COMPARATIVE STUDY OF LIDOCAINE, DILTIAZEM AND VERAPAMIL FOR STRESS ATTENUATION DURING EXTUBATION

A study of 120 cases

Dissertation submitted for the Degree of

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MADURAI

CERTIFICATE

This is to certify that the dissertation entitled **"COMPARATIVE STUDY OF LIDOCAINE , DILTIAZEM AND VERAPAMIL FOR STRESS ATTENUATION DURING EXTUBATION ",** is a bonafide record work done by **DR. P.K.ABIRAMI**, in the Department of Anaesthesiology, Government Rajaji Hospital, Madurai Medical College, Madurai.

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Last ,but not the least, I sincerely thank all the patients who have subjected themselves wholeheartedly for this project.

DECLARATION

I, ***DR .P.K. ABIRAMI ,*** solemnly declare that the dissertation titled ***"COMPARATIVE STUDY OF LIDOCAINE, DILTIAZEM AND VERAPAMIL FOR STRESS ATTENUATION DURING EXTUBATON ",*** has been prepared by me.

This is submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the requirements for the award of M.D. Degree Examination (Branch X) Anaesthesiology to be held in SEPTEMBER 2006 .

Place: Madurai.

Date :

DR. P.K.ABIRAMI

CONTENTS

I
NTRODUCTION

The conduct of a General Anesthesia is generally compared to a flight travel – here the intubation is akin to take off and extubation to landing. Hence the intubation and extubation are the most stressful events to the patient. Though the art of attenuating the stress response to intubation is practiced widely, the practice of caring about the stress response to extubation is not practiced widely. But the stress during extubation can be detrimental and life threatening in a wide group of patient population.

Though a pilot gives equal attention to landing and take off, we anesthesiologist are mostly concentrating on intubation rather than on extubation in relation to stress response. The present study attempts to redress this imbalance.

HISTORY

The introduction of anaesthesia dates back to 16 october 1846, when W.T.G Mortan of Boston anaesthetised Gilbert Abbott.

Endotracheal techniques were popularised by Ivan W.Magil and E.Stanley Rowbotham in early 1920's. Controlled respiration was then established following the use of curare by Harold Griffith and G.Enid johnson of Montreal in 1942. Macintosh described his curved laryngoscope in Oxford in 1943.

From then on, anaesthesia has become much safer with the subsequent introduction of various techniques and newer drugs to deal with untoward complications. Subsequently the rude way of anaesthetising a patient has evolved into a systematic and well organised job with subsequent researches studying and concentrating on the most tiny details. This paved the way for the evolution of anaesthesia into an individual speciality. Of late, anaesthesiologists have been trying very

hard to maintain the near normal physiological vitals throughout anaesthesia using the relevant drugs and techniques.

The cardiovascular responses to laryngoscopy and endotracheal intubation have been recognised since 1951. Consequently drugs were used to control the stress response during intubation and to a minor degree during extubation. Subsequently, the mortality and morbidity during anaesthesia decreased.

AIMS OF THE STUDY

- To quantify the amount of cardiovascular stress response during extubation

- To prove the effectiveness of intravenous diltiazem, verapamil and lidocaine in attenuating stress response during extubation.

To know whether these drugs can have an effect on the quality of extubation.

GENERAL ANAESTHESIA

In 1957, P.WOODBRIDGE defined general anasthesia as comprising of four components:

1. sleep or unconsciousness
2. blockade of undesirable reflexes
3. motor blockade
4. sensory blockade.

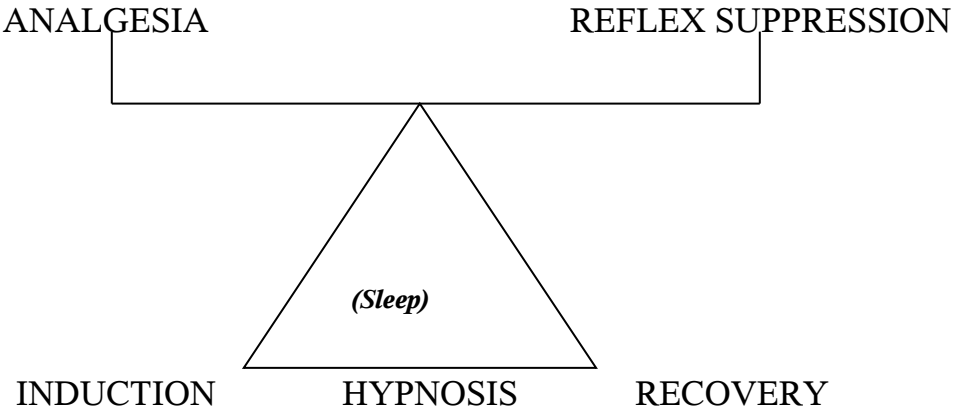
These ideas have been discussed and modified by M.Pinsker into 3 components.

1. paralysis
2. unconsciousness
3. attenuation of stress response.

Lundy's balanced anaesthesia is another formulation of the idea that several drugs can be used in continuation to produce the state of unconsciousness and analgesia that we define as general anaesthesia.

General anaesthesia can also be defined as a carefully controlled reversible modification or depression of various modalities of central nervous system, autonomic nervous system and peripheral nervous system by using small, incremental, titrated doses of various pharmacological agents to achieve a specific physiological goal, the goal being the protection of the patient from the detrimental effects of various reflexes.

General anaesthesia comprises of three aspects, well known as the "Triad of Anaesthesia" (i.e) Hypnosis, Analgesia, Reflex Suppression.



This triad can be achieved by using small, titrated, incremental doses of various pharmacological agents, thereby gaining maximum benefit of each drug, at the same time avoiding their side effects.

General Anaesthesia is usually provided by endotracheal intubation and controlled ventilation. At the end of the anaesthesia endotracheal extubation is done. Tracheal extubation can be associated with various problems.

General Anaesthesia with endotracheal intubation is considered as the safest form of anaesthesia, since, here the airway is under the control of the anaesthesiologist. But this is not absolutely safe since problems during the last but not the least step (ie.) extubation can be fatal.

PROBLEMS DURING EXTUBATION

1. **Difficult extubation:**

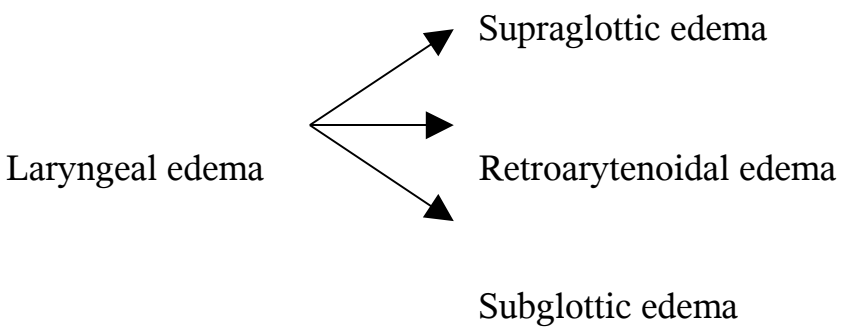
Difficulty in removing a tracheal tube at the end of a General Anaesthesia is a rare, but dangerous and occasionally fatal complication of difficult intubation.

