International Journal of Clinical Trials
Bhalke R et al. Int J Clin Trials. 2017 Feb;4(1):49-57
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: http://dx.doi.org/10.18203/2349-3259.ijct20170309

Original Research Article

Comparison of esmolol versus combination of esmolol and fentanyl in preventing cardiovascular stress response to intubation

Rahul Bhalke[1], Maroti S. Karale[2]*, Umesh Deshmukh[3]

[1]Department of Anaesthesia, G.M.C.H. Aurangabad, Maharashtra, India
[2]Department of medicine, [3]Department of Anaesthesia, G.M.C.H. Latur, Maharashtra, India

Received: 25 October 2016
Revised: 29 November 2016
Accepted: 05 December 2016

***Correspondence:**
Dr. Maroti S. Karale,
E-mail: drmskarale13@gmail.com

ABSTRACT

Background: A number of cardiovascular responses occur during laryngoscopy and intubation which can have serious consequences during anaesthesia.We planned to conduct a study to evaluate effectiveness of intravenous Esmolol and intravenous Fentanyl in attenuating hemodynamic stress response to laryngoscopy and endotracheal intubation.
Methods: A prospective, observational, randomized, double blind comparative clinical study, conducted on 60 cases of ASA grade I/II patients undergoing elective abdominal surgery under general anesthesia. The data obtained was divided in the two groups based on drug used 5 min prior to induction, Group 1 (I.V. Esmolol 2 mg/kg) and Group 2 (I.V. Esmolol 2 mg/kg & I.V. Fentanyl 2 µg/kg). Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were measured at various time intervals.
Results: There was no significant difference in HR, SBP, DBP, MAP after premedication and induction in both the groups. However at intubation, both groups showed an increase in HR, SBP, DBP and MAP but the rise was attenuated in both groups. Increase in HR was more in group 1 as compared to group 2 and it was statistically significant at 01 and 02 minutes post intubation. The increase in SBP was statistically significant at 00, 01 and 02 minutes post intubation. The increase in MAP was statistically significant immediately after induction, at 00, 01, 02, 05 and 10 minutes post intubation.
Conclusions: Combination of intravenous Esmolol and intravenous Fentanyl is more effective in attenuating heart rate, systolic, diastolic and mean arterial pressure response to intubation than intravenous Esmolol alone.

Keywords: Esmolol, Fentanyl, Cardiovascular Stress, Laryngoscopy, Endotracheal intubation

INTRODUCTION

Laryngoscopy and intubation violate the patient's protective airway reflexes and lead to physiological changes involving various systems of body. A number of responses occur including hypertension, tachycardia, arrhythmias, raised intracranial and intraocular pressure. In this marked circulatory effects like reflex tachycardia (rise up to 20%) and hypertension (rise up to 40-50%) is encountered during endotracheal intubation.[1] These cardiovascular responses may have serious consequences, including myocardial ischemia, dysrhythmias, pulmonary oedema, sudden left ventricular failure, cerebrovascular haemorrhage and at times even cardiac arrest.[2] These changes are tolerated quite well by healthy patients, however patients suffering from coronary artery disease, hypertension, valvular heart disease, stroke, intracranial lesions, and penetrating eye injuries are not able to withstand them. In these patients, myocardial reserve is decreased and tachycardia associated with laryngoscopy and intubation cause myocardial ischemia.[3]

In principle these responses may be modified by using methods which act locally, centrally or peripherally. Block of sensory receptors and of afferent nerves is accomplished by topical application and infiltration of nerves. Topical surface anaesthetics like Tetracaine (1% to 2%), Lidocaine (4% or 10%), Procaine (4%) have been used.[4-7] Lignocaine hydrochloride has been used in various forms like viscous lignocaine and inhalation of lignocaine prior to induction.[3,5,8] Recent studies, however have questioned the efficacy of lignocaine. Singh et al and Van den Berg et al found intravenous Lignocaine 1.5 mg/kg to be ineffective in controlling the hemodynamic response following intubation.[9,10] Lignocaine is effective in preventing pressor response to tracheal intubation, whatever its route (intravenous or intra-tracheal) but not increase in heart rate.[11]

Central nervous system block is achieved by narcotics like Fentanyl, Alfentanil and Remifentanil.[12-20] These drugs are used for intraoperative analgesia; therefore there is no additional cost involved.

Vasodilator Sodium Nitroprusside have been tried. However, associated hypotension and risk of coronary hypo perfusion are unacceptable.[21] Calcium channel blockers like Verapamil, Diltiazem and Nicardipine proved to be useful in preventing pressor response but not tachycardia.[22] They have antihypertensive, antianginal and antiarrhythmic action. But they cannot be administered safely with volatile anaesthetic agents, beta blockers and in patients having poor left ventricular function. They also potentiate neuromuscular blockade.[22]

Oral clonidine pre-anaesthetic medication 5 µg/kg attenuates pressor response, decreases plasma catecholamines and enhances post-operative analgesia. It is associated with side effects like hypotension, bradycardia, sedation and xerostomia.[23] Gabapentin also attenuate pressor response to laryngoscopy and intubation in a dose of 800 mg tablet given orally 1 hour before surgery.[24] The mechanism by which gabapentin attenuates the pressor response is unidentified.

