

## Comparison of Dexmedetomidine, Lignocaine, and their combination in attenuation of cardiovascular responses to tracheal extubation in controlled hypertensive patients

Dr. Hardul V. Modi<sup>1\*</sup>, Dr. Monika<sup>2</sup>, Dr. S.K. Shah<sup>3</sup>

1. Assistant professor, Department of Anaesthesia, B.J. Medical College & Civil Hospital, Ahmedabad
2. Resident, Department of Anaesthesia, B.J. Medical College & Civil Hospital, Ahmedabad
3. Professor, Department of Anaesthesia, B.J. Medical College & Civil Hospital, Ahmedabad

**Corresponding Author:** Dr. Hardul V. Modi

**Email:** [hardul@gmail.com](mailto:hardul@gmail.com)



### Abstract

**Background & Aims:** Tracheal extubation is associated with acute, transient, significant and undesirable hemodynamic and airway responses that may persist into the recovery period. This study was designed to compare the efficacy of dexmedetomidine plus lignocaine with each drug alone in suppressing the hemodynamic changes during extubation in controlled hypertensive patients in elective ENT surgeries. **Material and Method:** In this double-blind randomized study 80 adult patients of age 18 years to 60 years of either sex belonging to ASA grade II having SBP >160 mmhg and/ or DBP >90 mmhg prior on preoperative visit undergoing elective ENT surgeries were randomly divided into 4 groups: Group D received dexmedetomidine [0.1 mcg/kg] iv, Group L received Lignocaine [1mg/kg] iv, Group D+L received Dexmedetomidine [0.1 mcg/kg] iv+ Lignocaine[1mg/kg] iv and Group C received Normal Saline iv before reversal. Hemodynamic parameters in form of heart rate, systolic and diastolic blood pressure, mean arterial pressure, rate pressure product, oxygen saturation was recorded at 1,2,3,5,10 min after extubation. Any side effects during study were noted. **Results:** It was found that heart rate, mean arterial pressure, rate pressure product increased temporarily after tracheal extubation in patients receiving Lignocaine. However, these hemodynamic responses were completely inhibited in those receiving Dexmedetomidine plus lignocaine, but suppressed to some extent with Dexmedetomidine group alone. **Conclusions:** Dexmedetomidine plus lignocaine is an effective and safe prophylaxis for attenuating the cardiovascular responses to tracheal extubation in hypertensive patients and is superior to each drug alone. Dexmedetomidine alone suppressed the hemodynamic variables and airway reflexes comparable to combination group.

**Keywords:** Dexmedetomidine, lignocaine, tracheal extubation, hypertensive patients

### Introduction

Tracheal extubation is associated with acute, transient, significant and undesirable hemodynamic and airway responses that may persist into the recovery period. Stimulation of the respiratory tract at the supraglottic and subglottic levels and an increase in the circulatory catecholamines produce these responses<sup>1</sup>. The reflexes range from tachycardia, hypertension, coughing, bucking, agitation to bronchospasm, laryngospasm, laryngeal edema, negative pressure pulmonary oedema, arrhythmias, left ventricular failure, myocardial ischemia, increased bleeding, raised intraocular and intracranial pressure and cerebro-vascular haemorrhage

in susceptible individuals<sup>2</sup>. Although most of the patients can tolerate these transient effects without any significant consequences, but this could be detrimental in patients operated for cardiac, neurosurgery, patient with poor cardiac reserve, patient with coronary artery disease or ophthalmic lesions. As per Difficult Airway Society basic extubation guideline, cardiovascular and airway factors need to be optimized before extubation<sup>3,4,5</sup>.

Several techniques, as well as drugs, have been used to attenuate these responses during tracheal extubation. Techniques like extubation in deeper plane of anaesthesia, substitution of the Endotracheal Tube with a laryngeal mask airway and drugs like low dose Propofol, Beta blockers like Esmolol, combined alpha and beta blockers like Labetalol, Ca<sup>2+</sup> channel blockers like Diltiazem, Verapamil, Nicardipine, intravenous Lignocaine, Lignocaine spray, intracuff lignocaine, central sympatholytic like Clonidine, Dexmedetomidine, low dose intravenous Fentanyl, Remifentanyl, Alfentanil, vasodilators like Nitrates, Prostaglandin and MgSO<sub>4</sub> have been studied as a sole agent or in comparison with each other to control hemodynamic changes and upper airway tract events with variable success rates<sup>6</sup>.