Causes:

- ❖ Failure to deflate the tracheal tube cuff.
- ❖ An excessively large cuff catching on the vocal cords.
- ❖ Adhesion of the tube to the tracheal wall because of the absence of lubricant.
- ❖ Tube being transfixed by a suture.

2. **CARDIO VASCULAR RESPONSE TO EXTUBATION**
3. **Trauma to vocal cords and upper and lower airway**
4. **Tracheal collapse, due to tracheomalacia**
5. **Airway obstruction.**

Laryngospasm



Vocal cord paralysis

6. **Pulmonary edema**
7. **Laryngeal incompetence**

Laryngeal incompetence leading to aspiration of gastric contents or foreign bodies at tracheal extubation.

CARDIOVASCULAR RESPONSES TO EXTUBATION AND ITS IMPLICATIONS

Tracheal extubation is performed usually with the patient in a light stage of anaesthesia and produces significant increases in heart rate and arterial pressure.

The exact mechanism of these cardiovascular response in man is unknown, but it is believed to be associated with the release of catecholanines causing increases in heart rate, myocardial contractility and systemic vascular resistance.

CLINICAL SIGNIFICANCE:

The majority of patients are able to tolerate the hemodynamic responses to tracheal extubation without any significant consequences. However, patients with coexisting disease may be unable to tolerate these responses, while others will have an exaggerated response which

may be poorly tolerated.

CARDIOVASCULAR SYSTEM:

In patients with coronary artery disease, the haemodynamic responses to extubation may upset the delicate balance between myocardial oxygen supply and demand, resulting in myocardial ischemia. An ischemic myocardial metabolic response to tracheal extubation has also been demonstrated in some patients after coronary artery surgery.

Although suppression of the hemodynamic response to extubation is unlikely to influence the outcome in the majority of patients with stable coronary arteries, there remains a small number of patients in whom a single hyperdynamic episode may produce a clinical catastrophe. Thus it is reasonable to attempt to minimize the stress response to tracheal extubation.

In both treated and untreated hypertensive patients, tracheal extubation is associated with significant increases in heart rate and arterial pressure. These increase mimic in size those associated with

laryngoscopy and tracheal intubation. Such hypertensive crisis may result in cardiac decompensation, pulmonary edema or cerebral haemorrhage.

CENTRAL NERVOUS SYSTEM:

In patients who have undergone neurosurgical operations, the hypertensive response to tracheal extubation may be detrimental. In such patients, autoregulation of cerebral blood flow may be disturbed and a sudden increase in arterial pressure may lead to increases in both cerebral blood flow and intracranial pressure. These increases may result in either herniation of brain contents or decrease in cerebral perfusion pressure, leading to cerebral ischemia. It seems reasonable, therefore, to attempt to prevent or suppress the haemodynamic response to extubation in such patients.

Thus the sympatho-adrenal response to extubation may be harmful in those suffering from systemic hypertension, myocardial ischaemia, intracranial hypertension, cerebrovascular disease and valvular heart disease.

Further, the integrity of cerebral and aortic aneurysms is largely a

function of transmural pressure. A sudden increase in blood pressure during extubation can lead to rupture of these vessels and sudden deterioration.

CARDIOVASCULAR REFLEXES:

Both the sympathetic and parasympathetic nervous systems play a role in the cardiovascular responses to extubation.

The hypertension and tachycardia response to extubation are mediated through sympathetic efferents via cardio accelerator nerves and sympathetic chain ganglia. This reflex is polysynaptic in nature. This reflex is mediated by the glossophayngeal nerve, when the stimuli occurs superior to the anterior surface of the epiglottis and by the vagus nerve, when stimuli occur from the level of posterior surface of the epiglottis down into the lower airway. These stimuli passes through the brainstem and spinal cord and results in diffuse autonomic responses, which includes widespread release of noradrenaline from adrenergic nerve terminals and secretion of adrenaline from adrenal medulla.

Some of the hypertensive responses to endotracheal extubation also result from activation of renin-angiotensin system, with the release of renin from the renal juxtaglomerular apparatus.

REVIEW OF LITERATURE

Edde RR in 1979 demonstrated the cardiovascular responses to extubation. He suggested that tracheal extubation was performed usually with the patient in a light stage of anaesthesia and produced significant increases in heart rate and arterial pressure.

Wohlner and Colleagues in 1979, studied the hemodynamic responses to tracheal extubation in patients after coronary artery surgery. They demonstrated significant increases in heart rate, mean arterial pressure, cardiac index and systemic vascular resistance index. They also demonstrated similar significant increases in the mean pulmonary artery pressure, pulmonary artery occlusion pressure and pulmonary vascular resistance index.

Dyson et al in 1990 demonstrated in 10 ASA I and II patients who were not receiving cardiovascular or antihypertensive medication, in whom extubation was performed, an increase of 20% or more in both

heart rate and systolic arterial pressure, in 70% of the patients.

Lowrie A et al in 1992 showed a significant increase in the plasma concentration of adrenaline, but not of noradrenaline, after tracheal extubation in a small group of patients who had undergone major elective surgery.

Prys – Roberts C et al in 1971 have shown that the cardiovascular responses to intubation is associated with the release of catecholamines causing increases in heart rate, myocardial contractility and systemic vascular resistance.

Hodgkinson R et al in 1980 studied parturiants with severe preeclampsia and suggested that the cardiovascular response to tracheal extubation is as dramatic as the response to tracheal intubation. They demonstrated mean maximal increases of 45 mm Hg in mean systemic arterial pressure, 20mm Hg in mean pulmonary arterial pressure and 20 mm Hg in pulmonary artery occlusion pressure, in relation to tracheal extubation.

Bidwai AV et al in 1978 demonstrated that the tracheal administration of lignocaine, 60 mg ,3-5 min before extubation and

lignocaine, 40 mg at extubation ,prevented increases in heart rate and arterial pressure during and after tracheal extubation. They subsequently in the year 1979 demonstrated that iv administration of lignocaine 1mg per kg, 2 mins before tracheal extubation also prevented the stress of extubation.

Dyson et al in 1990 demonstration that esmolol attenuates the cardiovascular stress response to extubation.

Fujjii Y et al in 1999 showed that combined diltiazem and lidocaine is more effective prophylaxis than diltiazem or lidocaine alone for attenuating the cardiovascular responses to tracheal extubation.

Shajur MA et al in 1999 demonstrated that remifentanil bolus dose of 1mg/kg prevented the in HR and MAP at the time of extubation without any effect on recovery.

Kihara S et al in 1998 showed that the administration of diltiazem produced greater attenuation of the haemodynamic response to tracheal extubation than nicardipine.

