverses the membrane in its lipophillic form (B+), reionises in the axoplasm and approaches the LA receptor through the intracellular mouth of the channel. It is the cationic form of local anaesthetic (BH+), which primarily binds to the LA receptor. The receptor has higher affinity or is more accessible to local anaesthetic in the activated state compared to the resting state. Binding of LA to its receptor stabilizes the channel in the inactive state and thus reduces the probability of channel opening.

Action of receptors within the sodium channel accounts for 90% of nerve blocking effect. Non-specific membrane expansion accounts for the remaining 10% of the action and is analogous to the electrical stabilization produced by a number of non-polar, purely lipid solvable substances such as barbiturates, general anaesthetics and benzocaine.

PHARMACOLOGICAL ACTION:

1. LOCAL - Minimal local irritant action and blocks sensory nerve endings, nerve trunks, neuro-muscular junction, ganglionic receptors.

2. REGIONAL - Autonomic fibers are generally more susceptible than somatic fibers. Among the somatic afferents, the order of blockade is pain temperature touch deep pressure.

3. SYSTEMIC - Effect is mainly on CVS or CNS.

CVS : In cardiac tissue, a therapeutic serum concentration (1.5 to 6. micrograms / ml) of lignocaine will produce the following effects:

- depression of slow spontaneous depolarization (phase 4), that is the automaticity of isolated, non-polarised purkinjee fibres, while having little effect on conduction velocity, membrane responsiveness or cardiac output. Automaticity induced by stretch, hypoxia or catecholamines can also be suppressed by lignocaine.

- Shortening of action potential period and effective refractory period of purkinjee and ventricular cells.

Thus it has a stabilizing effect on cell membrane of cardiac tissue. It also stabilizes aberrant conduction.

CNS : Low plasma concentration of LA are likely to produce numbness of tongue and circumoral tisses. As plasma concentration increases it crosses blood-brain-barrier and produces restlessness, vertigo, tinitus and difficulty in focusing. Then slurred speech and skeletal muscle twitching occur.

Lignocaine causes drowsiness before seizures. Seizures are classically followed by CNS depression, which may be accompanied by hypotension and apnoea.

PHARMACOKINETICS

Following IV injection, the blood level of lignocaine declines with a half-life of 7 to 10 mins., within the first hour due to rapid distribution into various tissues including the heart. After this initial phase, the half-life is 90 to 120 mins (metabolism and excretion). Absorption is slow in regional anaesthesia.

METABOLISM AND EXCRETION

The principle metabolic pathway of lignocaine is oxidative dealkylation in the liver to monoethylgycinexylidine following by hydrolysis of this metabolite to xylidine. Monoethylglycine xylidine has approximately 80% of the activity of lignocaine for protecting against cardiac dysrhythmias. This metabolite has a prolonged elimination half time. Xylidine has approximately 10% of the activity of lignocaine. Hepatic disease or decrease in hepaticflow, which may occur during general anaesthesia, decreases the rate of metabolism of lignocaine. Excretion is through the kidneys. Approximately 90% of the dose is excreted as metabolites and less than 10% is excreted unchanged in the urine.

DOSAGE

For cardiac arrythmias, therapeutic serum concentration of lignocaine is 5 to 20 micromol/L or 1.5 to 6.0 micrograms/ ml.

A single intravenous dose of 1mg/kg should be given over 1 to 2 mins, to obtain therapeutic blood levels rapidly. The initial effect will occur in 2 to 4 mins, and may last as long as 20 mins. This should be followed within 10 mins, by a continuos infusion at the rate of 2 to 4 mgs/min. The initial dose may be repeated by two more injections at 15 to 20 min intervals to maintain therapeutic blood levels but no more than 300mg of lignocaine should be administered within a 1 hr period. Since it has a very narrow therapeutic window, infusion should promptly stopped when there is an undue prolongation of PR interval or QRS complex.

To attenuate the cardiovascular stress response to intubation, lignocaine 1.5mg/kg IV 3 min prior to laryngoscope should be given.

ADVERSE EFFECTS /TOXCICITY:

- Due to high plasma levels as a result of excessive dosage, rapid absorption, delayed elimination or inadvertent IM injection during local anaesthetic use.

- CNS: Lightheadedness, disorientation, confusion, psychois, nervousness, agitation, drowsiness, euphoria, tinnitus, blurred vision,

slurred speech, numbness, twitcfhing, tremors, convulsions, unconsiousness, seizures, coma, respiratory depression and arrest.

- CVS: Hypotension, CVS collapse, arrahythmias, heart block and bradycardia which may lead to cardiac arrest. Meth-hemoglobineamia may occur following IV administration.

- HYPERSENSITIVITY: Rare with lignocaine.

- NEUROLOGICAL SYSTEM : Persistent anaestheisa, paresthesia, weakness, paraplegia of lower extremeities and loss of sphincter control may occur.

PRECAUTIONS

The safety and effectiveness of lignocaine depends upon proper dosage, correct technique, adequate precautions and readiness for emergencies.

1. Lignocaine should be given cautiously in patients with severe bradycardia, cardiac conduction disturbances, severe digitalis intoxication, severe shock and hypovolemia.

2. Serum Potassium level should be normalized prior to administration of lignocaine as anti-arryhthmic drugs may be ineffective in hypokaelemic patients.

DRUG INTERACTIONS

Propanolol and metaprolol reduce the metabolism of intravenously administered lignocaine. It is possible that this effect will be repeated with other beta - adrenergic blockers.

1. Phenytoin, phenobarbitone, primidone and carbamazapine appears to enhance the metabolism of lignocaine, possible due to an induction of microsomal enzyme.

