Original Research Paper

Volume - 12 | Issue - 10 | October - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Emergency Medicine

A COMPARATIVE STUDY BETWEEN EFFICACY OF INTRAVENOUS ESMOLOL AND INTRAVENOUS LIGNOCAINE FOR ATTENUATING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A PROSPECTIVE RANDOMIZED NON BLINDED COMPARATIVE CLINICAL STUDY.

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KEYWORDS :

INTRODUCTION

Endotracheal intubation and laryngoscopy are very essential tools in the hands of anesthesiologist in maintaining the airway. Laryngoscopy and Endotracheal intubation can cause striking changes in hemodynamics[1-3].

These changes are characterized by elevation in systolic and diastolic pressure and heart rate there by increases the myocardial oxygen demand within five seconds of laryngoscopy which further increases during insertion of the endotracheal tube into the trachea. Increase in heart rate, and blood pressure occurs most commonly from reflex sympathetic stimulation in response to laryngotrachel stimulation, which in turn leads to increased plasma Norepinephrine concentration[4] Average rise in systemic blood pressure is about 25 – 50 mm of Hg. A plateau at or about this peak pressure is maintained for 1 – 2 minutes followed by gradual return to pre – laryngoscopic BP within five minutes. These reflexes are of little significance in healthy patients but may be fatal in patients with Hypertension, Coronary artery disease, Valvular heart diseases, Myocardial ischemia, Thyrotoxicosis, Cerebrovascular disease, Intracranial aneurysm, the effect of these hemodynamic changes can evoke life threatening conditions[5,6].

Tachycardia and Hypertension associated with laryngoscopy and Endotracheal intubation should be prevented to maintain the delicate balance between myocardial oxygen supply and demand during induction of general anesthesia. Many attempts have been made in modifying the hemodynamic responses e.g. premedication, deep anesthesia, topical anesthesia. Numerous agents like Opiods, Calcium channel blockers, Magnesium sulphate and Local anesthetics have been used to blunt the stress response[7-9]. Several studies have looked at the efficacy of Lignocaine [10-12] and Esmolol[13,14,19,21,23,24] to blunt the hemodynamic response to Laryngoscopy and Endotracheal intubation. And other agents like Nitroglyserine[15] low dose Fentanyl[17,22] Propofol, Clonidine and Gabapentine[18] have also been used to blunt the stress response.

In this backdrop we considered it worthwhile to undertake a study to compare the efficacy of intravenous Lignocaine and intravenous Esmolol for attenuating pressor response to laryngoscopy and endotracheal intubation in patients undergoing elective neurosurgeries in terms of attenuating Heart rate, Systolic blood pressure, Diastolic pressure, Mean blood pressure, Pulse pressure, Rate pressure product.

MATERIALS AND METHODS

With the an aim to ascertain the effectiveness of Esmolol (1.5ml/kg IV bolus administered 3 minutes before laryngoscopy and endotracheal intubation) and Lignocaine (1.5 ml/kg 3 minutes before laryngoscopy and endotrachel intubaton) in suppressing the sympathetic response to laryngoscopy and endotracheal intubation. After obtaining approval from hospital scientific and ethics committee, and written informed consent, 60 patients who met all inclusion criteria and non of exclusion criteria were enrolled in this study.

The primary objective of the study is to compare the effect on sympathetic response measured through monitoring heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, systemic pulse pressure and rate pressure product.

The study population includes patients of either sex, ASA grade I-II, in age group between 25-65 years, all patients posted for elective neurosurgical procedures who undergone laryngoscopic intubation were included in this study. The study was conducted in Prospective, Randomized, Controlled, Non blinded manner at in-patients of Department of Neurosurgery,Seven Hills hospital, Visakhapatnam between July 2015- July 2016. Patients were randomly categorized into either of the study groups *Group.A*-was given Esmolol 1.5mg/kg diluted to a total volume of 20ml with normal saline (0.9%) i.v. slowly. *Group.B* -was given Lignocaine 1.5mg/kg in the volume of 10ml (with distilled water) i.v. without any bias using a computer based software program.