None of these pharmacological approaches have proved entirely satisfactory for prevention of cardiovascular stress response to laryngoscopy and intubation.

Cardiovascular response to laryngoscopy and intubation is a reflex phenomenon with afferent stimuli carried over both glosso-pharyngeal and vagal pathways which activate suprasegmental and hypothalamic sympathetic centres to cause peripheral sympathoadrenal response with release of adrenaline and nor-adrenaline.

Elevation of blood pressure is associated with nor-epinephrine release whereas changes in heart rate are epinephrine related.[25] Nor-epinephrine levels may increase on laryngoscopy and intubation (from 60 to 310 pg/ml) and continue to rise for 4 to 8 minutes. Epinephrine levels may rise 4 times from 70 to 280 pg/ml; simultaneous endocrine stress is evident by increase in β-endorphins of 15 pg/ml.[26]

Anaesthetists have employed multitude of regimens to block afferent and efferent limbs responsible for hemodynamic responses to intubation of the trachea. Fentanyl in dose greater than or equal to 5 µg/kg has been reported to be effective.[15] However, such dose of fentanyl may lead to excessive sedation, apnoea and chest wall rigidity preoperatively and to nausea, vomiting and respiratory depression postoperatively. While agent such as Esmolol avoids these complications, it has variable effectiveness in recommended doses (100-200 mg). We postulated that 'fentanyl modulation' of nociceptive input and 'Esmolol blockade' of adrenergic receptors should enable their combination to provide effective blunting of the response to intubation, while minimizing the undesirable effects of larger doses of each agent alone.

With this background we conducted a observational study to evaluate the effectiveness of I.V. Esmolol 2 mg/kg versus combination of I.V. Esmolol 2 mg/kg and I.V. Fentanyl 2 µg/kg single bolus dose given 5 minutes prior to induction in attenuating hemodynamic stress response to laryngoscopy and endotracheal intubation

METHODS

This was a prospective, observational, randomized, double blind clinical study conducted at Government Medical College, Aurangabad, during June 2014 to June 2016. The present study was carried out to evaluate and compare effect of intravenous Esmolol versus Esmolol & Fentanyl combination in preventing cardiovascular stress response to intubation. It was conducted on 60 ASA Grade I/II patients (30 in each group) of either sex and of 20 – 45 years age group with weight between 50- 70 kilograms undergoing elective abdominal surgeries under general anesthesia. Pregnant females and patients with known asthma, chronic obstructive pulmonary disease, drug allergy and those with baseline bradycardia, heart block or hypertension were excluded from study. Elderly patients were excluded from the study as most of them were on drugs like antihypertensive, antidepressants etc. which can modify the cardiovascular effects of Esmolol and can affect the pharmacokinetic profile of Fentanyl. Ethical approval was taken from the institutional ethics committee. Patients scheduled for elective abdominal surgeries were thoroughly evaluated and assessed pre-operatively for inclusion into study.

All patients were investigated for hemoglobin, complete blood count, urine analysis, bleeding time, clotting time, liver function test, kidney function test, chest X-Ray and electrocardiogram as appropriate. Other investigations if required were carried out as advised by experienced anesthetist and physician. Patients satisfying inclusion and exclusion criteria were explained about nature of the study in their vernacular language and informed consent was obtained for participation in study from all patients.

The patients were divided randomly into Group-I and Group-II based on medication they received prior to induction.

Group I: Injection Esmolol 2 mg/kg intravenously 5 minutes prior to induction.

Group II: Injection Esmolol 2 mg/kg & Injection Fentanyl 2 µg/kg intravenously 5 minutes prior to induction.

Tablet Diazepam 10 mg was given one night prior and morning 6 am on the day of surgery. Written informed consent was obtained from all patients for surgery. Nil by mouth status was confirmed prior to procedure. Patients were taken on tipping top operation table. Intravenous line was secured with 18 G Angiocath with 500 ml of ringer lactate fluid. Chest leads, NIBP and pulse oximeter were applied for cardiorespiratory monitoring. Heart rate and blood pressure (systolic, diastolic & mean arterial pressure on NIBP) were measured and ECG lead-II and V5 were observed during induction, intubation and surgery. Premedication given with injection Midazolam 0.02 mg/kg 5 minutes prior to induction along with study drugs. Patients were classified in to Group-I and Group-II based on drug they received prior to induction for prevention of cardiovascular stress response (I.V. Esmolol 2 mg/kg or combination of I.V. Esmolol 2 mg/kg & Injection Fentanyl 2 µg/kg). Patient pre-oxygenated with 100% O2 for 5 minutes and induction of anaesthesia was done with Injection Thiopentone Sodium 5mg/kg in 15 sec. Intubation was facilitated with Suxamethonium hydrochloride 2 mg/kg. All these procedures were carried out as routine anaesthesia protocols and no separate interventions were carried out for study purpose.