2. Lignocaine prolongs the duration of suxamethonium.

INDICATIONS

1. Local anaesthesia, nerve blocks and regional analgesia.

2. Anti-arrhythmic agent.

3. To obtund intubation response

4. Brain Protection.

5. Myocardial infarction.

6. To relieve arterial spasm following accidental intra-arterial injection of Thiopentone.

REVIEW OF LITERATURE

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RIED & BRACE (1940) postulated that reflex circulatory responses to laryngeal instrumentation were mediated through the vagus nerve and they named it as "Vaso Vagal Reflex".

KING et al (1951) used deep ether anaesthesia to abolish the reflex circulatory response to tracheal intubation.

WYCOFF C.C. (1960) in his study stated that topical anaesthesia of the pharynx along with superior laryngeal nerve blocks, reduced the increase in mean arterial pressure after intubation.

STEINHANS GASKIN (1963) found that intravenous lignocaine suppressed the cough reflex. It is very easy to predict that if the cough is suppressed, the rise in blood pressure and pulse rate and intra cranial pressure noticed on laryngeal instrumentation would be blunted by this technique.

FORBES and DALLY (1970) observed that laryngoscopy and endo-tracheal intubation is immediately associated with an average increase in mean arteral pressure of 25mm Hg in all 22 normotensive patients. These responses were interpreted as due to reflex sympathetic adrenal stimulation.

MASSON AND ECKANKOFF (1971) proved that the hypertensive response in patients can be significantly decreased by simple lignocaine spray.

PRY ROBERT et al (1971) found that the increase in heart rate and blood pressure are much more exaggerated in hypertensive patients.

DENLINGEAR J.K. and ELLISON N.E. (1974) have used intratracheal lignocaine spray which causes a 50% reduction in the hypertensive response.

VICTORIA FARIA BALNC and NORMAND A.G. (1974) in their article of "complications of tracheal Intubation" have classified the neurogenic or reflexly mediated complication into three different categories.

i. **Laryngo Vagal Reflexes** - Which give rise to spasm of the glottis, bronchospasm, apnoea, bradycardia, cardiac dysrrhythmias and arterial hypotension. The mere presence of the tracheal tube seem to be the most common cause of bronchospasm in anesthetised asthmatic patients.

ii. **Laryngo Sympathetic Reflexes** - Which include tachycardia, tachyarrhythmias, acute arterial hypertension as frequent complication. The hypertensive hyperdynamic state during

laryngoscopy may be related in some cases to an increased nor-adrenaline fraction of the total catecholamines.

iii. **Laryngo Spinal Reflexes** - Which include coughing, vomiting and bucking.

RICHARD McCAMMAN (1981) studies the effects of propranolol and they significantly proved that better protection was given by the administration of topical lignocaine or intravenous lignocaine in patients who were on chronic propranolol therapy.

DONAL E. MARTIN (1982) have also proved the efficacy of a low dose fentanyl along with an induction dose of thiopentone, but in these series, it was also found that the incidence and occurrence of tachycardia was not prevented.

TAM.S. et at (1985) found attenuation of circulatory responses to laryngoscopy and endotracheal intubation using intravenous lignocaine; a determination of the optimal time as 3 minutes before intubation.

DONAL R MILLER and RAYMOND J. MARTINEAN (1989) used bolus dose of esmolol for treating hypertension, tachycardia and myocardial ischaemia intra operatively.

T. NISHINO, K. HIRAGA and K. SUGIMORI in (1990) proved that intravenous lignocaine had a dose dependent effect on the expiration reflex,

cough reflex in patients anaesthetized with enflurane, and that 1.5mg/kg of lignocaine intravenous can suppress the cough reflex and other related reflexes during intubation, extubation, bronchoscopy and laryngoscopy when duration of these procedures is relatively brief.

C.D. MILLER and S.J. WARREN (1990) observed that intravenous lignocaine given within three minutes had no significant effect on cardiovascular effects of laryngoscopy and Intubation.

STEVEN M. HELFMAN, MARTIN I GOLD, EVERTARD, A DE LESSER and CLAIRE A. HERRINGTON (1991) observed that esmolol provides consistent and reliable protection from increase in both heart rate and systolic blood pressure during and after intubation where as lignocaine and fentanyl failed to protect against increase in heart rate but did not provide protection against increase in systolic blood pressure equivalent to that provided by esmolol.

MATERIALS AND METHODS

A prospective study comparing Diltiazem and Lignocaine in attenuating the haemodynamic response to laryngoscopy and intubation in E.N.T. patients comprised of 40 patients aged between 20 to 50 years. Both male and female patients who were scheduled for E.N.T. procedures like FESS, mastoidectomy, myringoplasty, Stepedectomy etc. requiring endotracheal intubation were chosen for the study. All patients belonged to ASA I physical status. Patients with cardio-respiratory problems and patients suspected to have a difficult intubation were excluded from the study. All the patients were informed of the study and their consent was obtained. The surgeon was also informed of the study.

Patients were assessed by a detailed examination, including, X-ray chest, ECG and routine laboratory tests. In this study, patients were randomly assinged into 2 groups.

Group `A' - 20 patients received Diltiazem by intravenous bolus administration in a dose of 0.2 mg/Kg body weight, 1 min prior to intubation.

Group `B' - 20 patients received Lignocaine by intravenous administration in a dose of 1.5 mg/kg body weight, 3 mins prior to intubation.

ANAESTHESIA PROTOCOL

Preoprative visit was done to allay anxiety, and a good rapport was established with the patient.