Inclusion Criteria:

1.Patients of either sex.
2.Age between 25-65 years.
3.Patients with ASA grade I-II.
4.Patients scheduled for elective neurosurgeries.

Exclusion Criteria:

1.Emergency surgeries.
2.Anticipated difficult intubation.
3.Intubation time more than 20sec.
4.More than one attempt of intubation.
5.Patients with ASA grade III or higher.
6.Patients on Beta blockers or Calcium channel blockers.
7.Patients with Asthma and Heart blocks.
8.Patients with history of allergy to Lignocaine and Esmolol.

Randomization was done according to computer based software (www.graphpad.com) and patients have been allocated either Group A or Group B.

Patients were advised absolute fasting for a period of at least 8hours. All the patients were pre medicated with tablet Alprazolam 0.5mg and tablet Ranitidine 150 mg night before and on the morning of surgery. In the operation room after establishing IV access, monitors such as Heart rate, Electrocardiography, Noninvasive blood pressure, Pulse oximetry, and Respiratory rate were connected. Invasive monitoring such as radial artery cannulation was performed under local anesthesia. Base line parameters i.e. heart rate (HR), systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial pressure(MAP) were recorded before administration of test drugs.

All patients were pre oxygenated for 3 minutes; and premedicated with inj. Midazolam 0.03 mg/kg, Glycopyrrolate 10µg/kg, Fentanyl 2 µg/kg. Precalculated doses of Esmolol and Lignocaine has given intravenously slowly in group A and B respectively, followed by induction of anesthesia with Thiopental sodium 2.5% , 5mg/kg in incremental doses. Plane of anesthesia was assessed by loss of eyelash reflex.

Neuromuscular blockade was achieved by injection Vecuronium bromide 0.15 mg/kg. After 3 minutes, intubation completed with appropriate sized cuffed endotracheal tube by a single operator in all the cases. Total duration of laryngoscopy was noted. Patients whose total duration of laryngoscopy more than 20 seconds were excluded from the study.

Anesthesia was maintained with 66% nitrous oxide in oxygen (O 2 : N 2 O: 33:66), Sevoflurane, intermittent boluses of injection Vecuronium and Fentanyl. Ventilation was adjusted to maintain an end-tidal carbon dioxide (ETCO 2) value between 30 and 35 mmHg. The ETCO 2 values were kept between 30 and 35 in cases with probability of increased ICP secondary to their pathology. After completion of surgery, neuromuscular blockade was reversed with injection Neostigmine 40 µg/kg and injection Glycopyrrolate 10 µg/kg and patients were extubated.

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded before study drug administration, after study drug administration, after induction and 1, 2, 3, 5, 7, 10 minutes after Endotracheal intubation.

From the time of Pre induction, Post induction (Pre-laryngoscopy & intubation), and from the onset of Laryngoscopy & Intubation for 1, 3, 5, 7 and 10 minutes. heart rate, systolic and diastolic BP, Mean BP, systemic pulse pressure, rate pressure product.

Pharmacology

Esmolol hydrochloride is a beta – selective (cardio selective) adrenergic receptor blocking agent with rapid onset of action, short duration of action, nad no intrinsic sympathomimetic or membrane stabilizing activity at therapeutic doses. Esmolol inhibits the beta one receptors located chiefly in the cardiac muscle, but at 40 -100 fold higher doses it also inhibits beta 2 recptors chiefly in the bronchial and vascular musculature respectively.

Lignocaine stabilises the neuronal membrane and prevents the initiation and transmission of nerve impulses, thereby effecting local anaesthetic action. The onset of action is rapid and the blockade may last from 1 to 1.5 hours.

Data Analysis

Statistical analysis was performed using Microsoft excel 2007.Data was collected from the study proformas, tabulated, coded and analysed. Demographic data was analyzed by using chisquare test and independent samples Kruskal-Wallis test. Hemodynamic characters were analyzed by using independent students t' test. Incidence of complications were analyzed by using one-way ANOVA test. Data was reported as a mean value+/-standard deviation. A P value of <0.05 was considered statistically significant(s) between two groups.

