Original Research Article

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Comparative Study between Esmolol and Xylocard for Attenuation of Pressor Responses during Laryngoscopy and Intubation

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Abstract

Background: Cardiovascular complications are one of the most common causes of anesthesia-related morbidity and mortality.The present work was undertaken to compare the effect of lignocaine (Xylocard) with esmolol on blunting the hemodynamic responses to endotracheal intubation.

Methods: Laryngoscopy and intubation was done within 15 to 20 seconds.In group I: Inj. Lignocaine (Xylocard) i.v. was administered 3 minutes before laryngoscopy and intubation.In group II: Inj. Esmolol i.v. was administered 3 minutes before laryngoscopy and intubation. Changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were measured before induction of general anesthesia (baseline), 1, 3, and 5 min after tracheal intubation.

Results: The heart rate response between lignocaine (Xylocard) and esmolol was very significant at all times starting from 1 to 10 minutes ($p \leq 0.05$) with esmolol showing a favorable response towards attenuation of heart rate. In systolic blood pressure, Esmolol group showed a better attenuation compared to lignocaine group (Xylocard) until 3 minutes post-laryngoscopy. Attenuation of diastolic blood pressure was significant with esmolol than with lignocaine (Xylocard) group until 3 minutes ($p<0.05$). In mean arterial pressure, Esmolol caused significant attenuation of pressor response ($p<0.05$) at 1 minute and 3 minute post-laryngoscopy.

Conclusion: Esmolol is more efficient than lignocaine (Xylocard) in attenuating the sympathetic responses to laryngoscopy and intubation.Esmolol at a bolus dose of 1.5 mg/kg i.v. administered 3 minutes before laryngoscopy appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

Keywords: Esmolol; Xylocard; Laryngoscopy; Intubation; Hemodynamic; Bangalore.

Introduction

Cardiovascular complications are one of the most common causes of anesthesia-related morbidity and mortality. Pressor response during laryngoscopy and endotracheal intubation has been known from years. These responses though transient, will be tolerated by normal individuals, but can be potentially harmful in those individuals with cardiovascular compromise. In patients with IHD, HTN or cerebrovascular insufficiency there is increased risk of subarachnoid haemorrhage, arrhythmias and cardiac failure in response to intubation. Laryngoscopy and tracheal intubation induces changes in circulating catecholamine levels. Norepinephrine, epinephrine and dopamine levels rise, but the rise in norepinephrine levels is consistently associated with elevation of blood pressure and heart rate [1-5].

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Perioperative myocardial infarction is a leading cause of postoperative morbidity and mortality due to hypertension and tachycardia. Such anesthesia-related deaths could be reduced by controlling the hemodynamic changes that occur due to myocardial ischemia. There is increasing evidence that the control of the heart rate and blood pressure response to endotracheal intubation is essential in preventing adverse cardiovascular outcomes, as rate pressure product (RPP) acts as an indicator of oxygen demand by the heart at the onset of ischemia, there is therefore a need for assessment in this direction as there are currently no available studies in the Indian population on the efficacy of lidocaine and esmolol in attenuating hemodynamic responses during intubation.

Many strategies have been advocated to minimize these haemodynamic adverse responses to laryngoscopy and tracheal intubation at different levels of the reflex are [6] Block of the peripheral sensory receptors and afferent input – topical application and infiltration of local anaesthetic to superior laryngeal nerve; Block of central mechanisms of integration and sensory input – Fentanyl and morphine. The present work was undertaken to compare the effect of lignocaine (Xylocard) withesmolol on blunting the hemodynamic responses to endotracheal intubation.

Material and Methods

A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 50 patients posted for elective surgeries. Study was conducted in St. Martha's Hospital, Bangalore from 2015 to 2016. Institutional committee approved our study protocol. Informed consent was taken from enrolled patients. Patients undergoing various orthopedic, ENT, gynecological, general surgical and laparoscopic procedures were selected. The study criterion includes: Patients scheduled for elective surgeries; Age between 18 to 60 years of both the sexes; Patients with ASA grade I and II; Mallampati airway assessment of grade I and excludes: Emergency surgeries; Patients of anticipated difficult intubation; Patients with ASA grade III or higher; Patients with cardiovascular compromise; Patients on beta blockers or calcium blockers.

Presurgical Protocol

Patients were selected after thorough preanaesthetic assessment and investigations. 50 patients were randomly allocated into one of the two study groups containing 25 each.

Group I: patients received 1.5 mg/kg lignocaine intravenously 3 minutes before laryngoscopy and intubation.