Nishina K et al in 1995 concluded that a bolus dose of intravenous

fentanyl 2mg / kg given at the time of peritoneal closure was of value in attenuating the cardiovascular changes associated with tracheal extubation and that this did not prolong the recovery.

Kovac Ac in 2001 have shown that nicardipine in the doses of 0.03mg/kg attenuated the blood pressure but not heart rate response during emergence and extubation.

Wang Y Q et al in 2003 found that esmolol in 1.5mg/kg does not only controlled cardiovascular response to tracheal extubation, but also had no side effects.

Yorukoglu D et al in 1999 Showed that metoprolol effectively blocked the increases on heart rate after extubation and the increase in blood pressure was less when compared to the control groups.

Nishina K et al in 1996 showed that prostaglandin E1 infusion of 0.1mg/kg/min was effective in attenuating hypertensive responses during extubation but ineffective for tachycardia.

Zalunareto MP et al showed that a single preoperative iv dose of clonidine (3mg/kg) blunts the hemodynamic responses due to extubation

in noncardiac surgery of intermediate duration.

Yoshitake MD and his colleagues showed that combined diltiazem and lidocaine administration during tracheal extubation for stress attenuation was more effective than either drug alone.

Mikaeva Katsuya et al in 1997 showed that a combination of verapamil 0.1 mg/kg and lidocaine 1mg/kg injected iv two minutes before extubation was superior to either drug alone in attenuating stress response to extubation.

MATERIALS AND METHODS

After obtaining approval from the ethical committee of the Department of Anaesthosiology, Government Rajaji Hospital and Madurai Medical College, Madurai, the study was conducted in 120 patients posted for elective surgeries under general anaesthesia.

Informed consent was obtained from the patients before conducting the study.

Type of Study:

Prospective study

Double blind study.

Inclusion criteria:

Elective surgical patients between 20-65 yrs of age, who came under ASA physical status I were included in the study.

Exclusion criteria:

ASA physical status II, III & IV

Age < 20 & > 65 yrs.

Patients suffering from coexisting systemic illness and those taking cardiovascular or antihypertensive medications.

Patients who required postoperative ventilation.

Preoperative preparation:

Routine preoperative assessment as for any elective surgical patient was carried out.

The patients were randomly divided into four groups. (n=30 for each group).

Group S	Saline	control group
Group V	0.1mg/kg	verapamil group
Group D	0.2 mg/kg	diltiazem group
Group L	1.5mg/kg	lidocaine group

Premedication:

Once the patient was found to be fit, premedication was administrated.

All patients were premedicated with intramuscular atropine 0.6mg and intramuscular pentazocine 0.06mg/kg ,45 mins before the induction of anaesthesia.

The following emergency drugs and equipments were kept ready

- Boyle's machine with oxygen cylinder
- Laryngoscopes with varied blades
- Oropharyngeal airway
- Endotracheal tubes
- Drugs - atropine, adrenaline, ephedrine, dexamethasone, Deriphyline.

Baseline pulse rate and Blood pressure were recorded.

Intravenous line was secured with 18 G Cannula.

Patients were preoxygenated for 3 minutes with 100% oxygen via Mapleson's A circuit with mask.

Anaesthesia was induced with Inj thiopentone sodium 5mg/kg iv as 2.5% solution and tracheal intubation was facilitated with Inj succinylcholine 2mg/kg iv.

Anaesthesia was maintained with 66% nitrous oxide in oxygen and titrated, intermittent bolus doses of Inj pentazocine iv and inj pancuromium iv.

Monitoring during anaesthesia was done with pulse oximetry and non invasive BP.

Pulse rate, Blood pressure and SPO_2, were monitored throughout the surgery.

After surgery N_2O was discontinued and residual muscle relaxation was reversed with inj neostigmine, 0.04 mg/kg and inj atropine 0.02 mg/ kg. iv. Three minutes later saline (Group S) or verapamil (Group V) or diltiazem (Group D) or lidocaine (Group L) were given iv according to the group of the patient. These medications had been prepared before and in equivalent volumes and their identities were unknown to the anaesthetist. The trachea was extubated 2 minutes after administration of the study drugs. Immediately before tracheal extubation it was confirmed that the patients were able to breath spontaneously and open their eyes on command. The recovery from muscle relaxation was assessed by hand grip. Oropharyngeal secretions were aspirated immediately prior to

extubation. After tracheal extubation, 100% oxygen was given via face mask for 5 mins.

Monitored Parameters:

Systolic arterial pressure (SAP)

Diastolic arterial Pressure (DAP) &

Heart rate (HR)

were measured at the time of injection of neostigmine and atropine mixure.

Hemeodynamic data was then recorded every minute until 5 minutes after extubation.

The Systolic Arterial Pressure, Diastolic Arterial Pressure and Heart rate measured at the time of injection of neostigmine and atropine mixture was taken as the baseline value.

Haemodynamic data obtained from 3 min after the injection of neostigmine atropine mixture (i.e. at the time of injection of study medications) until 5 min after extubation were analysed to determine cardiovascular changes associated with tracheal extubation. Values for

SAP, DAP and HR found immediately before the induction of anaesthesia, at the time of injection of neostigmine –atropine mixture, at the time of injection of the study drugs (2min before tracheal extubation), 1 min after these drugs (1 min before tracheal extubation), at tracheal extubation and 1 min and 5 min after tracheal extubation were compared among the four groups.

QUALITY OF EXTUBATION:

The quality of tracheal extubation was evaluated using a five-point rating scale.

1 – no coughing or straining

2 – very smooth, with minimal coughing

3 – moderate coughing

4 – marked coughing or straining

5 – poor extubation, very uncomfortable.

CALCIUM CHANNEL BLOCKERS

(calcium entry blockers or calcium antagonists)

- These are a diverse group of structurally unrelated compounds that selectively interfere with inward calcium ion movement across myocardial and vascular smooth muscle cells.
- Calcium ions play a key role in the electrical excitation of cardiac cells and vascular smooth muscle cells.

Classification:

On basis of chemical structure into

(a) phenyl alkyl amines

(eg) verapamil

(b) 1,4 – dihydropyridines

(eg) nifedipine

(c) benzothiazepines

(eg) diltiazem.

Calcium Channels:

Three types of calcium channels have been described in smooth muscles and other excitable cells of the body.

They are:

a. Voltage sensitive channel

b. Receptor operated channel.

c. Leak channel.

Voltage sensitive Ca^{2+} Channels :

These are heterogenous – three major types have been identified

L - type,

T – type &

N – Type.

All voltage sensitive Ca^{2+} channels are membrane spanning funnel shaped glycoproteins that function as ion selective valves. They are composed of a major subunit, which encloses the ion channel and other modulatory subunits. The channels exist in multiple isoforms which may

be site specific. Only the voltage sensitive L – type channels are blocked by the CCBs. The three groups of CCBs bind to their own specific binding sites on the α_1 subunit- all restricting Ca^{2+} entry, though the characteristics of the channel blockade differ.

