

## Original Research Article

# Attenuation of haemodynamic responses to endotracheal extubation-diltiazem versus lidocaine

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### ABSTRACT

**Background:** Endotracheal extubation is one of the frequently performed procedure in the practice of anaesthesia. This study was done to observe the haemodynamic responses during tracheal extubation and to compare the efficacy of IV diltiazem 0.2 mg/kg versus IV lidocaine 1 mg/kg in attenuating the hemodynamic response to tracheal extubation.

**Methods:** 90 patients aged 20 to 60 yrs, belonging to ASA I and II, normotensive were included in the study and they were randomly allocated into 3 groups of 30 each. Group I received normal saline and served as control. Group II received 0.2 mg/kg of IV diltiazem 2 min before extubation. Group III received 1 mg/kg of lidocaine IV 2 min before extubation. At the end of the surgery, heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded served as base line values.

**Results:** After tracheal extubation, all the haemodynamic parameters increase from the basal level in the control group and decreased in the study group. The change in HR, SBP and DBP were significantly less in group II and group III compared to group I. The change in HR, SBP and DBP were significantly less in group II compared to group III.

**Conclusions:** Diltiazem hydrochloride, a calcium channel blocker belongs to the benzothiazepine group given in dose of 0.2 mg/kg IV 2 min before tracheal extubation in ASA grade I and grade II patients is a simple, effective and practical method of blunting cardiovascular responses to tracheal extubation. This suppressive effect of diltiazem was comparable to or even more potent than that of lignocaine 1 mg/kg IV 2 min before tracheal extubation.

**Keywords:** Diltiazem, Lignocaine, Endotracheal extubation, Hemodynamic parameters

### INTRODUCTION

Endotracheal extubation is one of the frequently performed procedure in the practice of anaesthesia. Endotracheal extubation is the translaryngeal removal of a tube from the trachea via the nose or mouth. Endotracheal extubation almost always associated with haemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. This increase in sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias.<sup>1,2</sup> This increase in blood

pressure and heart rate are usually transitory, variable, unpredictable. It is more hazardous to the patient with hypertension, myocardial insufficiency or cerebrovascular diseases.<sup>3</sup> Therefore, this haemodynamic response to tracheal extubation such as hypertension, tachycardia and arrhythmias have always been an interest to anesthesiologist. Many pharmacological methods have been devised to reduce the extent of hemodynamic events, including esmolol, alfentanil, fentanyl, diltiazem, high dose of opioids, local anesthetics like lignocaine and vasodilating drugs like nitroglycerine.<sup>1,3</sup> Topical anaesthesia with lignocaine applied to the larynx and trachea in

a variety of ways remains a popular method used alone or in combination with other techniques.<sup>4</sup> Intravenous lignocaine with its well established centrally depressant and antiarrhythmic effect was found to be a more suitable alternate method to minimize this pressor response.<sup>5</sup> Recently several studies have shown that calcium channel antagonist like diltiazem, with its direct vasodilation and direct negative chronotropic and dromotropic properties is also effective.<sup>1-3,6</sup> The present study was undertaken to compare the effect of intravenous lignocaine and intravenous diltiazem on blunting the hemodynamic response to endotracheal extubation.

## **METHODS**

This is a prospective, randomized comparative study conducted in the department of Anaesthesia Konaseema Institute of Medical Science Amalapuram from July 2018 to December 2019.

As per exclusion and inclusion criteria 90 ASA grade-I patients were enrolled for this study to examine the effects of intravenous diltiazem (0.1 or 0.2 mg/kg) and lignocaine 1 mg/kg). The patients were randomly assigned to one of three groups.

The patients who receive normal saline and served as control (n=30) served as group I.

The patients who receive diltiazem 0.2 mg/kg IV 2 min before extubation (n=30) considered as group II.

The patients who receive lignocaine 1 mg/kg IV 2 min before extubation (n=30) served as group III.

