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Original Research Article

Attenuation of cardiovascular response during laryngoscopy and intubation: A comparative study of I.V Esmolol and labetalol

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Abstract
Introduction: Laryngoscopy and endotracheal intubation causes reflex responses in the cardiovascular system which leads to changes in the blood pressure, heart rate and sometimes arrhythmia. These responses are of short duration and may be of little consequence in young healthy patients but can be detrimental to patients with hypertension, coronary artery disease, raised intracranial pressure, cerebral aneurysm and bronchial asthma.
Materials and Methods: A prospective study conducted at Department of Anaesthesiology in a Tertiary care teaching hospital from March 2019 to October 2019. 80 patients of age group 18- 60 years belonging to ASA Grade I and II of either sex posted for elective surgeries of various surgical units requiring endotracheal intubation under general anaesthesia were considered for study in a randomised single blinded manner. They were divided into 2 groups consisting of 40 patients each.
Group I(E): Received I.V Esmolol Hydrochloride 0.5mg/kg diluted to 10 ml with normal saline.
Group II(L): Received i.v Labetalol Hydrochloride 0.25mg/kg diluted to 10 ml with normal saline.
Result: In the esmolol group the initial mean heart rate of 85.52±7.72 increased to 107.35± 10.35 at intubation and 109.65± 10.03 at 1 minute and then decreased to 101.2±5.10, 96.52±6.14, 93.27±4.03, 87±6.20 at 3,5,10 and 15 minute interval respectively. In the labetalol group the initial heart rate was 85.37±11.62 which increased to 97.47±12.92 at intubation and 99.35±12.92 at 1 minute. It gradually decreased to 91.45±9.84, 85.97±7.78, 76.4±9.15, 80.2±7.93 at 3, 5, 10 and 15 minute interval respectively.
Conclusion: Labetalol was better than esmolol in attenuating the increase in heart rate and systolic blood pressure. Both Labetolol and Esmolol were ineffective in attenuating the increase in diastolic blood pressure. Labetalol was superior to Esmolol in suppressing the magnitude and duration of haemodynamic response to laryngoscopy and intubation as evident from the changes in rate pressure product.

Keywords: Laryngoscopy, esmolol, labetalol

Introduction

When the speciality of anaesthesiology was in its infancy, inhalational anaesthetics were the sole agents to induce and maintain anaesthesia associated with many problems [1]. In an attempt to achieve adequate muscle relaxation for better surgical access in the absence of any muscle relaxant, the patients had to be brought down to a very deep level of anaesthesia with its attendant problems like cardio-respiratory depression, loss of protective reflexes in maintaining a secured airway, extending over into the post-operative period [2]. However awareness and non-suppression of sympathetic activity in response to various stimulations were not the problem. Then came the era of modern day “balanced" anaesthesia. Induction of anaesthesia became rapid with intravenous agents, and muscle relaxation was also possible and complete with muscle relaxants. This required control of airway and ventilation. For that endotracheal intubation with the help of laryngoscope was essential [3].

Laryngoscopy and endotracheal intubation causes reflex responses in the cardiovascular system which leads to changes in the blood pressure, heart rate and sometimes arrhythmia [4]. These responses are of short duration and may be of little consequence in young healthy patients but can be detrimental to patients with hypertension, coronary artery disease, raised intracranial pressure, cerebral aneurysm and bronchial asthma [5]. Many pharmacological agents and techniques have been used to attenuate these haemodynamic response to laryngoscopy and endotracheal intubation, including minimizing the duration of laryngoscopy to less than 5 seconds, topical and intravenous lignocaine, intravenous opoids (fentanyl, Sufentanil, Alfentanil), deep inhalational anaesthesia [6].

Alpha and beta adrenergic blocker (clonidine, dexmedetomidine) vasodilators (sodium nitroprusside, nitroglycerine and nifedipine) etc. [7]. But no single method has gained widespread acceptance because of their advantages and disadvantages. Studies are still being carried out with revaluation of older ones. Keeping this in mind, an attempt was made to observe the effect of esmolol hydrochloride and labetalol on haemodynamic response to laryngoscopy and endotracheal intubation.

