Original Article

Attenuation of sympathomimetic response to laryngoscopy and intubation: Comparative study of esmolol and labetalol treatment

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Abstract

Background: The sequence of induction of anesthesia, laryngoscopy and tracheal intubation are associated with marked hemodynamic changes and autonomic reflex activity which may be a cause of concern in many high risk patients. It is a sympathetic reflex associated with increase plasma norepinephrine concentration and is not prevented by routine premedication. These changes may lead to a number of complication which include myocardial ischemia/infarction, cardiac failure, intracranial haemorrhage and increase in intracranial pressure. In the present study, the efficacy of intravenous Esmolol and Labetolol for attenuating cardiovascular response following larngoscopy and intubation have been compared and evaluated in normotensive surgical patients. **Aim and objective:** 1.To study rise in heart rate while laryngoscopy and intubation in Esmolol treated group compared to Labetalol treated group. 2. To study rise in SBP, DBP & MAP while laryngoscopy and intubation in Esmolol treated group compared to Labetalol treated group. **Material and methods:** Sixty patients of American Society of Anaesthesiologists (ASA) grade I and II undergoing elective surgical procedure, requiring general anaesthesia were divided into 2 groups, Group A patients (30) were given ESMOLOL 1 mg/kg n & Group B (30 patients) were given LABETOLOL 0.25mg/kg. **Results & Discussion:** There is significant difference among mean pulse rate changes from baseline among two groups up to 15 min after study drug. There was significant difference in mean changes in mean arterial pressure and systolic blood pressure from immediately after intubation up to 15 min post intubation. In diastolic blood pressure there was no significant difference in mean changes between two groups at all points of study, except 3 min after intubation which is an isolated finding. There was no significant difference in spo2 between two groups at all points of study.

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INTRODUCTION

Significant changes in blood pressure, heart rate and variety of cardiac arrhythmias are known to occur during laryngoscopy and tracheal intubation following induction of anaesthesia.[1, 2] It is a sympathetic reflex provoked by stimulation of the epipharynx and larngopharynx associated with increase plasma norepinephrine concentration and is not prevented by routine premedication. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals, but either or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases. These changes may lead to a number of complication which include myocardial ischemia/infarction, cardiac failure, intracranial haemorrhage and increase in intracranial pressure.[3] The method to attenuate the response to the reflex stimulus of laryngoscopy and intubation have included deep anaesthesia with intravenous/inhalational agents[4], reducing the duration of laryngoscopy to less than 15 seconds and administration of drugs like topical/I.V. lignocaine[5], opioids[6], intravenous/topical vasodilators[7],

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adrenergic blockers[8] and calcium blockers[9]. B-blockers have been shown to effectively block these haemodynamic responses. Both Esmolol hydrochloride and Labetalol are emerging as an important class of drugs for attenuating pressure response during direct laryngoscopy and intubation. Esmolol, is a selective short- acting B-adrenergic blocker whereas Labetalol is an adrenergic receptor blocking agent with mild alpha1 and predominant beta-adrenergic receptor blocking actions. In the present study, the efficacy of intravenous Esmolol and Labetolol for attenuating cardiovascular response following larngoscopy and intubation have been compared and evaluated in normotensive surgical patients

MATERIAL AND METHODS

Present study is a prospective, randomized, double blinded, comparative study done among 60 patients in a tertiary care centre. Duration of study was 2 years.

Inclusion Criteria

1. Patients of ASA grade I and II
2. Age between 18-60 years
3. Body weight between 45-90 kgs
4. Any elective surgery of duration of maximum 120 minutes

Exclusion Criteria

1. Age more than 60 years and less than 18 years
2. Body wt more than 90 kg and less than 45 kg
3. Pts on drugs affecting ANS and Pts with history of adverse drug reactions
4. Pts with airway abnormalities or expected difficult intubation and with any cardiovascular disease, respiratory disease, metabolic disease and central nervous system, diseases Pts with intracranial or intraocular pathology.
5. Pregnant patients. Sixty patients of American Society of Anaesthesiologists (ASA) grade I and II undergoing elective surgical procedure, requiring general anaesthesia were divided into 2 groups, Group A patients (30) were given ESMOLOL 1 mg/kg n and Group B (30 patients) were given LABETOLOL 0.25mg/kg.

