Original Article

Indian Journal of Anesthesia and Analgesia
2019; 6(6) (Part - I): 2049-2056
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6619.29

To Comparitive Study Lignocaine Over Esmolol in Attenuating the Sympathetic Responses to Laryngoscopy and Tracheal Intubation

P Kalyan Chakravarthy[1], Kotla Hemnath Babu[2], Sree Vidya Ramineedi[3], Konduru Sindhura[4], Metta Ramya[5], Vaddi Preethi[6]

[1,2]Associate Professor, [3,4,5,6]Post Graduate, Department of Anesthesia, Great Eastern Medical School and Hospital, Ragolu, Srikakulam, Andhra Pradesh 532484, India.

Abstract

Introduction: The stress response to laryngoscopy and endotracheal intubation activates the sympathetic nervous system, which may increase myocardial oxygen demand by increasing heart rate and arterial blood pressure. Activation of the sympathetic nervous system may also cause coronary artery vasoconstriction reducing the supply of oxygen to the myocardium, which in turn would pre-dispose to myocardial ischemia. *Aims:* To study the effectiveness of Lignocaine *2 mg/kg* and Esmolol 200 mg and to ascertain the superiority of Esmolol over lignocaine or vice versa in suppressing sympathetic response. *Materials and Methods:* A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 150 patients posted for elective surgeries under general anesthesia with endotracheal intubation for all the patients. Patients were allocated randomly to the Three Groups, Group 1 (Control), Group II (Lignocaine) and Group III (Esmolol) 50 patients in each group. *Results:* In patients with no drugs to attenuate the sympathetic responses to laryngoscopy and intubation the maximum rises in heart rate, systolic, diastolic and mean arterial blood pressures were statistically and clinically very highly significant and can be detrimental in high risk patients. Lignocaine significantly attenuates the sympathetic responses to laryngoscopy and tracheal intubation. Esmolol also very significantly attenuates the sympathetic responses. *Conclusion:* Esmolol is more efficient than lignocaine in attenuating the sympathetic responses to laryngoscopy and intubation. Esmolol at a bolus dose of *200 mg* I.V. administered. 3 minutes before laryngoscopy and intubation can be recommended to attenuate the sympathetic responses due to laryngoscopy and intubation.

Keywords: Laryngoscopy; Esmolol; Lignocaine; Sympathetic responses.

How to cite this article:

P Kalyan Chakravarthy, Kotla Hemnath Babu, Sree Vidya Ramineedi et al. To Comparitive Study Lignocaine Over Esmolol in Attenuating the Sympathetic Responses to Laryngoscopy and Tracheal Intubation. Indian J Anesth Analg. 2019;6(6 Part-I):2049-2056.

Introduction

Direct laryngoscopy and endotracheal intubation frequently induces a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation. The response is transient occurring *30 seconds* after intubation and lasting for less than *10 minutes*.[1] The stress response to laryngoscopy and endotracheal intubation activates the sympathetic nervous system, which may increase myocardial oxygen demand by increasing heart rate and arterial blood pressure. Activation of the sympathetic nervous system may also cause coronary artery vasoconstriction

Corresponding Author: Kotla Hemnath Babu, Associate Professor, Department of Anesthesia, Great Eastern Medical School and Hospital, Ragolu, Srikakulam, Andhra Pradesh 532484, India.

E-mail: hemnathbabu@rediffmail.com

Received on 21.07.2019, **Accepted on** 26.08.2019

reducing the supply of oxygen to the myocardium, which in turn would pre-dispose to myocardial ischemia. Of course, intubations using Glide Scope video laryngoscope causes lesser stress response in comparison to intubation with a Macintosh laryngoscope.[2]

Sympathoadrenal stimulation and subsequent catecholamine release may contribute to hemodynamic instability which is typically signified by an increase in heart rate and blood pressure however, the main mechanism is not clearly defined. These acute changes in hemodynamic status are particularly significant in pre-existing pre-disposing situations like hypertension, myocardial infraction, myocardial malfunction and cardiovascular diseases.[3] Various techniques have been examined for attenuating hemodynamic responses to laryngoscopy and tracheal intubation, including deeper anesthesia and numerous drugs, such as beta blockers, calcium channel blockers, opioids, sodium channel blockers, vasodilators, and alpha agonists. Opioids are the most commonly used drugs with satisfactory outcomes for preventing hemodynamic subsequence of intubation. These drugs are not cost-effective, however, and are associated with some unfavorable complications such as nausea, vomiting, consumedly sedation, and respiratory depression. Therefore, there has been a growing trend to find an effective substitute to reduce these side effects as much as possible.