Pharmacological actions of CCB:

The common property of all 3 subclasses of CCBs is to inhibit Ca^{2+} mediated slow channel component of the action potential in smooth / cardiac muscle cell.

Two important actions are

i. Smooth muscle (specially vascular) relaxation.
ii. Negative chronotropic, inotropic and dromotropic actions on the heart.

PHARMACOLOGY OF VERAPAMIL:

History:

Verapamil was developed in Germany in 1962 as a coronary dilator.

Fleckenstein in 1967 showed that it interfered with Ca^{2+} movement into the cell.

Verapamil is a synthetic hydrophilic papaverine congener belonging to the phenylalkylamine group of calcium channel blockers.

Physiochemical properties:

It is supplied as a racemic mixture.

The dextroisomer of verapamil is devoid of activity at slow calcium channels and instead acts on fast sodium channels, accounting for the local anaesthetic effects.

The levoisomer is specific for slow channel blockade and the predominance of this action accounts for the classification of verapamil as a calcium channel blocker.

Mechanism of action:

Verapamil binds to the intracellular portion of the α_1 subunit of the L-type channel subunit, when the channel is in an open state and actually physically occlude the channel. It further delays the recovery of the channel.

Pharmacokinetics:

Absorption:

Oral verapamil is almost completely absorbed.

Oral absorption > 90%

But oral bioavailability is only 10-20% because of extensive hepatic first pass metabolism with high hepatic extraction of 75-90% of orally administered drug. As a result oral dose is about 10 times the intravenous dose.

Protein binding:

Verapamil is highly protein bound upto 90%. The presence of other drugs like lidocaine, diazepam and propranolol can increase the

pharmacologically active, unbound portion of the drug.

Metabolism and clearance:

It is metabolilsed in liver and excreted in urine and bile.

Dimethylated metabolites of verapamil predominate, with norverapamil possessing sufficient activity to contribute to the antidysrhythmic properties of the parent drug.

70% of injected dose is recovered in urine as metabolites and 15% is excreted via bile.

Onset of action:

Oral	< 30 minutes
Intravenous	1 - 3 minutes

Therapeutic plasma concentration:

100 – 300 ng/ml

Volume of distribution (Vd):

5 liters / kg

Elimination half time:

4-6 hours

Dosage:

Oral - 80 – 160 mg tds

Intravenous - 75 –150 micro grams / kg

Availability:

40, 80 mg tablets.

120, 240 mg slow release tablets.

5mg / ml injection

EFFECTS OF VERAPAMIL ON VARIOUS SYSTEMS OF THE BODY

Cardiovascular system:

Of the many CCBs verapamil has the most prominent cardiac electrophysiological action.

Negative chronotropic effect:

This effect is due to slowing of the SA node. It results in reduced myocardial oxygen consumption. The direct negative chronotropic effects of verapamil are able to overcome any reflex sympathetic response to the lowering of blood pressure. This effect can depress the frequency of hyperactive tissue causing arrhythmias.

The basic action of verapamil is to depress Ca^{2+} mediated depolarization.

Suppresses automaticity or reentry dependent on slow response.

Phase 4 depolarization in SA node and purkinjee fibres is reduced resulting in bradycardia and extinction of latent pacemakers.

The most consistent action of verapamil is prolongation of AV nodal ERP. As a result AV conduction is markedly slowed and reentry involving AV node is terminated.

Intraventricular conduction, however, is not affected.

Negative inotropic effect:

This effect reduces myocardial oxygen consumption. Verapamil's direct negative inotropic effects are able to overcome any reflex sympathetic response to the lowering of blood pressure.

Negative dromotropic effect:

By slowing conduction through the AV node, verapamil increases the time needed for each beat. This results in reduced myocardial oxygen consumption.

Effect on smooth muscles:

Verapamil dilates the arterioles and has some α adrenergic blocking activity – decreases total peripheral resistance but the blood pressure is only modestly lowered. The heart rate generally decreases, AV conduction is slowed, but cardiac output is maintained by reflex sympathetic stimulation and decrease in aortic impedance.

Verapamil is a potent vasodilator of coronary vessels. This effect increases coronary blood flow, and reduces coronary vasospasm.

Indications:

1. **Paroxysmal supraventricular tachycardia :**

   Verapamil is a class IV antiarrhythmic drug.

   It terminates attacks of paroxysmal supraventricular tachycardia. It is also useful for preventing recurrences

2. **Atrial fibrillation or flutter:**

   To control ventricular rate in atrial fibrillation or flutter.

3. **Hypertension**:

   Lowers BP by decreasing peripheral vascular resistance without

   compromising cardiac output.

   The vasodilatory effects of verapamil are useful in treating mild to moderate hypertension, particularly low-renin hypertension.

intravenous verapamil may be effective in treating hypertensive emergencies.

4. Angina Pectoris:

Reduces frequency and severity of classical as well as variant angina. Benefit in classical angina appears primarily due to reduction in cardiac work- mainly as a result of reduced afterload due to peripheral vasodilatation.

It also increases coronary flow.

Exercise tolerance is increased.

Capacity of verapamil to prevent arterial spasm is responsible for the beneficial effect in variant angina.

Reduction of cardiac O_2 demand would also work in the same direction.

5. **Hypertrophic cardiomyopathy:**

   The negative inotropic action of verapamil can be salutary in the diastolic dysfunction in this condition.

6. **Premature labour:**

   Due to its action on smooth muscle → relaxant effect.

7. **Maternal and fetal tachy dysrhythmias:**

   Administered intravenously in parturients, verapamil prolongs atrioventricular conduction of the fetus despite limited placental transfer of the drug.

8. Nocturnal leg cramps.

Adverse effects:

Nausea,Constipation, Dizziness & Bradycardia are more common Flushing, Headache &Ankle Edema are less common

Contraindications:

1.CHF:

Patients with reduced ventricular function may not be able to counteract the inotropic and chronotropic effects of verapamil, the result being an even higher compromise of function.

2. SA node or AV conduction disturbances:

Use of verapamil is contraindicated in patients with SA or AV nodal abnormalities, because of its negative chronotropic and dromotropic effects

3. Low blood pressure:

Patients with systolic blood pressures below 90 mm Hg should not be treated with verapamil.

4. Digitalis toxicity:

Verapamil is contraindicated for atrial tachycardia caused by digitalis toxicity,because of pharmacokinetic interactions that may lead to increased blood digoxin levels.

4. Wolff-Parkinson-White syndrome induced atrial fibrillation:

Verapamil may paradoxically increase ventricular rate in some patients because of accessory conduction pathways.

Drug interactions:

1. β - Blockers:

Additive sinus depression.

I.V. verapamil should never be used concurrently with a beta-blocker; can result in AV block or severe depression of ventricular function and asystole may occur.

2. Digoxin:

Verapamil increases plasma concentration of digoxin – causing increased toxicity, presumably by decreasing its plasma clearance.

3.Qunidine and disopyramide:

Additive cardiac depression and reduced clearance.