Observations

All the patients participated throughout the study. There was no significant difference in the demographic characteristics between two groups. Table 1 illustrates the distribution, percentage mean age and sex distribution in the two groups, which was found to be comparable.

Table 1: Mean Distribution Of Age And Sex In Two Groups

Age (years)	Group A	Group B
25-35	3(10%)	4(13.33%)
36-45	11(36.67%)	7(23.33%)
46-55	10(33.33%)	13(43.33%)
56-65	6(20%)	6(20%)
Total	30(100%)	30(100%)
Mean ± SD	46.93±8.94	48.07±9.27
Female	11(36.67%)	12(40%)
Male	19(63.33%)	18(60%)

The mean heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, systemic pulse pressure and rate pressure product is significantly lower in the group A after study drug administration, post induction, post intubation 1 minute, 5 minutes. There was no significant difference in mean heart rate at other time points as shown in table 2,3 and 4.

DISCUSSIONS

A diversity of results exists about protective measures against hemodynamic and catecholamine response to laryngoscopy and intubation, but no single anesthetic technique has become generally accepted as being effective in preventing or attenuating these responses.[19] Many techniques have been recommended. The drugs used were either partially effective or had other undesirable effects on the patients.[20] Topical application of local anesthetics, infiltration or nerve blocks [21] beta blockers, calcium channel blockers, clonidine, sodium nitroprusside, lignocaine, fentanyl etc. are being used. No single drug or technique is satisficatory.

Some studies note a response of intravenous lignocaine in blunting rise in pulse, blood pressure, intracranial and intraocular pressure. Yukioka et al[14] showed that cough reflex was suppressed completely by IV lignocaine and also minimizes blood pressure fluctuations after tracheal intubation.

Table 2: Showing Changes In Heart Rate, Systolic Blood Pressure And Diastolic Blood Pressure At Various Time Intervals

Time Interval	HR			SBP			DBP		
	Group A	Group B	P value	Group A	Group B	P value	Group A	Group B	P value
Before study drug administration	79.17±9.12	82.93±8.62	0.105	125.13±8.50	127.4±7.22	0.270	75.53±7.15	76.6±6.08	0.536
After study drug administration	66.07±7.23	81.43±10.82	<0.0001	114.67±7.30	127.8±5.49	<0.0001	63.8±6.06	76.87±5.79	<0.0001
Post induction	64.73±6.31	80.40±7.83	<0.0001	102.33±6.08	117.73±6.25	<0.0001	61.6±4.31	66.07±5.26	0.0007
Post intubation 1 minute	98.67±8.09	117.67±6.62	<0.0001	126.47±6.49	124.07±5.88	0.138	84.93±6.70	78.53±7.21	0.0008
3 minutes	78.53±9.46	82.47±10.14	0.125	112.93±6.92	116±6.49	0.082	75.93±5.81	77.33±5.85	0.356
5 minutes	65.4±5.09	74.87±6.90	<0.0001	111.4±6.28	113.27±5.21	0.215	66.4±4.18	64.73±3.12	0.085
7 minutes	64.87±5.47	67.53±6.12	0.080	112.47±5.42	113.6±4.73	0.392	65.33±3.37	64.33±2.92	0.225
10 minutes	68.07±4.08	70±6.66	0.180	111.67±4.20	112.87±4.05	0.265	66.33±4.07	66.87±3.58	0.592

Previous studies also have shown that unique pharmacokinetic behavior of esmolol makes it well suited for controlling the cardiovascular response to tracheal intubation when used as a continuous infusion technique.[22] A simple alternative is using bolus doses of esmolol and many studies have investigated this and concluded it to be efficatious in attenuating the cardiovascular response to laryngoscopy and tracheal intubation.[23] In studies conducted before , 2mg/kg IV bolus esmolol injected prior to induction has been effective in attenuating cardiovascular response to laryngoscopy and intubation. Optimal time of administration is 3 minutes before laryngoscopy and intubation.[24] Esmolol also prevented the bispectral index during induction of anesthesia and orotracheal intubation.

