Original Article

Role of intravenous esmolol, fentanyl and lignocaine for attenuation of stress response in tracheal intubation-a comparative study

Nurul Islam[1], Amirul Islam[2], Idris Ali[3], Mohiuddin Shumon[1], Mozaffor Hossain[1], UH Shahera Khatun[4]

[1]Dept. of Anaesthesia & ICU, DMCH. [2]Dept. of Anaesthesia, Analgesia & Intensive Care Medicine, BSMMU, Dhaka. [3]Dhaka Dental College, Dhaka. [4]Head of the Department of Anaesthesia, Community Medial College Hospital, Dhaka.

Corresponding author: drnislamdmc@yahoo.com

Abstract

Background *Endotracheal intubation is an essential part of safe airway management but this stimulates the patient's airway reflexes and predictably leads to haemodynamic derangement. Many drugs have been suggested in modifying in haemodynamic responses to laryngoscopy and intubation.*

Objectives *To assess efficacy of three drugs - esmolol, fentanyl and lignocaine and to assess which one is more effective to attenuate haemodynamic response to direct laryngoscopy and endotracheal intubation.*

Methods *A total number of 90 patients ASA class I and II were selected randomly as per inclusion and exclusion criteria in three groups, 30 patients in each group. Group A received esmolol 1.5mg/kg in the volume of 10ml (with distil water) 2min before intubation, group B received fentanyl 1.5mg/kg IV 5min before intubation and group C received lignocaine 1.5mg/kg IV 90 sec before intubation. Per-operative data were recorded at 1min, 2min, 5min and 10min after intubation.*

Results *The mean heart rate, systolic, diastolic,mean arterial pressure before starting anaesthesia were similar in group-A (esmolol), B(fentanyl) and C(lignocaine). The mean values of heart rate and rate pressure product were significantly lower in group A(Esmolol) at 1 and 2 minute than group B(fentanyl) and at 1, 2 and 5 minute than group C(lignocaine). The mean values of systolic, diastolic and mean arterial pressure were slightly lower in group A(esmolol) at 5 minute than group B(fentanyl) and significantly lower at 1, 2 and 5 minute than group C(lignocaine).*

Conclusion *Esmolol 1.5mg/kg is superior to lignocaine 1.5mg/kg for attenuation of haemodynamic response (HR, SBP, DBP, RPP and MAP) to laryngoscopy and endotracheal intubation and also superior to fentanyl for attenuation of HR and RPP.*

Keywords *Esmolol, fentanyl, lignocaine, laryngoscoy, endotracheal intubation.*

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Introduction

Laryngoscopic stimulation of oropharyngeal structures may be an important factor in the haemodynamic stress response associated with tracheal intubation[1]. Instrumentation of pharynx and tracheal intubation may result in tachycardia, hypertension and increased plasma catecholamine concentrations that may evoke life threatening conditions among susceptible individuals especially those with cardiovascular disease[2]. Thus it has been proposed that an abrupt increase in catecholamine may be associated with potentially severe hypertension, tachycardia which may cause cardiac arrhythmias, myocardial ischaemia, left ventricular dysfunction and rupture of cerebral aneurysm, in susceptible individuals[3,4,5] Activation of sympathetic nervous system may cause coronary artery vasoconstriction, reducing the myocardial oxygen supply which in turn predispose to myocardial ischaemia. This condition is also aggravated by hypercoagulable state in the postoperative period-a stress response byADH[6].

Stress may be reduced by modifying or controlling the response to stress[7]. Several agents and regimens have been devised to control this stress induced haemodynamic responses. These are Local anesthetics, Ganglion blocker, Vasodilator, Opioids. But none of these gained wide spread popularity.Esmolol is a short acting beta I selective agent whose sole use is in arrhythmias. Its short duration and beta I selectivity means that it could be considered in some patients with contraindications to other beta blocking drugs[10]. The rapid onset and offset of effect is an advantage in the perioperative period, as any effects such as dose dependent bradycardia or hypotension are short lived. It is effective in preventing or controlling intraoperative tachycardia and hypertension[11]. Esmolol 1.4mg/kg IV was significantly more effective than either ligocaine or nitroglycerine in controlling the increase in HR, and it was also more effective than ligocaine in minimising the increase in MAP following tracheal intubation. In situation where opioid analgesics are contraindicated, esmolol would appear to be the cardiovascular drug of choice in maintaining haemodynamic stability during laryngoscopy and intubation[12]. There are some studies about preventing stress response due to tracheal intubation with either esmolol or fentanyl or lignocaine and there are some comparative studies with esmolol versus fentanyl, esmolol versus lignocaine or fentanyl versus lignocaine. But there are very limited study about comparing the effects of esmolol, fentanyl and lignocaine. So we have taken this study to see the role of intravenous esmolol, fentanyl and lignocaine for attenuation of stress response in tracheal intubation. It will help us to choice the better one to prevent per-operative MI, excessive bleeding & help for better recovery of the patient, ultimately patients good outcome.