Preoperative assessment of these patients was done on the previous day of operation. The written informed consent was obtained from all the patients. In laboratory data Hb, RBS, routine urine examination, sr. Creatinine, ECG and CXR were evaluated. Patients were instructed to remain NBM for at least 6 hours before surgery. Written informed consent was obtained from all patients. After securing intravenous line intravenous infusion was started with ringer lactate solution. All the patients were given inj. Glycopyrrolate 4 mcg/kg. Prior to injection of the study drug H.R., S.B.P., M.A.P., D.B.P. were recorded and designated as B- pre induction value. Patients of group A received Esmolol 1 mg/kg diluted to 10 ml 0.9% normal saline was given 2 min prior and group B received Labetolol 0.25 mg/kg 5 min before induction. Patients were induced with propofol 2 mg/kg followed by Succinylcholine 1.5 mg/kg intravenously. Intermittent positive pressure ventilation with 100% O_2 was given and after the onset of complete relaxation, laryngoscopy and tracheal intubation was performed within 30 seconds and anaesthesia was maintained with 50% Nitrous Oxide, 50% Oxygen and sevoflurane via closed circuit using controlled ventilation. Following recovery from Suxamethonium, vecuronium bromide 0.1mg/kg was given intravenously for maintaining muscle relaxation and inhalation anaesthetic agent sevoflurane was continued. Immediately after intubation at 1, 3, 5, 10, 20 and 30 minutes interval H.R., S.B.P., D.B.P, M.A.P., were recorded and designated as follows:

E	-Immediately after intubation
E+1	-One minute post intubation
E+3	-Three minutes post intubation
E+5	-Five minutes post intubation
E+10	-Ten minutes post intubation
E+20	-Twenty minutes post intubation
E+30	- Thirty minutes post intubation

Two anaesthesiologists were involved in the study. One loaded and injected the drug while other noted down the results to prevent observers' bias. Hypotension was defined as SBP < 20% of baseline value or 90 mm of Hg or less. Hypertension was defined as SBP >20 % of baseline value or 150 mm of Hg or more. Tachycardia was defined as HR > 20 % of baseline value Bradycardia was defined as HR < 60 beats per minute. Any patients who required prolonged laryngoscopy or a second attempt at intubation were excluded from the study. The results were obtained and statistically analysed by 't' test.

RESULTS

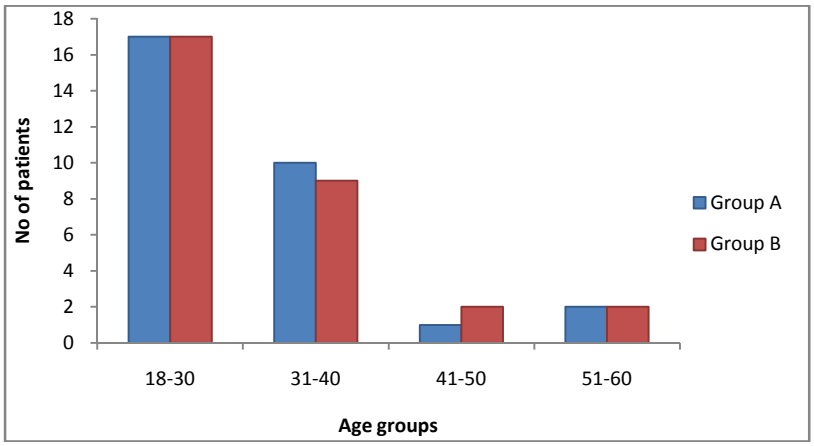

Figure 1: Distribution of patients according to age

Table 1: Comparison of change in mean pulse rate ± SD in two groups

Time of Assessment	Group A		Group B		P Value (comparison between group A and group B)
	Mean	SD	Mean	SD	
Pre anesthetic assessment	92.65	9.67	91.03	10.30	0.74
A-Baseline	101.58	19.94	98.53	14.46	0.57
B- pre induction after study drug	97.20	19.95	87.16	14.76	0.04
E-immediately after intubation	107.13	16.85	91.83	11.56	0.00
E +1- 1 MIN	101.27	16.67	89.4	10.67	0.00
E +3- 3 MIN	98.75	15.62	89.26	12.74	0.01
E +5- 5 MIN	93	15.07	85.03	12.77	0.03
E+10- 10 MIN	91.31	15.09	81.4	9.15	0.00
E+15- 15 MIN	90.03	13.80	82.76	11.68	0.02
E+20- 20 MIN	89.20	12.99	83.26	12.15	0.11
E+30- 30 MIN	87.20	13.15	81.73	8.91	0.09