No single agent has been established as the most appropriate for this purpose. Among the recommended procedures, intravenous Lignocaine, Fentanyl or Esmolol appear to best fulfill the above mentioned criteria.[4] Large doses of fentanyl may cause unwanted side effects, intravenous lignocaine has shown variable results. In one study conducted by Miller and Warren lignocaine failed to attenuate the cardiovascular responses to laryngoscopy and intubation. Esmolol is an ultra-short acting beta blocker and has been consistently associated with control of pressor response to laryngoscopy and intubation. The present study is undertaken to determine the efficacy of I.V. Lignocaine *2 mg/kg* bolus and I.V. Esmolol *200 mg* bolus in attenuating the sympathetic responses to laryngoscopy and tracheal intubation. The superiority of esmolol over lignocaine or *vice versa* will also be determined.

Materials and Methods

A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 150 patients posted for elective surgeries under General anesthesia was provided with endotracheal intubation for all the patients. Patients undergoing various Orthopaedic, ENT, Gynecological, General Surgical, Neurosurgical and Laparoscopic procedures were selected.

Inclusion Criteria

Patients age group between *20* and *60 years* of both the sexes, ASA Grade I, II or III. Patients posted for major surgical procedures lasting between *2* and *5 hours*.

Exclusion Criteria

Documented hypersensitivity to lignocaine, Patients with history of sore throat, recurrent history of tracheitis or laryngitis, asthma, COPD, Chronic smokers. Patient to be electively ventilated after surgery, Patients undergoing oropharyngeal surgeries.

Patients were allocated randomly to the Three Groups, Group 1 (Control), Group II (Lignocaine) and Group III (Esmolol) 50 patients in each group:

Group I was Control group. In this group no drug was administered for attenuating sympathetic response to laryngoscopy and intubation.

Group II was Lignocaine group. Here patients received *2 mg/kg* lignocaine I.V., *3 minutes* before laryngoscopy and intubation.

Group III was esmolol group. All the patients in this group received *200 mg* I.V. bolus *3 minutes* before laryngoscopy and intubation.

Pre-medication

All the patients were visited the day before surgery and pre-anesthetic counselling was done. All patients received Diazepam *10 mg* orally at night on the day before surgery. On the day of surgery intravenous line was secured with and following pre-medications were given *45 minutes* before induction. On entering the OT pulse oximeter, non-invasive blood pressure and ECG monitors were connected. A pre-induction heart rate, systolic and diastolic blood pressures were recorded. I.V. infusion of DNS solution was started.

Anesthesia Technique

All the patients were pre-oxygenated with 100% oxygen for *3 minutes* before induction. Induction was achieved with Inj. Thiopentone sodium *5 mg/kg* I.V. given in 2.5% solution. Inj. Glycopyrrolate *0.2 mg*

I.V. was given along with Thiopentone. After induction of anesthesia (loss of eyelash reflex), heart rate, systolic and diastolic blood pressures were recorded.

Succinylcholine was administered at a dose of *2 mg/kg* I.V. Laryngoscopy was done using rigid laryngoscope with standard Macintosh blade. Intubation was done with appropriate sized, disposable, high volume low pressure cuffed endotracheal tube. Oral intubation was done for all surgical procedures. Laryngoscopy and intubation was done within *15* to *20 seconds*. Heart rate, systolic and diastolic blood pressure were recorded at *1, 3, 5, 7* and *10 minute* intervals from the onset of laryngoscopy.

In Group I, patients were not administered with any kind of drug for attenuating pressor response. In Group II, I.V. lignocaine was administered *3 minutes* before laryngoscopy and intubation. In Group III, I.V. esmolol was administered *3 minutes* before laryngoscopy and intubation. Patients were connected to Bain's circuit and anesthesia was maintained with oxygen (33%), N_2O (67%), halothane 0.5% and non- depolarising muscle relaxant vecuronium bromide at a dose of *0.05 mg/kg* I.V. and IPPV. Adequacy of ventilation was monitored clinically and SpO_2 was maintained at 99–100%. Positioning, throat packing and surgery were withheld till the completion of recording. At the end of the surgery reversal was done with inj. Neostigmine 0.05 *mg/kg* and inj. Glycopyrrolate 0.01 *mg/kg* I.V. An observation was made related to adverse effects of drugs and anesthesia related problems and were attended to appropriately.