Group II: patients received 1.5 mg/kg esmolol intravenously 3 minutes before laryngoscopy and intubation.

The following routine investigations done in enrolled patients: complete blood count, ESR, Random Blood Sugar, Blood urea, serum creatinine, Bleeding time and Clotting time, Urine, albumin, sugar and microscopy, X-ray chest and PA view, ECG. All the patients were visited the day before surgery and preanaesthetic counseling was done. All patients received tab Alprazolam 0.5 mg orally at night the previous day and the morning of surgery. On entering the operation theatre, pulse oximeter, non-invasive blood pressure and ECG monitor were connected. A preinduction heart rate, systolic and diastolic blood pressures were recorded, i.v. infusion of ringer lactate solution was started.

Surgical Protocol

All patients were preoxygenated 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 anaesthesia (loss of eyelash reflex), heart rate, systolic and diastolic blood pressures were recorded. Inj. Succinylcholine was administered at a dose of 1.5 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 pressures were recorded at 1, 3, 5, and 10 minutes interval from the onset of laryngoscopy. In group I: Inj. Lignocaine (Xylocard) i.v. was administered 3 minutes before laryngoscopy and intubation. In group II: Inj. Esmolol i.v. was administered 3 minutes before laryngoscopy and intubation. Patients were connected to Bain's circuit and anaesthesia was maintained with oxygen (33%), nitrous oxide (67%), halothane (0.5%) and non-depolarizing muscle relaxant vecuronium bromide at a dose of 0.05 mg/kg i.v. and IPPV. Adequacy of ventilation was monitored with $ETCO_2$ and SpO_2 maintained at 99-100%. Positioning, epinephrine infiltration 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 anaesthesia related problems were attended to appropriately.

Statistical Analysis

All the collected data was tabulated. Statistical analysis was done by student *t*-test and *P* values were calculated. Hemodynamic variables were represented by mean±SD. The comparison between the lignocaine (Xylocard) and esmolol groups are compared using Student's Independent sample (unpaired) "t" test. The difference is considered statistically significant, whenever $p \leq 0.05$ at all-time points measured. The statistical software used for analysis was SPSS. V. 15.0.

Results

Demographic profile related to age, sex and weight was comparable in the two groups statistically ($p>0.05$). Analysis by student unpaired "t" test showed that there was no significant difference in heart rate at pre and post-induction levels between lignocaine and esmolol groups (p=0.844, p=0.319). The heart rate response between lignocaine (Xylocard) and esmolol was very significant at all times starting from 1 to 10 minutes ($p \leq 0.05$) with esmolol showing a favorable response towards attenuation of heart rate. In systolic blood pressure, Esmolol group showed a better attenuation compared to lignocaine group (Xylocard) until 3 minutes post-laryngoscopy.

At 5, 7 and 10 minutes there was no significant difference between the two groups statistically. Attenuation of diastolic blood pressure was significant with esmolol than with lignocaine (Xylocard) group until 3 minutes ($p<0.05$). In mean arterial pressure, Esmolol caused significant attenuation of pressor response ($p<0.05$) at 1 minute and 3 minute post-laryngoscopy.

Discussion

Laryngoscopy and intubation is associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias. Variations of heart rate changes decrease with increasing age. Young patients show more extreme changes [7]. Marked fluctuations in haemodynamic responses are often seen in geriatric patients [8,9]. In our study, we selected the age range of 18 to 60 years. There was no significant difference between lignocaine (Xylocard) and esmolol groups ($p>0.05$). There was no significant difference observed in sexwise distribution of the cases between lignocaine (Xylocard) and esmolol group. The most significant laryngoscopic factor influencing cardiovascular responses is found to be the duration of laryngoscopy [7]. A linear increase in heart rate and mean arterial pressure during the first 45 seconds has been observed. Further prolongation has little effect. In our study, the duration of laryngoscopy and intubation was limited to 20 seconds.Adequate care was taken to achieve the required depth of anaesthesia avoiding hypoxia and hypercarbia which can influence the haemodynamic variations.

Analysis of Heart Rate

Lignocaine (Xylocard) group, the mean heart rate and standard duration at preinduction were 79.16±5.47. After induction, there was an increase of 3.2% with the mean of 81.76±5.95. At 1 minute from the onset of laryngoscopy, the heart rate increasedto 104.64±6.93 with an increase of 32% from preinduction values. At 3 minutes, heart rate was observed to be 101.64±10.05. Subsequently, the mean heart rate decreased is 91.12±7.21 (15%) and 86.36±5.92 (9%) at 5 and 7 minutes respectively. At the end of 10 minutes, hear t rate was 81.60±4.42 which was 3% above the baseline at preinduction [Table 2].