### ***Inclusion criteria***

Patients aged between 20-60 yrs of either sex, weight of the patients between 40-80 kgs, height of the patients between 150 to 170 cm, patients belonging to ASA status I and II were included.

### ***Exclusion criteria***

Patients with neurological disorders, cardio respiratory disease, bleeding disorders, gastrointestinal disorders and psychiatric illness, patients with history of allergy to opioids and local anaesthetic agents, pregnant breast feeding and menstruating women, morbidly obese patients were excluded.

### ***Ethics***

Before start of the study institutional ethics committee approval was taken and a written informed consent was taken from all patients before enrolling them for study.

Pre-anesthetic evaluation was done on the evening before surgery. A routine preanaesthetic examination was conducted assessing general condition of the patient,

nutritional status and weight of the patients, a detailed examination of the cardiovascular system, a detailed examination of respiratory system, other associated diseases.

Routine investigations were done for all patients.

All patients were tested for any hypersensitivity reaction to local anaesthetics and informed consent was obtained from all the patients.

All patients were kept nil per oral from 12 midnight to the day of surgery.

All the patients were premedicated with tab. diazepam 10 mg and tab. pantoprazole 40 mg orally at bed time the previous day.

On the arrival of the patient in the operating room, an 18 gauge or 20 gauge intravenous cannula was inserted and an infusion of dextrose with normal saline was started. The patient were connected to multi channel monitor which records heart rate, non-invasive blood pressure (NIBP), end tidal carbon dioxide concentration, continuous ECG monitoring and oxygen saturation.

The base line blood pressure and heart rate were recorded from the same non invasive monitor and cardiac rate and rhythm were also monitored from a continuous display of electrocardiogram from lead II.

Inj. midazolam 1 mg IV and inj. pentazocine 15 mg IV was given IV to all the patients before induction as a premedication.

### ***Induction of anaesthesia***

Anaesthesia was induced with inj. thiopentone 5 mg/kg as 2.5% solution and endotracheal intubation was facilitated with succinylcholine 1.5 mg/kg. After confirming bilateral equal air entry, the endotracheal tube was secured. Anaesthesia was maintained using 66% nitrous oxide and 33% of oxygen. After the patients recovered from succinylcholine further neuromuscular blockade was maintained with non depolarizing muscle relaxants.

At the end of the surgery, heart rate, systolic and diastolic BP were recorded. These served as baseline values. Then the patients received inj. neostigmine 0.05 mg/kg IV and atropine 0.02 mg/kg IV. Then after 3 min of giving reversal and 2 min before extubation drugs were given.

### ***Monitoring***

The cardiovascular parameters were recorded in all the patients as heart rate (HR) in beats per minutes (BPM), systolic blood pressure (SBP) in mmHg, diastolic blood pressure (DBP) in mmHg.

The above cardiovascular parameters were noted at the end of the surgery served as baseline. then after giving reversal at 1 min and 2 min, at the time of administration of study drug, 1 min after administration of study drug, at the time of extubation, after extubation at 1 min, 2 min, 3 min, 4 min, 5 min, and 20 min.

The results were statistically evaluated using student ‘t’ test comparing between the groups and within the group. The quality of tracheal extubation was evaluated using a five point rating scale.

- No cough or strain.
- Very smooth, minimal coughing.
- Moderate coughing.
- High degree of coughing or straining.
- Poor extubation, very uncomfortable.

**Statistical analysis**

Results are presented as mean±SD. The statistical analysis was done using student ‘t’ test and Chi square test. The results were statistically evaluated using student ‘t’ test comparing between the groups and within the group. P<0.05 was considered to be statistically significant, p<0.001 highly significant, p>0.05 not significant

**RESULTS**

In the present study, 30 patients received normal saline, they serve as control group, 30 patients received inj.

diltiazem 0.2 mg/kg and 30 patients received inj. lignocaine 1 mg/kg and these constitute the study group. Results are presented as mean±SD.

In group II, basal HR was HR was 78.9 BPM. One minute after extubation it was 82.9 BPM representing a rise of 4 BPM. Subsequently elevated heart rate started settling down.