PREMEDICATION

All patients were given inj. Glycopyrrolate 5 micrograms/kg body weight and inj. Pentazocine 0.6 mg/kg body weight intramuscularly 45 mins before surgery. Pre-operative heart rate and blood pressure were recorded.

INDUCTION AND INTUBATION

Pre-oxygenation was done for 3 mins. Baseline heart rate, blood pressure and ECG were recorded. Then the patient was induced with inj. Thiopentone 5 mg/kg body weight followed by inj. vecuronium 0.1 mg/kg body weight. Intubation was done 4 Min. after induction Intubation was done 1 min after test drug diltiazem and 3 mins after the test drug Lignocaine with the appropriate size cuffed endo-tracheal tube.

MAINTENANCE

Anaesthesia was maintained with Nitrous oxide and Oxygen. No surgical stimulation was permitted for 5 mins after intubation.

MONITORING

Monitoring devices - NIBP, ECG, Pulse-oximeter were connected to the patient. Blood pressue was recorded every minute upto 5 mins.

PROFORMA

COMPARISON OF DILTIAZEM AND LIGNOCAINE FOR ATTENUATING INTUBATION RESPONSE

Name : Age : Sex : Wt :

IP No : ASA Physical Status :

Diagnosis : Procedure :

Pre medication : Glycopyrrolate 0.2 mg IM
Pentazocine 0.6 mg/kg body wt.

Induction : Thiopentone sodium 5 mg/kg body wt.

Intubation : vecuronium 0.1 mg/kg body wt.

Trial drug : Group A - diltiazem 0.2 mg/kg body wt. 1 min prior to intubation

Group B - Lignocaine 1.5 mg/kg body wt 3 min prior to intubation.

Intubation was done 4 minutes after induction.

Time	**Pre induction**	**1 min after Trial Drug**	**Intubation**	**1 min**	**2 min**	**3 min**	**4 min**	**5 min**
HR								
Systolic BP								
Diastolic BP								
MAP								

OBSERVATION AND RESULTS

40 patients under this study were categorised into two groups. They comprised both sexes in the age group of 20 to 50 years. The age and sex distribution was equal in all the two groups.

The groups are :

1. Diltiazem (Group- A) : Consisting of 20 patients who received inj. Diltiazem 0.2 mg/kg body weight, bolus 1 min. prior to laryngoscopy.

2. Lignocaine (Group `B') consisting of 20 patients who received Inj. Lignocaine 1.5 mg/kg body weight, 3 mins prior to Laryngoscopy.

Heart rate and Blood pressure were recorded before induction, 1 min after test drug, at the time of intubation and every 1 min for 5 mins.

Table 1

PATIENTS CHARACTERISTICS

	Group A (Diltiazem)	**Group B (lignocaine)**
Patients (n)	20	20
Age (yr)	31 +/- 7.244 (mean +/- SD)	30.5 +/- 8.007 (mean +/- SD)
Sex (M/F)	11/9	10/10
Weight (Kg)	55.7 +/- 5.63 (mean +/- SD)	52.6 +/- 6.866 (mean +/- SD)

P value for age = 0.79

P value for body weight = 0.06

Table 2

HEART RATE

	Group	N	Mean	SD	Students t-test and Mean difference with 95% CI	Statistical Significance
Pre induction	Diltiazem	20	83.25	7.412	t=0.93 p=0.36	NS
	Lignocaine	20	80.65	10.111		
One min after drug	Diltiazem	20	100.40	6.541	t=1.65 p=0.11	NS
	Lignocaine	20	96.40	8.647		
Intubation	Diltiazem	20	106.25	6.455	t=1.99 p=0.05	S
	Lignocaine	20	111.85	10.888	5.6(1-11)	
One minute	Diltiazem	20	105.05	7.543	t=2.74 p=0.01	S
	Lignocaine	20	113.05	10.674	8(2-14)	
Two minutes	Diltiazem	20	102.40	7.816	t=2.53 p=0.02	S
	Lignocaine	20	110.15	11.207	7.8(2-14)	
Three minutes	Diltiazem	20	98.40	7.923	t=3.89 p=0.001	S
	Lignocaine	20	110.05	10.787	11.7(6-18)	
Four minutes	Diltiazem	20	97.85	7.286	t=3.4 p=0.002	S
	Lignocaine	20	107.85	10.946	10(4-16)	
Five minutes	Diltiazem	20	95.15	5.613	t=3.60 p=0.001	S
	Lignocaine	20	105.65	11.775	10.5(5-17)	

C.I. = Confidence Interval
p value < 0.05 is significant

The data were analysed using Analysis of variance and results were considered statistically significant if is p value is < 0.05