In esmolol group, the mean preinduction heart rate in this group was 79±5.66. Post-induction heart rate increased by 4.5% to 82.6±5.9. There was a further increase by 22.8% at 1 minute post laryngoscopy with a mean value of 96.96±9.96. A small fall in heart rate was observed at 3 minutes with a mean of 95.48±10.14. Heart rate further declined from the 5^{th} minute with a mean of 89.02±6.22 and further to 83.7±5.6 and 80.32±3.96 at 7^{th} and 10^{th} minutes respectively. Analysis by student unpaired "t" test showed that there was no significant difference in heart rate at pre and post-induction levels between lignocaine and esmolol groups (p=0.844, p=0.319). The heart rate response between lignocaine (Xylocard) and esmolol was very significant at all times starting from 1 to 10 minutes ($p\leq 0.05$) with esmolol showing a favorable response towards attenuation of heart rate. Intravenous lignocaine failed to attenuate the cardiovascular responses to laryngoscopy and intubation in a study by Miller CS and Warren SJ, its efficacy was noted by others [10-3]. It is recommended to use at a dose of 1.5 to 2 mg/kg i.v. optimal time for administration is 3 minutes before laryngoscopy and intubation [12].

Analysis of Systolic Blood Pressure

Lignocaine (Xylocard) group, preinduction systolic blood pressure was 131.2±12.76. At post-induction there was only 1% fall in systolic blood pressure with a mean of 129.8±12.26. There was 15% increase in systolic blood pressure following 1 minute after laryngoscopy with a mean value of 151.84±13.75 [Table 2]. The systolic blood pressure started to decrease at 3 minutes with the mean of 149.8±15.03. It further decreased till the end of 10 minutes to 2% below the baseline systolic blood pressure with a mean value of 128.44±12.02. Esmolol group, preinduction systolic blood pressure was 129.88±11.65. At post-induction, there was a fall in systolic blood pressure by 2.3%. There was 9.5% increase in systolic blood pressure following 1 minute after laryngoscopy with a mean value of 133.8±11.3. Systolic blood pressure increased slightly with a mean of 134.32±10.02 at 3 minutes post-laryngoscopy. From there on the systolic blood pressure started to

Table 1: Type of Surgery involved

Type of Surgery	Lignocaine	Esmolol	Total
Diagnostic lap	1	2	3
Exostosis excision	-	1	1
FESS	1	2	3
Fibroadenoma excision	-	1	1
Fibroadenoma excision	1	-	1
GJ pyloroplasty	-	1	1
Hemithyroidectomy	1	1	2
Hernia repair	-	1	1
Hysterectomy	1	1	2
I and D cold abscess	-	1	1
Ileocaecal mass excision	-	1	1
Laminectomy	2	1	3
Lap appendicectomy	1	-	1
Lap cholecystectomy	1	1	2
Lap cystectomy	1	1	2
Lap mesh repair	1	-	1
Laparotomy	2	-	2
Lymph node excision	1	-	1
Mastoidectomy	3	3	6
Myringoplasty	-	1	1
ORIF & DCP	1	-	1
ORIF & plating	1	-	1
ORIF internal fixation	-	1	1
Plating & bone graft	1	-	1
Septoplasty	1	-	1
Split skin graft	-	1	1
SSG	1	-	1
Submandibular gl. Exc.	1	-	1
Tension band wiring	-	1	1
Thyroidectomy	-	1	1
TO mass excision	1	-	1
Tonsillectomy	1	1	2
Vagotomy & GJ	-	1	1
Total	25	25	50

Table 2: Comparison between Lignocaine and Esmolol group of heart rate

HR	Lignocaine			Esmolol			t value	p value
	Mean	SD	% difference	Mean	SD	% difference		
Pre-induction	79.16	5.47	-	79.00	5.66	-	0.198	0.844
Post-induction	81.76	5.95	3.2	82.60	5.90	4.5	1.007	0.319
1 minute	104.64	6.93	32	96.96	9.96	22.8	8.598	0.000
3 minutes	101.64	10.05	28	95.48	10.14	20.7	5.388	0.000
5 minutes	91.12	7.21	15	89.02	6.22	12.7	2.513	0.015
7 minutes	86.36	5.92	9	83.70	5.60	6	3.789	0.000
10 minutes	81.60	4.42	3	80.32	3.96	1.67	2.392	0.021