In group III, basal HR was 93.6 BPM. One minute after extubation, it was 98.33 BPM, representing a rise of 5 BPM. Subsequently elevated heart rate started settling down.

Statistical evaluation between the groups showed that the increase in HR observed in group III is statistically significant when compared to increased in HR in group II.

In group I, the Basal heart rate was 92.6 BPM. One minute after extubation, it was 114.80 BPM, representing a rise of 22 BPM subsequently elevated heart rate started settling down. Statistical evaluation between the groups showed that increase in HR observed in group I was statistically highly significant (p<0.001) when compared to increase in HR in group II and group III.

In group II, the basal value of SBP was 131.6 mmHg. One minute after extubation it was 117.6 mmHg, representing a fall of 14 mmHg. Thereafter it started coming down as shown in the Table 2.

**Table 1: Changes in mean heart rate between group II and III.**

	Group II (mean±SD)	Group III (mean±SD)	‘t’ value	P value	Remarks
<b>Basal</b>	78.9±10.9	93.6±11.5	5.08	<0.001	HS
<b>Extubation E1</b>	82.9±17.8	98.33±9.23	2.04	<0.05	S
<b>E2</b>	81.8±10.0	86.63±8.36	2.04	<0.05	S
<b>E3</b>	74.7±16.2	82.93±9.14	2.42	<0.05	S
<b>E4</b>	73.8±10.2	81.40±8.78	3.09	<0.01	S
<b>E5</b>	72.53±9.83	79.90±8.96	3.03	<0.01	S
<b>E20</b>	71.10±9.74	78.63±8.90	3.13	<0.01	S

S=significant, HS=highly significant. The statistical analysis was done using student ‘t’ test. Terms used for statistical significance.

**Table 2: Changes in mean systolic blood pressure between group II and group III.**

	Group II (mean±SD)	Group III (mean±SD)	‘t’ value	P value	Remarks
<b>Basal</b>	131.6±8.89	126.46±7.83	2.376	<0.05	S
<b>Extubation E1</b>	117.6±11.7	123.8±6.76	2.513	<0.05	S
<b>E2</b>	118.83±6.18	122.73±6.9	2.30	<0.05	S
<b>E3</b>	111.77±5.90	118.43±5.16	4.65	<0.001	HS
<b>E4</b>	109.1±10.6	116.86±5.81	3.516	<0.001	HS
<b>E5</b>	111.3±5.1	108.40±4.68	2.295	<0.05	S
<b>E20</b>	107.6±6.30	104.17±57.1	2.255	<0.05	S

S=significant, HS=highly significant. The statistical analysis was done using student ‘t’ test. Terms used for statistical significance.

**Table 3: Changes in mean diastolic blood pressure between group II and group III.**

	Group II (mean±SD)	Group III (mean±SD)	't' value	'P' value	Remarks
	81.6±4.82	82.23±4.32	0.533	>0.05	NS
<b>Extubation E1</b>	79.0±3.3	84.67±4.01	5.98	<0.001	HS
<b>E2</b>	78.37±3.37	83.8±3.8	5.856	<0.001	HS
<b>E3</b>	77.0±3.2	80.97±3.04	4.487	<0.001	HS
<b>E4</b>	75.0±3.6	79.5±3.20	3.980	<0.001	HS
<b>E5</b>	75.0±3.5	79.83±3.44	5.391	<0.001	HS
<b>E20</b>	74.0±3.7	79.9±3.2	6.606	<0.001	HS

NS= non-significant, S=significant, HS=highly significant. The statistical analysis was done using student 't' test. Terms used for statistical significance.