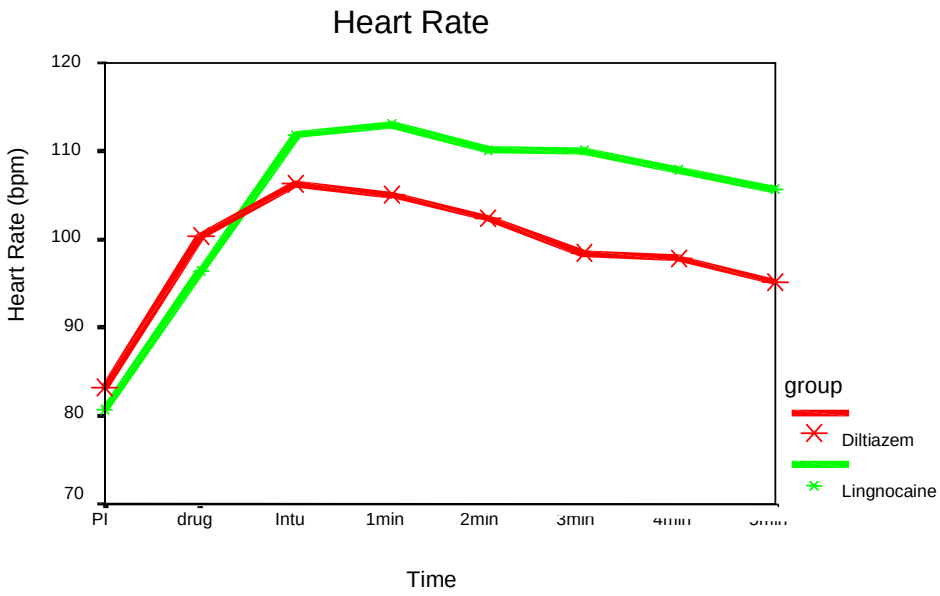
Table 3

BLOOD PRESSURE (mm of Hg)

	Group	N	Mean	SD	students t- test and Mean difference with 95% CI	Statistical Significance
Pre induction _sbp	Diltiazem	20	119.90	9.486	t=0.48 p=0.64	NS
	Lignocaine	20	118.50	9.168		
Pre induction _dbp	Diltiazem	20	79.05	7.584	t=0.67 p=0.51	NS
	Lignocaine	20	80.50	6.022		
one min drug sbp	Diltiazem	20	106.70	11.361	t=3.36 p=0.002 10.9(4-17)	S
	Lignocaine	20	117.60	9.058		
one min drug _dbp	Diltiazem	20	69.55	9.451	t=4.03 p=0.001 9.8(5-15)	S
	Lignocaine	20	79.30	5.292		
intubation_sbp	Diltiazem	20	121.00	10.657	t=4.03 p=0.001 22.9(17-29)	S
	Lignocaine	20	143.85	8.437		
intubation_dbp	Diltiazem	20	80.05	8.217	t=7.52 p=0.001 14.9(11-19)	S
	Lignocaine	20	94.90	4.962		
one min_sbp	Diltiazem	20	132.00	11.300	t=6.92 p=0.001 11.5(5-18)	S
	Lignocaine	20	143.50	8.859		
one min_dbp	Diltiazem	20	88.40	8.042	t=3.58 p=0.001 6.8(3-11)	S
	Lignocaine	20	95.20	4.927		
two min_sbp	Diltiazem	20	130.20	9.390	t=3.22 p=0.003 12.3(7-18)	S
	Lignocaine	20	142.45	8.049		
two min_dbp	Diltiazem	20	87.95	6.770	t=4.43 p=0.001 5.1(2-8)	S
	Lignocaine	20	93.05	4.662		
three min_sbp	Diltiazem	20	127.75	8.735	t=2.78 p=0.009 11.5(6-17)	S
	Lignocaine	20	139.25	8.908		
three min_dbp	Diltiazem	20	85.85	7.058	t=4.12 p=0.001 5.7(2-10)	S
	Lignocaine	20	91.55	5.083		
four min_sbp	Diltiazem	20	125.50	10.195	t=2.93 p=0.006 9.5(4-15)	S
	Lignocaine	20	135.00	6.875		
four min_dbp	Diltiazem	20	84.35	6.831	t=3.46 p=0.001 5.9(2-9)	S
	Lignocaine	20	90.20	3.651		
five min_sbp	Diltiazem	20	121.70	8.749	t=4.59 p=0.001 11.6(7-18)	S
	Lignocaine	20	133.30	7.168		
five min_dbp	Diltiazem	20	80.90	5.830	t=4.51 p=0.001 7.3(4-11)	S
	Lignocaine	20	88.20	4.287		