Results

Table I *Distribution of the patients by age & body weight of groups*

Mean ± SD	Group-A	Group-B	Group-C	p value*
Age (in years)	29.07 ± 9.38	33.13 ± 8.57	34.37 ± 8.29	0.054
Weight (in kg)	51.17 ± 10.58	54.80 ± 7.52	56.00 ± 8.51	0.100

*ANOVA test was done to measure the level of significance.

Mean ages of the patients of group A, group C and group B were 29.07 ± 9.38, 34.37 ± 8.29, and 33.13 ± 8.57 years respectively. No statistically significant difference was observed among groups at 0.05 level in term of age & mean weights of the patients of group A, group C and group B were 51.17 ± 10.58, 56.00 ± 8.51 and 54.80 ± 7.52 kg respectively. No statistically significant difference was observed among groups in term of body weight at 5% level.

Table II *Comparison of groups in term of heart rate (Heart rate at different follows up period)*

Heart rate	Group			p
	Group-A	Group-B	Group-C	value*
Before induction				
0 minute	94.67 ± 11.88	90.63 ± 12.39	91.93 ± 7.87	0.348
After intubation				
1 minute	98.53 ± 18.81	111.37 ± 25.49	118.57± 12.18	0.001
2 minute	94.37 ± 17.74	100.17±10.69	114.60± 17.52	<0.001
5 minute	91.73 ± 12.86	87.17 ± 11.10	87.17 ± 11.10	<0.001
10 minute	85.70 ± 11.77	83.40 ± 10.00	86.80 ± 8.73	0.426

*One way ANOVA was done to measure the level of significance

Table shows the mean heart rate before induction and after intubation among the patients of different groups in different follows up period. Significance differences were observed among groups in term of heart rate at 1 minute, 2 minute and 5 minute.

Table III *Comparison of groups in term of systolic blood pressure (Systolic blood pressrue at different follows up period)*

Systolic BP	Group			p value*
	Group-A	Group-B	Group-C	
Before induction				
0 minute	123.80 ± 12.85	122.13 ± 8.11	125.47 ± 8.74	0.447
After intubation				
1 minute	143.33 ± 14.69	142.13 ± 11.02	152.90 ± 11.50	0.002
2 minute	138.20 ± 12.38	135.90 ± 8.73	145.07 ± 9.90	0.003
5 minute	118.67 ± 12.21	120.17 ± 8.65	131.13 ± 13.58	0.000
10 minute	115.00 ± 12.77	117.97 ± 10.60	121.50 ± 12.12	0.111

*One way ANOVA was done to measure the level of significance

Table shows the mean systolic blood pressure before induction of anaesthesia and after intubation among the patients of different groups in different follows up period. Significant differences were observed among groups at 1 minute, 2 minute and 5 minute.

Table IV *Comparison of groups in term of diastolic blood pressure (Diastolic blood pressure at different follows up period)*

Diastolic BP	Groups			p value*
	Group-A	Group-C	Group-B	
Before induction				
0 minute	80.50 ± 7.39	80.87 ± 7.24	80.83 ± 9.40	.981
After intubation				
1 minute	103.30 ± 14.85	101.17 ± 6.24	113.60 ± 14.55	.000
2 minute	97.47 ± 11.27	93.37 ± 11.08	104.43 ± 15.68	.005
5 minute	83.50 ± 9.73	86.07 ± 8.86	91.63 ± 12.79	.012
10 minute	81.17 ± 10.83	77.33±7.32	80.53 ± 9.73	.244

*One way ANOVA was done to measure the level of significance

Table shows the mean diastolic blood pressure before induction and after intubation among the patients of different groups in different follows up period. Significance differences were observed among groups at 1 minute, 2 minute and 5 minute.

Table V *Comparison of groups in term of mean arterial pressure (Mean arterial pressure at different follows up period)*

Mean arterial pressure	Groups			p value*
	Group-A	Group-B	Group-C	
Before induction				
0 minute	94.93 ± 8.66	94.62± 5.11	95.71± 7.63	0.837
After intubation				
1 minute	116.64 ± 13.64	114.82 ± 6.41	126.70 ± 12.51	0.000
2 minute	111.04 ± 10.74	107.54 ± 7.82	117.98 ± 12.87	0.001
5 minute	95.22 ± 10.10	97.43 ± 7.86	104.80 ± 12.78	0.002
10 minute	92.44 ± 10.98	90.88 ± 7.38	94.19 ± 8.63	0.376

*One way ANOVA was done to measure the level of significance

Table shows the mean arterial blood pressure before and after induction among the patients of different groups in different follows up period. Significance differences were observed among groups at 1 minute, 2 minute and 5 minute.

Table VI *Comparison of groups in term of rate pressure product (Mean rate pressure product at different follows up period)*

Rate pressure product	Group			p value*
	Group-A	Group-B	Group-C	
Before induction				
0 minute	11729.1±1935.7	11076.0±1741.5	11507.7±966.6	.281
After intubation				
1 minute	14065.2±2986.2	15801.3±3670.1	18134.2±2325.6	.000
2 minute	13000.4±2657.3	13601.0±1605.2	16618.1±2764.7	.000
5 minute	10894.5±1925.3	10508.0±1710.2	12922.8±1640.6	.000
10 minute	9859.1±1787.7	9836.2±1409.0	10548.9±1514.4	.145

*One way ANOVA was done to measure the level of significance

Table shows the mean rate pressure product before and after induction among the patients of different groups in different follows up period. Significance differences were observed among groups at 1 minute, 2 minute and 5 minute.

Table VII *Distribution of assessment of intubation conditions by groups*

Assessment	Group			p value*
	Group-A	Group-B	Group-C	
Excellent	23 (76.7)	27 (90.0)	22 (73.3)	0.233
Good	7 (23.3)	3 (10.0)	8 (26.7)	
Total	30 (100.0)	30 (100.0)	30 (100.0)	

*Chi-square test was done to measure the level of significance.

#Figure within parentheses indicates in percentage.

Table shows the clinical assessment of patients after induction of drugs among groups. Maximum patients of all groups show excellent result. No significant difference was observed in term of assessment results among groups at 5% level.

Discussion

Laryngoscopic stimulation of oropharyngeal structures may be an important factor in hemodynamic stress response associated with tracheal intubation[1]. Instrumentation of pharynx and tracheal intubation may result in tachycardia, hypertension and increased catecholamine concentration that may evoke life threatening condition among susceptible individuals specially those with cardiovascular disease[2]. Intubation is associated with a cardiovascular respose of elevated blood pressure and pulse, occasional dysrrhythmias, cough reflexes, increased intracranial pressure, and increased intraocular pressure. If no specific measures are taken to prevent hemodynamic response, the HR can increase from 26%-66% depending on the method of induction, and SBP can increase from 36%-45%.

Stress may be reduced by modifying or controlling the response to stress[7]. Premedication is used to provide sedation, anxiolysis and to enhance quality of induction, maintenance and recovery from

anesthesia. A recent study has suggested that different premedication may lead to an alteration in sympathoadrenal stress responses during intubation and surgery[8]. Several agents and regimens have been deviced to control this stress induced hemodynamic responses. These are local anesthetics, ganglion blockers, vasodilator, opioids, deep inhalational anesthesia, Large dose of thiopental sodium. But none of them gained wide spread popularity. Local anesthetic in large dose may cause cardiac depression, Opioid in large doses, fentanyl >50 mcg/kg; morphine >2mg/kg has been shown to produce stress free condition in cardiac surgery[9,] which is inappropriate in noncardiac surgery. Vasodilator and ganglion blocker cause hypotension and reflex tachycardia. Deep inhalational anesthesia cause intracranial hypertension, large dose thiopental causes cardiac depression. These effects are not desirable and limit their usefulness.

A randomized placebo-controlled, double-blind study was carried out by Harbhej Singh et al. to compare the safety and efficacy of lidocaine, esmolol and nitroglycerine in modifying the hemodynamic response to laryngoscopy and intubation on 40 ASA I&II patients undergoing general anesthesia. Patients were divided into 4 groups, group 1 received 5 ml saline, group 2 received lidocaine 1.5 mg/kg, group 3 esmolol 1.4 mg/kg group 4 nitroglycerine 2mcg/kg. MAP and HR were recorded every min for 20 min following induction of anesthesia. Following laryngoscopy and intubation, MAP increased significantly in all 4 groups' control (49% ± 19%), lidocaine, (55% 26%), esmoll (25%±11%), nitroglycerine (45% ± 21%) compared with preinduction baseline values. In the esmoll group, the increase in HR was significantly lower (20%± 3%) compared with nitroglycerine (37%± 8%), lidocaine (52%± 8%), and control (29%±4%) groups. Esmolol 1.4 mg/kg IV was significantly more effective than either lidocaine or nitroglycerine in controlling the HR and MAP in response to laryngoscopy and intubation ($p<0.05$) [12].

A randomized study was done by Ajay Gupta et al. for comparison of esmolol and lidocaine for attenuation of cardiovascular stress response to laryngoscopy and endotracheal intubation on 60 ASA (I&II) patients divided into 3 groups, each group containing 20 patients. Group C received no drug, group L received lignocaine 1.5mg/kg IV, group E 1.5mg/kg IV esmolol 3min before intubation. Immediately after intubation and further on there was statistically significant ($p>0.05$) increase in HR in group C compared to group E and the difference remained significant till 2 min after intubation. The attenuation of HR response in group E was greater than L. After intubation the attenuation of increase in SBP & DBP in group-E was statistically significant as compared to group-C and L. They concluded that IV esmolol 1.5mg/kg as a bolus attenuates the response more effectively without any deleterious effects[13].

A prospective randomized double blind study was performed by Bakiye Ugur et al.[14] to investigate the effects of esmolol, lidocaine, fentanyl, on 120 (ASA I&II), divided into 4 equal groups. Group C received 5% dextrose 5ml, group-E esmolol 1.5mg/kg IV, group-F fentanyl 1mcg/kg IV, and group-L lignocaine 1.5mg/kg IV 2 min before endotracheal intubation. HR, MAP, and RPP were recorded before and after induction of anesthesia, immediately after intubation and 1, 3, 5, 7 and 10 min after intubation. An increase in HR was observed immediately after intubation in all groups except the group-E. The decrease in HR began 3 min after intubation, occurred earliest in group-E, and was significant in all groups 10 min after intubation ($p<0.0083$). MAP increased after intubation in all groups but was lower in fentanyl group. MAP decreased first in the group-E 3 min after intubation and than in other grup 5 min after intubation ($p<0.05$). Calculated RPP increased immediately after intubation in all groups compared with baseline values. Increased RPP values began to decrease first in the group-E 3 min after intubation ($p<0.05$). They concluded that Esmolol 1.5 mg/kg can be given 2 min before laryngoscopy and intubation to prevent RPP and tachycardia and can be beneficial when administered before layngoscopy and tracheal intubation in patients with tachycardia.

Arandomized placebo controlled double-blined study was done by Steven M. et al[15]. to investigate which drug prevents tachycardia and hypertension associated with tracheal intubation: lidocaine, fentanyl, or esmolol? 80 patients (ASA II, III & IV)

divided into 4 groups to receive preintuation dose of either placebo, 200 mg lidocaine, 200 mcg fentanyl, 150mg esmolol. After induction of anesthesia 1-1.5mg/kg succinylcholine was given at 1 min. laryngoscopy and tracheal intubation were performed at 2 min after anesthesia maximum percent increase in HR(mean±SE) during and after intubation were similar in the placebo (44% ± 6%), lidocaine (51% ± 10%), and fentanyl (37% ± 5%) groups, but lower in esmolol (18% ± 5%) group ($p<0.05$). Maximum SBP increases were lower in the lidocaine (20% ± 6%), fentanyl (12% ± 3%), and esmolol (19% ± 4%) groups than in the placebo (36% ± 5%) group ($p<0.05$). They concluded that esmolol 150 mg provides consistent and reliable protection from increases in both HR and SBP during and after intubation. Lidocaine 200 mg and fentanyl 200 mcg fail to protect against increases in HR but do provide protection against increase in SBP equivalent to that provided by esmolol.

Attenuation of cardiovascular response to laryngoscopy and tracheal intubation has been described by Feng CK, and et al[16]. consists of administering 2 mg/kg lidocaine and 2 mg/kg esmolol. All patients were premedicated with diazepam 0.1 mg/kg 30 min before induction of general anaesthesia. Each designated drug was given upon induction of anaesthesia. There was no difference in the demographic data between the two groups. After intubation, the incidence of hypertension (SBP>180 mmHg) was found in 20% patients in esmolol group than 70% patients in lidocaine group. The results of this study showed that only esmolol could reliably offer protection against the increase in both HR and SBP and 2 mg/kg lidocaine had no effect to blunt adverse haemodynamic responses during laryngoscopy and tracheal infubation.

In this prospective study ninety patients have been randomly selected into one of the three groups by a computer generated random number table and by card sampling. Each patient has been given cards to take any one blindly from three groups. There were no significant differences between three groups in age, body weight, gender and ASA grading. Before induction of anaesthesia heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), rate pressure product (RPP) and mean arterial pressure (MAP) were not statistically significant($p>0.05$) in three groups.

One minute after intubation, these parameters were significantly raised ($p<0.05$) in all groups. The findings of our study are comparable to those of Bakiye et al[14]. Who found a rise in HR, MAP and RPP, just after and 1 min after intubation and also comparable to those of Steven et al[15] who show an increase in HR and SBP during and 1 min after intubation and comparable to those of King et al[17] who found a rise of HR, SBP, DBP, RPP and MAP 1 min after intubation. They also found gradual return of these parameters to baseline as anaesthesia deepened.

Our study demonstrated highly significant reduction in HR,SBP, DBP, RPP and MAP in groups A and B compared with group C, at 1, 2 and 5 minutes after intubation. The reduction of HR, SBP, DBP, MAP and RPP were significantly more in group A (Esmolo) than those of group C (lignocaine) (fig I-V). The reduction of HR and RPP were significantly more in group A (esmolol) than group B(fentanyl) at 1 and 2 min after intubation which is consistent with the study of Feng et al[16]. Who found that esmolol 2 mg/kg is more effective than fentanyl 3 mcg/kg in preventing HR and RPP and showed that only esmolol could reliably offer protection against the increase in both HR and SBP. In our study five minutes after intubation, HR, SBP, DBP, RPP and MAP returned to almost baseline values in esmolol and fentanyl group but in lignocaine group it took 10 min to return to base line.These findings are in agreement with that of Bakiye Ugur et al., and Steven et al. Bakiye Ugur et al. showed that esmolol 1.5 mg/kg can be given 2 min before laryngoscopy and intubation to prevent RPP and tachycardia. Steven et al. showed that Esmolol 150 mg provides consistent and reliable protection from increases in both HR and SBP during and after intubation.

It is also comparative with that of Ajay Gupta et al[52]. for comparison of esmolol and lidocaine for attenuation of cardiovascular stress response to laryngoscopy and endotracheal intubation who showed that IV lignocaine 1.5mg/kg given 3 min before intubation is not very effective in attenuating hemodynamic response to laryngoscopy and intubation, while esmolol 1.5mg/kg as a bolus attenuates the response more

effectively without any deleterious effects. They showed that there were greater attenuation of HR, SBP and DBP in group E compared to group L from just after intubation to 2 min after intubation.

We observed that esmolol attenuated tachycardia and fentanyl prevented hypertension; RPPdecreased in both the esmolol and fentanyl groups, but the decrease was more marked in esmolol group and lignocaine could not prevent tachycardia and hypertension. The dose of esmolol, fentanyl and lignocaine evaluated in this study did not cause any adverse effects. This study has one limitation-we only tested the 1.5 mg/kg Esmolol, 1.5 mcg/kg Fentanyl and 1.5 mg/kg Lignocaine and administered the anaesthetic agents through the intravenous route. Therefore the results of the study are applicable to the doses tested in combination with the anaesthesia induction technique used.

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