Attenuation of Cardiovascular Responses to Tracheal Extubation: Esmolol versus Propofol

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Abstract
The present study attenuation of cardiovascular responses to tracheal extubation: esmolol versus propofol was a randomized study conducted to evaluate haemodynamic response to extubation with use of IV Propofol, IV Esmolol 2 minutes prior to extubation. After taking approval from institutional ethical committee and satisfying the inclusion and exclusion criteria; valid written informed consent was obtained from 60 adult patients were randomly allocated the two study groups. Patients were given following drugs two minutes prior to Extubation: Group E: patients received i.v. Esmolol 1.5 mg/kg and Group P patients received i.v. Propofol 0.5 mg/kg 2 minutes prior to extubation. Patients were given general anaesthesia as per protocol of our study. Haemodynamic parameters were monitored throughout the whole procedure, the study drug was given 2 minutes prior to Extubation. Heart rate , Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, was monitored and recorded just before study drug administration (T) [i.e. baseline in our study], and before extubation (T-1), one (T-2), three (T-3), five (T-4) and ten (T-5) minutes after Extubation. On comparison of mean heart rate (HR) in both the study groups at different times of observation (T0-T5), when compared to the baseline; mean heart rate (HR) was observed to decline much more in group E than in group P. Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure were comparable at baseline (T-0),declined up to 5 minutes after extubation. No major complication occurred in any patients included in our study. It was concluded that attenuation of haemodynamic response to extubation by injection esmolol was more effective than injection propofol. Even though less effective IV propofol too attenuated the hemodynamic response to extubation effectively.

Keywords: Esmolol, Propofol, Extubation, Hemodynamic Response, Attenuation.

Introduction
Tracheal intubation secures the airway in patients who are undergoing surgical procedures under general anaesthesia. At the end of the surgery, tracheal extubation is carried out i.e. the removal of endotracheal tube from the trachea. Tracheal intubation is frequently associated with cardiovascular stress response characterized by...
hypertension, tachycardia and increased serum concentration of catecholamines and similar phenomenon is also seen during extubation\cite{1,2}. For a smooth extubation, there should be no straining, movement, coughing, breath holding or laryngospasm\cite{3}.

Several techniques, as well as drugs, have been used to attenuate hemodynamic responses during tracheal intubation. Several techniques, as well as drugs, have been used to attenuate hemodynamic responses during tracheal extubation. Techniques like extubation in a deeper plane of anaesthesia,\cite{4} substitution of the endotracheal tube with a laryngeal mask airway,\cite{5} Drugs like low-dose propofol, \(\beta_1\) blockers like esmolol, landiolol; \(Ca^{2+}\) channel blockers like nicardipine lidocaine spray low dose iv opioids like fentanyl remifentanil, central sympatholytics like clonidine, dexmedetomidine; vasodilators like nitrates, prostaglandin and \(MgSO_4\) have been studied as sole agents or in comparison with each other /placebo to attenuate haemodynamic changes and upper airway tract events with variable success rates.

Esmolol is a selective \(\beta_1\) antagonist with a very short duration of action. It has very little, if any, sympathomimetic action and it lacks membrane stabilizing action. Esmolol is administered IV and used when \(\beta\) blockade of short duration is desired or in critically ill patients in whom adverse effects of bradycardia, heart failure or hypotension may necessitate rapid withdrawal of the drug\cite{6}.

Propofol a 2-6 disopropylphenol has high lipid solubility, which allows for a rapid induction and recovery from anaesthesia, as well as good haemodynamic maintenance when used during the intraoperative period\cite{7}. It produces its anaesthetic effect by positive regulation of GABA, an inhibitory neurotransmitter through ligand gated GABA\(a\) receptors. The result is decrease in cardiac output with little or no change in heart rate.

**Materials & Methods**

The present study was conducted on patients admitted in Mahathma Ghandi Hospital and Medical College Warangal Telangana, undergoing elective surgeries under general anaesthesia after obtaining permission from the Institutional Ethical Committee. The participants were informed regarding the purpose, procedures, risks and benefits of the study. Written and Informed Consent was obtained from all participants.

A randomized controlled trial was conducted in 80 adult patients of American Society of Anaesthesiologists (ASA) physical status I or II undergoing various elective surgeries, aged between 20-50 years of both genders were included. Patients with ASA grade III & IV, Allergic reaction to any above drugs, difficult airways, Patients with history of bronchospasm, cardiac arrhythmias, heart disease and hypertension were excluded. The patients were randomly divided into two groups of 40 patients in each group - P and E. Group - P received 0.5 mg kg\(^{-1}\) propofol and group - “E” received 1.5 mg kg\(^{-1}\) esmolol IV 2 min before extubation. A detailed history of the patient was taken and complete general and systemic clinical examination was done. Vital parameters including pulse rate, blood pressure & respiratory rate were measured. Mallampatti grading was done to rule out for possibility of difficult intubation. Base line Pulse rate (PR), SpO2, systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean blood pressure and E.C.G. were measured before induction as baseline. After induction of general anesthesia with thiopenton sodium 6 mg/kg and vecuronium 0.12 mg/kg, endotracheal intubation was done with appropriate size portex disposable cuffed endotracheal tubes. Air entry was checked bilaterally. Endotracheal tube was fixed and attached to anaesthesia work station with suitable & appropriate circuit. Patients were maintained on oxygen (33%), Nitrous oxide (66%) and isoflurane 0.5% with controlled mechanical ventilation. Muscle relaxation maintained with 0.8mg inj. Vecuronium as and when required.
Vital parameters were recorded throughout the procedure. At the time of completion of surgical procedure, Isoflurane was discontinued 5 minutes before the end of surgery and Nitrous oxide just before reversal of neuromuscular blockade with inj. neostigmine 0.05mg/kg + inj. Glycopyrolate 0.008mg/kg intravenously. The study drug was given 2 minutes prior to Extubation. Patients were given 100% Oxygen between injections of drug and tracheal Extubation. After gentle & through Oropharyngeal suction Endotracheal extubation was done. Quality of Extubation was scored on 4 point scale as suggested by Eshak (0-No cough or strain, 1-Moderate coughing, 2- High degree of coughing or straining, 3 - poor extubation with larygospasms).

Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, was monitored and recorded just before study drug administration (T0) and before extubation (T-1), one (T-2), three (T3), five (T-4) and ten (T-5) minutes after extubation. ECG was monitored continuously and dysarrythmias, if any, were noted. Oxygen saturation was continuously monitored recorded at above mentioned intervals. Complications if any were noted during the study in all the three groups. Patients were also observed for any complications. Statistical analysis was done using computer software package SPSS version 23.0 Student's unpaired t test was applied for comparing continuous variables like hemodynamic parameters and Chi-square test was used for comparing categorical variables which are presented as frequencies and percentages. A P-value of <0.05 was considered significant where as the p-value of <0.001 was considered as highly significant.

**Results**

The present study was conducted to compare the efficacy of intravenous esmolol 1.5 mg/kg bolus and propofol 0.5 mg/kg bolus in attenuation of haemodynamic responses following tracheal extubation when administered 2 minutes prior to endotracheal extubation.

**Demographic data**

The demographic parameters like age, weight, height and BMI which were comparable in all the four groups. There is no significant difference among the two study groups .The details were sown in table1

**Hemodynamic parameters**

The heart rate, systolic blood pressure, diastolic blood pressure, Mean arterial pressure, oxygen saturation (SPO2) was monitored and recorded just before study drug administration (T0) and before extubation (T-1), after extubation at one (T-2), three (T-3), five (T-4) and ten (T-5) minutes in both the study groups.

**Table 1. Comparison of Demographic data in study groups**

| Parameters | Group P(propofol) | Group E (esmolol) |
|------------|-------------------|-------------------|
| Age (yrs)  | 38.87 ± 12.55     | 37.13 ± 11.99     |
| M/F        | 22/15             | 19/21             |
| Wt. (Kg)   | 66.2 ± 9.13       | 61.5 ± 11.45      |
| Ht (Cm)    | 157.07±10.07      | 163.77 + 9.44     |

P >0.05 not significant

**Heart rate**

In the present study, the baseline (T0) mean heart rate was observed to be 87.80±4.06 bpm in group E and 89.2±6.01 bpm in group P and the mean Heart rate (HR) was found to be comparable in both study groups. On comparison of mean heart rate (HR) in both the study groups at different times of observation (T0-T5), when compared to the baseline; mean heart rate (HR) was observed to decline much more in group E than in group P. The decrease in the mean heart rate (HR) was highly significant statistically in group E (P<0.001) as compared to group P (P<0.05). Esmolol was found to be more effective in decreasing the mean heart rate as compared to propofol.
Mean systolic pressure: (SBP)
In the present study, the mean baseline i.e. (T-0) systolic blood pressure (SBP) was observed to be 128.92±4.23 mm Hg in group E and 124.95±5.36 mm Hg in group P. The two study groups were observed to be comparable in terms of their baseline mean SBP.
On comparison of mean SBP in both the study groups at different times of observation (T0-T5), when compared to the baseline; it was declined much more in group E than in group P up to (T-4)5 minutes. The decrease in the mean systolic blood pressure (SBP) was highly significant statistically in group E as compared to group P.

Mean arterial pressure
In the present study, the mean arterial pressure (MAP) at (T-0) i.e. baseline was observed to be 189.64±3.42 mm Hg in group E and 181.64±5.36 mm Hg in group P. The two study groups were observed to be comparable in terms of their baseline MAP. On comparison of MAP in both the study groups at different times of observation (T0-T5), when compared to the baseline; mean arterial pressure (MAP) was observed to decline much more in group E than in group P in group P. The decrease in the mean arterial pressure (MAP) was highly significant statistically in group E as compared to group P.

Mean diastolic blood pressure
In the present study, the mean baseline (T-0) diastolic blood pressure (DBP) was observed to be 88.37±2.63 mm Hg in group E and 84.47±2.34 mm Hg in group P comparable with each other. The DBP in both the study groups at different times of observation (T0-T3) decline much more in group E than in group P when compared to the baseline. The decrease in the diastolic blood pressure (DBP) was highly significant statistically in group E as compared to group P.
Comparison of Mean Arterial Pressure (MAP) In Both the Study Groups.

The mean SPO2 was observed to be 99.77±0.23 in group E and 98.12±0.41 % in group P before study drug was given/administered (T-0) i.e. baseline in the present study. On comparison of mean SPO2 in both the study groups at different times of observation (T0-T5), when compared to the baseline; mean SPO2 was observed to decrease in group E and group P. The decrease in mean SPO2 in both study groups however was not significant statistically. (P>0.05) At no point the mean SPO2 reduced below 98%.

**Sedation score**
Sedation Scoring was done by using 5 point Sedation Scoring Scale as follows 0 -Awake, alert, 1- Mild sedation, easy to rouse, 1S- Asleep, easy to rouse and 2- Moderate sedation, unable to remain awake
Propofol was observed to cause more sedation in 7 patients and in esmolol group no sedation was observed in any of the patients after 10 minutes. The two study groups were observed to be comparable in terms of sedation.

**Extubation**
Quality of extubation was scored by 4 point scale as suggested by Eshak as 0-No cough or strain, 1- Moderate coughing, 2-High degree of Coughing, 3-Poor extubation with laryngospasm. Three patients in group E showed moderate cough. In both study groups were found to be comparable regarding quality of extubation (p>0.05). Hence both the drugs i.e. esmolol and propofol were able to attenuate cough and strain of extubation in ≥ 95% of the patients. Oxygen saturation was well maintained in all the patients, irrespective of the study group. No significant ECG changes were observed in any of the patients of the two study groups.

**Discussion**
Extubation is associated with awakening, pain, anxiety and airway irritation which may lead to haemodynamic responses similar to intubation, resulting in hypertension, tachycardia and arrhythmias. It is more hazardous in a patient with hypertension, myocardial insufficiency or cerebral vascular disease and is associated to increased incidence of cerebral haemorrhage, myocardial ischemia and pulmonary oedema. Therefore, attenuation of hemodynamic responses to tracheal extubation is of paramount importance to anaesthesiologists.

The present study was a randomized controlled study to assess and compare the efficacy of intravenous esmolol 1.5 mg/kg bolus and propofol 0.5 mg/kg bolus in attenuation of haemodynamic responses following tracheal extubation when administered 2 minutes prior to extubation. Esmolol is a selective short-acting beta-blocker, and Beta-adrenergic blockers are also frequently used to suppress adrenergic activity caused by extubation. Considering the fact that esmolol is of very short half-life, the present study IV infusion of esmolol was used. Propofol a 2-6 diisopropylphenol has high lipid solubility, which allows for a rapid induction and recovery from anaesthesia, as well as good haemodynamic maintenance when used during the intraoperative period.

Tracheal extubation like intubation often provokes increase in arterial blood pressure and heart rate. Many factors are responsible for these hemodynamic changes at extubation. Firstly, extubation is often performed with patients in lighter plane of anaesthesia. Extubation is also associated with mechanical irritation to airway
causing coughing, bucking and straining. Other factors involved are pain from surgery and emergence from general anaesthesia [11]. Moreover it has been demonstrated that tracheal extubation increase plasma catecholamine levels which in turn cause tachycardia, increased myocardial contractility and increased systemic vascular resistance [12]. The different studies [13,14,15,16] with esmolol found to be attenuate HR during emergence and recovery from anesthesia. esmolol controlled both systolic blood pressure and heart rate, but the larger dose produced significant decreases in systemic blood pressure [17,18].

In the study by Hosseinzadeh H et al [19] emphasizing the fact that esmolol is of excellent early recovery and extubation profiles. In the study by Shrestha S et al [20] Concluded that esmolol 1.5 mg/kg given 3 min prior to extubation attenuated the heart rate at the time of extubation. In the study by Cheng Y-C et al [21] In propofol group, the HR during extubation and thereafter had no significant difference compared with those before induction, while they were significantly lower than those before giving propofol. The incidence of cough, restlessness was significantly lower in the propofol group than that in the urapidil group after extubation (P<0.05). There were no episodes of hypotension, laryngospasm, or severe respiratory depression. There was no statistical difference in recovery time between two groups.

In the study by Tendulkar MP et al [18] Regarding sedation, it was observed that patients in the Dexmedetomidine group, were significantly sedated as compared to Esmolol and Control group, but this aided a smooth extubation without any agitation.

**Conclusion**

In the present study, IV esmolol 1.5 mg/kg and IV propofol 0.5 mg/kg bth drugs attenuated the haemodynamic response to extubation more effectively when given 2 minutes prior to extubation. The attenuation was immediate and remained effective till 10 minutes post extubation, without any side effects. Esmolol was more effective than Propofol.

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