Statistical Analysis

Excel 2010 and SPSS Version 21.0 will be used for statistical analysis. *p*-value < 0.05 will be considered significant for all statistical purposes. Data will be pooled and expressed as mean and standard deviations. Comparison between groups will be done by ANOVA and independent student '*t*' test.

Results

Table 1: Demographic distribution in present study

Variables	Control	Lignocaine	Esmolol
Age (Mean ± SD)	31.5 ± 10.225	32.12 ± 10.153	33.6 ± 10.83
Male/female	25/25	26/24	21/29
Weight (Mean ± SD)	51.72 ± 5.9	52.84 ± 6.6	52.12 ± 8.7

There is no significant difference between the three groups in age and weight ($p > 0.05$). In control group, 50% of the patients were males and 50% of patients were females. In lignocaine group, 52% of the patients were males and 48% of patients were females. In esmolol group, 42% of the patients were males and 58% of patients were females, (**Table 1**).

Increases in heart rates were clinically significant until the end of *7 minutes* in control and *5 minutes* in lignocaine but were not clinically significant at all times in esmolol group. Analysis by '*z*' test showed significant variations in heart rate before and after induction and at time intervals of *1, 3, 5, 7 and 10 minutes* from the onset of laryngoscopy and intubation. There was no significant difference in heart rate at pre and post induction levels between lignocaine and esmolol groups. ($p = 0.75$ and $p = 0.97$). The heart rate response between lignocaine and esmolol was very significant at all times starting from *1 to 10 minutes* ($p < 0.001$) with esmolol showing a favourable response towards attenuation of heart rate, (**Table 2**).

No significant variations were noted in all groups in systolic blood pressure pre- and post-induction. In comparison to control group and lignocaine group attenuation of systolic blood pressure is significant in lignocaine group. A rise of systolic blood pressure by 14.4% was observed in lignocaine group as compared to control group 18.9% ($p < 0.05$).

Table 2: Comparison of heart rates in present study

	Heart rate						*p*-value			
	Control		Lignocaine		Esmolol		*p*-value between groups	i-ii	ii-iii	i-iii
	Mean ± SD	(%) Diff.	Mean ± SD	(%) Diff.	Mean ± SD	(%) Diff.				
Pre-Induction	85.16 ± 8.1		78.3 ± 6.9		77.4 ± 6.6		0	0	0.54	0
Post-Induction	92.28 ± 10.9	8.3	80.7 ± 6.1	3	81.96 ± 6.09	5.9	0	0	0.436	0
1 Minute	119.94 ± 10.78	40.8	103.74 ± 8.1	32.4	88.08 ± 5.8	13.8	0	0	0	0
3 Minute	119.94 ± 11.57	40.4	102.40 ± 8.7	30.7	89.46 ± 6.0	15.6	0	0	0	0
5 Minute	107.72 ± 13.16	26.4	88 ± 13.6	12.3	86.44 ± 4.9	11.6	0	0	0.491	0
7 Minute	94.72 ± 11.47	11.2	84.4 ± 5.7	7.7	80.92 ± 3.9	4.5	0	0	0.026	0
10 Minute	86.98 ± 8.6	2.1	80.58 ± 5.5	2.8	78.22 ± 3.7	1	0	0	0.065	0

In comparison to control group, the rise in systolic blood pressure was only 3.76% in esmolol group which is statistically highly significant ($p < 0.001$). Esmolol group showed a better attenuation compared to lignocaine group in systolic blood pressure until *3 minutes* post laryngoscopy. Immediately post laryngoscopy at *1 minute* the difference was very significant ($p < 0.001$). At *5, 7* and *10 minutes* there was not much significance between the two Groups statistically, (**Table 3**).

Over *5*, and *7 minutes* the diastolic blood pressure decreased to 79.22 ± 3.888 and 77.90 ± 3.965 respectively. At the end of *10 minutes* it was 2.1% above the baseline with a mean of 77.02 ± 3.846. A maximum rise of 12.5% as compared to 18% was noted between lignocaine and control groups. Attenuation of diastolic blood pressure by lignocaine as compared to control group is very significant until *7 minutes* ($p < 0.001$). A maximum rise of only 7% of diastolic blood pressure was seen in esmolol group which is statistically highly significant ($p < 0.001$). Attenuation of diastolic blood pressure was very significant with esmolol than with lignocaine group until *5 minutes* ($p < 0.001$), (**Table 4**).