Materials and Methods

A prospective study conducted at Department of Anaesthesiology in a Tertiary care teaching hospital from March 2019 to October 2019. 80 patients of age group 18-60 years belonging to ASA Grade I and II of either sex posted for elective surgeries of various surgical units requiring endotracheal intubation under general anaesthesia were considered for study in a randomised single blinded manner.

Exclusion criteria

Patents having diabetes, any endocrinal disease, hypertension, under treatment with beta blocker, known hypersensitivity to the drugs, any cardiovascular disease were excluded from the study.

Those patients requiring laryngoscopy and intubation for more than 30 seconds were excluded from the study.

They were divided into 2 groups consisting of 40 patients each,

Group I(E): received i.v Esmolol Hydrochloride 0.5mg/kg diluted to 10 ml with normal saline.

Group II(L): received i.v Labetalol Hydrochloride 0.25mg/kg diluted to 10 ml with normal saline.

Pre-operative assessment

All the patients were examined before operation to assess the condition of patients. All routine investigations like haemogram, examination of urine and stool, blood urea and serum creatinine, blood sugar, cardiological evaluation, ECG, X ray chest etc. were done. Abnormalities detected were appropriately treated and the suitability of patients to undergo surgery under anaesthesia was assessed.

Anaesthetic Procedure

All patients were premedicated with Tab Diazepam 10 mg orally at bed time on the previous night of surgery and advised to remain nil per orally after midnight. On the day of operation, intravenous line secured with a 18 G cannula and Lactated ringer's solution started at 75ml/hr. Patients were premedicated with inj. Glycopyronium Bromide 0.2 mg i.v, inj. Midazolam Hydrochloride 0.02 mg/kg, inj. Butorphanol Tartarate 0.03 mg/kg i.v. On arrival in the operation theatre, standard monitors connected and continuous monitoring of SPO_2, HR, NIBP, ECG and parameters were noted at different time intervals. Any abnormalities in ECG were observed. Rate Pressure product was calculated (SBP × HR) till 15 minutes of laryngoscopy and intubation.

Induction and Intubation

Study drug I (Esmolol), Preoxygenation was done with 100% oxygen for 3 minutes. Study drug I was given over 2 minutes. Then Inj. thiopentone sodium was given 5mg/kg or sleep dose (till loss of eye lash reflex) followed by inj. Succinylcholine chloride 1.5 mg/kg. IPPV was continued. Intubation was performed with a cuffed endotracheal tube of appropriate size after visualisation of the laryngeal inlet under direct laryngoscopy with a Macintosh laryngoscope.

Study drug II (Labetalol), Preoxygenation was done with 100% oxygen for 3 minutes. Study drug II (labetalol) was given over 2 minutes. Inj. thiopentone sodium was given 5mg/kg or sleep dose (till loss of eye lash reflex) followed by inj. Succinylcholine chloride 1.5 mg/kg. IPPV was continued. Intubation was performed with a cuffed endotracheal tube of appropriate size after visualisation of the laryngeal inlet under direct laryngoscopy with a Macintosh laryngoscope.

Result

Table 1: Age distribution of patients in the present study

	Group I		Group II	
Age in yrs	**No**	**%**	**No**	**%**
30 – 39	21	52.5	17	42.5
40--49	14	35	16	40
50 - 59	5	12.5	7	17.5

The age distribution of both groups were comparable (p>0.05)

Table 2: Sex distribution of patients in the present study

	Group I		Group II	
Sex	**No**	**%**	**No**	**%**
Male	22	55	20	50
Female	18	45	20	50

The sex distribution of both groups were comparable (p>0.05)

Table 3: Distribution of weight of the patients in the present study

	Group I		Group II	
Body Wt(kg)	**No**	**%**	**No**	**%**
45 - 50	12	30	16	40
51 - 55	14	35	8	20
56 - 60	12	30	12	30
61-65	2	5	0	0