Dexmedetomidine is a new alpha 2 agonist with eight times more affinity for alpha 2 adrenoreceptors compared to clonidine, which has shown only partial agonist activity and is known to decrease the plasma catecholamines level and suppress the release of catecholamines level and suppress the release of catecholamines. Dexmedetomidine induce fewer changes in hemodynamic values during the extubation period. This drug may be useful in anaesthetic management requiring smooth emergence from anaesthesia. The net effect of dexmedetomidine action is a significant reduction in circulating catecholamines, with a slight decrease in blood pressure and a modest reduction in heart rate<sup>7</sup>. Lignocaine, an amide local anaesthetic, injected intravenously or topically applied to larynx and trachea, attenuates the hemodynamic responses to tracheal extubation by its myocardial depressant effects, central stimulant effect. It also prevents the rise in intracranial pressure associated with tracheal suctioning. It also decreases myofilament calcium sensitivity and has been shown to suppress coughing and prevent reflex bronchoconstriction<sup>8-11</sup>. Therefore, the present randomized placebo-controlled study was designed to compare the efficacy of dexmedetomidine plus lignocaine with each drug alone in suppressing the hemodynamic changes during extubation in controlled hypertensive patients in elective surgery.

### **Aims and objectives:**

- To study the various cardiovascular responses to laryngoscopy and extubation in controlled hypertensive patients undergoing elective ENT surgeries under general anaesthesia.
- To study the compared efficacy of Dexmedetomidine, Lignocaine and their combination, for attenuation of hemodynamic responses to laryngoscopy and extubation in hypertensive patients.
- To compare any side effects or complications like laryngospasm, bronchospasm, hypertension, hypotension, bradycardia, arrhythmias, ECG changes, hypoxemia, respiratory depression, myocardial ischemia, desaturation, vomiting intra-operatively or post-operatively.

### **Material and Method**

In our study 80 adult patients Age between 18 years to 60 years of either sex belonging to ASA grade II having SBP >160 mmhg and/ or DBP > 90 mmhg were selected. They were posted for elective ENT surgeries under general anaesthesia. All the patients with history of hypersensitivity to dexmedetomidine / Lignocaine, Mallam Pati grade III & IV, existence of considerable pathology in pharynx/larynx, patient with GERD, patient with cardiovascular diseases like ischemic heart disease, bronchial asthma were excluded. After obtaining institutional ethical committee approval, written informed consent was obtained. Patients were randomly divided into 4 groups with 20 patients in each group.

All patients were visited on the day prior to surgery and explained about the anaesthetic technique and perioperative course. Each patient had a pre anaesthetic check-up which includes any significant present and past medical/surgical history, physical examination, vital parameters like BP, pulse, temperature & respiratory rate. All routine and specific investigations (ECG, CBC, chest-x-ray, RFT, LFT, serum electrolytes). Informed consent of the patients for the study was taken.

**Study design:** Hospital Based Double Blind Randomized Comparative and Interventional Study.

**Sample size:** A sample size of 20 cases in each group with 30% prevalence of hypertension was adequate at 95% confidence limit and 80% power to verify the expected difference. This sample size was adequate to cover all other study variables too.

**Study groups:**

- Group L (n=20) –Inj. Dexmedetomidine 0.1mcg/kg i.v. as single bolus diluted in 10 ml normal saline given before reversal.
- Group D (n=20) – Inj. Lignocaine 1mg/kg i.v. as single bolus diluted in 10 ml normal saline given before reversal
- Group DL(n=20) –Inj. Dexmedetomidine 0.1mcg/kg+ inj. Lignocaine 1.0 mg/kg i.v. as single bolus diluted in 10ml normal saline given before reversal.
- Group C(n=20) --Control group received Inj. Normal saline.