4.Volatile anaesthetics:

One of the possible mechanism of cardiac depression by volatile

agents is interference with calcium movement across the cell membrane.

The myocardial depression and peripheral vasodilation produced by volatile agents could be exaggerated by similar actions of verapamil.

5.Neuromuscular blocking agents:

Verapamil potentiate the effects of depolarizing and nondepolarising muscle relaxant.

The local anaesthetic effect of verapamil reflecting inhibition of sodium ion flux via fast sodium channels – may contribute to the potentiation of these agents.

Further the antagonism of neuromuscular blockade may be impaired because of diminished presynaptic release of acetylcholine due to verapamil.

6.Local anaesthetic:

Verapamil increases the risk of local anaesthetic toxicity.

7.Potassium containing solutions:

Verapamil slows the inward movement of potassium ions.

So there is a risk of hyperkalemia when administered with

potassium containing solutions (or) with stored blood.

8.Dantrolene:

Verapamil alters the normal homeostatic mechanisms for regulation of plasma potassium concentrations and may result in hyperkalemia from dantrolene induced potassium release.

PHARMACOLOGY OF DILTIAZEM

Diltiazem is a Benzothiazepine calcium channel blocker.

Mechanism of action:

- Act at the L-Type calcium channel on the α_1 subunit. But the mechanism of action is not well understood.
- It may act on sodium – potassium pump, decreasing the amount of intracellular sodium available for exchange with extracellular calcium.
- It may inhibit calcium calmodulin binding.

Pharmacokinetics:

Absorption:

Oral absorption is excellent >90%

Bioavailability:

Only 40% due to first-pass hepatic extraction of about 70-80% after oral administration.

Protein binding:

70-80% bound to proteins.

Metabolism and clearance:

Extensively metabolized in liver and excreted as active metabolites principally in bile (60%) and to a lesser extent in urine (35%)

Onset of action:

Oral --30 minutes

Intravenous --1-3 minutes

Therapeutic plasma concentration:

100 -250 nanograms / ml

Volume of distribution :

3 liters / kilogram

Elimination half time:

5-6 hrs

Dosage:

Oral 60-90 mg 8^{th} hourly

Intravenous 75-150 mg / kg

Availability:

60 mg and 30 mg oral tablets.

90 mg slow release tablets.

25 mg / 5 ml intravenous injections.

Effects on cardiovascular system:

Diltiazem has a modest direct negative inotropic action, but direct depression of SA mode and AV conduction are equivalent to verapamil.

Effects on smooth muscle:

Less potent vasodilator than verapamil.

Usual clinical doses produce consistent fall in BP with little change or decrease in heart rate.

Large dose or iv injection decreases total peripheral resistance markedly which may elicit reflex cardiac effects.

It dilates the coronaries.

Indications:

Similar to that of verapamil.

1. Paroxysmal suprarentricular tachycardia:

Used as an alternative to verapamil.

2. Atrial fibrillation and flutter:

   To control the ventricular rate.

3. Angina pectoris.
4. Hypertension.

Contraindications:

1. Patients with sick sinus syndrome
2. 2^{nd} or 3^{rd} degree AV block
3. Patients with severe hypotension or cardiogenic shock
4. Hypersensitivity to the drug.
5. Patients on intravenous β - blockers.
6. Patients with atrial fibrillation or flutter associated with an accessory bypass tract such as in WPW syndrome or short PR interval.
7. Patients with ventricular tachycardia – ventricular fibrillation may be precipitated.

Adverse effects:

Are mild and transient.

Hypotension, injection-site reactions, vasodilatation, arrythmias – junctional bradycardia, chestpain, CCF, pruritis, constipation, nausea, dizziness, vomiting, headache, paresthesia, amblyopia, exfoliative dermatitis.

Drug interactions:

1. Anaesthetic drugs:

The depression of cardiac contractility, conductivity and automaticity as well as the vascular dilatation associated with anaesthetics may be potentiated by diltiazem.

2. Digitalis:

Since both digitalis and diltiazem affect AV nodal conduction, patients should be monitored for excessive slowing of the heart rate and AV block.

3. Beta blockers:

Due to additive action, the possibility of bradycardia, AV block, depression of myocardial contractility should be considered.

PHARMACOLOGY OF LIDOCAINE

Lidocaine is a synthetic amide-linked local anaesthetic of intermediate potency and duration. In 1943 Lofgren synthesized lidocaine in Sweden. First used by Gordh in 1948.

Lidocaine is the standard to which all other local anaesthetics are compared. It is currently the most widely used local anaesthetic. In addition, it is a popular antiarrythmic. It can be given by almost any route.

Mechanism of action:

Lidocaine prevent transmission of nerve impulses by inhibiting passage of sodium ions through ion-selective sodium channels in the nerve membranes. This slows the rate of depolarization such that the threshold potential is not reached and thus action potential is not propagated. But resting membrane potential is not altered. Lidocaine binds to the inner portion receptor (i.e sodium channel) after entering the cell membrane.

Physiochemical properties:

Molecular weight 234.

Weak base with a pka 7.6 – 7.8.

Very stable, not decomposed by boiling, acids or alkalies.

It is less lipid soluble than that of Bupivacaine.

Pharmacokinetics:

Absorption:

It is absorbed from the site of application or injection into the blood stream. Rate of absorption depends on the blood flow to the area and use of epinephrine.

Metabolism:

Metabolised in liver by oxidative dealkylation to monoethylglycine xylidide followed by hydrolysis of this metabolite to xylidide. Metabolism is dependant on hepatic blood flow.

Monoethylglycine xylidide has 80% activity of the parent drug.

Xylidide has 10% activity of the parent drug.

75% of xylidide is excreted in the urine as 4 – hydroxyl – 2,6, -dimethylaniline.

Onset of action:

Rapid onset of action.

- Topical anaesthesia 5-10 mins
- Conduction anaesthesia
  - For small nerves 5-10 mins
  - For large nerves 10-15 mins
- Intravenous administration 1-2 mins

Protein binding:

It is 70% bound to α_1 acid glycoproteins.

Volume of distribution:

91 liters

Distribution:

Lignocaine has a triphasic distribution.

Rapid distribution phase (α) :

In this phase, the drug is distributed to highly vascular regions.

t ½ α is 1 min.

Slow disappearance phase (β) :

The drug is distributed to slowly equilibrating tissues.

t ½ β is 9.6 min.

Slow transformation and excretion phase (δ) :

t ½ δ is 1.6 hrs.

Clearance is 0.95 litres per minute.

Availability:

a. 5% heavy 2 ml ampoules which contain 50mg of lignocaine / ml

   with 75 mg – 100 mg of dextrose.

b. 2% lignocaine (xylocard) without preservative – 50 ml vial for intravenous use.
c. 2% lignocaine – plain – 30 ml vial – contains methyl and propyl paraben as preservative.
d. 4% lignocaine with 1 in 200000 Adrenaline ─ 30─ ml vial.
e. 4% Lignocaine viscus
f. 4% lignocaine aqueous solution
g. 10% lignocaine spray
h. 2% lignocaine jelly
i. 2% lignocaine ointment

j. 5% lignocaine ointment

Pharmacodynamics:

Local actions:

Causes nerve blockade with loss of pain and temperature sensation, touch, motor power and vasomotor tone in the region supplied by the nerves blocked.