Attenuation of pressor response by lignocaine when compared to control is significant ($p < 0.001$). Maximum rise in 13.5% in lignocaine group as to 19% in control group. When compared to control group attenuation by esmolol group is very highly significant ($p < 0.001$). Among the two study groups esmolol is significant in attenuating pressor response compared to lignocaine ($p < 0.05$), (**Table 5**).

Table 3: Comparison of systolic blood pressure

	Systolic Blood Pressure						*p*-value			
	Control		Lignocaine		Esmolol		*p*-value between groups	i-ii	ii-iii	i-iii
	Mean ± SD	(%) Diff.	Mean ± SD	(%) Diff.	Mean ± SD	(%) Diff.				
Pre-Induction	129.46 ± 10.856		130.94 ± 11.541		128.04 ± 11.746		0.45	0.52	0.21	0.53
Post-Induction	127.74 ± 11.702	2.2	130 ± 11.402	0.7	124.52 ± 10.983	2.8	0.06	0.32	0.017	0.16
1 Minute	155.44 ± 11.483	20	149.88 ± 13.654	14.4	132.86 ± 10.546	3.76	0	0.02	0	0
3 Minute	154.08 ± 11.637	18.9	146.82 ± 13.837	12.1	133.58 ± 10.059	4.3	0	0	0	0
5 Minute	142.72 ± 13.087	10.2	135.72 ± 11.221	3.6	132.12 ± 9.835	3.1	0	0	0.118	0
7 Minute	133.88 ± 11.126	3.4	129.34 ± 10.714	1.2	130.12 ± 9.512	1.6	0.07	0.32	0.71	0.07
10 Minute	128.52 ± 9.896	0.7	127.28 ± 10.597	2.8	128.94 ± 9.382	0.7	0.69	0.53	0.407	0.83

Table 4: Comparison of diastolic blood pressure in present study

	Diastolic blood pressure						*p*-value			
	Control		Lignocaine		Esmolol		*p*-value between groups	i-ii	ii-iii	i-iii
	Mean ± SD	(%) Diff	Mean ± SD	(%) Diff	Mean ± SD	(%) Diff				
Pre-Induction	72.28 ± 6.07		75.76 ± 5.7		75.40 ± 5.083		0.91	0.67	0.75	0.91
Post-Induction	73.0 ± 6.4	3	74.66 ± 5.3	1.5	73.12 ± 4.3	3	0.24	0.12	0.15	0.91
1 Minute	88.84 ± 5.2	18	85.24 ± 5.32	12.5	80.02 ± 4.4	6.1	0	0	0	0
3 Minute	88.4 ± 5.1	17.4	84.66 ± 5.2	10.4	89.74 ± 3.8	7	0	0	0	0
5 Minute	83.6 ± 6.1	11	78.62 ± 4.2	3.8	79.22 ± 3.8	5	0	0	0.537	0
7 Minute	78.18 ± 5.5	3.8	74.96 ± 4.66	1	77.9 ± 3.9	3.3	0	0	0.002	0.76
10 Minute	75.86 ± 5.39	0.7	73.96 ± 4.4	2.4	77.0 ± 3.8	2.1	0	0.04	0.001	0.21

Table 5: Comparison of mean arterial blood pressure

	Mean arterial blood pressure						*p*-value			
	Control		Lignocaine		Esmolol		*p*-value between groups	i-ii	ii-iii	i-iii
	Mean ± SD	(%) Diff	Mean ± SD	(%) Diff	Mean ± SD	(%) Diff				
Pre-Induction	93.24 ± 6.6		94.16 ± 6.5		92.98 ± 5.7		0.62	0.47	0.36	0.84
Post-Induction	91.3 ± 6.9	2.1	93.16 ± 6.0	1	90.32 ± 4.99	2.8	0.06	0.13	0.02	0.42
1 Minute	111 ± 6.19	19	106.86 ± 6.9	13.5	97.62 ± 5.17	5	0	0	0	0
3 Minute	110.36 ± 6.2	18	104.78 ± 7.1	11.3	98.42 ± 4.7	5.8	0	0	0	0
5 Minute	103.36 ± 6.9	10.5	97.76 ± 5.2	3.8	96.86 ± 4.6	4.1	0	0	0.43	0
7 Minute	96.76 ± 6.3	3.8	93 ± 5.4	1.2	95.32 ± 4.4	2.5	0	0	0.034	0.19
10 Minute	93.42 ± 5.53	0.2	91.76 ± 5.5	2.5	94.36 ± 4.5	1.5	0	0.11	0.014	0.37