sbp : Systolic blood pressure
dbp : diastolic blood pressure

Graph I

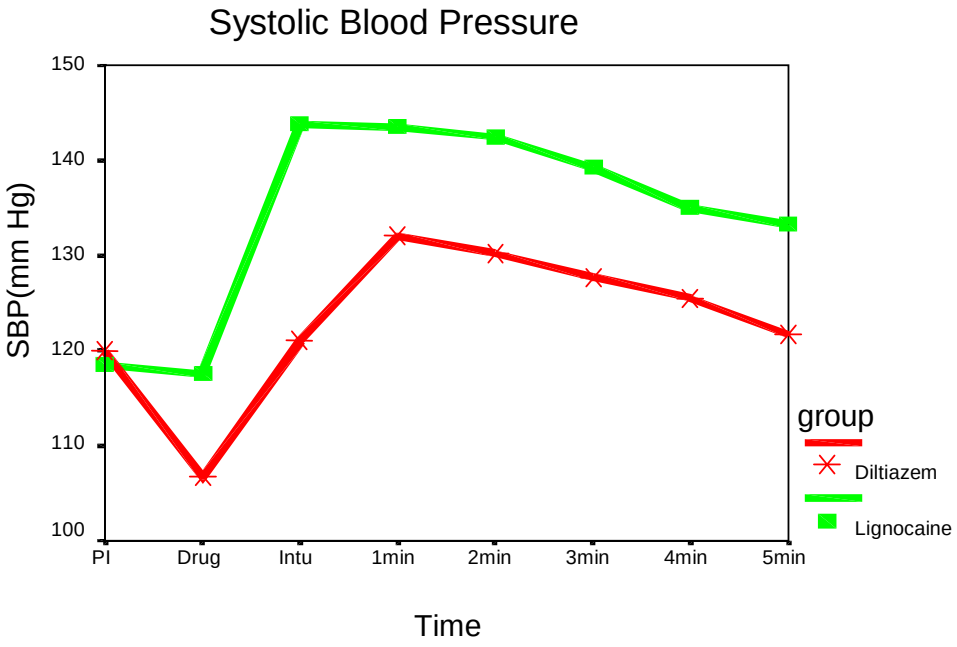


PI = Pre induction

drug = 1 min after Test drug

Intu = Intubation

Graph II

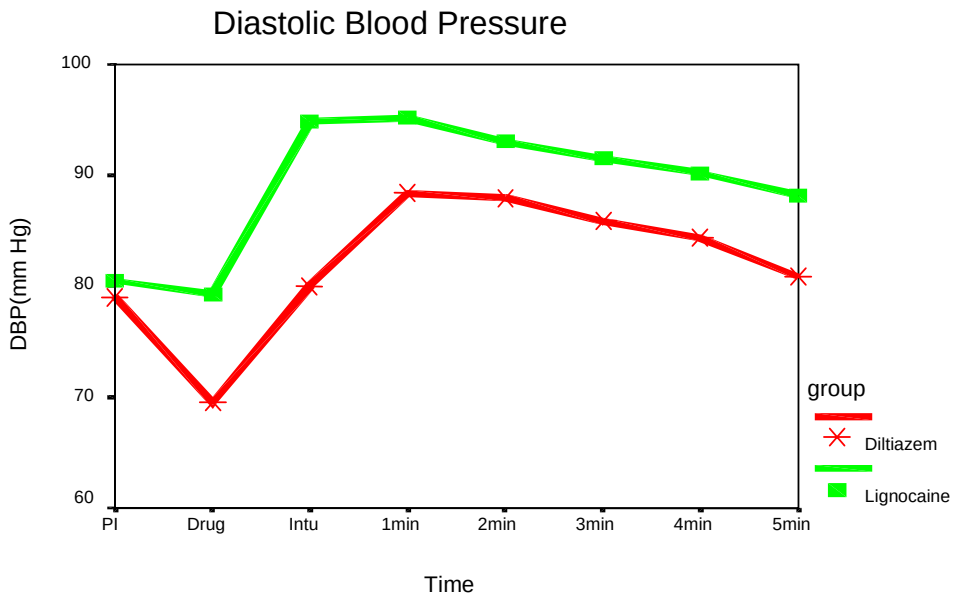


PI = Pre induction

drug = 1 min after Test drug

Intu = Intubation

Graph III



PI = Pre induction

drug = 1 min after Test drug

Intu = Intubation

Table 4

PRE INDUCTION - MEAN HEART RATE

Group	N	Mean	SD	Students t_test and Mean difference with 95% CI
Diltiazem 'A'	20	83.25	7.412	t = 0.93
Lignocaine 'B'	20	80.65	10.111	P = 0.36

By student t-test and mean difference with 95% confidence Interval

Heart rate : No significant difference.

Table 5

1 MIN AFTER TEST DRUG - MEAN HEART RATE

Group	N	Mean	SD	Students t_test and Mean difference with 95% CI
Diltiazem 'A'	20	100.40	6.541	t = 1.65
Lignocaine 'B'	20	96.40	8.647	P = 0.11

Heart rate not significant

Table 6

INTUBATION - MEAN HEART RATE

Group	N	Mean	SD	Students t_test and Mean difference with 95% CI
Diltiazem 'A'	20	106.25	6.455	t = 1.99
Lignocaine 'B'	20	111.85	10.888	P = 0.05 5.6 (1-11)

If P value is < 0.05 significant

Table 7

HEART RATE - 1-5 MINS AFTER INTUBATION

Group		N	Mean	SD	Students t_test and Mean difference with 95% CI
1 min	Diltiazem 'A'	20	105.05	7.543	t = 2.74, p = 0.01 8 (2 - 14)
	Lignocaine 'B'	20	113.05	10.674	
2 mins	Diltiazem 'A'	20	102.40	7.816	t = 2.53, p = 0.02 7.8 (2-14)
	Lignocaine 'B'	20	110.15	11.207	
3 mins	Diltiazem 'A'	20	98.40	7.923	t = 3.89 p = 0.001 11.7 (6 - 18)
	Lignocaine 'B'	20	110.05	10.787	
4 mins	Diltiazem 'A'	20	97.85	7.286	t = 3.4, p = 0.002 10 (4 - 16)
	Lignocaine 'B'	20	107.85	10.946	
5 mins	Diltiazem 'A'	20	95.15	5.613	t = 3.60 p = 0.001 10.5 (5-17)
	Lignocaine 'B'	20	105.65	1.775	

P value < 0.05 is significant

In 1- 5 mts after intubation there is a significant difference variation is 2-18 bpm.

Table 8

MEAN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE AT PRE INDUCTION

	Group	N	Mean	SD	Students t_test and Mean difference with 95% CI
SBP	Diltiazem 'A'	20	119.90	9.486	t = 0.48
	Lignocaine 'B'	20	118.50	9.168	P = 0.64
DBP	Diltiazem 'A'	20	79.05	7.584	t = 0.67
	Lignocaine 'B'	20	80.50	6.022	p = 0.51

Not significant

Table 9

MEAN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE 1 MIN, AFTER TEST DRUG

	Group	N	Mean	SD	Students t_test and Mean difference with 95% CI
SBP	Diltiazem 'A'	20	106.70	11.361	t = 3.36 P = 0.002
	Lignocaine 'B'	20	117.60	9.058	10.9 (4 - 17)
DBP	Diltiazem 'A'	20	69.55	9.451	t = 4.03 p 0.01
	Lignocaine 'B'	20	79.30	5.292	9.8 (5 - 15)

P value is < 0.05. This is signifant,

Systolic BP diference is 4 - 17 mm of Hg

Diastolic BP difference is 5 - 15 mm of Hg

This difference is significant.