Table 2: Comparison of change mean in systolic and diastolic blood pressure ± SD in two groups

	Systolic blood pressure					Diastolic blood pressure				
	Group A		Group B		P value	Group A		Group B		P
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	value
Pre anesthetic assessment	119.33	10.37	123	10.55	0.93	77.58	7.86	79.33	6.91	**0.38**
A-Baseline	123.46	22.55	126.2	8.14	0.27	78.13	8.14	80.2	4.21	**0.23**
B- pre induction after study drug	116.8	11.43	117.2	9.09	0.88	74.51	7.72	77.93	5.93	**0.07**
E-immediately after intubation	131.33	9.17	120.86	10.35	0.00	79.72	7.81	76.53	6.49	**0.08**
E +1- 1min	134.13	7.31	122.13	6.62	0.00	78.13	7.85	75.4	6.39	**0.13**
E +3- 3min	124.6	6.81	110.7	7.22	0.00	76	6.96	72.66	5.01	**0.02**
E +5- 5min	116.5	6.78	110.6	7.01	0.00	73.17	7.20	71.2	3.46	**0.15**
E+10- 10 min	114.73	8.50	107.06	8.39	0.00	72	7.72	70.26	4.29	**0.30**
E+15- 15 min	110.2	20.11	105.13	8.16	0.01	72	5.85	69.8	4.18	**0.10**
E+20- 20 min	110.4	7.93	108.46	7.45	0.33	72.48	4.97	71.13	3.81	**0.17**
E+30- 30 min	110.26	7.89	107.46	7.66	0.16	72.41	5.10	70.93	3.92	**0.15**

Table 3: Comparison of change in mean arterial pressure ± SD in two groups

Mean blood pressure	Group A		Group B		P Value
	Mean	±SD	Mean	±SD	
Pre anesthetic assessment	91.49	8.45	93.88	7.58	0.26
A-Baseline	93.05	8.57	95.53	4.82	0.21
B- pre induction after study drug	88.39	8.75	91.02	5.81	0.23
E-immediately after intubation	96.75	5.24	92.55	5.44	0.00
E +1- 1MIN	96.78	6.36	92.8	3.86	0.00

E +3- 3MIN	92.13	5.74	85.35	5.09	0.00
E +5- 5MIN	87.58	6.75	84.35	4.22	0.02
E+10- 10 MIN	86.18	7.64	82.53	4.94	0.02
E+15- 15 MIN	84.73	6.25	81.57	4.94	0.03
E+20- 20 MIN	89.20	12.99	83.26	12.15	0.11
E+30- 30 MIN	87.20	13.15	81.73	8.91	0.09

Table 4: Comparison of change in mean SPO2 ± SD from the baseline value in two groups

SPO_2	Group A		Group B		P value
	Mean	±SD	Mean	±SD	
Pre-anesthetic	99.89	0.40	99.66	0.66	0.10
A-Basaline	99.93	0.25	99.86	0.62	0.59
B-after study drug	99.96	0.32	99.93	0.44	0.74
E-immediately after intubation	99.16	0.37	99.06	0.36	0.30
E+1 MIN	99.06	0.63	99.06	0.25	1
E+3 MINS	99.36	0.48	99.2	0.40	0.76
E+5 MINS	99.13	0.43	99	0.52	0.28
E+10 MINS	99.27	0.45	99.1	0.40	0.13
E+15 MINS	99.24	0.43	99.06	0.44	0.09
E+20 MINS	99.10	0.40	99.80	0.55	0.21
E+30 MINS	99.1	0.30	99	0.26	0.17