Table 3: Showing Changes In Mean Arterial Pressure, Pulse Pressure And Rate Pressure Product At Various Time Intervals

Time Interval	MAP			PP			RPP		
	Group A	Group B	P value	Group A	Group B	P value	Group A	Group B	P value
Before study drug administration	92.06±6.65	93.52±6.21	0.382	49.6±7.90	50.8±3.88	0.458	9935.2±1485.6	10547.7±1102.4	0.074
After study drug administration	80.75±5.75	93.84±4.88	<0.0001	51.13±6.51	50.93±6.20	0.903	7591.8±1089	10425.1±1577	<0.0001
Post induction	75.17±4.11	83.26±4.63	<0.0001	41.06±6.05	51.73±6.68	<0.0001	6646.2±950.5	9396.4±1236.1	<0.0001
Post intubation 1 minute	98.77±4.68	93.71±4.97	0.0002	42.06±9.28	45.6±9.84	0.158	12466.2±1037.1	14585.4±917.5	<0.0001
3 minutes	88.29±5.07	90.22±5.26	0.153	37.33±7.48	38.67±6.41	0.462	8882.2±1298.8	9553.8±1188.4	0.041
5 minutes	81.39±4.06	80.91±2.64	0.589	45±6.11	48.87±5.64	0.013	7280.9±656.7	8458.5±827.8	<0.0001
7 minutes	81.27±2.75	80.74±2.46	0.443	47.13±6.88	49.26±5.66	0.195	7289.2±635.5	7675.3±809.6	0.044
10 minutes	82.19±2.37	81.44±2.96	0.283	45.67±5.58	46.33±5.51	0.643	7322±1341.4	7901.7±807.43	0.047

In our attempt to ascertain effectiveness lignocaine and esmolo it can be seen that mean HR was increased in esmolol and lignocaine groups by an average of 19.5 bpm and 34.74 respectively bpm (p value <0.0001) one minute after intubation. These values were normalized to base line value only after three minutes of intubation in both the groups (p value 0.125). After that mean heart rate was decreased

significantly in both groups. SBP was decreased by 10.46mmHg after administration of esmolol but there is no significant decrease in SBP after administration of lignocaine (p value < 0.0001). SBP was returned to base line value after one minute of intubation in both the groups (p value 0.138). After that SBP decreased significantly in both the groups.

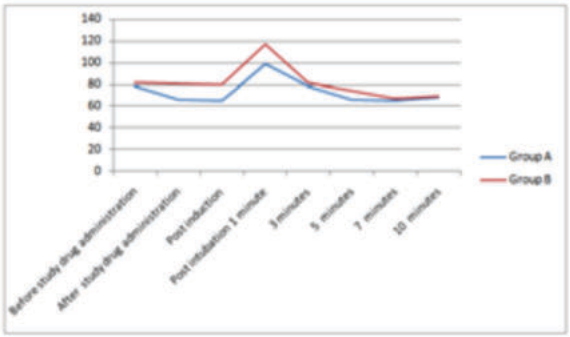

Fig: 1 Comparison of mean heart rate at different points between two groups

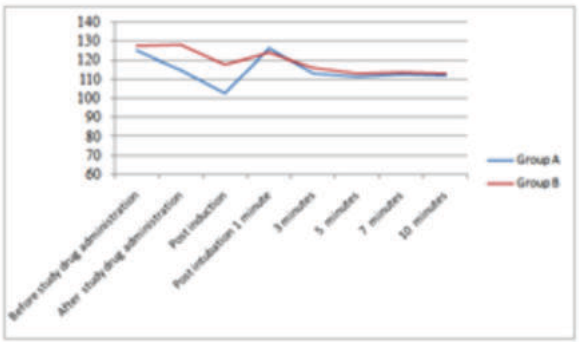

Fig 2: Comparison of mean systolic blood pressure at different points between two groups

