



## A PROSPECTIVE RANDOMIZED COMPARATIVE STUDY OF PROPOFOL AND LIGNOCAINE IN TERMS OF ATTENUATION OF CARDIOVASCULAR RESPONSES DURING TRACHEAL EXTUBATION

<sup>1</sup>\*Dr Nalini Gangwar, <sup>2</sup>Dr Richa Agarwal, <sup>3</sup>Dr. Rajeew Kumar Gupta

<sup>1</sup>\*Assistant Professor, Department of Anaesthesiology, J K Cancer Institute, Kanpur  
Email- [nalinigangwar@gmail.com](mailto:nalinigangwar@gmail.com)

<sup>2</sup>Assistant Professor, Department of Anaesthesiology, J K Cancer Institute, Kanpur

<sup>3</sup>Assistant Professor Cardiology, Rama Medical College Hospital & Research Centre, Mandhana, Kanpur, 209217

**\*Corresponding Author:** Dr Nalini Gangwar

<sup>1</sup>Assistant Professor, Department of Anaesthesiology, J K Cancer Institute, Kanpur

\*Email- [nalinigangwar@gmail.com](mailto:nalinigangwar@gmail.com)

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### ABSTRACT

**Introduction:** Ivan Magill's, the Father of endotracheal anaesthesia, and Joun Lundy's development of balanced anaesthesia were significant milestones that paved the way for modern anaesthesia practices. Controlled ventilation techniques have indeed become a cornerstone of anaesthesia care, allowing for safer and more effective management of patients undergoing surgery. The stress response during tracheal extubation can indeed trigger significant hemodynamic changes, posing risks for hypertensive patients and those with CVD. The study was undertaken to compare the effect of Propofol and Lignocaine in attenuating cardiovascular responses during extubation as compared to controls.

**Aims:-** The aim of study is to compare the effect of Propofol and Lignocaine in attenuating cardiovascular responses during extubation as compared to controls.

**Objective:-** To assess the cardiovascular responses of extubation when Propofol and Lignocaine was given in terms of

- change in systolic arterial pressure (SAP)
- change in diastolic arterial pressure (DAP)
- change in mean arterial pressure (MAP)
- change in heart rate (HR)

**Material and Method:** This was a cross sectional randomized study which had included 75 patients undergoing surgical intervention under general anaesthesia after obtaining approval from the Ethics committee of Apollo Hospital, Jubilee hills, Hyderabad. Informed consent was obtained from eligible patients who fulfilled the inclusion criteria and patients were divided randomly into 3 groups according to the drug administered.

**Results:** In our study we found that both Lignocaine and Propofol significantly attenuated the rise in heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure response to extubation. Decrease in heart rate was more in Propofol group when compared to Lignocaine but was not statistically significant at 1 minute, 2 minutes, 5 minutes and at 10 minutes post extubation ( $p > 0.05$ ). Lignocaine significantly attenuated the rise in systolic blood pressure response as compared to Propofol at 1 minute, at 2 minutes, 5 minutes and at 10 minutes post extubation ( $p < 0.05$ ). Diastolic blood pressure was also decreased by Lignocaine more effectively than Propofol at extubation.

**Conclusion:** Intravenous Propofol and Lignocaine both decrease cardiovascular responses as compared to baseline or control group. Intravenous Lignocaine is more effective in attenuating these responses.

**Keywords:** Attenuation cardiovascular responses, propofol, Lignocaine

## INTRODUCTION

The release of endogenous catecholamines during laryngoscopy and intubation can indeed lead to significant hemodynamic instability, posing risks for patients, especially those with cardiovascular disease [1]. Managing this response is crucial to prevent adverse events like tachycardia, hypertension, and arrhythmias.

Kern MJ et al in 1990 [2] studied effect of abruptly increased intrathoracic pressure, which can occur during extubation, on coronary blood flow, arterial pressure and heart rate.

Several pharmacological strategies have been studied in past to blunt these cardiovascular changes of extubation in deeper plane of anaesthesia and using drugs such as Verapamil

[3] Diltiazem [4], Remifentanyl [5], Esmolol [6], Fentanyl [7], Lignocaine and Propofol. The choice of agent often depends on the patient's specific needs, the procedure, and the anesthesiologist's preference.