The weight distribution of both groups were comparable (p>0.05)

Table 4A: Heart rate at different time intervals in the two groups before and after intubation

Groups	1	2	3	4	5	6	7
I – Esmolol (mean±SD)	85.52±7.72	107.35±10.35	109.65±10.03	101.2±5.10	96.52±6.14	93.27±4.30	87.17±6.20
II – Labetalol (mean±SD)	85.37±11.62	97.47±12.92	99.35±12.60	91.45±9.84	85.97±7.78	76.4±9.15	80.2±7.93

In the esmolol group the initial mean heart rate of 85.52±7.72 increased to 107.35± 10.35 at intubation and 109.65± 10.03 at 1 minute and then decreased to 101.2±5.10, 96.52±6.14, 93.27±4.03, 87±6.20 at 3,5,10 and 15 minute interval respectively.

In the labetalol group the initial heart rate was 85.37±11.62 which increased to 97.47±12.92 at intubation and 99.35±12.92 at 1 minute. It gradually decreased to 91.45±9.84, 85.97±7.78, 76.4±9.15, 80.2±7.93 at 3, 5, 10 and 15 minute interval respectively.

Table 4B: Heart rate per minute of various time intervals before and after intubation in patients of both groups (intra group comparison)

Comparison	'p' value(Group – I)	'p' value(Group – II)
1 vs 2	0.2	0.94
1 vs 3	0.09	0.91
1 vs 4	0.2	0.89
1 vs 5	0.04	0.83
1 vs 6	0.14	0.70
1 vs 7	0.31	0.70

The mean rise in heart rate was not significant (p>0.05) at intubation and throughout the study period in both the groups

Table 4C: Mean heart rate observed at various time interval in the two groups before and after intubation (inter group comparison)

Time of observation		Groups(Esmolol vs Labetalol)
1	'p' value	>0.05
2	'p' value	<0.001**
3	'p' value	<0.001**
4	'p' value	<0.001**
5	'p' value	<0.001**
6	'p' value	<0.001**
7	'p' value	<0.001**

The mean heart rate was significantly lower in labetalol group at all-time intervals.

Table 5A: Systolic blood pressure (mm Hg) at different time interval in the two groups before and after intubation

Groups	1	2	3	4	5	6	7
I – esmolol (mean±SD)	120.87±8.70	152.92±15.20	158.2±14.35	138.12±13.45	127.17±12.44	121.6±11.08	120.12±8.63
II –labetalol (mean±SD)	126.27±10.34	140.92±11.84	139.3±10.98	125.4±11.66	117.62±10.95	113.07±11.07	114.25±10.87

In the esmolol group the initial mean systolic blood pressure (in mm Hg) of 120.87±8.70 increased to 152.92±15.20 at intubation and 158.2±14.35 at 1 minute interval and then decreased to 138.12±13.45, 127.17±12.44, 121.6±11.08, 120.12±8.63 at 3,5,10 and 15 minute interval respectively.

In the labetalol group the initial mean systolic blood pressure (in mm Hg) was 126.27±10.34 which increased to 140.92±11.84 at intubation and decreased to 139.3±10.98 at 1 minute.

It gradually decreased to 125.4±11.66, 117.625±10.95, 113.07±11.07, 114.25±10.87 at 3, 5, 10 and 15 minute interval respectively.

Table 5B: Significance of mean difference in systolic blood pressure (mm Hg) at various time interval before and after intubation in patients of both groups (intra comparison)

Comparision	'p' value(Group-I)	'p' value(Group-II)
1 vs 2	0.69	0.86
1 vs 3	0.60	0.75
1 vs 4	0.48	0.51
1 vs 5	0.58	0.47
1 vs 6	0.7	0.40
1 vs 7	0.7	0.40

The mean rise in systolic blood pressure was not significant (p>0.05) throughout the study period in both the groups.