Laryngoscopy was done by experienced anesthetist who was trained in technique and endotracheal intubation was done. Macintosh 3 laryngoscope blade was used for laryngoscopy. After cuff inflation and confirmation of air entry, patients were maintained on O_2 + N_2O + Halothane + Inj Atracurium (0.5 mg/kg). Heart rate and blood pressure (systolic, diastolic and mean arterial pressure on NIBP) were measured 10 minutes before induction, 5 minutes before induction, during induction, during intubation (0 min), 1 minute, 2 minutes, 5 minutes, and 10 minutes after intubation.

The data was analyzed by using microsoft excel and SPSS software. The heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure at various times in each groups were compared by using Students paired t-test with two-tailed distribution. Unpaired t-test with two-tailed distribution was used as a test of significance when comparing two groups at various time-points. The Chi-square test was used to compare between qualitative data. All values are expressed as Mean± SD.

RESULTS

The data obtained was divided in the following two groups.

- Group I: Injection Esmolol 2 mg/kg and
- Group II: combination of Injection Esmolol 2 mg/kg & Injection Fentanyl

As shown in Table 1 below, mean age of Group-I was 34.50±4.61 years and that of Group-II was 35.57±5.41 years, this difference was statistically not significant (P-0.4147). Similarly, the mean weight of Group-I was 54.93±3.23 kg and that of Group-II was 56.93±5.29 kg. This difference was statistically not significant (P=0.0810). The mean height of Group-I was 156.50±3.09 cm and that of Group-II was 154.70±4.36 cm. this difference was statistically not significant (P=0.1878). The sex was compared with Chi-Square test. Both the groups were comparable in terms of age, sex, weight, height as shown in Table 1.

As shown in Table 2, mean basal heart rate i. e. heart rate 10 minutes before induction in Group I was 85.47±6.86 and in Group II was 85.27±6.40. This difference was statistically not significant (P =0.9075).

Systolic blood pressure 10 minutes before induction in Group I was 122.90±7.58 and in Group II was 121.80±7.29. The difference in the two groups was statistically not significant (P =0.5810). Diastolic blood pressure 10 minutes before induction in Group I was 74.13±4.69 and in Group II was 73.97±3.24. The difference in the two groups was statistically not significant (P =0.8735). Mean arterial pressure 10 minutes before induction in Group I was 90.27±4.59 and in Group II was 88.30±4.19. The difference in the two groups was statistically not significant (P =0.0887).

Thus, at baseline, the heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure in both groups were comparable.

Table 1: Demographic data.

Parameters	Group I	Group II	'P' value
Age # (Years)	34.5±4.61	35.57±5.41	0.4147
Weight # (Kg)	54.93±3.23	56.93±5.29	0.0810
Height # (cm)	156.5±3.09	154.70±4.36	0.1878
Sex χ (M/F)	15/15	15/15	1

- by unpaired Student's t-test. χ - by Chi- Square test.

Table 2: Comparison of baseline hemodynamic parameters.

Parameters	Group I	Group II	'P' value
Heart rate (beats per minute)	85.47±6.86	85.27±6.40	0.9075
Systolic blood pressure (mm of Hg)	122.9±7.58	121.80±7.29	0.5810
Diastolic blood pressure (mm of Hg)	74.13±4.69	73.97±3.24	0.8735
Mean arterial pressure (mm of Hg)	90.27±4.59	88.30±4.19	0.0887

The time required for intubation and duration of surgery in both the groups was comparable (P=0.6232 and P=0.6771 respectively) as shown in Table 3.

From the Table 4a it was observed that there was no significant difference in heart rate after premedication and induction in both groups but at intubation, both groups showed increase in heart rate. Increase in heart rate was more in Esmolol group as compared to Esmolol and Fentanyl group.

Table 4b demonstrates that the maximum change in heart rate was seen in 1 minute post intubation in group I and during intubation (0 min) in group II. The difference between the two groups was statistically significant at 1 and 2 minutes post intubation.

Table 3: Time required for intubation and duration of surgery.

Parameters	Group I	Group II	P value
Time required for intubation (seconds)	11.40±1.88	11.63±1.77	0.6232
Duration of surgery (minutes)	96.63±9.08	97.53±7.49	0.6771

Table 4a: Comparison of heart rate

Time	Heart rate (beats per minute)		'P' value
	Group I	Group II	
10 minutes before induction	85.47±6.86	85.27±6.40	0.9075
5 minutes before induction	84.60±7.21; P = 0.1289	84.30±5.29; P = 0.0627	0.8549
Immediately after induction	85.53±7.32; P = 0.8875	86.20±5.23; P = 0.0971	0.6866
During intubation (0 minute)	91.60±7.09; P <0.0001	90.97±5.28; P <0.0001	0.6964
1 minute post intubation	91.63±7.61; P <0.0001	87.10±6.36; P <0.0001	0.0152
2 minute post intubation	86.70±7.58; P <0.0001	81.40±6.00; P <0.0001	0.0040
5 minute post intubation	82.47±7.47; P <0.0001	79.13±6.09; P <0.0001	0.0633
10 minute post intubation	80.37±7.49; P <0.0001	77.50±5.87; P <0.0001	0.1045
30 minute post intubation	75.73±7.48; P <0.0001	72.70±5.75; P <0.0001	0.0837
60 minute post intubation	72.80±7.15; P <0.0001	71.03±5.02; P <0.0001	0.2731

Table 4b: Comparison of percentage change in heart rate at various time-points with respect to baseline heart rate.