Discussion

Induction of general Anesthesia, direct laryngoscopy and tracheal intubation induce marked cardiovascular changes as well as autonomic reflex activity. Laryngoscopy and intubation of the trachea following induction of anesthesia may be associated with hypertension and tachycardia. Less commonly bradycardia may occur as a result of vagal stimulation Ghaus *et al.* (2002).[5] Although the responses of blood pressure and heart rate are short lived, they might have determinal effects in high risk patients, especially in those with cardiovascular disease. These cardiovascular responses are associated with increased plasma levels of catecholamines.[6]

The main reason for the intubation induced hypertension seems to be release of noradrenaline and to a lesser extent, adrenaline. In addition, increased levels of Adrenocorticotrophic Hormone (ACTH) and dopamine have also been reported. A variety of factors have been shown to have an effect on this stress response: The choice and dosages of pre-medication and induction agents D,[7] the skill of the operator, and probably the technique being used. Numerous studies have demonstrated an increased stress response during direct laryngoscopy, fibre optic intubation and insertion of the laryngeal mask.[8]

Variations of changes in heart rate decrease with increasing age. Young patients show more extreme changes.[9] A linear increase in heart rate and mean arterial pressure during the first *45 seconds* of laryngoscopy was observed. Further prolongation had little effect. As the duration of laryngoscopy is normally less than *30 seconds*, the results of studies in which it takes longer than this have less clinical relevance. The force applied during laryngoscopy has only minor effect.[9] In our study, the duration of laryngoscopy and intubation was limited to *20 seconds*. Marked fluctuations in hemodynamic responses are often seen in geriatric patients.[8] In our study. we have selected the optimal age range of *20* to *50 years*.

An average rise in mean arterial pressure of *25 mm Hg* and *47.7 mm Hg* have been documented.[10] An increase in mean arterial pressure of *26.5 mm Hg* and *20* to *40 torr* when compared with awake control levels and *35* to *60 torr* when compared with pre-intubation values have been reported after placement of endotracheal tube.[11] A rise in mean heart rate of *29.9 beats/min* has also been noted. Many factors influence the cardiovascular changes associated with laryngoscopy and intubation. Age, drugs, type and duration of procedures, depth of anesthesia, hypoxia, hypercarbia etc., influence the pressor response. Patients on anti-hypertensive drugs may exhibit a decrease in pressor response. We excluded the patients on anti-hypertensive mediations from our study.

A variable combination of drugs used for pre-medication, induction, relaxation and maintenance of anesthesia can influence the sympathetic response to laryngoscopy and intubation. The pressure response to laryngoscopy and intubation in form of tachycardia and hypertension occurs frequently; even alpha-adrenoceptor blockade minimizes increases in heart rate and myocardial contractility (primary determinants of O_2 consumption) by attenuating the effects of increased adrenergic activity. This is particularly derivative in patients with IHD.[12]

More attention is given to the use of selective beta-adrenergic antagonists to prevent the reflex sympathoadrenal discharge-mediated tachycardia and hypertension during procedure of laryngoscopy and endotracheal intubation and these include Esmolol.[13] Esmolol has been used in various bolus doses or in an infusion form. Esmolol, *2 mg/kg*, as a single bolus successfully attenuated the pressor response. There was minimal increase in heart rate than the other group but the blood pressure showed a rise although it was less than other groups after laryngoscopy and endotracheal intubation. Again our study correlates with the study of Liu Philip *et al.* who used esmolol infusion to control hemodynamic responses associated with intubation. They found significant decreases in Rate Pressure Product prior to induction and post-intubation. The increase was 50% less in the esmolol-treated patients compared to the placebo group.[14] Christopher *et al*. used esmolol *1 mg/kg* and concluded that the increase in heart rate and blood pressure associated with laryngoscopy and endotracheal intubation were significantly lower in comparison to the control group.[15] Sabahat *et al*. used esmolol *1 mg/kg* and concluded that esmolol partially attenuated the hemodynamic response but did not abolish it completely. Esmolol in bolus doses *100 mg* and *200 mg* attenuates tachycardia and hypertension after tracheal intubation.[16]