Propofol is a substituted isopropylphenol that is administered intravenous (IV). It decreases Blood pressure (BP) and Heart rate (HR) by inhibition of sympathetic vasoconstrictor nerve activity [8]

Lignocaine is amide type of local anaesthetic and also classified as antiarrhythmic drug of class 1b. Intravenous Lignocaine produces central sedation, suppress autonomic reflexes and may protect ischemic myocardium from ultra structural damage associated with high level of catecholamine [9]

Among these drugs, in this study Lignocaine and Propofol were compared in their efficacy to attenuate these cardiovascular responses because both can decrease heart rate and blood pressure.

This research aimed to study the attenuation of cardiovascular responses to tracheal extubation with lignocaine as compared with Placebo and propofol.

**Material and Method:** This cross sectional randomized study was approved by Ethics Committee of Apollo Hospital Jubilee hills, Hyderabad between June 2012-June 2013 ..... After written informed consent was taken, 75 patients, ASA grade 1 or 2, aged between 20-46 years, scheduled for surgical intervention under general anaesthesia were assessed for eligibility. Patients were divided randomly into 3 groups according to the drug administered.

Patients with contradictions to the study drugs, history of respiratory problem, angina, palpitation, syncope, or those with coronary ischemic diseases of any degree, renal failure, on any type of beta blockers and Baseline HR  $< 60$ /min and patient with history of laryngeal/tracheal pathology or surgery were excluded.

All patients coming to Apollo hospital for surgery met the above mentioned criteria are included in the study. Patients were randomized using a list of numbers generated in random order.

Patients were divided into three groups using random drawing of lots and study proforma was filled out for each patient.

Group 1- control group receiving 5 ml saline

Group 2- Lignocaine group receiving 1.5 mg/kg

### Group 3- Propofol group receiving 0.5 mg/kg

All patients were visited day before the surgery and pre-anaesthetic check-up of selected patients done. They received ranitidine 150 mg and alprazolam 0.25mg at night on day before surgery. Patients were kept nil by mouth (NBM) from 12 midnight.

On the day of surgery intravenous line was secured. Patients are pre-medicated 0.1mg/kg ondansetron prior to induction.

Preoxygenation with 100% oxygen was done for 3 min. Anaesthesia was induced intravenously with fentanyl 2 microgram/kg and Propofol 2mg/kg. Tracheal intubation was facilitated by 0.5 mg/kg Atracurium intravenously.

Anaesthesia was maintained with 33% oxygen, 67% nitrous oxide, sevoflurane 1-2% . End tidal carbon dioxide was maintained at 28-38 mmHg. Peripheral arterial oxygen saturation was monitored throughout the period of anaesthesia. Blood pressure was recorded before induction of anaesthesia and monitored every five min during anaesthesia using automated non-invasive blood pressure monitor. Heart rate was monitored by ECG (leadII).

Blood pressure and heart rate was maintained between 80% and 120% of preoperative value by increasing or decreasing the concentration of sevoflurane until the completion of surgery. Muscle relaxation was maintained with intermittent boluses of atracurium. Anaesthesia was standardized in all procedure, multimodal analgesia with diclofenac ,if not contraindicated, and small doses of fentanyl was used.

After the end of surgery nitrous oxide and sevoflurane were discontinued and residual muscle relaxation was reversed with Neostigmine 0.05 mg/kg and Glycopyrrolate 0.01 mg/kg. Gentle pharyngeal suction was done. After observing for predefined **extubation criteria** like Clear oropharynx /hypopharynx,Intact gag reflex,Sustained head lift for 5 seconds, sustained hand grip, Adequate pain control, Minimal end expiratory concentration of inhaled anaesthesia, Trachea is extubated. After extubation 100% oxygen by face mask is given for 5 min and patient were shifted to recovery room.

Considering the Primary outcome of cardiovascular changes in terms of SAP, DAP,MAP, HR before and after of drug administration, at the time of administration, its changes within 1, 2, 5min and 10 after intubation

Statistical Analysis was entered into the electronic proforma spread sheet and analysed using statistical package with biostatistical assistance. Quantative data is presented as mean + standard deviation. Comparison among study group is done with the help of student t Test. Qualitative data is presented as percentage. For this study P value < 0.05 was considered as statistically significant. Data entry and analysis is done in Excel.