**Sampling:**

RANDOMISATION - 80 eligible patients undergoing Surgery were selected for study purpose on first come first serve basis and were allocated in 4 groups using sealed envelope method.

DOUBLE BLINDING- Both the drugs were clear, transparent but still we covered these with white paper with a marking of A&B. The anaesthetist who gave the medicine was different from the anaesthetist who recorded study variable. Patients were told that some drug for maintaining hemodynamic was given to them.

Upon entering the operation theatre, all standard monitors (Electrocardiogram, Non-invasive blood pressure and Saturation probe) were applied and the baseline blood pressure, pulse rate, oxygen saturation and respiratory rate were recorded. Intravenous access was secured. Patient was given premedication with inj. Ondansetron 0.15mg/kg, inj. Fentanyl 2mcg/kg and inj. Glycopyrrolate 0.004 mg/kg. Patient was preoxygenated with 100% oxygen for 3 minutes. Anaesthesia was induced with inj. Propofol 2mg /kg iv and tracheal intubation was done after inj. Succinylcholine 2mg/kg iv. Anaesthesia was maintained with 0.2-2% Sevoflurane and 50% N<sub>2</sub>O in oxygen. Intra - operative monitoring included HR, SBP, DBP, MAP, SpO<sub>2</sub> and ECG (lead II) was monitored. The BP was recorded immediately before the induction of anaesthesia and every five minutes during anaesthesia using automated non-invasive BP monitor. The ECG was monitored by ECG lead II. The BP and HR was maintained between 80% and 120% of the preoperative values by altering the concentration of sevoflurane before completion of surgery. Muscle relaxation was maintained by intermittent boluses of inj. Vecuronium 0.1 mg/kg i.v.

At the end of surgery sevoflurane was switched off and we waited for return of spontaneous respiration. Before the reversal, the study medicines i.e., Dexmedetomidine (0.1 mcg/kg) or Lignocaine (1mg/kg) was given i.v. These medicines were prepared beforehand by an assistant and their identities were unknown to the anaesthetist. The total volume of study medicines was made to 10ml in both the groups. Residual muscle relaxation was reversed with inj. Neostigmine 0.05mg/kg iv and inj. Glycopyrrolate 0.008mg /kg i.v. on appearance of spontaneous ventilation. A thorough oropharyngeal suction was done before extubation. Then trachea was extubated once Return of spontaneous respiration with adequate tidal volume, obeying verbal commands (eye opening) and good hand grip. Immediately after tracheal extubation patient was given 100% oxygen by a facemask for 5 minutes. All parameters (HR, SBP, DBP, MAP, SPO<sub>2</sub>) were recorded at baseline,

after premedication, before induction, after induction, just before study drug administration, just before extubation, at 1,2,3,5 and 10 mins after extubation.

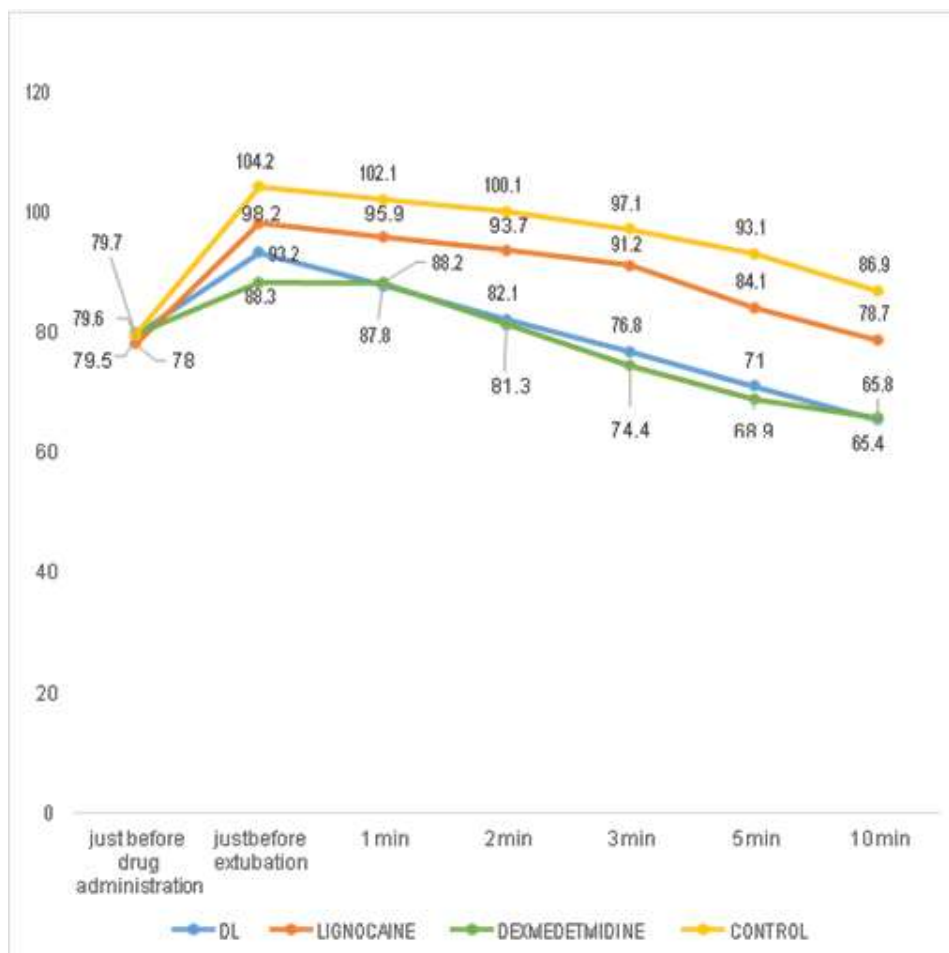
## Result

**Table 1: Demographic data**

Variables	Group A DL( $\mu\pm\sigma$ )	Group B LIGNOCAINE ( $\mu\pm\sigma$ )	Group C DEXMEDET MIDIN E( $\mu\pm\sigma$ )	Group D CONTROL ( $\mu\pm\sigma$ )	P Value
Age (Yrs.)	38.4 $\pm$ 9.96	34.1 $\pm$ 10.39	35.9 $\pm$ 14.14	36.45 $\pm$ 8.09	0.662869
Weight (Kg)	74.4 $\pm$ 9.2	71 $\pm$ 11.9	69.2 $\pm$ 12.6	73 $\pm$ 8.6	0.436519
Sex Ratio	13:07	7:13	12:08	12:08	

All four groups were comparable in age and sex as shown in table 1 and there was no statistically significant difference between these three groups.

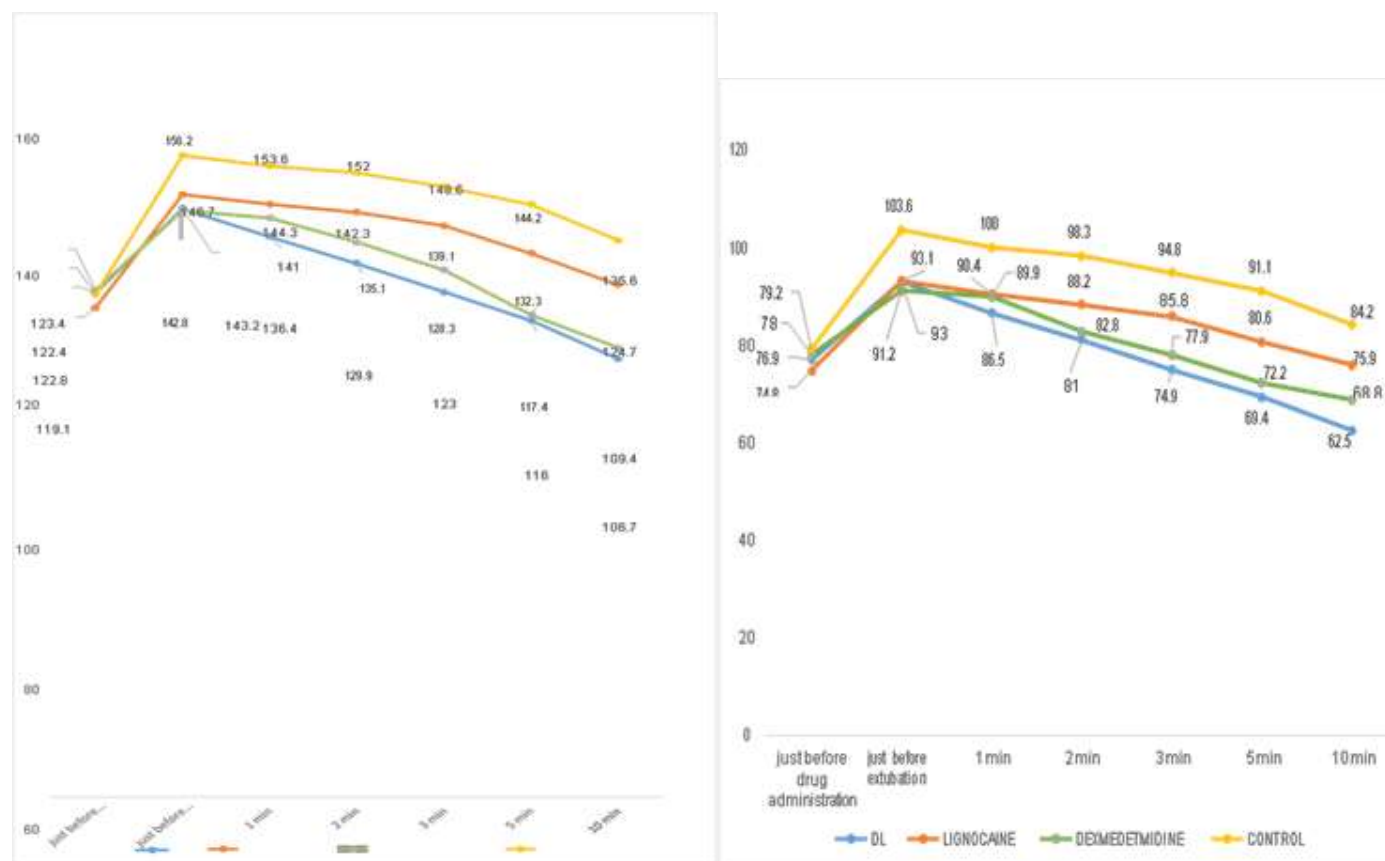
**Image 1: Comparative changes in mean Heart rate during the different study periods**



The HR increased significantly immediately after tracheal extubation in all groups. The HR remained increased for 2 mins in group D and group DL and for 5 mins in group L. The HR remained increased for 10 mins in group C. There was no significant difference in change of HR in group D and group DL. There was significant statistical difference ( $p < 0.01$ ) in mean HR among group DL and group L, group DL and group C [Image 1].

**Image 2: Comparative changes in SBP during the different study periods**

**Image 3: Comparative changes in DBP during the different study periods**

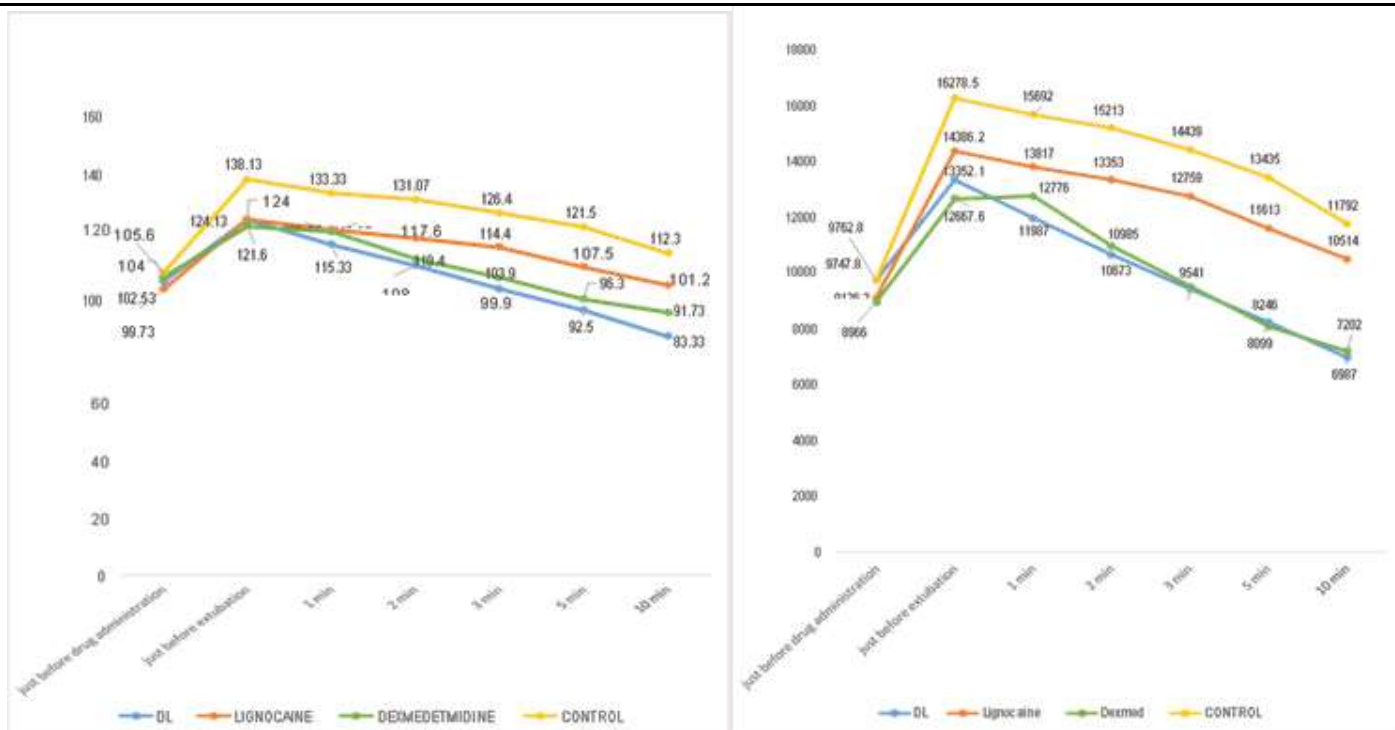


These data's showing among all the study groups, depicted that Group DL effectively attenuated the rise of SBP, DBP and MAP during and after tracheal extubation. No statistical differences were seen in baseline parameters in all the study groups. The SBP, DBP and MAP increased during extubation in all the study groups. The MAP remained high for initial 3 mins after extubation in Group DL and later it returned to baseline values [ Image 2,3,4]

There was significant statistical difference seen among Group DL and group L, Group DL and group C, Group D and group L, Group D and group C, Group L and group C. There was no statistical difference seen in group DL and group D at different time interval except at 10 mins interval in DBP and MAP.

**Image 4: Comparative changes in MAP during the different study periods**

**Image 5: Comparative changes in RPP during the different study periods**



In group DL, there was no significant increase in RPP after tracheal extubation during the study period. In group D, RPP increased significantly only immediately after tracheal extubation. In group L, there was significant increase in RPP immediately after tracheal extubation and remain increased for 3 mins. In group C, there was significant increase in RPP after tracheal extubation during the study period [Image 5]

**Table 2: Side effects and Complications**

SIDE EFFECTS & COMPLICATIONS	GROUP DL	GROUP L	GROUP D	GROUP C
Bradycardia	2	-	3	-
Hypotension	2	1	2	-
Hypertension	-	-	-	-
Arrhythmia	-	-	-	-
Laryngospasm	-	-	-	-
Bronchospasm	-	-	-	-
Hypoxemia	-	-	-	-
ECG changes	-	-	-	-
Myocardial ischemia	-	-	-	-

As shown in table 2, side effect and complications like bradycardia, hypotension, hypertension, arrhythmias, ECG changes, hypoxemia, respiratory depression, laryngospasm, bronchospasm, myocardial ischemia etc. encountered were very few and could be easily treated. In our study, none of the patients sustained bradycardia or hypotension sufficient to require pressor or sympathomimetic drug after extubation. No arrhythmias, evidence of myocardial ischemia, or hypoxemia was observed.

## Discussion

In the current study, it was found that HR, SBP, DBP, MAP, RPP increased temporarily after tracheal extubation in patients receiving Lignocaine (Group B). However, Hemodynamic changes related were completely inhibited in those receiving Dexmedetomidine plus Lignocaine (Group A) but suppressed to some extent with those receiving Dexmedetomidine (group C). The immediate changes in RPP after tracheal extubation compared with the baseline were less in group A (DL) than in either group. Patients with coronary insufficiency are liable to develop myocardial ischemia when the RPP exceeds 15000 and values above 20000 should be considered highly dangerous. Nevertheless, RPP after tracheal extubation was not more than 20000 (bpm×mmHg) in any of the groups, suggesting that critical increases in RPP may be avoided by administering Dexmedetomidine, Lidocaine, or their combination. The quality of extubation using the five point's extubation score was better in group DL than in group L or group D. Compared to Dexmedetomidine, Lignocaine was better in attenuated attenuating airway reflexes either alone or in combination.

*Ashraf MAMoustafa et al.*<sup>12</sup> carried out to compare the efficacy of Dexmedetomidine (0.25 ug/kg) Lidocaine (1.0 mg/kg) combination with each drug alone in suppressing the hemodynamic and catecholamine stress responses during tracheal extubation and emergence from general anaesthesia in 60 hypertensive patients undergoing elective surgery. They concluded that the Dexmedetomidine Lidocaine combination was superior to each drug alone in attenuating the cardiovascular changes in hypertensive patients. *Guler et al.*<sup>13</sup> studied the effect of single dose of Dexmedetomidine 0.5mcg/kg as bolus intravenously and suggested that Dexmedetomidine effectively attenuated airway circulatory reflexes during extubation. *AH Shruthi et al.*<sup>14</sup> carried out a study to compare the ability of Dexmedetomidine(0.5ug/kg) to attenuate the hemodynamic responses during extubation in a group of 80 patients received standard anaesthesia and concluded that Dexmedetomidine given before extubation attenuates hemodynamic reflexes during emergence from anaesthesia without causing undue sedation, but prolongs time to extubation. *Sowmya N swamy et al.*<sup>15</sup> studied and compared the efficacy of combination of I.V. Diltiazem with different doses (0.1mg/kg and 0.2 mg/kg) with Lignocaine (1mg/kg) on a group of 105 patients with ASA I-II and concluded that combined Diltiazem and Lidocaine are more effective prophylaxis than Lidocaine alone for attenuating the cardiovascular responses to tracheal extubation. *Hemanshu Prabhakar et al.*<sup>16</sup> compared the effect of the Dexmedetomidine (0.5 ug/kg) and Lignocaine (1.5 mg/kg) given at the end of procedure on attenuation of airway and pressor responses following tracheal extubation on a group of sixty ASA I III patients scheduled to undergo spinal surgery at the level of thoracic, lumbar or sacral region. Airway responses was better controlled with use of Dexmedetomidine allowing a smooth easy tracheal extubation, thereby providing a more comfortable recovery and early neurological examination.

There are few limitations to the study. We did not measure the plasma epinephrine level in the study groups which was increased by stress response of tracheal extubation. Hence, cannot predict the drug response on catecholamines level produced by stress response of tracheal extubation. We studied the single doses of Dexmedetomidine and Lignocaine for attenuation of hemodynamic parameters and airway reflex.

## Conclusion

From present study, it is concluded that dexmedetomidine plus lignocaine is an effective and safe prophylaxis for attenuating the cardiovascular responses to tracheal extubation in hypertensive patients and is superior to each drug alone. Also, lignocaine intravenous was more beneficial in the suppression of cough or straining that may occur with extubation. Dexmedetomidine alone suppressed the hemodynamic variable and airway reflexes comparable to combination group.

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