Esmolol group did not reveal any rhythm abnormality. No ST segment changes were seen in any patients. Narcotics may block afferent nerve impulses resulting from stimulation of the pharynx and larynx during intubation. Fentanyl has also been used in different doses varying from 2 to 15 *mg/kg* to blunt haemodynamic responses

to laryngoscopy and endotracheal intubation. Low doses of fentanyl, *2 mg/kg* were used in our study and the efficacy was compared with esmolol group. 4 It was found that with fentanyl, *2 mg/kg* elevation of heart rate and blood pressure after intubation was lower than control group, although not statistically significant.

Yushi *et al*. in his study concluded that *2 mg/kg* fentanyl suppresses the hemodynamic response to endotracheal intubation more than the response to laryngoscopy.[17] It was shown that supplementation of anesthetic induction with fentanyl *2 mg/kg* significantly attenuated the increase in heart rate, arterial pressure and rate pressure product after laryngoscopy and intubation, and fentanyl *6 mg/kg* completely abolished pressure response.[61] Doses of Fentanyl that are low enough to cause little post-operative respiratory depression significantly blunt post-intubation hypertension when used as adjuncts to thiopental. This was demonstrated in a study conducted by Donald E Martin *et al*. who used fentanyl, *8 mg/kg* in patients undergoing major vascular surgery.[18]

Low doses of fentanyl were employed because a large dose lead to muscular rigidity, bradycardia, nausea and vomiting. Large doses may also cause post-operative respiratory depression; especially in surgery with short duration of less than *1 hour*. McClain *et al*. reported apnoeic episodes in four out of seven patients who received *3.2–6.5 mg/kg* fentanyl.[19] b-blocker esmolol possesses several properties which make it a valuable agent to obtund the cardiovascular response. Firstly, it is a cardio selective agent, and secondly it has ultra short duration of action (*9 min*) and finally, significant drug interaction with commonly used anesthetics has not been reported. Korpinen *et al*. (1998) reported that the administration of esmolol bolus *2 mg/kg*$^{-1}$ I.V. *2 min* before laryngoscopy and intubation suppressed the increase in the heart rate rather than arterial blood pressures.[20] Bostana and Eroglu (2012) reported that I.V. esmolol in dose of *1 mg/kg*$^{-1}$ before intubation was effective in suppressing the heart rate and arterial blood pressure.[21] Kumar *et al*. (2003) have also claimed optimal results while using higher doses of esmolol in Asian population, *i.e*., *2 mg kg*$^{-1}$ without any incidence of unplanned hypotension or bradycardia. However, no consensus has been reached regarding the optimum dose and timing of its delivery.[22]

Lidocaine has been a popular agent for attenuating circulatory responses. The beneficial effect of lidocaine is due to its direct cardiac depression and peripheral vasodilation, its ability to suppress airway reflexes elicited by irritation of tracheal mucosa and its analgesic as well as anti-arrhythmic properties. Some studies have reported beneficial effects while others showed no effect of intra-venous lignocaine administered *1, 2* or *3 min* before laryngoscopy.[23] Midazolam *et al*. dose of *0.2 mg/kg* I.V. decreases the blood pressure and increases the heart rate similar to thiopentone, However, pre-medication with *0.05 mg/kg* I.V. of midazolam has no effect on sympathetic response to laryngoscopy and intubation. Pentazocine an opioid agonist antagonist may increase the blood pressure, heart rate and catecholamine levels. Glycopyrrolate pre-medication can moderately increase the heart rate. Thiopentone was selected for induction since it still continues to be the most popular agent for induction. In normovolemic patients thiopentone *5 mg/kg* I.V. can transiently decrease *10–20 mm Hg* of blood pressure and increase the heart rate by *15–20 beats/min*. There is increase in catecholamine levels, both noradrenaline and adrenaline.