Table 3: Comparison between lignocaine and Esmolol group of SBP

SBP	Lignocaine			Esmolol			t value	p value
	Mean	SD	% difference	Mean	SD	% difference		
Pre-induction	131.20	12.76	-	129.88	11.65	-	0.382	0.704
Post-induction	129.80	12.26	1	125.28	11.13	-2.3	1.365	0.179
1 minute	151.84	13.75	15	133.80	11.30	9.5	5.068	0.000
3 minutes	149.80	15.03	14	134.32	10.02	8.9	4.284	0.000
5 minutes	135.68	11.40	3	132.72	9.77	2.8	0.986	0.329
7 minutes	130.72	11.76	-0.3	130.44	9.69	-0.3	0.092	0.927
10 minutes	128.44	12.02	-2	129.80	10.02	-1.1	0.435	0.666

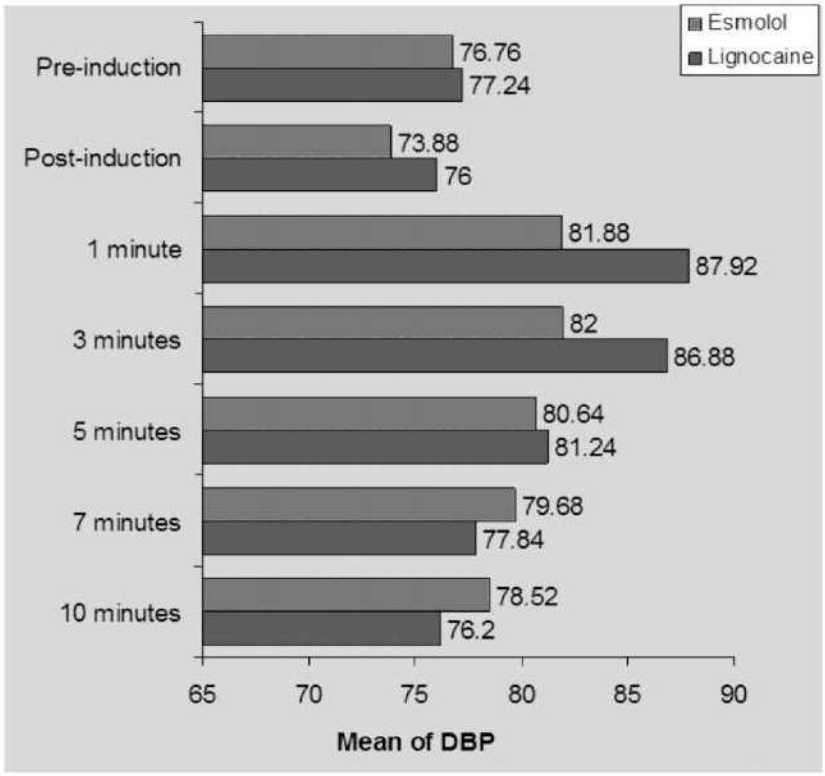

Fig. 1: Comparison between lignocaine and Esmolol group of DBP

fall with a mean of 132.72±9.77 at 5 minutes and 130.44±9.69 at 7 minutes. At 10 minutes post-laryngoscopy the systolic blood pressure almost returned to baseline with a mean value of 129.8±10.02. Esmolol group showed a better attenuation compared to lignocaine group (Xylocard) until 3 minutes post-laryngoscopy. At 5, 7 and 10 minutes there was no significant difference between the two groups statistically. Previous studies have shown that the unique pharmacokinetic behavior of esmolol makes it well suited for controlling the cardiovascular responses to tracheal intubation when used as continuous infusion technique [14-16].

A single alternative is using a bolus doses of esmolol and many studies have investigated this and concluded it to be efficacious [17-20].

Analysis of Diastolic Blood Pressure

Lignocaine (Xylocard) group, Mean preinduction diastolic blood pressure in this group was found to be 77.24±5.83. A decrease by 1.6% to 76±5.74 was noted after induction. It increased by 13% to 87.92±4.53 at 1 minute after laryngoscopy. It came down to 86.88±4.53 at 3 minutes and continued to fall at 5 and 7 minutes to 81.24±3.53 and 77.84±3.82 respectively [Figure 1]. By the end of 10 minutes the diastolic blood pressure was 76.20±4.82, a 1.3% below the baseline.

In Esmolol group,Diastolic blood pressure in this group before induction was 76.76±5.86. After induction 2.77% fall to 73.88±4.7 was noted. An increase by 9% to 8.2±4.65 at 1 minute post laryngoscopy was noted. Diastolic blood pressure started to decrease at 5 minutes to 80.64±4.88 and at 7 minutes to 79.68±4.55. At the end of 10 minutes, it was 0.5% above the baseline with a mean of

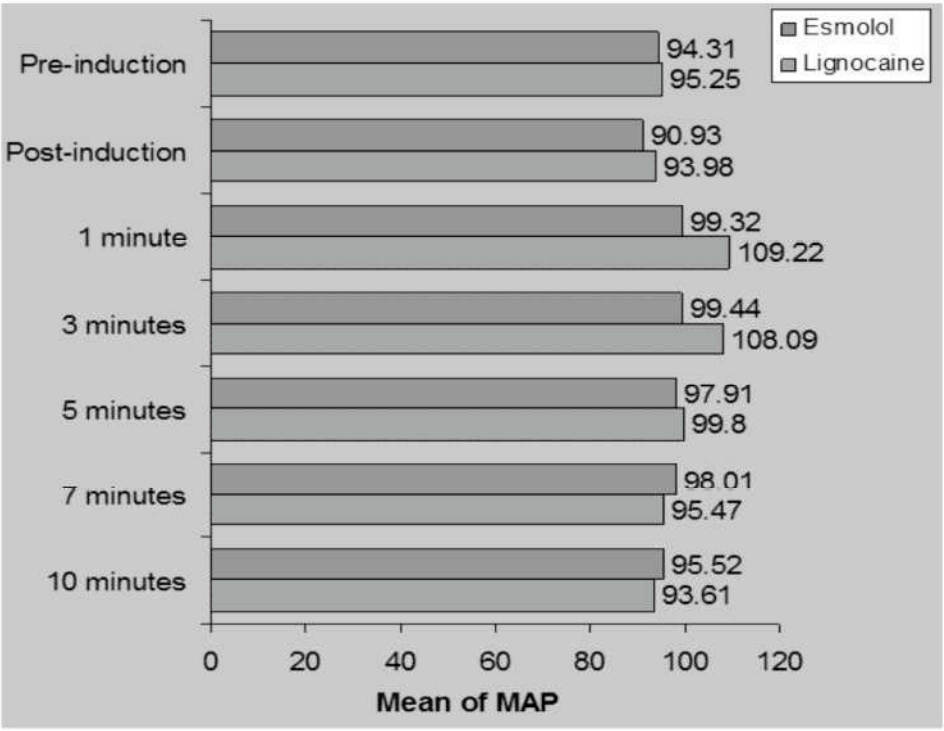

Fig. 2: Comparison between lignocaine and Esmolol group of MAP

78.52±3.99.Among the two study groups esmolol showed a better attenuation of diastolic blood pressure compared to lignocaine (Xylocard) till 3 minutes post-laryngoscopy.

Analysis of Mean Arterial Pressure

In Lignocaine (Xylocard) group, Preinduction mean value in this group was 95.25±7.08. Post-induction fall was 1.3% to 93.98±6.64. There was an increase by 14.6% to 109.22±6.26 at 1 minute and marginal fall is 108.09±7.92 at 3 minutes.

It decreased further over 5, 7 and 10 minutes [Figure 2]. At 10 minutes post-laryngoscopy, it showed a decrease of 1.7% below the baseline to 93.61±6.11. In Esmolol group, Preinduction mean arterial blood pressure was 94.31±6.24 in this group. There was an increase by 10.4% to 99.32±5.72 at 1 minute post-laryngoscopy. It started to decrease at 3 minutes to 99.44±5.28 and 5 and 7 minutes being 97.91±5.25 and 98.01±9.99 respectively. At 10 minutes, post-laryngoscopy it was 0.2% below the baseline to 95.52±4.89.

Esmolol caused significant attenuation of pressor response ($p<0.05$) at 1 minute and 3 minute post-laryngoscopy. Efficacy of intravenous lignocaine 1.5 mg/kg and two doses of esmolol 1mg/kg and 2 mg/kg for attenuating the cardiovascular responses to laryngoscopy and intubation was evaluated by Kindler et al. They found that esmolol 1 to 2 mg/kg was reliably effective in attenuating the hemodynamics response [18]. In our study, we have used 1.5 mg/kg i.v. bolus of esmolol.

Conclusion

Intravenous Lignocaine (Xylocard) and esmolol are effective agents significantly attenuates the sympathetic responses to laryngoscopy and tracheal intubation without any deleterious effect. Esmolol is more efficient than lignocaine (Xylocard) in attenuating the sympathetic responses to laryngoscopy and intubation. Esmolol at a bolus dose of 1.5 mg/kg i.v. administered 3 minutes before laryngoscopy appears to be very effective and should be viewed as potential treatment strategy for attenuating hemodynamic changes during induction of anesthesia.

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