Time	Percentage change in heart rate (%)	
	Group I	Group II
10 minutes before induction	Baseline	Baseline
5 minutes before induction	-1.01	-1.13
immediately after induction	0.08	1.09
during intubation (0 minute)	7.18	6.68
1 minute post intubation	8.31	2.15
2 minute post intubation	1.44	-4.53
5 minute post intubation	-3.51	-7.19
10 minute post intubation	-5.97	-9.11
30 minute post intubation	-11.39	-14.74
60 minute post intubation	-14.82	-16.69

The systolic blood pressure was significantly lower than baseline in both the groups after induction of anesthesia. There was no significant difference in systolic blood pressure after premedication and induction in both groups. However at intubation, both groups showed an increase in systolic blood pressure. The rise in systolic

blood pressure was more in Esmolol group as compared to Esmolol and Fentanyl group. Systolic blood pressure was better controlled by combination of Esmolol and Fentanyl than Esmolol alone, with statistically significantly difference at 0, 01 and 02 minutes post intubation (P =0.0016, P =0.0007, P =0.0211 respectively) as given in Table 5.

Table 5: Comparison of systolic blood pressure.

Time	Systolic blood pressure (mmHg)		'P' value
	Group I	Group II	
10 minutes before induction	122.9±7.58	121.8±7.29	0.5810
5 minutes before induction	121.9±6.58; P = 0.1340	121.0±5.93; P = 0.4244	0.5803
Immediately after induction	122.0±5.94; P <0.0001	110.0±6.67; P <0.0001	0.1311
During intubation (0 minute)	132.7±7.19; P <0.0001	125.9±8.65; P <0.0001	0.0016
1 minute post intubation	129.4±8.20; P <0.0001	120.4±11.21; P <0.0001	0.0007
2 minute post intubation	122.0±8.25; P <0.0001	117.1±7.75; P <0.0001	0.0211
5 minute post intubation	113.3±7.78; P <0.0001	111.5±8.14; P <0.0001	0.3939
10 minute post intubation	105.6±7.53; P <0.0001	102.6±8.05; P <0.0001	0.1372
30 minute post intubation	104.2±7.07; P <0.0001	101.8±6.99; P <0.0001	0.1856
60 minute post intubation	104.1±6.29; P <0.0001	102.1±4.59; P <0.0001	0.1680

Table 6: Comparison of diastolic blood pressure.

Time	Diastolic blood pressure (mmHg)		'P' value
	Group I	Group II	
10 minutes before induction	74.13±4.69	73.97±3.24	0.8735
5 minutes before induction	73.60±3.29; P = 0.3405	74.07±2.99; P = 0.8585	0.5682
Immediately after induction	68.73±2.75; P <0.0001	63.77±3.89; P <0.0001	<0.0001
During intubation (0 minute)	86.97±3.40; P <0.0001	79.00±4.18; P <0.0001	<0.0001
1 minute post intubation	85.33±3.55; P <0.0001	74.90±4.59; P <0.0001	<0.0001
2 minute post intubation	81.13±3.10; P <0.0001	72.33±4.44; P <0.0001	<0.0001
5 minute post intubation	71.97±3.70; P <0.0001	68.03±4.03; P <0.0001	0.0002
10 minute post intubation	66.27±3.89; P <0.0001	64.03±4.13; P <0.0001	0.0354
30 minute post intubation	60.57±3.19; P <0.0001	60.60±2.78; P <0.0001	0.9658
60 minute post intubation	60.97±2.38; P <0.0001	60.33±2.41; P <0.0001	0.3107

Table 7: Comparison of mean arterial pressure.

Time	Mean Arterial Pressure (mmHg)		'P' value
	Group I	Group II	
10 minutes before induction	90.27±4.59	88.30±4.19	0.0887
5 minutes before induction	88.93±3.03; P =0.0161	88.30±3.60; P =1.00	0.4647
Immediately after induction	83.30±2.97; P <0.0001	77.97±4.58; P <0.0001	< 0.0001
During intubation (0 minute)	102.3±3.27; P <0.0001	94.63±4.82; P <0.0001	< 0.0001
1 minute post intubation	100.00±4.62; P <0.0001	90.47±4.93; P <0.0001	< 0.0001
2 minute post intubation	94.77±4.46; P <0.0001	87.23±4.86; P <0.0001	< 0.0001
5 minute post intubation	85.70±4.45; P <0.0001	82.60±4.68; P <0.0001	0.0110
10 minute post intubation	79.43±3.87; P <0.0001	77.03±4.81; P <0.0001	0.0377
30 minute post intubation	75.13±3.56; P <0.0001	74.37±3.23; P <0.0001	0.3868
60 minute post intubation	75.33±2.84; P <0.0001	73.90±2.38; P <0.0001	0.0387

At intubation, both groups showed an increase in diastolic blood pressure. However the rise was attenuated in both groups. The rise was more in Esmolol group as compared to Esmolol and Fentanyl group. Diastolic blood pressure was better controlled by combination of Esmolol and Fentanyl than Esmolol alone, with statistically significantly difference immediately after induction at 00, 01, 02 and 05 minutes post intubation (P <0.0001, P <0.0001, P <0.0001, P =0.0002 respectively). as given in Table 6.