Perhaps timing of administration of lignocaine is equally important. Tam *et al*.[100] in their article "Intravenous lidocaine: Optimal time of injection before tracheal intubation", showed that, when given intra-venously *3 minutes* before intubation, esmolol and lidocaine appear to have similar efficacies to attenuate moderate hemodynamic changes secondary to emergency intubation in patients with isolated blunt head injury. Wang *et al*.[24] showed that the values of systolic and diastolic pressures *1 min* after intubation were significantly less in groups where lignocaine was given either *3* or *5 minutes* before intubation. However, in Miller and Warren's study, I.V. lignocaine failed to attenuate the cardiovascular response to laryngoscopy and tracheal intubation irrespective of the timing of administration *i.e*., *1, 2,* or *3 min* before laryngoscopy. Wilson *et al*.[25] showed that irrespective of the timing of administration of injection of lignocaine *2, 3 or 4 minutes* before tracheal intubation, there was a significant increase in heart rate of 21–26% in all groups. There was no significant increase in MAP in response to intubation in any group of patients given lignocaine before intubation, but in the placebo group, MAP increased by 19% compared to baseline values. In our study, heart rate increased by a maximum of 40.8% when compared to pre-induction value in the control group ($p < 0.001$). Similar increases in lignocaine was 32.4% and in esmolol group by 15.6%. Both lignocaine and esmolol attenuated the heart rate significantly ($p < 001$). It reaches a level which is clinically less significant by the end of

7 minutes in control group and by the end of *5 minutes* in lignocaine and esmolol group. Attenuation of maximum rise in the heart rate by esmolol is evident and statistically highly significant when compared with lignocaine ($p < 0.001$).

In control group systolic blood pressure increased maximally after *1 minute* from the onset of laryngoscopy and intubation. It gradually decreased to pre-induction values over *10 minutes*. With lignocaine group the maximum rise in systolic blood pressure was 14.4% above pre-induction values and with esmolol it was only 4.3% above pre-induction values by the end of *1 minute*. Both drugs compared with control showed significant attenuation ($p < 0.05$). Among the two drugs studied esmolol showed a better attenuation over lignocaine up to *5 minutes* post-laryngoscopy ($p < 0.001$). Maximal rise in diastolic blood pressure was 17.4% when compared to pre-induction values in the control group ($p < 0.001$). In lignocaine group the maximal increase was 12.5% and in esmolol group it was 7%. Attenuation of diastolic blood pressure is very significant in the two groups as compared to control group until the end of *5 minutes* ($p < 0.001$). Among the two study groups esmolol showed a better attenuation of diastolic blood pressure compared to lignocaine.

Similarly mean arterial pressure was increased by 19% in control group while it increased by 13.5% in lignocaine group and only by 5.8% in esmolol group compared to pre-induction values by *1 minute* post-laryngoscopy. Attenuation of mean arterial pressure is significant in esmolol group as compared to both lignocaine and control group ($p > 0.05$). The efficiency of esmolol over lignocaine in attenuation of cardiovascular responses similar to our study has been verified by many other studies. A combination of both lignocaine and esmolol has been recommended for better responses.

Conclusion

Based on the present clinical comparative study the following conclusions can be made. In patients with no drugs to attenuate the sympathetic responses to laryngoscopy and intubation the maximum rises in heart rate, systolic, diastolic and mean arterial blood pressures were statistically and clinically very highly significant and can be detrimental in high risk patients.

Lignocaine significantly attenuates the sympathetic responses to laryngoscopy and tracheal intubation. Esmolol also very significantly attenuates the sympathetic responses. Esmolol is more efficient than lignocaine in attenuating the sympathetic responses to laryngoscopy and intubation. Esmolol at a bolus dose of *200 mg* I.V. administered *3 minutes* before laryngoscopy and intubation can be recommended to attenuate the sympathetic responses due to laryngoscopy and intubation.

References

1. Jakuoenko N, Kopeika U, Mihelsons M, *et al*. Comparison of stress response performing endotracheal Intubation by Direct Laryngoscopy, fibreoptic intubation and intubation by the Glidescope Laryngoscope. Proceedings of the Latvian Academy of Sciences. 2008;62(4/5) Section B:176–81.
2. Sugiura S, Seki S, Hidaka K, *et al*. "Hemodynamic effects of landiolol, an ultra-short-acting β1-selective blocker, on endotracheal intubation in patients with and without hypertension. Anesthesia and Analgesia. 2007;104(1):124–29.
3. Min JH, Chai HS, Kim YH *et al*. Attenuation of hemo-dynamic responses to laryngoscopy and tracheal intubation during rapid sequence induction: Remifentanil vs Lidocaine with esmolol. Minerva Anestesiologica. 2010;76(3):188–92.
4. Van den Berg AA, Halliday EM, Soomro NA, *et al*. Reducing cardiovascular responses to laryngoscopy and tracheal intubation: A comparison of equipotent doses of tramadol, nalbuphine and pethidine, with placebo. Middle East Journal of Anesthesiology 2004;17(6):1023–36.
5. Ghaus M Saif, Singh Vinita, Kumar A, *et al*. A study of cardiovascular response during laryngoscopy and intubation and their attenuation by ultra short acting: Beta-blockers–Esmolol. Indian J Anesth. 2002;104.
6. Derbyshire Dr, Chmielewski A, Fell D, *et al*. Plasma catecholamine responses to tracheal intubation. British journal of Anesthesia. 1983; 55:855–60.
7. Bucx MJL, Van Geel RTM, Scheck PAE, *et al*. Cardiovascular effects of forces applied during laryngoscopy. The importance of tracheal intubation. Anesthesia. 1992;47:1029–33.
8. Hickey S, Cameron AE, Asbury AJ. Cardivascular response to insertion of Brain's laryngeal mask. Anesthesia. 1990;45:629–33.
9. Bucx MJL, Van Geel RTM, Scheck PAE *et al*. T cardiovascular effects of forces applied during laryngoscopy. Anesthesia. 1995;50:17–22.
10. Khan RM, Khan TZ, Eqbal Ahmed *et al*. Nifedipine and attenuation of blood pressure and pulse rate changes in response to laryngoscopy and tracheal intubation. Ind J Anesth. 1987;35(5):346–49.

11. Menkhaus PG, Reves Jg, Kissin I. Cardiovascular effects of Esmolol in anesthetized humans. Anesth Analg. 1985;64:327.
12. Sam Chung K, Raymond S, Jonathan D. A comparison of fentanyl, Esmolol and their combination for blunting the hemodynamic response. Anesth Analg. 1991;72:482–86.
13. Oxorn D, Hill J. Bolus doses of esmolol for the prevention of pre-operative hypertension and tachycardia. Can Jr Anesth. 1990;37:206–9.
14. Philips L. Esmolol for the control of increase in heart rate and blood pressure during tracheal intubation after thiopentone and succinylcholine. Can Anesth Soc J. 1986;33:556–62.
15. Kindler CH, Schumacher PG, Orwyler A. Effects of intravenous lidocaine and or Esmolol on hemodynamic response to laryngoscopy and intubation: A double blind, controlled clinical trial. J Clin Anesth. 1996;8:491–96.
16. Trariq S, Aziz A, Wahid A. Saca congress. 3rd edition. Karachi: Attenuation of hemodynamic response to intubation with Esmolol. 1997.
17. Yushi U, Maiko S, Hideyuki H. Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy. Anesth Analg. 2002;95:233–37.
18. Martin DE, Rosenberg H, Aukburg SJ, *et al*. Low dose fentanyl blunts responses to tracheal intubation. Anest Analg. 1982;82:680–84.
19. Me clain DA, Hug CC Jr. Intravenous Fentanyl kinetics. Clin Pharmacology ther. 1980;28:106–14.
20. Korpinen R, Simola M, Saarnivaara L. Effect of esmolol on the hemodynamic and electrocardiographic changes during laryngomicroscopy under propofol-alfentanil anesthesia. Acta Anesthesiol Belg. 1998;49:123–32.
21. Bostana H, Eroglu A. Comparison of the clinical efficacies of fentanyl, esmolol and lidocaine in preventing the hemodynamic responses to endotracheal intubation and extubation. J Curr Surg. 2012;2:24–28.
22. Shroff PP, Mohite SN, Panchal ID. Bolus administration of esmolol in controlling the hemodynamic response to tracheal intubation. J Anesthesiol Clin Pharmacol. 2004;20:69–72.
23. Pandey CK, Raza M, Ranjan R. Intravenous lidocaine suppresses fentanyl-induced coughing: A double-blind, prospective, randomized placebo-controlled study. Anesth Analg. 2004;99:1696–98.
24. Wang YM, Chung KC, Lu HF, *et al*. Lidocaine: The optimal timing of intravenous administration in attenuation of increase of intraocular pressure during tracheal intubation. Acta Anesthesiol Sin. 2003; 41(2):71–75.
25. Wilson IG, Meiklejohn BH, Smith G. Intravenous lignocaine and sympathoadrenal responses to laryngoscopy and intubation. Anesthesia. 1991;46:177–80.