In group A the minimum age was 18 years and maximum age was 55 years with a mean age of 29.46 ±10.20 yrs. In group B the minimum age was 18 years and maximum age was 60 years with a mean age of 30.47 ±11.42 yrs. In group A there were 11 males and 19 females. In group B there were 16 males and 14 females. Table no 1showed that there is significant difference among mean pulse rate changes from baseline among two groups up to 15 min after study drug. The difference being statistically not significant at pre-anesthetic and base line value. (p >0.05) The difference being statistically very highly significant at intubation (p=0.00013) and 1 min (p= 0.0019) and highly significant at 3 min (p = 0.0146) and 5 min post intubation (p= 0.0366) At 10^{th} min heart rate was again significantly lower in Labetalol group than in Esmolol group (p = 0.0036) Table no 2 shows comparison of two groups with regard to mean change in systolic blood pressure ± SD and diastolic blood pressure ± SD from base line value, at various time intervals. The preanesthetic and basal values were comparable between the two groups. In systolic blood pressure P<0.05 shows that there is significant difference among mean changes from baseline among two groups from immediately after intubation to 15 min after study drug. In diastolic blood pressure P value > 0.05 showed that there was no significant difference in mean changes between two groups at all points of study, except 3 min after intubation which is an isolated finding. Table 3 shows comparison of two groups with regard to mean arterial pressure ± SD from baseline value, at various time intervals. P value < 0.05 showed that there was significant difference in mean changes in mean arterial pressure from immediately after intubation up to 15 min post intubation. Table 4 showed no significant difference in spo2 between two groups at all points of study.

DISCUSSION

Two groups were comparable with respect to age. This helped us to judge the clinical significance of our study. The distribution, metabolism, excretion and action of drugs vary according to different age groups. Therefore, clinically insignificant variation in age helped us to alleviate these confounding factors. Pulse rate in Labetalol group was lower than Esmolol group at all time after giving study drug. In a similar study conducted by Singh *et al*[10] there was no significant effect of Esmolol on pulse rate when compared to the placebo group. Labetalol had a significantly (P<0.05) better effect than Esmolol in controlling pulse rate at all points during their study. Our study is supported by Kim *et al*.[11] who reported that a single dose of Labetalol of dosage 0.25 mg/kg given preoperatively 5 min before intubation decreases HR significantly after intubation up to 10 min. Roelofse *et al*[1] found that Labetalol of dosage 1 mg/kg given as an IV bolus 1 min before laryngoscopy was not effective in the attenuation of HR. This failure of the study can be explained by the different time of administration of the study drug because Labetalol has peak effect after 5-10 min. In systolic blood pressure P<0.05 shows that there is significant difference among mean changes from baseline among two groups from immediately after intubation to 15 min after study drug. In the study conducted by Singh *et al*, [10] Esmolol was completely ineffective in preventing the increases in SBP as there was no significant difference between values of Esmolol and placebo groups during the study period (P>0.05). Labetalol prevented the

increase in SBP significantly throughout the study period as compared to placebo and Esmolol groups (P<0.05). Ramanathan *et al.*[13] used 20 mg Labetalol and observed that it prevent rise in SBP successfully. Inada *et al.*[14] found 10 mg (0.14 mg/kg) Labetalol ineffective in attenuating the rise in systolic pressure. This difference might be because of the lower dose they used and the timing of giving of Labetalol (2 min prior to intubation) because of which the peak effect of drug was lost at intubation. Maharaj *et al.*[15] failed to blunt the blood pressure response with 0.25 and 0.5 mg/kg Labetalol. However, they did not mention the timing of giving the drug. After giving study drug, diastolic blood pressure reduced in both the groups but the difference was not statistically significant (p=0.07). In the study conducted by Singh *et al*[10], in intergroup comparison of Esmolol and Labetalol, none of them was found to be better (P>0.05) for controlling diastolic blood pressure, both showed equal decrease in DBP MAP was significantly lower in the Labetalol group at intubation (p =0.002), at 1 min (p = 0.003), at 3 min (p = 0.000), 5 min (p = 0.024), 10 min (p =0.029) and 15 min (p = 0.035) which is significant. In the study of Singh *et al*, Where the Labetalol group was compared with the placebo group, the MAP was significantly less at all points (P<0.05) except at 10 min post intubation when the values were comparable. Our study correlate well with studies of Sharma *et al*[16] and Bakiye *et al*[17] who reported that compared to the placebo groups Esmolol group had a significantly less MAP at intubation although Esmolol was not at all effective in controlling MAP after laryngoscopy and intubation.

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