Table 10

MEAN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE AT INTUBATION

	Group	N	Mean	SD	Students t_test and Mean difference with 95% CI
SBP	Diltiazem 'A'	20	121.00	16.657	t = 4.03 p = 0.001 22.9 (17-29)
	Lignocaine 'B'	20	143.85	8.437	
DBP	Diltiazem 'A'	20	80.05	8.217	t = 7.52 p = 0.001 14.9 (11-19)
	Lignocaine 'B'	20	94.90	4.968	

Mean systolic Blood Pressure varies between 17-29 mm of Hg

Mean Diastolic Blood Pressure varies between 1-19 mm of Hg

Both values are significant.

Table 11

MEAN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE 1-5 MINS. AFTER INTUBATION

Group			N	Mean	SD	Students t_test and Mean difference with 95% CI
1 min	SBP	Diltiazem 'A'	20	132.00	11.300	t = 6.92 p = 0.001 11.5 (5 - 18)
		Lignocaine 'B'	20	143.50	8.859	
	DBP	Diltiazem 'A'	20	88.40	8.042	t = 3.58 p = 0.001 6.8 (3 - 11)
		Lignocaine 'B'	20	95.20	4.927	
2 mins	SBP	Diltiazem 'A'	20	130.20	9.390	t = 3.22 p = 0.003 12.3 (7 - 18)
		Lignocaine 'B'	20	142.45	8.049	
	DBP	Diltiazem 'A'	20	87.95	6.770	t = 4.43 p = 0.001 5.1 (2-8)
		Lignocaine 'B'	20	93.05	4.662	
3 mins	SBP	Diltiazem 'A'	20	127.75	8.735	t = 2.78 p = 0.009 11.5 (6-17)
		Lignocaine 'B'	20	139.25	8.908	
	DBP	Diltiazem 'A'	20	85.85	7.058	t = 4.12 p = 0.001 5.7 (2 - 10)
		Lignocaine 'B'	20	91.55	5.083	
4 mins	SBP	Diltiazem 'A'	20	125.50	10.195	t = 2.93 p = 0.006 9.5 (4 - 15)
		Lignocaine 'B'	20	135.00	6.875	
	DBP	Diltiazem 'A'	20	84.35	6.831	t = 3.46 p = 0.001 5.9 (2 - 9)
		Lignocaine 'B'	20	90.20	3.651	
5 mins	SBP	Diltiazem 'A'	20	121.70	8.749	t = 4.59 p = 0.001 11.6 (7 - 18)
		Lignocaine 'B'	20	133.30	7.168	
	DBP	Diltiazem 'A'	20	80.90	5.830	t = 4.51 p = 0.001 7.3 (4 - 11)
		Lignocaine 'B'	20	88.20	4.287	

In 1 to 5 mts after intubation there is significant difference in systolic and Diastolic blood pressure

Syst. BP varies between 4 - 18 mm of Hg

Diastolic BP varies between 2 - 11 mm of Hg.

Increase in Heart rate following intubation upto 5 mts is less with diltiazem group when compared to Lignocaine group and the difference is statistically significant. There was a slight increase in heart rate immediately following the administration of diltiazem however this is not statistically significant (Table 2) The results were plotted in a graph (Graph - I)

The rise in both systolic and diastolic blood pressure following intubation is less with diltiazem group when compared to lignocaine group. The result is statistically significant ($P < 0.05$) blood pressure were measured upto 5 mts after intubation (Table 3) There was a slight transient fall in the BP immediately after administrate of diltiazem which is not statistically significant (> 0.05). The results were plotted in a graph which confirm the statistics (Graph II & III).

- The demographic profile is similar in both the groups. (Table 1)

- There was no statistically significant difference in pre induction heart rate between the two groups. (p value 0.36).

- From the time of laryngoscopy and intubation upto five minutes following intubation there is a statistically significant difference in the heart rate between the two groups. (p values at laryngoscopy, 1,2,3,4 & 5 mins following intubation are 0.01, 0.02, 0.001, 0.002 & 0.001 respectively. And from the graph it is evident that heart rate following intubation was lesser in diltiazem group than lignocaine group.

- There is a statistically insignificant difference in the systolic & diastolic, at the time of pre induction, and at the time of test drug delivery.

- From the graph it is evident that there is a statistically significant drop in the mean systolic pressure and diastolic pressure in the diltiazem group with respect to lignocaine group.

- There is a statistically significant difference in the mean systolic and diastolic pressure between the 2 groups from the time of laryngoscopy till 5 min following intubation. It is evident from the graph that they are lesser in diltiazem group than lignocaine group.

This shows Diltiazem is better than the Lignocaine in attenuating stress response to laryngoscopy and intubation.

DISCUSSION

Hypertension and tachycardia usually accompany laryngoscopy and intubation.[1] This response is undersirable, especially in patients with cardiovascular and intracranial disease. Increase in heart rate and blood pressure occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased norepinephrine levels [4].

Many attempts have been made to attenuate the pressor response by many persons with varying success rate.

KING et al (1951), [13] used ether to attenuate the pressor response while Wycoff [28] et al (1960) [6], and J.KENNETH (1974) tried a combination of topical anaesthesia of larynx together with Superior laryngeal nerve block to attenuate the stress response to intubation.