Table 5C: Systolic blood pressure (mm Hg) observed at various intervals in the two groups before and after intubation (inter group comparison)

Time of observation		Groups (Esmolol vs Labetalol)
1	'p' value	>0.05
2	'p' value	<0.001**
3	'p' value	<0.001**
4	'p' value	<0.001**
5	'p' value	<0.001**
6	'p' value	<0.001**
7	'p' value	<0.001**

The mean systolic blood pressure was significantly lower in labetalol group at all time intervals.

Table 6A: Diastolic blood pressure (mm Hg) at different time interval in the two groups before and after intubation

Groups	1	2	3	4	5	6	7
I – Esmolol mean±SD	79.2±4.72	98.6±8.74	94.85±10.62	87.2±8.74	82.77±6.43	78.92±6.12	79.17±5.22
II – labetalol mean±SD	81.2±7.8	100.5±11.55	97.67±11.26	90.25±7.55	83.1±8.09	77.07±8.18	79.05±7.74

In the esmolol group the initial mean diastolic blood pressure (in mm Hg) of 79.2±4.72 increased to 98.6±8.74 at intubation and decreased to 94.85±10.62 at 1 minute interval and then decreased to 87.2±8.74, 82.77±6.43, 78.92±6.12, 79.17±5.22 at 3,5,10 and 15 minute interval respectively.

In the labetalol group the initial mean diastolic blood pressure (in mm Hg) was 81.2±7.8 which increased to 100.5±11.55 at intubation and decreased to 97.67±11.26 at 1 minute. It gradually decreased to 90.25±7.55, 83.1±8.09, 77.07±8.18, 79.05±7.04 at 3, 5, 10, and minute interval respectively.

Table 6B: Diastolic blood pressure (mm Hg) at various time interval before and after intubation in both groups (intra group)

Comparision	'p' value-Group I	'p' value-Group II
1 vs 2	0.19	0.39
1 vs 3	0.13	0.41
1 vs 4	0.13	0.55
1 vs 5	0.21	0.57
1 vs 6	0.29	0.57
1 vs 7	0.56	0.57

Mean change in diastolic blood pressure was not significant (p>0.05) at intubation, and throughout the study period in both the groups

Table 6C: Diastolic blood pressure (mm Hg) observed at various intervals in the two groups before and after intubation

Time of observation		Groups (Esmolol vs Labetalol)
1	'p' value	>0.05
2	'p' value	>0.05
3	'p' value	>0.05
4	'p' value	>0.05
5	'p' value	>0.05
6	'p' value	>0.05
7	'p' value	>0.05

The mean diastolic blood pressure was comparable in both groups at all time intervals (p>0.05).

Table 7A: Mean blood pressure (mm Hg) at different time interval in the two groups before and after intubation

Groups	1	2	3	4	5	6	7
I – esmolol mean±SD	92.75±5.31	116.32±9.57	115.9±10.29	104±7.10	97.6±5.83	93.07±5.70	92.77±5.57
II – labetalol mean±SD	96.02±7.97	113.95±11.45	111.5±10.92	102±8.26	94.55±7.79	89.1±7.79	90.77±6.99

In the esmolol group the initial mean of mean blood pressure (in mm Hg) of 92.75±5.31 increased to 116.32±9.57 at intubation and decreased to 115.9±10.29 at 1 minute interval and then decreased to 104±7.10, 97.6±5.83, 93.07±5.70, 92.77±5.57 at 3,5,10 and 15 minute interval respectively.

In the labetalol group the initial mean of mean blood pressure (in mm Hg) was 96.02±7.97 which increased to 113.95±11.45 at intubation and decreased to 111.5±10.92 at 1 minute. It gradually decreased to 102±8.26, 94.55±7.79, 89.1±7.67, 90.77±6.99 at 3, 5, 10 and 15 minute interval respectively.