**Table 4: Results of the present study.**

Variable	Group I	Group II	Group III
<b>Mean age (yrs)</b>	36.78	44.37	40.80
<b>Sex ratio (M:F)</b>	20:10	20:10	13:17
<b>Mean weight (kg)</b>	70.2	58.07	65.97
<b>Changes in HR (BPM) compared to baseline values at 1 min after extubation</b>	↑22	↑4	↑5.28
<b>Changes in SBP (mmHg) compared to baseline values at 1 min after extubation</b>	↑7.13	↓19	↓2.66
<b>Changes in DBP (mmHg) compared to baseline values at 1 min after extubation</b>	↑9	↓2	↑2.00

In group III, the basal value of SBP was 126.46 mmHg, one minute after extubation, it was 123.8 mmHg, representing a fall of 3 mmHg. Thereafter it started coming down as shown in the Table 2.

Statistical evaluation between the groups showed that increase in SBP in group III was statistically significant when compared to increase in SBP in group II.

In group I, the basal value of SBP was 127 mmHg. One minute after extubation, it was 134.13 mmHg, representing a rise of 7 mm Hg. Subsequently it started coming down.

Statistical evaluation of between the groups showed that the increase in SBP in group I was statistically highly significant (p<0.001) when compared to increase in SBP in group II and group III.

In group II, the basal value of DBP was 81.6 mmHg. One minute after extubation it was 79 mmHg, representing a fall of 2 mmHg. Thereafter the pressure started coming down shown in the Table 3.

In the group III, the basal value of DBP was 82.23 mmHg. one minute after extubation, it was 84.67 mmHg representing a rise of 2 mmHg, therefore the elevated pressure started coming down as shown in Table 4. Statistical evaluation between the groups showed that increase in DBP in group III was statistically highly significant (p <0.001) when compared to increase in DBP in group II.

In group I, the basal value of DBP was 83.6 mmHg. One minute after extubation, it was 92 mmHg representing a rise of 9 mmHg. There after the elevated pressure started coming down.

Statistical evaluation between the groups showed that increase in DBP in group-I was statistically HS (p<0.001) when compared to increase in DBP in group II and group-III.

There was marked rise in HR, SBP and DBP 1 min following tracheal extubation in group I where no drug was employed for attenuation of cardiovascular responses to tracheal extubation.

Both lignocaine and diltiazem were effective in attenuating the pressor response to extubation. In our study diltiazem effectively decreased the SBP and DBP than lignocaine because of proper sedation, good analgesia and shorter duration of surgery.

**DISCUSSION**

Tracheal extubation is as hazardous as tracheal intubation and at times is stormy causing severe hypertension, tachycardia, arrhythmias, coughing, laryngospasm, bronchospasm and cerebrovascular accidents more so in patients with hypertension, coronary artery disease and cerebrovascular disease. A number of pharmacological agents including lidocaine, esmolol, alfentanil, fentanyl and prostaglandin E1 have been recommended for the control of these haemodynamic changes.<sup>7</sup> Beta blockers

like Esmolol was employed by Dyson et al to attenuate the cardiovascular responses associated with extubation.<sup>8</sup> They showed that the increase in HR that occurs during extubation can be successfully attenuated by bolus injection of 1 mg/kg of esmolol, although this dose is insufficient to effectively block increases in SBP. Prostaglandin E1 was employed by Nishina et al in their study but prostaglandin E1 in infusion of 0.1 micrograms/kg/min was effective in attenuating hypertensive response but ineffective for tachycardia.

### **Heart rate changes and blood pressure changes**

**Group I:** In our study basal HR was 92.6 BPM. One min after extubation it was 114.80 BPM representing a rise of 22 BPM. 5 min after extubation it was 99.48 BPM representing a rise of 6.8 BPM.

Basal value of SBP and DBP was 127 mmHg and 83.6 mmHg respectively. One min after extubation the rise in SBP was 134.13 mmHg representing a rise of 7.13 mmHg and DBP 92.0 mmHg representing a rise of 9 mmHg. 5 min after extubation the SBP was 119.43 mmHg representing a fall of 7.6 mmHg and DBP was 82.4 mmHg representing a fall of 1.2 mmHg.

**Group II:** In our study where diltiazem was used Basal HR was 78.9 BPM. One min after extubation it was 82.9 BPM representing a rise of 4 BPM. 5 min after extubation it was 72.53 BPM representing a fall of 6.17 BPM.

Basal value of SBP and DBP was 131.6 mmHg and 81.6 mmHg respectively. One min after extubation the rise in SBP was 117.6 mmHg representing a fall of 19 mmHg and DBP 79 mmHg representing a fall of 2 mmHg. 5 min after extubation the SBP was 111.3 mmHg representing a fall of 20.3 mmHg and DBP was 75 mmHg representing a fall of 6.6 mmHg.

Nishina et al in their study found that diltiazem is effective in blunting the haemodynamic responses associated with extubation.<sup>1</sup> Diltiazem at high doses (4.5 microg/ml) inhibits the release of catecholamines but the drug at doses used in clinical setting (0.2-0.6 mcg/ml) is unlikely to suppress catecholamine release.

Recently Mikawa et al, Fujii et al and Nishina et al have reported that calcium channel antagonists like diltiazem, verapamil and nicardipine are also effective in controlling the hemodynamic responses associated with extubation in normotensive as well as in hypertensive patient.<sup>1,3,6</sup>

Fujii et al have reported that inhibitory effects of diltiazem 0.2 mg/kg on the cardiovascular responses to tracheal extubation were greater than those of nicardipine 30 mcg/kg.<sup>6</sup>

**Group III:** In our study where lignocaine was used Basal HR was 93.6 BPM. One min after extubation it was 98.88

BPM representing a rise of 5.28 BPM. 5 min after extubation it was 79.90 BPM representing a fall of 13.70 BPM.

Basal value of SBP and DBP was 126.46 mmHg and 82.23 mmHg respectively. One min after extubation the rise in SBP was 123.8 mmHg representing a fall of 2.66 mmHg and DBP 84.67 mmHg representing a rise of 2 mmHg. 5 min after extubation the SBP was 108.4 mmHg representing a fall of 18.06 mmHg and DBP was 79.83 mmHg representing a fall of 3 mmHg.

Lignocaine has been successfully used to blunt the haemodynamic responses to extubation.

Recently Nishina et al showed lignocaine 1mg/kg iv successfully attenuated the cardiovascular responses associated with extubation.<sup>9</sup> Nishina et al in their study compared the effect of two different doses of diltiazem 0.2 mg/kg and 0.1 mg/kg with lignocaine 1 mg/kg during extubation in patients undergoing elective abdominal gynaecologic surgery and showed that the inhibitory effect on cardiovascular responses was greatest with diltiazem 0.2 mg/kg while the extent of attenuation by diltiazem 0.1 mg/kg was similar to lignocaine 1 mg/kg.<sup>10</sup> In our study the change in HR, SBP and DBP were significantly less in group II (diltiazem) and group III (lignocaine) compared to group I. The change in the HR, SBP and DBP were significantly less in group II (diltiazem) compared to group III (Lignocaine), which is similar to the findings of Nishina et al.<sup>10</sup>

We noticed that diltiazem in the dose of 0.2 mg/kg given 2 min before extubation significantly attenuated the pressor response to extubation. Here there is decrease in SBP and DBP probably because of good analgesia, proper sedation and shorter duration of surgery. We noticed that lignocaine in the dose of 1 mg/kg given 2 min before extubation significantly attenuated the cough reflex. In the present study when intravenous lignocaine and diltiazem were compared we noticed that diltiazem gave better protection than intravenous lignocaine against the cardiovascular responses to extubation.

### **CONCLUSION**

Diltiazem hydrochloride, a calcium channel blocker belongs to the benzothiazepine group given in dose of 0.2 mg/kg IV 2 min before tracheal extubation in ASA grade I and II patients is a simple, effective and practical method of blunting cardiovascular responses to tracheal extubation. This suppressive effect of diltiazem was comparable to or even more potent than that of lignocaine 1 mg/kg given IV 2 min before tracheal extubation.

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