STEINHAN AND GASKIN (1963) [22] used IV Lignocaine, JAMES et al (1981) used Lignocaine intratracheal spray, MASSON & ECKANKOFF (1971) and DENLINGER J.K. AND STOELTING (1978) [25] used a combination of viscous Lignocaine and topical intratracheal lignocaine.

FASSUOULAKI A, KANNIASIS P used intranasal administration of Nitro-glycerine to attenuate the pressor response. Anti-hypertensives like phentolamine have also been used to attenuate the pressor response by DEVAULT M et al.

Calcium channel blockers have been used to attenuate the pressor response by PURI GD & BATRA YK & NISHI KAWA, T, NAMIKIA.

Lignocaine has been found to be ineffective in attenuating the intubation response. SING H. VICHITVEJPAISAL et al [22] (1955) showed in their study that lignocaine 1.5 mg/kg body weight intravenously was ineffective in controlling the heamodynamic response following laryngoscopy and intubation.

CHAREMMER JORGERREN et al found no beneficial effect when Lignocaine 1.5 mg/kg body weight was given 2 mins prior to laryngoscopy. SJ WARREN (1990) found that Lignocaine 1.5 mg/kg body weight given more than 3 mins before laryngoscopy failed to attenuate the pressor response.

Narcotics used to attenuate the intubation response may produce respiratory depression whereas inhalational agents may produce cardiovascular depression. Use of vasodilators like Sodium nitroprusside may result in reflex tachycardia and lability of blood pressure.

Calcium channel blockers effectively prevents increase in Heart rate and Blood pressure following laryngoscopy by suppressing A-V nodal conduction and vasodilatation.

In this study the rise in heat rate following intubation is less with Diltiazem group than lignocaine group Fujii et al (1995) and Hasegawaj et al have observe that diltiazem effectively prevents tachycardia following laryngoscopy.

Mikawa K et al (1990) and Fujii Y et al (1998) have found that diltiazem attenuates the pressor response following intubation. This concurs with our study in which the rise in blood pressure following laryngoscopy is less with the diltiazem group than the lignocaine group.

No patient in this study developed severe hypotension. The lowest systolic and diastolic pressure were recorded 88/56. This concurs with the study of K.Mikawa et al (1996).

This study shows that Diltiazem is better alternative to lignocaine in attenuating the cardiovascular responses to tracheal intubation. This results are consistents with the findings of Fujii Y et al (1998).

There were no difference between the diltiazem ad lignocaine group in the clinical out come (intra-operative and post operative morbidity and mortality) possibly because this study was conducted only in ASA I patients, without cardiovascular or cerebro vascular diseases.

SUMMARY

This study was done on patients undergoing E.N.T procedures to compare the efficacy of IV Lignocaine and IV Diltiazem for attenuating the haemodynamic response to laryngoscopy and intubation.

A prospective study was carried out in 40 E.N.T patients in the age group 20-50 years requiring endotracheal intubation. The patients were randomly assigned into 2 groups. Group I received diltiazem 0.2 mg/kg body weight one minute prior to intubation and Group II received lignocaine 1.5 mg/kg body weight, 3 minutes prior to intubation.

The pulse rate systolic and diastolic blood pressure were recorded every minute for 5 minutes following laryngoscopy and intubation.

The study showed that diltiazem was better than lignocaine in attenuating the haemodynamic response to laryngoscopy and intubation in E.N.T procedures. The side effects associated with IV diltiazem are negligible hence the drug diltiazem is better alternative to lignocaine in attenuating the intubation response.

CONCLUSION

From this study it is concluded that diltiazem, given as bolus in a does of 0.2 mg/kg body weight 1 minute prior to intubation, is a better alternative to lignocaine in attenuating the cardiovasuclar responses to laryngoscopy and intubation.

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PROFORMA

COMPARISON OF DILTIAZEM AND LIGNOCAINE FOR ATTENUATING INTUBATION RESPONSE

Name : Age : Sex : Wt :

IP No : ASA Physical Status :

Diagnosis : Procedure :

Pre medication : Glycopyrrolate 0.2 mg IM
Pentazocine 0.6 mg/kg body wt.

Induction : Thiopentone sodium 5 mg/kg body wt.

Intubation : vecuronium 0.1 mg/kg body wt.

Trial drug : Group A - diltiazem 0.2 mg/kg body wt. 1 min prior to intubation

Group B - Lignocaine 1.5 mg/kg body wt 3 min prior to intubation.

Intubation was done 4 minutes after induction.

Time	**Pre induction**	**1 min after Trial Drug**	**Intubation**	**1 min**	**2 min**	**3 min**	**4 min**	**5 min**
HR								
Systolic BP								
Diastolic BP								
MAP								

GROUP 'A' (DILTIAZEM) BLOOD PRESSURE - SYSTOLIC AND DIASTOLIC (mm of Hg)