The mean blood pressure was significantly lower than baseline in both the groups after induction of anesthesia and at intubation, both groups showed an increase in mean blood pressure. The rise was more in Esmolol group as compared to Esmolol and Fentanyl group. Mean

blood pressure was better controlled by combination of Esmolol and Fentanyl than Esmolol alone, with statistically significantly difference immediately after induction at 00, 01, 02, 05 and 10 minutes post intubation (P <0.0001, P <0.0001, P <0.0001, P <0.0001, P=0.0110, P=0.0377 respectively) as given in Table 7.

Rate pressure product was also calculated at intubation (0 minute) and in both groups and it was 12169±1320 (Mean±SD) in Esmolol group versus 11439±906.9 in Esmolol and Fentanyl group which was statistically significant (p =0.0154). At 1 minute post- intubation it was 11880±1437 in Esmolol group versus 10485±1188 in Esmolol and Fentanyl group which was statistically significant (p =0.0001). Significant hypertension or hypotension (> 30% change from baseline) was not found in any group at intubation.

Post-operative adverse effects

In this study postoperative nausea and vomiting was developed in two patients (6.67%) of group I and three (10%) patients of group II.

DISCUSSION

Laryngoscopy and endotracheal intubation are known to cause increase in arterial blood pressure, heart rate and may be associated with various dysrhythmias.[1] Deep anaesthesia, Remifentanil, Calcium channel blockers like Verapamil, Nitro-glycerine, Clonidine, Gabapentin, Beta-blockers like Esmolol, etc.[1,20,22,23.27-35] have been tried to prevent cardiovascular response and other serious consequences with varying success but unfortunately none of these pharmacological manipulations can consistently and effectively attenuate these adverse cardiovascular responses, nor are they free from complications.

We conducted a observational study to evaluate the effectiveness of I.V. Esmolol 2 mg/kg versus combination of I.V. Esmolol 2 mg/kg and I.V. Fentanyl 2 µg/kg single bolus dose given 5 minutes prior to induction in attenuating hemodynamic stress response to laryngoscopy and endotracheal intubation.

Injection Midazolam (0.02 mg/kg) was given as pre-medication. We have chosen midazolam (0.02 mg/kg) as a pre-medication agent as it has sedative, anxiolytic properties and has rapid and short duration of action. Patients in both groups were comparable in terms of age, sex, weight and height. Time required for intubation was comparable in both groups (p =0.6232).

Heart rate, systolic, diastolic and mean arterial pressure recorded 10 minutes before induction, 5 minutes before induction, immediately after induction, during intubation (0 minutes) and 01, 02, 05 and 10 minutes post-intubation. Also, 30 and 60 minutes post-intubation readings were taken to know hemodynamic status. King et al, observed the onset of pressor response within 5 to 15 seconds of elevating the epiglottis during laryngoscopy and returning at the end of 5 minutes.[1] Bruder et al observed that the response lasts for 5 to 10 minutes. Hence we monitored the parameters till 10 minutes after intubation.[2]

In our study, there was no significant difference in heart rate 5 minutes before induction and immediately after induction in both groups. The percentage change in heart rate with respect to baseline in Esmolol group was -1.01% and for Esmolol and Fentanyl group was -1.13% at 5 minutes before induction. Immediately after induction it was 0.08% (p =0.1289) in Esmolol group and 1.09% (0.0627) in Esmolol and Fentanyl group. However after intubation there was significant increase in heart rate as compared to baseline in both groups. In Esmolol group the percentage change in heart rate with respect to baseline during intubation was 7.18% (P <0.0001) and in Esmolol and Fentanyl group it was 6.68% (P <0.0001). In Esmolol group this rise in heart rate remained up to 2 minutes post-intubation, reached to baseline between 2 to 5 minutes post-intubation and became significantly lower than baseline after 5 minutes post intubation. In Esmolol and Fentanyl group this rise in heart rate remained up to 1 minute post-intubation, reached to baseline between 1 to 2 minutes post-intubation and became significantly lower than baseline after 2 minutes post intubation (P <0.0001). Bruder et al stated a marked cardiovascular response to laryngoscopy and intubation with increase in heart rate up to 20% without any preservative medication.[2] Thus, Esmolol and combination of Esmolol and Fentanyl significantly attenuated the increase in heart rate during intubation. Though Esmolol group and Esmolol and Fentanyl group attenuated the rise in heart rate; the difference between two groups is statistically not significant (p =0.6964). This difference is statistically significant at 01 (p=0.0152) and 02 (p=0.0040) minutes post-intubation. Sam Chung found 12% change in heart rate in Esmolol group versus 34% in Esmolol and Fentanyl group and difference was statistically significant (p<0.05).[29] Rathore et al found change in mean heart rate immediately after intubation by 11.7 beats/min with 100mg of Esmolol versus 9.5 beats/min with 150 mg of Esmolol.[31] Sheppard et al found changes in mean heart rate immediately after intubation by 5 beats/min with 200mg of Esmolol.[33] Singh et al found change in mean heart rate immediately after intubation by 11.8 beats/min with 0.5 mg of Esmolol.[34] Chung et al interpreted that the combination of low dose Fentanyl (2 µg/kg) and Esmolol (2 mg/kg) is more effective than the same dose of either agent alone in blunting tachycardia and hypertensive response to laryngoscopy and intubation.[29]