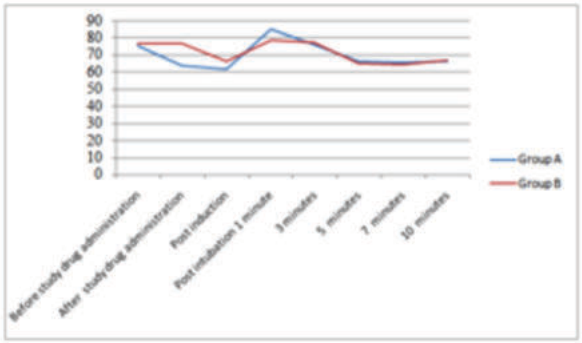

Fig 3: Comparison of mean diastolic blood pressure at different points between two groups

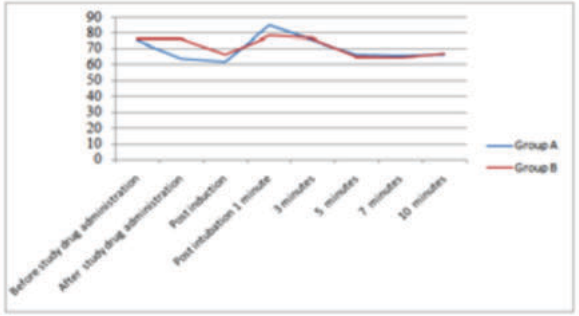

Fig 4: Comparison of mean MAP at different points between two groups

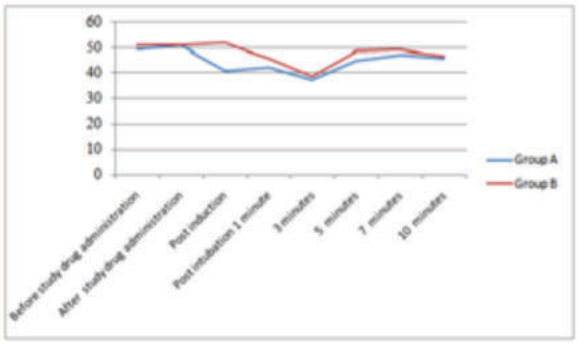

Fig 5:Comparison of mean pulse pressure at different points between two groups

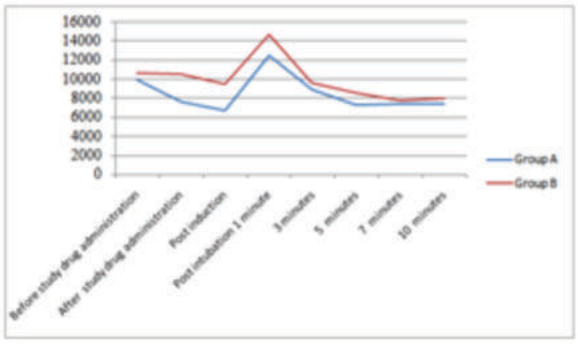

Fig 6: Comparison of mean rate pressure product at different points between two groups

DBP was decreased by 11.73 mmHg after administration of esmolol but there is no significant decrease in DBP after administration of lilgncaine (p value <0.0001). DBP was increased by 9.4mmHg in esmolol group and 1.93mmHg in lignocaine group one minute after intubation (p value 0.0008). DBP was normalized to base line value after three minutes of intubation in both the groups. After that DBP was decreased significantly in both the groups. MAP was decreased by 11.31mmHg after administration of esmolol but there is no significant decrease in MAP after administration of lignocaine (p value <0.0001). MAP was increased by 6.7 mmHg in esmolol group and 0.91 mmHg in lignocaine group one minute after intubation (p value 0.0002). MAP was normalized to base line value after three minutes of intubation in both the groups. After that MAP was decreased significantly in both the groups.

There is no significant difference in PP in both the groups except at the time point of after induction (p value <0.0001) and 5 min after intubation (p value 0.013). The mean RPP is significantly lower in the group A after study drug administration, post induction, post intubation 1 minute, 3 minutes, 5minutes, 7 minutes and 10 minutes.

CONCLUSION

From this study it can be concluded that both the drugs with specified quantities are not effective in blunting hemodynamic stress response produced by laryngoscopy and endotracheal intubation However , Esmolol is better than Lignocaine to attenuate the stress response

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