## RESULTS:

In our study, 75 patients were included in the study, which was divided in 3 group- Group1- Baseline, Group2-Lignocaine and Group3- Propofol For the study conducted, following observation were made, Systolic BP, Diastolic BP, mean arterial pressure and heart rate recorded at the time of **preinduction (Baseline)**, at extubation, 1min, 2 min , 5min and 10 min after extubation .Statistical differences were not found to be significant between any of the three groups for age, weight, sex and duration of surgery (Table 1)

There was attenuation of heart rate response after giving Propofol injection (Group 3) before extubation that was statistically significant at 1,2,5 and 10 minutes post extubation when group 3 response was compared to group 1 response. (p values <0.05) (Table 2).Attenuation of heart rate response to extubation was more in Propofol group when compared to Lignocaine

Attenuation of rise in systolic blood pressure due to injection of Lignocaine was statistically significant ( p<0.05) at the time of extubation and highly significant ( p<0.001) at 1 and 2 minutes post extubation. Attenuation of systolic blood pressure rise by Lignocaine was found to be of moderate significance ( p<0.01) at 5 minutes after extubation when group 2 was compared with

group I. There was no significant difference between group 2 and group 1 with respect to rise of systolic blood pressure at 10 minutes post extubation. (p>0.05)

Attenuation of rise of SBP was significantly greater in group 2 as compared to group 1 (Placebo). Attenuation of rise in systolic blood pressure due to injection of Lignocaine was statistically significant (p<0.05) at the time of extubation and highly significant (p<0.001) at 1 and 2 minutes post extubation, whereas it was found to be of moderate significance (p<0.01) at 5 minutes after extubation when group 2 was compared with group I.

Lignocaine (group 2) significantly attenuated the rise in systolic blood pressure response as compared to Propofol (group 3) (Table 3)

At extubation rise in mean diastolic blood pressure (Table 4) in Lignocaine group (group 2) was lesser than seen in Placebo group (group 1) but did not reach significance (p>0.05). Lesser rise in mean diastolic pressure was seen with Lignocaine which was highly significant at 1 minute, and at 2 minutes (p<0.001) after extubation and still reached significance (p<0.05) at 5 min, 10 min post extubation.

At extubation rise in mean diastolic blood pressure was more in Propofol arm (group 3) as compared to Placebo (group 1), but was statistically non significant (p>0.05). Rise in mean diastolic pressure was significantly lesser with Propofol (group 3), at 1 min and 2 min (p<0.05). At 5 min after extubation when compared with group 1 the rise in mean diastolic pressure was slightly lesser in group 3 but did not reach to a significant level (P>0.05). At 10 minutes post extubation rise in mean diastolic pressure in group 2 remained lesser and non significant (p>0.05). Hence Drug Lignocaine (group 2) was more effective in attenuating the rise in mean diastolic blood pressure response at extubation, at 1 minute, 2 minutes, 5 (p<0.001) and 10 minutes (p<0.01) post extubation when compared with Propofol (group 3).

At extubation, rise in mean blood pressure (Table 5) in Lignocaine arm (group 2) was lesser and non significant as compared to placebo (group 1) which became highly significant at 1 and 2 min, moderately significant at 5 minutes (p<0.01) but there was no significant attenuation at 10 minutes after extubation (p>0.05). When compared with group 3, Lignocaine arm (group 2) significantly attenuated rise in mean blood pressure which was significant at the time of extubation and was moderately significant (p<0.01) at 1, 2 and 5 minutes post extubation.

**Table 1: Demographic and Clinical data of Patients between groups**

| Groups  | Age (yrs)  | Weight (kgs) | Sex |    | ASAI | ASAII |
|---------|------------|--------------|-----|----|------|-------|
|         |            |              | M   | F  |      |       |
| Group 1 | 37±7.46    | 59.8±7.43    | 13  | 12 | 13   | 12    |
| Group 2 | 35.84±6.58 | 61.06±9.45   | 14  | 11 | 13   | 12    |
| Group 3 | 34.88±5.88 | 61.8±9.91    | 12  | 13 | 12   | 13    |

Values are expressed as mean ± DP and numbers

**Table 2- Comparison of heart rates between the groups**

| GROUP          | BASELINE     | AT Ext       | 1 min after ext | 2 min after ext | 5 min after ext | 10 min after ext | P value         |
|----------------|--------------|--------------|-----------------|-----------------|-----------------|------------------|-----------------|
| <b>GROUP-1</b> | 84.00+ 6.4   | 92.76 + 5.55 | 98.64 +4.71     | 95.88 +3.55     | 97.52+2.85      | 97.28 +3.69      | <b>&gt;0.05</b> |
| <b>GROUP-2</b> | 88.32 + 8.64 | 92.32 + 8.20 | 93.12 +6.84     | 93.72 +6.62     | 93.56 + 5.45    | 94.72 +6.32      | <b>&gt;0.05</b> |
| <b>GROUP-3</b> | 87.20 + 6.70 | 91.08 + 5.53 | 91.92 +4.63     | 89.96 +4.42     | 90.44 +4.87     | 90.64 +4.88      | <b>&gt;0.05</b> |

**Table 3: Comparison of systolic blood pressure in different groups**

| GROUP | BASELINE | AT Ext | 1 min | 2 min | 5 min | 10 min | P value |
|-------|----------|--------|-------|-------|-------|--------|---------|
|-------|----------|--------|-------|-------|-------|--------|---------|

|                |                |                | after ext      | after ext      | after ext      | after ext      |                 |
|----------------|----------------|----------------|----------------|----------------|----------------|----------------|-----------------|
| <b>GROUP-1</b> | 125.96 + 9.54  | 137.16 + 7.63  | 154.12 + 10.01 | 151.56 + 10.48 | 142.56 + 13.50 | 131.12 + 10.06 | <b>&gt;0.05</b> |
| <b>GROUP-2</b> | 129.08 + 12.17 | 131.15 + 11.14 | 133.78 + 11.40 | 133.36 + 10.69 | 132.84 + 9.64  | 128.08 + 10.24 | <b>&gt;0.05</b> |
| <b>GROUP-3</b> | 121.40 + 7.38  | 125.64 + 6.44  | 134.92 + 9.54  | 136.92 + 9.23  | 133.92 + 9.74  | 133.00 + 9.15  | <b>&gt;0.05</b> |

**Table 4: Diastolic blood pressure in the three groups at different time intervals**

| GROUP          | BASELINE    | AT Ext       | 1 min after ext | 2 min after ext | 5 min after ext | 10 min after ext | P value         |
|----------------|-------------|--------------|-----------------|-----------------|-----------------|------------------|-----------------|
| <b>GROUP-1</b> | 73.80+ 6.73 | 77.56 + 6.23 | 89.36+ 7.65     | 89.84 + 5.24    | 85.56 + 6.63    | 78.64 + 5.66     | <b>&gt;0.05</b> |
| <b>GROUP-2</b> | 75.76+ 6.27 | 78.20 + 4.87 | 81.76 + 5.82    | 82.28 + 4.55    | 81.80 + 6.42    | 77.76 + 6.23     | <b>&gt;0.05</b> |
| <b>GROUP-3</b> | 80.96+ 6.3  | 87.24 + 6.45 | 91.48 + 7.67    | 93.60 + 7.63    | 91.08+ 8.25     | 85.52+ 8.64      | <b>&gt;0.05</b> |

**TABLE 5 – COMPARISON OF MEAN BLOOD PRESSURE IN 3 GROUPS**

| GROUP           | BASELINE   | AT Ext     | 1 min after ext | 2 min after ext | 5 min after ext | 10 min after ext | P value         |
|-----------------|------------|------------|-----------------|-----------------|-----------------|------------------|-----------------|
| <b>GROUP -1</b> | 91.00+6.43 | 97.24+5.81 | 110.36+8.20     | 110.48+6.36     | 104.44+7.43     | 96.24+6.15       | <b>&gt;0.05</b> |
| <b>GROUP -2</b> | 93.56+6.48 | 95.56+5.29 | 98.64+6.78      | 99.28+5.40      | 98.76+6.39      | 94.56+6.72       | <b>&gt;0.05</b> |
| <b>GROUP -3</b> | 94.04+6.05 | 99.64+5.86 | 105.80+7.55     | 107.48+7.82     | 105.98+ 8.15    | 100.64+8.38      | <b>&gt;0.05</b> |

When compared with group 3, Lignocaine arm (group 2) significantly attenuated rise in mean blood pressure which was significant at the time of extubation and was moderately significant ( $p < 0.01$ ) at 1, 2 and 5 minutes post extubation.

## Discussion

Tracheal extubation causes significant hemodynamic stimulation resulting in transient increase in blood pressure and heart rate.

As Lowrie et al [10] evaluated the impact of tracheal extubation on changes in plasma concentration of epinephrine and norepinephrine in 12 patients undergoing major elective surgery. Epinephrine levels were significantly increased from 0.9 to 1.4 pmol/ml only 5 min after extubation. Norepinephrine levels remained unchanged. Increased epinephrine concentration can cause increased sympathetic activity, leading to hypertension and tachycardia, particularly due to stimulation of pharyngeal and laryngeal stimulation.

In 2013 Mohammad Taghy Moein Vaziri et al [11] studied the effect of low dose Propofol in attenuating cardiovascular response at tracheal extubation and concluded that Propofol can reduce SBP, DBP, MAP, HR at the time of injection but there were no significant changes in these parameters after extubation. In our study also we found that.

Hence, this randomized study was conducted to determine and compare the attenuation of hemodynamic responses to tracheal extubation in 75 patients of ASA I and II undergoing elective surgery by using Propofol, Lignocaine and saline (placebo).

In this study, total 75 patients were randomly divided into 3 groups each contain 25 patients. Average age was 37+7.46 years in group I, 35.84+6.58 years in group II and 34.88+5.88 years in

group III. Average weight was  $59.8 \pm 7.43$  kg in group I,  $61.08 \pm 9.45$  kg in group II and  $61.8 \pm 9.91$  kg in group III. On statistical analysis the difference in age, weight, gender and ASA was not found to be significantly different between 3 study groups ( $p > 0.05$ )

In our study, there was an increase in HR, SBP, DBP and MBP in saline (placebo) group i.e. group I at extubation and 1, 3, 5, & 10 minutes post extubation

Many investigators have also shown that cardiovascular stimulation is usually inconsequential, certain patients may experience unfavorable or undesirable sequelae. As in 1986 Coriat et al. [12] demonstrated that patients with coronary artery disease experience significant decreases in ejection fractions (from  $55\% \pm 7\%$  to  $45\% \pm 7\%$ ) after extubation. The changes in ejection fraction occurred in the absence of electrocardiographic signs of myocardial ischemia. Also in 1984 Wellwood et al. [13] reported that patients with a cardiac index of less than  $3.0 \text{ L min}^{-1} \text{ m}^{-2}$  did demonstrate an ischemic response to the stress of postoperative tracheal extubation after myocardial revascularization. These patients experienced decreases in myocardial lactate extraction, left ventricular compliance, and cardiac performance.

In our study, SBP, DBP and MAP was decreased in both groups but when compared statistically, there was a significant difference between group II and group III. In group II there was a significant decrease i.e.  $p < 0.001$ .

Our study also supports the observation of Mohammad Taghy Moein Vaziri et al. [14] who studied the effect of low dose Propofol in attenuating cardiovascular response at tracheal extubation. They observed significant changes in the SBP, DBP, MAP and HR during injection of drugs. But at the time of extubation they didn't see any significant difference regarding hemodynamic changes between the two groups. So, they concluded that Propofol can reduce SBP, DBP, MAP, HR at the time of injection but there were no significant changes in these parameters after extubation.

Our results are also comparable with the results of Bidwai AV et al. [15] who demonstrated in their study that injection of Lignocaine  $1 \text{ mg/kg}$ , 2 min prior to extubation prevented an increase in BP and HR during and after extubation.

In 1987 Wallin et al. [16] evaluated the effect of continuous iv infusion of Lignocaine on sympathoadrenal stress response to surgery. Increase in HR and BP after tracheal intubation was not significantly different in 2 groups, but tachycardia and hypertension associated with extubation was prevented in the Lignocaine group. Significant blunting of increase in SBP and HR was observed in patients who received Lignocaine at 5 and 10 minutes post extubation. Our study also shows that although Lignocaine and Propofol both attenuate cardiovascular changes associated with tracheal extubation, Lignocaine is more effective than Propofol with this regard.

**Conclusion:** Our study showed that Tracheal extubation causes significant cardiovascular responses. Intravenous Propofol and Lignocaine both decrease cardiovascular responses as compared to control. Intravenous Lignocaine is more effective in attenuating these responses. No serious adverse event was encountered during the study.

**Conflict of Interests:** The authors declare no conflict of interest

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