Systemic actions:

Result of systemic absorption from the site of admistration or intravenous administration.

Cardiovascular system:

It has a stabilizing effect on the cell membranes of cardiac tissue.

Lignocaine depresses myocardial automaticity by antagonizing the spontaneous phase IV depolarization and reduces the duration of effective refractory period.

Myocardial contractility and conduction velocity are depressed at higher concentrations.

These effects result from direct cardiac muscle membrane changes

(ie.) cardiac sodium channel blockade.

It stabilizes the membrane of damaged and excitable cells, tending to suppress ectopic foci..

Respiratory system:

Lignocaine depresses hypoxic drive (the ventilatory response to low P_aO_2 .)

Apnea can result from phrenic and intercostal nerve paralysis or depression of the medullary respiratory center following direct exposure to the local anaesthetic agents.

Relax bronchial smooth muscle.

Intravenous lignocaine may be effective in blocking the reflex bronchoconstriction associated with intubation.

Vascular smooth muscle:

Produces vasodilatation.

Central nervous system:

Produces a sequence of stimulation followed by depression.

Produces sedation on intravenous administration.

Intravenous administration decreases cerebral blood flow and attenuates the rise in intracranial pressure that accompanies intubation.

Infusion of lignocaine is capable of reducing the MAC of volatile anaesthetics by 40%

Musculoskeletal:

Lignocaine is myotoxic leading to lytic degeneration, edema and necrosis.

Haematological :

It decreases coagulation and enhances fibrinolysis.

Indications:

1. For infiltration block, peripheral nerve blocks, epicdural, spinal and topical anaesthesia & intravenous regional anaesthesia.
2. Antiarrythmic:

Lignocaine is a class I B antiangthrimic.

- Ventricular tachydrythmias
- Arythmias following acute MI during cardiac surgery
- In digitalis toxicity – because it does not worsen AV-

block.

3. Prevention or treatment of increases in intracranial pressure during intubation.

   - antitussive effect may be the reason.

4. Reflex induced bronchospasm is also attenuated by iv administration of lignocaine.
5. Suppresses noxious reflexes such as coughing & sympathetic stimulations associated with endotracheal suctioning and intubation.
6. Used as an antiepileptic agent intravenously.
7. Used intravenously as an analgesic for certain chronic pain states.
8. Used as a supplement to general anaesthesia.

Contraindications:

- Hypersensitivity.
- Should not be used with vasoconstrictor in digits of hand, feet and penis.
- Stokes Adams syndrome, severe degree of heart block

Dose:

Maximum recommended dose

(a) plain - 3 mg/kg

(b) with adrenaline - 7 mg/kg

(c) for reflex suppression - 1.5mg/kg iv.

Drug interactions:

β Blockers:

Coadministration of betablockers, increases serum levels of lignocaine and its toxicity by decreasing lignocaine's metabolism.

Anticonvulsant agents:

Increases lignocaine's metabolism.

Non depolarizing muscle relaxant:

Blockade is potentiated by lignocaine.

Opioids and α_2 adrenergic agonists:

Potentiate lignocaine's pain relief.

Antiarrythmic agents:

Potentiate the cardiac effects of lignocaine.

Toxicity:

Mostly due to systemic absorption of locally administered

lignocaine or due to accidental intravenous administration of large doses of lignocaine.

The cental nervous system is mostly vulnerable.

Blood levels and symptoms

4mg/ml: lightheadedness, tinnitus, circumoral and tongue numbness [anticonvulsant and antiarrhythmic activity]

6mg/ml: visual disturbances.

8mg/ml: muscular twitching

10mg/ml: convulsions

12mg/ml: unconsciousness

15mg/ml: coma

20mg/ml: respiratory arrest

26mg/ml: cardiovascular collapse

Treatment of toxicity:

Continuous monitoring of CVS and RS status.

- If convulsions occur barbiturates or benzodiazepines can be given.
- Succinylcholine 1mg/kg to paralyse the patient
- Cardiac toxicity like fibrillation can be treated by

defibrillation.

- ❖ Ventilatory support –100% oxygenation , intubation etc.,
- ❖ Maintain B.P. by rapid infusion of I.V. fluids, use of vasopressors and put the patient in Trendelenberg's position.
- ❖ Maintain fluid and electrolyte balance.

Adverse effects:

1. Allergic and hypersensitivity reactions:

Due to the preservative used - methyparaben.

2. Neurotoxicity:

Transient radicular irritation

Cauda equina syndrome

Anterior spinal artery syndrome.

3. CVS:

Bradycardia, hypotension.

OBSERVATION AND RESULTS

Data among groups are analysed by using one-way analysis of variance and are assessed by using NeumanKeuls post-hoc test. Data within each group are analysed by using two-way analysis of variance followed by using Bonferroni's correction of t-test.

DEMOGRAPHIC DATA

1. Comparison between groups with respect to Sex

		Sum of Squares	Df	Mean Square	F	Sig.
PRDIFF	Between Groups	293.461	1	293.461	.705	.403
	Within Groups	49096.539	118	416.072		
	Total	49390.000	119			
SDIFF	Between Groups	103.187	1	103.187	.225	.636
	Within Groups	54135.738	118	458.777		
	Total	54238.925	119			
DDIFF	Between Groups	62.430	1	62.430	.416	.520
	Within Groups	17693.27	118	149.943		

Total	0 17755.70 0	119			

Comments: The difference between the group with respect to sex is not significant. Hence the groups are comparable with respect to sex

2. Comparison between groups with respect to Age

		Sum of Squares	df	Mean Square	F	Sig.
PRDIFF	Between Groups	659.994	2	329.997	.792	.455
	Within Groups	48730.00 6	117	416.496		
	Total	49390.00 0	119			
SDIFF	Between Groups	1153.184	2	576.592	1.27 1	.284
	Within Groups	53085.74 1	117	453.724		
	Total	54238.92 5	119			
DDIFF	Between Groups	395.440	2	197.720	1.33 3	.268
	Within Groups	17360.26 0	117	148.378		
	Total	17755.70 0	119			

Comments: The difference between the group with respect to age is

not significant.

Hence the groups are comparable with respect to age.

3. Comparison between groups with respect to Weight

		Sum of Squares	Df	Mean Square	F	Sig.
PRDIFF	Between Groups	1163.778	2	581.888	1.412	.248
	Within Groups	48226.225	117	412.190		
	Total	49390.000	119			
SDIFF	Between Groups	1351.657	2	675.828	1.495	.228
	Within Groups	52887.268	117	452.028		
	Total	54238.925	119			
DDIFF	Between Groups	215.859	2	107.929	.720	.489
	Within Groups	17539.841	117	149.913		
	Total	17755.700	119			

Comments: The difference between the group with respect to Weight is not significant.