None of the patients in both groups had tachycardia, bradycardia or arrhythmia during intubation. Chung et al observed that one patient of Esmolol group and three patients of Esmolol and Fentanyl group experienced a decrease in heart rate to less than 50 beats/min prior to

intubation.[29] However heart rate reached baseline immediately after induction of anesthesia.

Surgery was started after 10 minutes of intubation so further values were not considered in relation to cardiovascular stress response to intubation. 30 minutes and 60 minutes post intubation reading in Group I were -1.39% &14.74% and in Group II were -4.82% & -16.69; showed heart rate being significantly lower than baseline indicating controlled hemodynamic status.

In our study, there was no significant difference in systolic blood pressure 5 minutes before induction and immediately after induction in both groups. The percentage change in systolic blood pressure with respect to baseline in Esmolol group was -0.81% and for Esmolol and Fentanyl group was -0.68% at 5 minutes before induction (p =0.5803). Immediately after induction it was -8.36% in Esmolol group and -9.61% in Esmolol and Fentanyl group which was statistically not significant (p =0.1311). After intubation (0 minutes) in Esmolol group it was 7.98% and in Esmolol and Fentanyl group it was 3.34% which was statistically significant (p =0.0016). Bruder et al stated a marked cardiovascular response to laryngoscopy and intubation with increase in blood pressure up to 40 to 50%without any preventive medication.[2] Thus in our study both groups significantly attenuated the increase in systolic blood pressure during intubation; but Esmolol and Fentanyl combination was significantly more effective than Esmolol alone at 00 minute (p =0.0016) and 01 minute (p =0.0007) post-intubation.

Comparable results were obtained by Chung et al, they recorded maximum percentage change in systolic blood pressure from baseline and it was 24% for Esmolol group versus 20% for Fentanyl group versus for Esmolol and 15% for Fentanyl group.[29] Rathore et al found change in systolic blood pressure from baseline during intubation was 30 mmHg with 100 mg of Esmolol and 21mmHg with 150 mg of Esmolol (p <0.01).[31] Singh et al found 31mmHg increase in systolic blood pressure from baseline during intubation with 2 mg/kg of Esmolol.[34] Chung et al found increase in systolic blood pressure of 15 mmHg from baseline during intubation with 3 µg/kg of Fentanyl.[17]

There was no significant difference in diastolic blood pressure 5 minutes before induction in both groups. The percentage change in diastolic blood pressure with respect to baseline in Esmolol group was -0.72% and for Esmolol and Fentanyl group was -0.14% at 5 minutes before induction which was statistically not significant (p =0.5682). Immediately after induction it was -7.28% in Esmolol group and -13.79% in Esmolol and Fentanyl group which was statistically significant (p <0.0001). After intubation (0 minutes) in Esmolol group it was 17.31% and in Esmolol and Fentanyl group it was 6.80% which was statistically significant (p <0.0001)

Comparable results were obtained by previous investigators in the study of Esmolol and Fentanyl. Chung et al found diastolic blood pressure paralleled changes in systolic blood pressure throughout the study.[29] Singh found 18 mmHg rise in diastolic blood pressure above baseline during intubation with 2 mg/kg Esmolol.[34] Chung et al found 20 mmHg rise in diastolic blood pressure above baseline with 3 µg/kg of Fentanyl.[17]

Difference in mean blood pressure 5 minutes before induction in both groups was not significant. The percentage change in mean blood pressure with respect to baseline in Esmolol group was -1.65% and for Esmolol and Fentanyl group was -0.05% at 5 minutes before induction which was statistically not significant (p =0.4647). Immediately after induction it was -7.77% in Esmolol group and -11.68% in Esmolol and Fentanyl group which was statistically significant (p <0.0001). After intubation (0 minutes) in Esmolol group it was 13.08% and in Esmolol and Fentanyl group it was 7.17% which was statistically significant (p <0.0001). Comparable results were obtained by previous investigators in the study of Esmolol and Fentanyl.