S.No.	Pre induction		1 min after Test drug		Intubation		1 min		2 min		3 min		4 min		5 min	
	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D
1.	101	67	94	64	104	78	128	84	129	86	118	78	110	74	108	66
2.	127	86	110	76	122	82	138	92	136	90	130	88	128	86	124	78
3.	123	73	108	66	118	80	140	88	138	86	130	84	128	82	118	80
4.	114	71	98	60	110	72	129	84	128	84	126	82	116	80	116	78
5.	140	88	126	78	134	88	156	100	134	100	130	98	148	99	140	90
6.	124	82	110	76	122	80	138	94	136	92	134	90	130	88	128	88
7.	110	72	102	64	108	66	128	88	128	84	126	86	120	84	113	80
8.	116	80	104	68	114	78	130	90	130	90	128	87	126	88	120	82
9.	108	66	100	56	110	66	122	83	128	80	128	80	118	78	112	78
10.	130	90	126	84	130	84	148	100	148	100	140	96	136	90	138	86
11.	117	83	88	56	118	82	101	67	107	72	106	74	105	74	107	75
12.	116	74	95	67	141	96	145	97	149	99	150	99	144	99	126	76
13.	114	82	130	92	128	91	126	90	124	90	123	89	122	88	121	88
14.	128	83	104	60	130	73	129	72	130	87	122	72	133	77	130	77
15.	128	90	98	64	116	78	130	90	122	84	129	88	123	81	119	78
16.	113	75	102	70	140	94	123	87	119	83	119	84	121	85	118	88
17.	124	81	110	72	120	81	132	90	130	88	128	84	126	82	124	80
18.	125	80	109	74	119	80	131	90	128	88	128	82	126	80	126	80
19.	110	70	100	64	108	70	128	88	124	84	126	86	120	84	118	82
20.	130	88	120	80	128	82	138	94	136	92	134	90	130	88	128	88

GROUP `B' (LIGNOCAINE) BLOOD PRESSURE - SYSTOLIC AND DIASTOLIC (mm of Hg)

S.No.	Pre induction		1 min after Test drug		Intubation		1 min		2 min		3 min		4 min		5 min	
	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D
1.	110	73	106	72	136	90	135	90	133	87	130	84	130	84	128	83
2.	123	84	128	80	150	93	153	102	150	100	148	98	140	90	140	90
3.	119	83	116	82	132	97	150	97	148	94	148	86	133	93	130	90
4.	131	86	123	82	155	102	153	103	150	97	147	93	146	93	144	90
5.	100	77	102	73	134	92	133	90	130	90	128	87	124	86	122	83
6.	106	70	113	76	139	89	129	90	137	87	127	85	124	86	122	80
7.	115	83	110	79	145	105	144	103	144	100	140	96	138	94	136	94
8.	130	90	130	83	153	96	150	90	149	98	148	96	133	94	132	92
9.	120	82	118	80	158	97	149	96	148	96	146	92	140	90	144	87
10.	124	74	124	80	150	96	154	96	150	90	148	87	140	90	133	93
11.	112	75	108	74	134	88	137	92	135	89	132	86	132	84	130	85
12.	125	86	130	82	150	91	151	94	150	93	127	96	140	90	140	90
13.	104	76	110	74	136	87	127	86	127	86	127	85	124	86	122	80
14.	128	86	124	80	140	98	140	99	138	96	137	95	130	90	128	88
15.	122	83	120	81	142	96	148	98	146	96	145	95	140	92	138	90
16.	115	82	110	79	143	100	143	98	143	87	142	96	140	94	136	90
17.	110	70	106	68	130	88	129	89	128	88	126	86	126	86	125	85
18.	126	80	126	86	148	98	149	99	148	98	147	98	136	94	138	88
19.	130	90	130	91	154	98	150	96	149	94	148	96	140	94	140	94
20.	120	80	118	84	148	97	146	96	146	95	144	94	144	94	138	92

GROUP 'A' (DILTIAZEM) HEART RATE (BEATS PER MINUTE)

S.No.	Pre induction	1 m after Test drug	Intubation	1 min	2 min	3 min	4 min	5 min
1.	82	94	106	114	110	101	106	100
2.	95	108	117	117	115	109	111	105
3.	90	98	113	106	104	96	96	94
4.	84	96	108	104	106	104	102	98
5.	72	98	102	100	100	98	98	94
6.	80	100	104	109	98	92	90	92
7.	80	104	100	98	96	92	90	92
8.	78	98	106	105	104	105	100	97
9.	78	96	94	90	86	82	87	84
10.	90	116	110	108	100	96	94	94
11.	97	109	118	117	117	110	112	106
12.	90	98	113	106	104	96	96	94
13.	80	100	104	104	98	92	90	92
14.	84	96	108	104	106	104	102	98
15.	82	94	106	114	110	108	106	100
16.	79	96	93	89	86	82	87	83
17.	78	97	105	104	103	102	99	96
18.	96	115	110	108	100	96	94	93
19.	72	98	102	99	101	98	97	94
20.	78	97	106	105	104	105	100	97

GROUP 'B' (LIGNOCAINE) HEART RATE (BEATS PER MINUTES)

S.No.	Pre induction	1 m after Test drug	Intubation	1 min	2 min	3 min	4 min	5 min
1.	77	100	108	108	99	97	93	97
2.	69	94	103	107	99	101	96	89
3.	80	102	111	113	116	114	113	105
4.	79	100	120	122	123	118	119	114
5.	86	98	123	124	120	120	118	117
6.	84	100	118	117	117	117	119	125
7.	63	79	90	91	92	90	90	87
8.	75	86	103	104	105	107	105	103
9.	96	102	129	129	128	127	120	120
10.	90	106	115	117	113	112	110	108
11.	68	94	103	107	98	101	96	89
12.	97	101	109	108	98	97	93	95
13.	84	100	118	117	117	117	114	112
14.	79	100	120	123	118	119	115	114
15.	83	97	121	124	120	121	118	117
16.	90	106	115	117	113	112	110	108
17.	75	86	103	104	105	107	105	103
18.	63	74	90	91	92	90	90	87
19.	95	101	127	126	125	120	120	118
20.	80	102	111	112	105	114	113	105