Hence the groups are comparable with respect to Weight.

1. Multiple comparison (pulse rate reduction)

Dependent Variable	(1) Group	(J) group	Mean Difference (I-J)	Std.Error	Sig	95% Confidence Interval	
						Lower Bound	Upper Bound
Pulse Rate Difference	Control	Verapamil	44,0000*	2.7303	.000	36.6713	51.3287
		Diltiazem	35,3000*	2.7303	.000	27.9713	42.6287
		Lidocaine	39.5000*	2.7303	.000	32.1713	46.8287
	Verapamil	Control	-44.0000*	2.7303	.000	-51.3287	-36.6713
		Diltiazem	-8.7000*	2.7303	.011	-16.0287	-1.3713
		Lidocaine	-4.5000	2.7303	.612	-11.8287	2.8287
	Diltiazem	Control	-35.3000*	2.7303	.000	-42.6287	-27.9713
		Verapamil	8.7000*	2.7303	.011	1.3713	16.0287
		Lidocaine	4.2000	2.7303	.760	-3.1287	11.5287
	Lidocaine	Control	-39.5000*	2.7303	.000	-46.8287	-32.1713
		Verapamil	4.5000	2.7303	.612	-2.8287	11.8287
		Lidocaine	-4.2000	2.7303	.760	-11.5287	3.1287

*. The Mean difference is significant at the .05 level

MULTIPLE COMPARISION(PULSE RATE REDUCTION)

The differences in **Pulse-rate reductions** of verapamil , lidocaine and diltiazem were –44, –39.5 and -35.3 respectively. All the differences against control were statistically significant. The effects of verapamil found to be superior, followed by lidocaine. However, the difference in the effects between them was not statistically significant. Their effects were almost the same. Comparing verapamil against diltiazem (-44-(-35.3) = -8.7), the difference is statistically significant. That is, verapamil was superior to diltiazem. But, lidocaine was not statistically superior to

the effects of diltiazem.

1. All the treatments had better effect than the control

2. The leading drug is verapamil having the difference of (-44) with control

3. Lidocaine is the next leading drug making the difference of (-39.5) with control. But, the difference found between verapamil and lidocaine is not statistically significant.

4. Diltiazem was the least among the three. The effect of verapamil was found to be superior to diltiazem. But, lidocaine did not differ significantly from diltiazem.

2. Multiple comparison (systolic blood pressure reduction)

Dependent Variable	(1) Group	(J) group	Mean Difference (I-J)	Std.Error	Sig	95% Confidence Interval	
						Lower Bound	Upper Bound
Systolic Blood Pressure difference	Control	Verapamil	47.3000*	2.9606	.000	39.3529	55.2471
		Diltiazem	33.0667*	2.9606	.000	25.1196	41.0137
		Lidocaine	39.5333*	2.9606	.000	31.5863	47.4804
	Verapamil	Control	-47.3000*	2.9606	.000	-55.2471	-39.3529
		Diltiazem	-14.2333*	2.9606	.000	-22.1804	-6.2863
		Lidocaine	-7.7667	2.9606	.059	-15.7137	.1804
	Diltiazem	Control	-33.0667*	2.9606	.000	-41.0137	-25.1196
		Verapamil	14.2333*	2.9606	.000	6.2863	22.1804
		Lidocaine	6.4667	2.9606	.186	-1.4804	14.4137
	Lidocaine	Control	-39.5333*	2.9606	.000	19.8440	30.4893
		Verapamil	7.7667	2.9606	.000	11.3773	22.0227
		Lidocaine	-6.4667	2.9606	.000	15.5440	26.1893

*. The Mean difference is significant at the .05 level

Multiple comparison (Systolic blood pressure reduction)

Comments: The differences in **Systolic BP** of verapamil , lidocaine and diltiazem were –47.3, –39.5 and –33.07 respectively. All the differences against control were statistically significant. The effects of verapamil found to be superior, followed by lidocaine. However, the difference in the effects between them was not statistically significant. Their effects were almost the same. Comparing verapamil against diltiazem (-47.3-(-33.07) = -14.23), the difference is statistically significant. That is, verapamil was superior to diltiazem. But, lidocaine was not statistically superior to the effects of diltiazem.

1. All the treatments had better effect than the control
2. The leading drug is verapamil having the difference of (-47.3) with control
3. Lidocaine is the next leading drug making the difference of (-39.5) with control. But, the difference found between verapamil and lidocaine is not statistically significant.
4. Diltiazem was the least among the three. The effect of verapamil was found to be superior to diltiazem. But lidocaine did not differ significantly from diltiazem.

3. Multiple comparison (diastolic blood pressure reduction)

Dependent Variable	(1) Group	(J) group	Mean Difference (I-J)	Std.Error	Sig	95% Confidence Interval	
						Lower Bound	Upper Bound
Diastolic Blood Pressure Difference	Control	Verapamil	25.1667*	1.9829	.000	19.8440	30.4893
		Diltiazem	16.7000*	1.9829	.000	11.3773	22.0227
		Lidocaine	20.8667*	1.9829	.000	15.5440	26.1893
	Verapamil	Control	-25.1667*	1.9829	.000	-30.4893	-19.8440
		Diltiazem	-8.4667*	1.9829	.000	-13.7893	-3.1440
		Lidocaine	-4.3000	1.9829	.193	-9.6227	1.0227
	Diltiazem	Control	-16.7000*	1.9829	.000	-22.0227	-11.3773
		Verapamil	8.4667*	1.9829	.000	3.1440	13.7893
		Lidocaine	4.1667	1.9829	.227	-1.1560	9.4893
	Lidocaine	Control	-20.8667*	1.9829	.000	-26.1893	-15.5440
		Verapamil	4.3000	1.9829	.193	-1.0227	9.6227
		Lidocaine	-4.1667	1.9829	.227	-9.4893	1.1560

*. The Mean difference is significant at the .05 level

Multiple comparison (diastolic blood pressure reduction)

Comments:

The differences in **Diastolic BP** of verapamil , lidocaine and diltiazem were -25.17,-20.87,-16.7 respectively. All the differences against control were statistically significant. The effects of verapamil found to be superior, followed by lidocaine. However, the difference in the effects between them was not statistically significant. Their effects were almost the same. Comparing verapamil against diltiazem (-25.17-(-16.7) = -14.23), the difference is statistically significant. That is, verapamil was superior to diltiazem. But, lidocaine was not statistically superior to the

effects of diltiazem.

1. All the treatments had better effect than the control
2. The leading drug is verapamil having the difference of (-25.17) with control

3. Lidocaine is the next leading drug making the difference of (-20.87) with control. But, the difference found between verapamil and lidocaine is not statistically significant.