None of the patients in both groups had significant hypertension or hypotension (30% changes with respect to baseline) during intubation. Chung et al, found that one patient of Esmolol group and three patients of Esmolol and Fentanyl group experienced a decrease in heart rate to less than 50 beats/min prior to intubation.[29] However the heart rate reached the baseline immediately after induction of anesthesia. They also experienced apnea in one patient after receiving 5 µg/kg of Fentanyl.

Rate pressure product was also calculated at intubation (0 minute) and in both groups and it was 12169±1320 (Mean±SD)in Esmolol group versus 11439±906.9 in Esmolol and Fentanyl group which was statistically significant (p =0.0154). At 1 minute post- intubation it was 11880±1437 in Esmolol group versus 10485±1188 in Esmolol and Fentanyl group which was statistically significant (p =0.0001).

CONCLUSION

Combination of intravenous Esmolol and intravenous Fentanyl is more effective in attenuating heart rate and blood pressure (systolic, diastolic and mean arterial pressure) response to intubation than intravenous Esmolol alone.

ACKNOWLEDGEMENTS

I solemnly express my gratitude to all my teachers of department of Anaesthesiology, Dr. S.S. Kulkarni, Dr. S. L. Jewalikar, Dr. R. Virshid, Dr. R.V. Bengali, Dr. J. Kulkarni, Dr. Pradeep Raut, Dr. Mukund Parchundekar, Dr. Poornima Sonkamble, and Dr. Samina Khatib for their constant help and encouragement.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. King BD, Harris LC Jr, Griefenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory response to direct laryngoscopy and tracheal intubation. Anaesthesiol. 1951;12:556-66.
2. Bruder N, Ortega D, Granthil C. consequences and prevention methods of hemodynamic changes during laryngoscopy and intratracheal intubation. Ann Fr Anaesth Reanim.1992;11(1):57-71.
3. Slogoff S, Keats AS. Does perioperative myocardial ischemia lead to postoperative myocardial infarction? Anaesthesiol. 1985;62(2):107-8.
4. Stoelting RK. Circulatory response to laryngoscopy and tracheal intubation with or without prior oropharyngeal viscous Lidocaine. Anaesth Analg. 1977;56(5):618-21.
5. Venus B, Polasssani V, Pham CG. Effects of aerosolized Lidocaine on circulatory responses to laryngoscopy and tracheal intubation. Crit Care Med. 1984;12(4):391-4.
6. Sklar BZ, Jurie S, Ezri T, Krichelli D, Savir I, Soroker D. Lidocaine inhalation attenuates the circulatory response to laryngoscopy and endotracheal intubation. J Clin Anaesth. 1992;4(5):382-5.
7. Takita K, Morimoto Y, Kemmotsu O. Tracheal Lidocaine attenuates the cardiovascular response to endotracheal intubation. Can J Anaesth. 2001;48(8):732-6.
8. Mostafa SM, Murthy BV, Barret PJ, McHugh P. Comparison of the effects of topical Lignocaine spray applied before or after induction of anaesthesia on the pressor response to direct laryngoscopy and intubation. Eur J Anaesthesiol. 1999;16(1):7-10.
9. Singh H, Vichitvejpaisal P, Guines AY, White PF. Comparative effects of Lidocaine, Esmolol, and Nitroglycerine in modifying the hemodynamic response to laryngoscopy and intubation. Am J Clin Anaesth. 1995;7(1):5-8.
10. Van den Berg AA, Savva D, Honjol NM. Attenuation of hemodynamic responses to noxious stimuli in patients undergoing cataract surgery: A comparison of Magneshium Sulphate, Esmolol, Lignocaine, Nitroglycerine and Placebo given IV with induction of anaesthesia. Eur J Anaesthesiol. 1997;14(2):134-47.
11. Wilson IG, Meiklejohn BH, Smith G. Intravenous Lignocaine and sympathoadrenal responses to laryngoscopy and intubation: the effect of varying time of injection. Anaesthesia.1991;46(3):177-80.
12. Malde AD, Sarode V. Attenuation of hemodynamic response to endotracheal intubation: Fentanyl versus Lignocaine. Int J Anaesthesiol. 2007;12:1.
13. Seong-Hoon Ko, Dong-Chan Kim, Young-Jin Han, He-Sun Song. Small- Dose Fentanyl: Optimal time of injection for blunting the circulatory responses to tracheal intubation. Anaesth Analg. 1998;86:658-61.
14. Helfman SM, Martin I Gold, Everard A, DeLisser, Claire A, Herrington RN. Which drug prevents tachycardia and hypertension associated with tracheal intubation: Lidocaine, Fentanyl, Esmolol? Anaesth Analg. 1991;72:482-6.
15. Dahlgreen N, Messeter K. Treatment of stress response to laryngoscopy and intubation with Fentanyl. Anaesthesia. 1981;36:1022-6.
16. Kautto UM. Attenuation of circulatory response to laryngoscopy and intubation by Fentanyl. Acta Anaesth Scand. 1982;26:217
17. Chung F, Evans D. Low-dose Fentanyl: hemodynamic response during induction and intubation in geriatric patients. Can Anaesth Soc. 1985;32(6):622-8.
18. Martin DE, Rosenberg H, Aukburg SJ, Bartkowski RR, Edwards MW, Greenhow DE. Low dose Fentanyl blunts circulatory responses to tracheal intubation. Anaesth Analg. 1982;61:680-4.
19. Yushi U, Adachi, Satomoto M, Higuchi H, Watanabe K. Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy. Anaesth Analg. 2002;95:233-7.
20. Maguire AM, Kumar M Parker JL, Rowbotham DJ, Thompson JP. Comparison of effects of Remifentanil and Alfentanil on cardiovascular response to tracheal intubation in hypertensive patients. Br J Anaesth. 2001;86(10):90-3.
21. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with Sodium Nitroprusside. Anaesth Analg. 1979;58:116-24.
22. Wig J, Sharma M, Baichoo N, Agarwal A. Nicardipine and Verapamil attenuate the pressor response to laryngoscopy and intubation. Can J Anaesth. 1994;41(12):1185-8.
23. Kulka PJ, Tryba M, Zenz M, MD. Dose-response effects of intravenous Clonidine in stress response during induction of anaesthesia in coronary artery bypass graft patients. Anaesth Analg. 1995;80:263-8.
24. Kamran M, Parviz K, Azim H, Mohammadreza S, Anahita H. Attenuation of the pressor response to direct laryngoscopy and tracheal intubation: oral Clonidine vs. oral Gabapentin premedication. JRMS. 2011;16:377-86.
25. Takki S, Tammisto T, Nikki P. Effect of laryngoscopy and intubation on plasma catecholamine levels during intravenous induction of anaesthesia. Br J Anaesth. 1972;44:1323-8.
26. Cork RC, Weiss JL, Homerroff SR, Bentley J. Fentanyl preloading in rapid sequence induction of anaesthesia. Anaesth Analg. 1984;63:60-4.

27. Hill AB, Bowley CJ, Nahrwold ML, Knight PR, Kirsh MM, Denliger JK. Intranasal administration of Nitroglycerine. Anaesthesiol. 1981;54:346-8.
28. Koc S, Memis D, Sut D. The preoperative use of Gabapentin, Dexamethasone and their combination in varicocele surgery: A randomized control trial. Anaesth Analg. 2007;105(4):1137-42.
29. Chung KS, Raymond SS, Jonathan DH, Darcy P, David GS. A comparison of Fentanyl, Esmolol, and their combination for blunting the haemodynamic responses during rapid-sequence induction. Can J Anaesht 1992;39(8):774-9.
30. Miller DR, Martineau RJ, Wynands JE, Hill J. Bolus administration of Esmolol for controlling the haemodynamic response to tracheal intubation: the Canadian multicentre trial. Can J Anaesth. 1991;38(7)849-58.
31. Arti Rathore, Gupta HK, Tanwar GL, Rehman H. Attenuation of the pressure response to laryngoscopy and endotracheal intubation with different doses of Esmolol. Indian J Anaesth. 2002;46(6):449-52.
32. Ghaus MS, Singh V, Kumar A, Wahal R. Bhatia VK, Agarwal J. A study of cardiovascular response during laryngoscopy and intubation and their attenuation by ultrashort acting alpha-blocker Esmolol. Indian J Anaesth. 2002;46(2):104-6.
33. Sheppard S, Chris JE. A bolus dose of Esmolol attenuates tachycardia and hypertension after tracheal intubation. Can J Anaesth. 1990;37(2):202-5.
34. Singh SP, Quadir A, Malhotra P. Comparison of Esmolol and Labetalol, in low doses, for attenuation of sympathomimetic response to laryngoscopy and intubation. Saudi J Anaesth. 2010;4(3):163-8.
35. Gupta S, Tank P. A comparative study of efficacy of Esmolol and Fentanyl for pressure attenuation during laryngoscopy and endotracheal intubation. Saudi J Anaesth. 2011;5(1):2-8.
36. Derbyshire DR, Chmielewski A, Fell D, Vater M, Achola K, Smith G. Plasma catecholamine responses to tracheal intubation. 1983;55(9):855-6.
37. Harris CE, Murray AM, Anderson JM, Grounds RM, Morgan M. Effects of Thiopentone, Etomidate and Propofol on the haemodynamic response to tracheal intubation. Anaesthesia. 2007;43(1):32-5.
38. Singhal SK, Neha. Haemodynamic response to laryngoscopy and intubation; Comparison of McCoy and Macintosh laryngoscope. Intern J Anaesth. 2008;17:1.
39. Burnstein CL, Woloshin G, Newman W. Electrocardiographic studies during endotracheal intubation: Effect during anaesthesia and intravenous Procaine. Anaesthesiol. 1950;11:299-14.

Cite this article as: Bhalke R, Karale MS, Deshmukh U. Comparison of esmolol versus combination of esmolol and fentanyl in preventing cardiovascular stress response to intubation. Int J Clin Trials 2017;4(1):49-57.