Table 7B: Significance at mean difference in mean blood pressure (mm Hg) at various time intervals before and after intubation in both groups (intra group comparison)

Comparision	'p' value-Group I	'p' value-Group II
1 vs 2	0.51	0.61
1 vs 3	0.47	0.57
1 vs 4	0.36	0.61
1 vs 5	0.36	0.58
1 vs 6	0.29	0.53
1 vs 7	0.78	0.56

The mean rise in mean blood pressure was not significant (p>0.05) at intubation and throughout the study period in both groups

Table 7C: Statistical comparison (between groups) of the corresponding mean of mean blood pressure (mm Hg) observed at various interval in the two groups before and after intubation

Time of observation		Groups (Esmolol vs Labetalol)
1	'p' value	>0.05
2	'p' value	>0.05
3	'p' value	>0.05
4	'p' value	>0.05
5	'p' value	>0.05
6	'p' value	<0.05
7	'p' value	>0.05

The mean diastolic blood pressure was comparable in both groups at all time intervals except at 10 minutes where it is statistically lower in labetalol

Table 8A: Rate pressure product at different time interval in the two groups before and after intubation

Groups	1	2	3	4	5	6	7
I – Esmolol mean±SD	10340±1200	16252±2280	17130±2610	14066±1204	12286±1522	11345±1191	10488±1217
II – Labetalol mean±SD	10726±1354	13689±1850	13813±1901	11453±1511	10111±1288	8607±1069	9134±1003

In the esmolol group the initial mean rate pressure product (in mm Hg) of 10340.93±1200.99 increased to 16252.43±2280.96 at intubation and 17130.25±2610.01 at 1 minute interval and then decreased to 14066.4±1204.612, 12286.58±1522.88, 11345.65±1191.35, 10488.45±1217.63 at 3,5,10 and 15 minute interval respectively.

In the labetalol group the initial mean rate pressure product (in mm Hg) was 10726.8±1354.64 which increased to 13689.93±1850.62 at intubation and 13813.55±1901.17 at 1 minute. It gradually decreased to 11453.28±1511.37, 10111.23±1288.99, 8607.02±1069.44, 9134.47±1003.97 at 3, 5, 10 and 15 minute interval respectively.

Table 8B: Rate pressure product at various time intervals before and after intubation in both groups (intra group comparison)

Comparision	'p' value –Group I	'p' value-Group II
1 vs 2	0.54	0.87
1 vs 3	0.46	0.77
1 vs 4	0.25	0.69
1 vs 5	0.21	0.59
1 vs 6	0.37	0.64
1 vs 7	0.51	0.61

The mean rise in rate pressure product was not significant (p>0.05) at intubation and throughout the study period in both the groups

Table 8C: Rate pressure product observed at various interval in the two groups before and after intubation (intergroup comparison)

Time of observation		Groups (Esmolol vs Labetalol)
1	'p' value	>0.05
2	'p' value	<0.001
3	'p' value	<0.001
4	'p' value	<0.001
5	'p' value	<0.001
6	'p' value	<0.001
7	'p' value	<0.001

The mean pressure product was comparable at preintubation in both groups and lower in labetalol group (p< 0.05) at all time intervals

Discussion

Intubation has become the main stay of modern anaesthesia for maintenance of good airway, prevention of aspiration, predictable delivery of FiO_2, elimination of carbon dioxide etc. It has been observed that laryngoscopy and endotracheal intubation lead to reflex cardiovascular stimulation produce an increase in heart rate and systemic blood pressure. These changes are due to an increase in sympathetic discharge via cardio accelerator fibres [8].

The reflex cardio acceleration during laryngoscopy occurs due to laryngoscope blade pressing on the base of tongue and raising the epiglottis. The afferent fibres of the reflex are through the sensory fibres of the vagus and efferent is traveling through the cervical sympathetic nerves [9].

The increased sympathetic activity caused by stimulation of upper respiratory tract has been supported by the observation that, increases in arterial pressure during endotracheal intubation is associated with an increase in plasma noradrenaline level (Russel W. J. 81). The initial rise in the heart rate and blood pressureare due to laryngoscopy and later slightly greater due to intubation [10].