4.Diltiazem was the least among the three. The effect of verapamil was found to be superior to diltiazem. But lidocaine did not differ significantly from diltiazem.

COMPARISION WITH RESPECT TO QUALITY OF EXTUBATION

	QUALITY				
DRUG	**1**	**2**	**3**	**4**	**5**
CONTROL	5(16.6%)	16(53.3%)	5(6.6%)	4(13.3%)	0
VERAPAMIL	26(86.6%)	4(13.3%)	0	0	0
DILTIAZEM	17(56.6%)	11(36.6%)	2(6.6%)	0	0
LIDOCAINE	21(70%)	9(30%)	0	0	0

86.6% of patients given Verapamil during extubation had no cough or strain.56.6% &70% of patients in diltiazem &lidocaine group had no cough or strain during extubation respectively.But only 16.6% of patients in the control group had the best quality of extubation. Thus Verapamil , lidocaine & diltiazem improved the quality of extubation.Verapamil is superior to lidocaine &diltiazem in this respect. Futher lidocaine is associated with better quality of extubation than diltiazem.

DISCUSSION

Anaesthesia is the process by which a patient is rendered, able to undergo Surgery. General anaesthesia uses drugs administered systemically to render the patient unaware of anything that is being done to or around him or her. It must be safe, not threating or unpleasant to the patient ,allow adequate surgical access to the operative site, and cause as little disturbance as possible to the internal homeostatic mechanisms.

General anaesthesia has many advantages such as making no psychological demand on the patient, allowing complete stillness for prolonged periods of time, facilitating complete control of the airway, breathing and circulation, permitting surgery to take place in widely separated areas of the body at the same time and adapting easily to procedures of unpredictable duration or extent. Despite these advantages administration of general anaesthesia has certain disadvantages. Apart from the less serious complications such as nausea, vomiting, sore throat, headache, shivering and delayed return to normal mental functioning the most feared aspect of general anaesthesia is its association with certain degree of physiological trespass. This physiological trespass can lead to major morbidity or mortality in a patient. The most susceptible phases of

general anaesthesia for this complication to occur are the phases of intubation and extubation. Thus the safe conduct of anaesthesia requires a high degree of preparation, vigilance and attention to detail till the process of extubation.

In this study the provocation of cardiovascular changes with marked increase in heart rate and arterial blood pressure by extubation is confirmed. The heart rate increase from the baseline value is 40.70±10.96 beats per minute during extubation. The systolic blood pressure increase is 33.20±12.50 mmHg from the baseline and the diastolic blood pressure increase is 19.73±1.86 mmHg from the baseline. Thus stress attenuation during extubation may be of value in preventing morbidity and mortality in specific patient groups such as hypertensives and those undergoing cardiovascular or neurosurgical procedures.

Myocardial ischemia may occur during tracheal extubation in patients with coronary arterial disease [19,20]. The occurrence of perioperative myocardial ischemia during anaesthesia is associated with postperative myocardial infarction. As heart rate is a major controllable determinant of myocardial oxygen balance, satisfactory suppression of

the tachycardic response to tracheal extubation may be beneficial.

Further in this study, it is confirmed that the stress response to tracheal extubation can be attenuated with 0.1mg/kg of verapamil or 0.2. mg/kg of diltiazem or 1.5mg/kg of lidocaine.

But the attenuative effect was greatest with 0.1mg/kg of verapamil followed by 1.5mg/kg of lidocaine which is followed by 0.2mg/kg of dilitazem.

Although the precise mechanism responsible for the cardiovascular changes during tracheal extubation remains to be elucidated, multifactorial stimuli during tracheal extubation, including wound pain, emergence from anaesthesia, and tracheal irritation, are involved in the events. The calcium channel blockers verapamil and diltiazem control the hypertension and tachycardia by their direct vasodilatory and negative chronotropic and dromotropic properties. In addition the potent local anaesthetic property of verapamil could have contributed to the attenuation of laryngeal irritation which may be the reason for the better quality of extubation. The beneficial effect of lidocaine on the hemodynamic sequences may be due, in part, to direct cardiac depression

and peripheral vasodilation. Intravenous lidocaine also suppresses the cough reflex.

In this study, none of the patients who received the drugs developed sustained bradycardia (HR <50bpm) or profound hypotension (SAP <80mmHg) or sinoatrial or atrioventricular block sufficient to require pressor or sympathomimetic drugs after extubation.

Further the quality of extubation is also enhanced by the use of these drugs during extubation. The quality of extubation is found to be superior with that of verapamil than that of lidocaine or diltiazam.

Verapamil is also highly cost effective than that of lidocaine or diltliazem. Lidocane is superior to diltiazem in cost effectiveness.

Considering all the above said factors verapamil in the dose of 0.1mg/kg is the drug of choice for tracheal extubation among the 3 drugs. Lidocaine 1.5mg/kg is the not drug of choice. If both verapamil and lidocaine are not available diltiazam in the dose of 0.2mg/kg may be used with substantial benefit.

CONCLUSION

1. Tracheal extubation is associated with increase in pulse rate and blood pressure.

   PR increase – 40.70 beats per min

   SBP increase – 33.20 mmHg

   DBP increase – 19.73 mmHg

2. Verapamil, lidocane and diltiazem all improve the quality of extubation.
3. Verapamil 0.1mg/kg is superior to lidocaine and diltazem in attenuating stress response during extubation. lidocaine 1.5mg/kg is superior to diltiazem in attenuating the stress response to extubation.
4. Verapamil, Lidocaine and Diltiazem all attenuate the stress response to extubation. 86.6% of patients given Verapamil had no cough or strain (quality1 extubation). 56.6% of patients in diltiazem group and 70% of patients in lidocaine group also had quality 1 extubation i.e., no cough or strain. But only 16.6% of patients in the control group had no cough or strain during extubation.

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PROFORMA

NAME :

AGE :

SEX :

WEIGHT :

DIAGNOSIS :

SURGERY DONE :

ASA PHYSICAL STATUS :

GROUP: CONTROL /VERAPAMIL / DILTIAZEM / LIDOCAINE

(TO BE TICKED OVER THE SPECIFIC GROUP)

QUALITY OF EXTUBATION:

1 ⟶ **NO COUGH OR STRAIN**

2 ⟶ VERY SMOOTH, MINIMAL COUGH

3 ⟶ MODERATE COUGH

4 ⟶ MARKED COUGH OR STRAIN

5 ⟶ POOR EXTUBATION

(TO BE TICKED OVER THE SPECIFIC QUALITY)

MONITORED PARAMETERS :

TIME	**PULSE RATE (Per Minute)**	**SYSTOLIC BLOOD PRESSURE (mm of Hg)**	**DIASTOLIC BLOOD PRESSURE (mm of Hg)**
PRE OPERATIVE			
0 MIN (end of surgery)			
1 MIN			
2 MIN			
3 MIN			
4 MIN			
5 MIN			
6 MIN			
7 MIN			
8 MIN			
9 MIN			
10 MIN			

SIDE EFFECTS: