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Original Research Article

A randomized controlled study of intravenous esmolol to attenuate the cardiovascular responses to laryngoscopy and endotracheal intubation

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ABSTRACT

Background: Objective is to compare the efficacy of intravenous Esmolol to attenuate the cardiovascular responses to laryngoscopy and endotracheal intubation with control group.
Methods: Study was done on 60 adults, ASA grade I or II normotensive patients, undergoing elective surgery under general anaesthesia and willing to participate. These patients where be randomly allocated in to either group C (Control) or E (Esmolol). Group 'C' Control group. Group 'E', patients were given intravenous Esmolol 1.5 mg/kg 2 minutes before start of laryngoscopy. All patients were premedicated, induced and intubated using Thiopentone and Succinyl Choline as per the protocol. Heart Rate (HR), SBP, DBP and MAP were recorded at baseline (taken half an hour prior to anaesthesia), Before sedation, After induction but before intubation, Immediately after endotracheal intubation and Thereafter at 1, 2, 3, 4, 5 and 10 minutes.
Results: Heart rate was lower in Group E as compared to Group C, and there was statistically significant difference immediately after intubation till 4 minutes after intubation. While Blood pressure was lower in Group E as compared to Group C, and there was statistically significant difference only immediately after intubation.
Conclusions: In Normotensive patients requiring general anaesthesia with laryngoscopy and intubation, authors conclude that intravenous Esmolol 1.5 mg/kg attenuated Heart rate response but fails to satisfactorily prevent rise in blood pressure.

Keywords: Esmolol, Hemodynamic, Intubation, Laryngoscopy, Response

INTRODUCTION

Laryngoscopy and endotracheal intubation are often accompanied with significant increases in heart rate and arterial blood pressure often leading to adverse outcome.[1] These responses are transient occurring 30 seconds after intubation and lasting less than 10 minutes.[2] The sympathoadrenal activation is also associated with dysrhythmias.[3]

Although these responses may be of short duration and of little consequence in healthy individuals, serious complications can occur in patients with underlying coronary artery disease reactive airways, or intracranial neuropathology.[4-6]

These reflexes are mediated by the cardioaccelerator nerves and sympathetic system. This response includes wide-spread release of norepinephrine from adrenergic nerve terminals and secretion of epinephrine from the adrenal medulla.[7]

Esmolol is an ultra-short acting, beta-adrenergic receptor antagonist with efficacy to provide hemodynamic stability during laryngoscopy and tracheal intubation without side-effects.[8] It inhibits Beta-1 receptors of myocardium thus attenuating positive chronotropic, to

very less extent it also inhibits Beta 2 receptors of smooth muscles of vascular walls thus attenuating positive inotropic effects.[9]

In this study, authors evaluate the effectiveness of Intravenous Esmolol in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

METHODS

Study period was May 2015 to May 2016. Study Population was 60 adult ASA grade I or II normotensive patients, undergoing elective surgery under general anaesthesia and willing to participate were the study population. Study design was it is a prospective randomized study. The approval for the study was obtained from the Institutional Ethics Committee.

Inclusion criteria

- Male and female of age group between 25 to 65 years. Undergoing elective surgery under general anesthesia. Weight 40 kg to 90kg. Resting systolic blood pressure less than 140 mmHg and diastolic pressure less than 90 mmHg. American Society of Anesthesiologist Grade I and II.

Exclusion criteria

- Ischemic heart diseases or ECG abnormalities indicating ischemic heart diseases. Patients with any overt cardiac, renal, pulmonary and liver diseases. Hypertensive patients. Any Patients with history of dyspnoea on exertion of grade III or more as per NYHA guidelines. Obesity (weight more than 90kg). Pregnancy. ASA grade III or IV patients. Anticipated difficult intubation. Any contraindication of Esmolol.

Pre-operative investigations and assessment

A preoperative evaluation was carried out in all patients with demographic data like age, gender, weight and detailed clinical history, physical examination including, associated medical co-morbidities, and current medications. Blood pressure was measured at three occasions at least 1 hour apart to confirm that it fulfils the selection criteria.

All routine and relevant investigations such as complete blood count, renal function test (serum electrolytes, serum creatinine, and blood urea levels), urine routine and microscopy, electrocardiogram, chest X-ray were carried out for all patients. The factors indicating difficult intubation on clinical examination were ruled out.

Pre-operative management

All patients received Tablet Pantoprazole 40 mg at night before surgery and 3 hours before surgery and Tablet Alprazolam 0.5 mg was given night before surgery. A 20G intravenous cannula was secured on non-dominant hand in appropriate vein in wards and intravenous fluid Ringers Lactate 500 ml as maintenance was started about 3 hours prior to surgery. About one hour prior to surgery, baseline readings were taken for pulse rate and blood pressures (Systolic, Diastolic and Mean) and were considered as preoperative baseline reading.

These patients where be randomly allocated in to either group C (Control) or E (Esmolol). Once group was decided, blinding was not maintained.

In operation theatre

In the preoperative area, monitoring of hemodynamic parameters such as Heart Rate, Non-invasive blood pressure monitoring (NIBP), oxygen saturation (SpO2) and Electrocardiography (ECG) was done. Five ECG leads were placed on chest and Lead II, Lead aVL and Lead V were continuously observed on monitor. In operation theatre monitoring of these parameters were continued. All the 3 groups received sedation with Intravenous Midazolam 0.02 mg/kg and Fentanyl 2 mcg/kg about 15 minutes before induction. Preoygenation with 100% oxygen by using facemask in closed circuit to achieve oxygen saturation (SpO2) of 98 - 99% was done.

- For Group ‘C’, patients were directly given inducing agent.
- For Group ‘E’, patients were given intravenous Esmolol 1.5 mg/kg 2 minutes before start of laryngoscopy.

Induction of anaesthesia was done with Intravenous Thiopentone 5mg/kg body weight given slowly till loss of eyelash reflex is seen. Then intravenous Succinylcholine was given in dose of 2 mg/kg.

Then facemask ventilation was done till twitches disappears and adequate relaxation obtained. Direct laryngoscopy was conducted by the same anaesthesia consultant for all cases, using standard McIntosh blade and an appropriate size cuffed endotracheal tube lubricated with non-anesthetic jelly and was inserted in single attempt and cuff will be immediately inflated with air to a pressure of 25 cm of water.

After confirming bilateral equality of air entry in lungs by auscultation, the endotracheal tube was secured with the adhesive tape. Ventilation was done by IPPV on ventilator. Ventilatory setting was set to provide tidal volume of 8-10 mg/kg and respiratory rate 14/minute for 10 minutes. No noxious stimulus or surgical incision was applied over 10 minutes after intubation. Supine position was maintained. Anaesthesia was maintained using 50% nitrous oxide and 50% oxygen with Isoflurane (MAC-1.0). Hemodynamic parameters were monitored as follows: Heart Rate (HR), Systolic Blood Pressure (SBP),

Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) by non-invasive technique.

The intervals for these measurements were

- Baseline (taken half an hour prior to anaesthesia)
- Before sedation
- After induction but before intubation
- Immediately after intubation
- Thereafter at 1, 2, 3, 4, 5 and 10 minutes.

After this monitoring for 10 minutes post-intubation, further operative and an aesthetic procedure were continued as per plan.

Statistical methods

Statistical analysis was carried out with the help of SPSS (version 20) for Windows package (SPSS Science, Chicago, IL, USA). The description of the data was done in form of mean±SD for quantitative data while in the form of % proportion for qualitative (categorical) data. p-values of <0.05 will be considered significant.

For quantitative data, Unpaired Student's t-test was used to test statistical significance of difference between two independent group means.

For comparison of categorical variables chi-square test was used.

RESULTS

Comparison of patient variables such as age, gender and weight show that there is no statistically significant demographical difference between group C and E. (Table 1).

Heart rate was lower in Group E as compared to Group C. There was no statistically significant difference at baseline, before sedation or after induction. Thereafter heart rate was statistically significant lower immediately after intubation till 4 minutes after intubation.

At 5 and 10 mins after intubation, heart rate was lower in group E but there was no statistically significant difference. (Table 2).

SBP was lower in Group E as compared to Group C. There was statistically significant lower SBP in Group E difference only immediately after intubation. At all other points of comparison there was no statistically significant difference (Table 3).

DBP was lower in Group E as compared to Group C. There was statistically significant lower DBP in Group E difference only immediately after intubation. At all other points of comparison there was no statistically significant difference (Table 4).

Table 1: Comparison of patient variable.

Variable		Groups		p value
		Group c	Group e	
Age		36.03±9.219	37.6±12.653	0.5849
Weight		60.8±10.965	63.93±7.856	0.2088
Gender	Male	20	19	0.786
	Female	10	11	

Table 2: Intergroup comparison of mean heart rate between group C and E.

	Group C (mean±sd)	Group E (mean±sd)	p-value
Baseline	81.20±12.024	80.63±6.891	0.824
Before sedation	84.60±11.171	81.60±7.233	0.232
After induction	84.77±10.513	79.33±10.410	0.077
Immediately after intubation	101.60±11.935	88.67±7.747	0.000*
1 min	99.10±11.514	88.77±8.016	0.000*
2 mins	96.10±11.400	87.53±7.519	0.002*
3 mins	93.73±11.453	86.53±7.615	0.009*
4 mins	90.13±11.658	84.37±7.308	0.034*
5 mins	85.93±11.310	82.73 ± 7.759	0.222
10 mins	83.63±11.731	80.93±7.843	0.316

*statistically significant

Table 3: Intergroup comparison of mean systolic blood pressure between group C and E.

	Group C (mean ± sd)	Group E (mean ± sd)	p-value
Baseline	121.83±8.526	120.80±9.368	0.603
Before sedation	125.37±8.704	119.93±9.584	0.220
After induction	119.70±8.647	117.07±8.998	0.241
Immediately after intubation	161.90±11.929	155.07±12.086	0.008*
1 min	151.10±10.114	150.73±10.696	0.877
2 mins	142.93±7.428	145.53±9.912	0.229
3 mins	137.67±7.950	141.00±9.040	0.104
4 mins	132.83±7.410	133.53±8.460	0.731
5 mins	127.90±8.168	126.27±9.752	0.460
10 mins	124.37±9.046	120.40±8.869	0.073

*statistically significant

MAP was lower in Group E as compared to Group C. MAP was statistically significant lower DBP in Group E difference from immediately after intubation till 2 mins after intubation. From baseline till after induction there was no statistically significant difference.

Similarly, from 3 mins after intubation till 10 mins after intubation there was no statistically significant difference (Table 5).

Table 4: Intergroup comparison of mean diastolic blood pressure between group C and E.

	Group C (mean±sd)	Group E (mean±sd)	p-value
Baseline	78.50±6.073	76.93±9.927	0.449
Before sedation	77.40±6.306	76.83±9.745	0.775
After induction	74.47±6.241	76.43±11.352	0.404
Immediately after intubation	94.13±7.366	89.53±8.016	0.015*
1 min	88.57±7.463	86.37±8.869	0.192
2 mins	86.57±6.590	84.23±9.591	0.174
3 mins	83.87±6.202	84.23±9.591	0.481
4 mins	82.40±6.344	80.63±9.608	0.319
5 mins	79.33±4.908	77.90±9.532	0.428
10 mins	77.27±5.382	73.80±8.919	0.051

*Statistically significant

Table 5: Intergroup comparison of mean MAP between group C and E.

	Group C (mean±sd)	Group E (mean±sd)	p-value
Baseline	90.90±8.057	91.53±6.485	0.749
Before sedation	91.63±7.695	89.50±6.431	0.226
After induction	86.27±7.755	86.27±6.787	1.000
Immediately after intubatic	115.73±11.922	109.80±7.911	0.045*
1 min	112.73±10.945	106.00±8.383	0.014*
2 mins	108.47±9.899	102.97±8.336	0.030*
3 mins	103.57±9.555	99.63±7.792	0.117
4 mins	99.93±8.706	97.00±7.297	0.183
5 mins	95.00±7.344	92.43±6.951	0.176
10 mins	90.93±7.148	88.57±7.055	0.226

*statistically significant

DISCUSSION

The hemodynamic response characterized by tachycardia and hypertension to manipulation in the area of the larynx, by means of laryngoscopy and intubation, is well-recognized. Stimulation of mechanoreceptors in the pharyngeal wall, epiglottis and vocal cords, is thought to be the cause for this hemodynamic response. Cardiovascular pressor response following laryngoscopy and tracheal intubation has been investigated extensively since these changes were initially reported.[10]

Myocardial ischemia might occur during the induction-intubation sequence in patients with coronary artery disease. Intraoperative ischemia has been associated with a high rate of perioperative myocardial infarction.[11] During procedure like direct laryngoscopy involving severe sympathetic stimuli prevention of tachycardia, hypertension and rise in total oxygen consumption may prove beneficial in patients with limited cardiac reserve.[12]

Esmolol is effective, in a dose-dependent manner, in the attenuation of the sympathomimetic response to laryngoscopy and intubation. Shrestha et al, noted that doses of Esmolol higher than 1.5 mg/kg did not completely prevent the pressor response to laryngoscopy and intubation. Sum et al, has also found a similar effect in addition to increase in intracranial pressure.[13,14]

Dyson et al, noted that Esmolol in doses 1 mg/kg was insufficient to control the increase in systolic blood pressure compared to 1.5 mg/kg and 2 mg/kg which controlled both systolic blood pressure and heart rate, but 2 mg/kg dose produced significant decreases in systolic blood pressure.[15]

Miller et al, in their study have reported that 100 mg of single bolus dose of Esmolol was effective for controlling the hemodynamic response to tracheal intubation in a Canadian multicenter trial.[16]

Study done by Sanjeev Singh et al, comparing Esmolol also showed significant increase in Heart Rate after intubation and remained significantly high at 3 and 5 mins.[17] They also found increase in SBP, DBP and MAP from the baseline in after Esmolol at 1 min with decreases at 3 and 5 min respectively after intubation. In this study also authors found Heart rate well controlled with Esmolol bolus but Blood pressure remained was controlled only for a short duration.

Unlike this study, Liu et al, who used Esmolol infusion to control hemodynamic responses associated with intubation, found significant decreases in an SBP prior to induction and post-intubation, compared to the placebo group.[18] This could be because in their study patients received infusion rather than bolus like this study.

In present study, pretreatment with Esmolol 1.5 mg/kg attenuated, but did not totally obtund, the cardiovascular response to tracheal intubation after induction of anesthesia and these findings are similar with previous studies.[17] β-adrenoceptor blockade minimizes increase in HR and myocardial contractility by attenuating the positive chronotropic and inotropic effects of increased adrenergic activity. But it failed to effectively attenuate hypertensive response to intubation.

CONCLUSION

In Normotensive patients requiring general anaesthesia with laryngoscopy and intubation, after induction with Fentanyl and Thiopentone, and Succinylcholine as muscle relaxant, authors found that intravenous Esmolol 1.5 mg/kg attenuated Heart rate response but fails to satisfactorily prevent rise in blood pressure.

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