After intubation there is gradual return of blood pressure and heart rate to prelaryngoscopic value. Various methods have been tried to attenuate these symptoms in high risk patients. These methods include deepening the plane of anaesthesia (King B.D.; 1951), topical anaesthesia of laryngopharynx and epiglottis (Delinger JK,1974), fentanyl and alfentanyl (Black TE, 1884), produced significant attenuation of cardiovascular response during intubation. [11] However, studies comparing esmolol (cardio selective beta blocker) and labetalol (mixed adrenergic blocker) are lacking. Considering the average time of the hemodynamic changes to last for about 15 min of laryngoscopy and intubation the study was undertaken over that time period [12].

Labetalol (II) had a significantly (P<0.05) better effect than esmolol (I) in controlling PR at all points in the study. Possibly labetalol maintains the PRs within normal ranges during process of laryngoscopy and intubation. When the effect of stimulus wear off, as occurs at 10 min postintubation, the drug's effect takes over and pulse rates go below baseline values. My study corroborates with the findings of Suman Shree *et al.* 2003 [13].

Esmolol (I) was completely ineffective as there was no significant difference between it and labetalol (II) during the study period (p > 0.05). Labetalol (II) prevented the increase in SBP significantly throughout the study period as compared to esmolol (II) groups (P<0.05). Ramanathan *et al.* used 20 mg labetalol to prevent rise in SBP successfully [14].

Inada *et al.* 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 [15].

Maharaj *et al.* failed to blunt the blood pressure response with 0.25 and 0.5 mg/kg labetalol [16]. However, they did not mention the timing of giving the drug. Esmolol even in doses exceeding >1mg/kg have been found to be ineffective in controlling systolic pressure rise. Our study corroborates with the findings of Kumar *et al.* 2003 [17]. However Rathore *et al.* successfully suppressed the SBP response even at doses of 50 mg [18].

The rise in DBP was not attenuated (P> 0.05) in any of the study groups. In intergroup comparison of esmolol and labetalol, none of them was found to be better (P > 0.05). My findings corroborates with that of Taneja B *et al.*, 2003 [19].

Between esmolol (I) and labetalol (II) there was no significant difference in values except at 10 min postintubation (labetalol having lower MAPs). This observation was again an isolated finding and no significant difference (P>0.05) was found at any other point of time during the study period.

Compared to esmolol (I) group, the labetalol (II) group had significantly lower values of RPP but even Labetalol could not prevent the increase in RPP completely. However, the magnitude of increase was less and never crossed the critical limit of 15000 mmHg /min. The values returned to baseline at 5 min postintubation as compared to esmolol (II) group where they achieved baseline values after 15 min. Therefore, labetalol (0.25 mg/kg) decreases the magnitude and duration of hemodynamic response to laryngoscopy as evident from the changes of RPP. Our findings corroborates with that of Leslie *et al.*, who used labetalol in doses of 0.25, 0.5, 0.75 and 1.0 mg/kg and found all doses effective in controlling the rise in RPP at laryngoscopy and intubation [20]. Rathore *et al.* 2002 showed esmolol(at doses of 50 mg) is ineffective in decreasing the rate pressure product [21].

The only side effect observed was that of labetalol in form of bradycardia, intraoperatively. Only two patients developed bradycardia (pulse rate <50 beats per minute) after the study period of 15 min and were managed with atropine in 0.2 mg increments (max. 0.01 mg/kg). There were no recurrent episodes of bradycardia. No abnormal ECG changes were recorded during the period of induction and intubation.

Conclusion

On comparing Labetalol (at doses of 0.25 mg/kg) and Esmolol (at doses of 0.5 mg/kg) for attenuation of cardiovascular response to laryngoscopy and intubation, the following conclusions were drawn from this study: Labetalol was better than esmolol in attenuating the increase in heart rate and systolic blood pressure. Both Labetolol and Esmolol were ineffective in attenuating the increase in diastolic blood pressure. Labetalol was superior to Esmolol in suppressing the magnitude and duration of haemodynamic response to laryngoscopy and intubation as evident from the changes in rate pressure product.

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