Original Research Article

Comparison of esmolol versus diltiazem for attenuation of cardiovascular response during laryngoscopy and endotracheal intubation in patients undergoing elective craniotomy

Iman Sinha[1], Ratul Basu[2,3],Aisha Sultan[3], Sayantan Mukhopadhyay[4*],Bibhukalyani Das[5],Sukanta Sen[6]

[1]Assistant Professor, Department of Anatomy,Institute of Post Graduate Medical Education and Research,Kolkata, West Bengal, India

[2]Assistant Professor, Department of Anaesthesiology,ICARE Institute of Medical Sciences and Research Haldia, Purba Medinipur 721645, West Bengal, India

[3]Senior Consultant, Neuroanaesthesiologist & Intensivist, Charnock Hospital, BMC 195, Teghoria, Biswa Bangla Sarani, Kolkata 700157, West Bengal, India

[4]Assistant Professor, Department of Anaesthesiology, Calcutta National Medical College & Hospital, Beniapukur, Kolkata,West Bengal,India

[5] Ex Professor & Head, Department of Neuronaesthesiology, ICU & Pain Clinic, Bangur Institute of Neurosciences, Institute of Post Graduate Medical Education and Research, Kolkata 700020, West Bengal, India

[6]Professor & Head, Department of Pharmacology,ICARE Institute of Medical Sciences and Research Haldia, Purba Medinipur , West Bengal, India

Received: 03-08-2020 / Revised: 29-09-2020 / Accepted: 09-10-2020

Abstract

Background: Laryngoscopy and tracheal intubation may cause undesirable increases in BP and/or heart rate in anaesthetized patients. Present study was done to evaluate and compare esmolol and diltiazem for attenuation of pressor responses to direct laryngoscopy and endotracheal intubation in patients undergoing elective craniotomy. **Materials & Methods:** The study was carried out in the department of Neuroanesthesiology & Critical Care at Bangur Institute of Neurosciences, IPGME&R, Kolkata, in 60 adult patients according to above stated selection criteria. They was randomly allocated into two groups – Group A (n=30) & Group B (n=30). Standard of heart rate, mean arterial pressure, SpO2, ECG was performed before induction of anaesthesia. Group A or esmolol group received esmolol 1mg/kg administered as a i.v. bolus 2 minutes before direct laryngoscopy and intubation, and Group B (n=30) received inj. diltiazem 0.2mg/kg i.v. bolus 60sec before direct laryngoscopy and intubation. After pre-oxygenation of at least 3 minutes, anaesthesia was induced with fentanyl 2µg/kg and inj. thiopentone sodium in increments of 50mg every 5 seconds until eye abolition of eyelash reflex. Inj. rocuronium 0.9mg/kg was administered by iv route to facilitate endotracheal intubation by appropriate sized non kinkable cuffed endotracheal tube. The tube was connected to capnometer and invasive intra-arterial pressure monitoring access was secured. Anaesthesia was maintained by N20/O2/Propofol and intermittent fentanyl injection. Muscle relaxation was maintained by continuous atracurium infusion. Hypoxia and hypercarbia was avoided throughout the procedure. Reversal from neuro-muscular blockade was done with inj neostigmine 0.05 mg/kg and inj glycopyrrolate 0.2 mg per mg of inj neostigmine. Extubation was done when the patient was fully awake, obeying commands, haemodynamically stable and after complete recovery from neuromuscular block. Thorough oro-pharyngeal suction was done before extubation. **Results:** In the present study esmolol given in group A in a dose of 1 mg /kg 120 seconds, prior to laryngoscopy and intubation caused a highly significant decline in SBP prior to laryngoscopy. There was a significant rise of mean SBP after intubation but at 2 and 5 minutes the SBP declined significantly. The MAP decreased highly significantly before laryngoscopy, that surged non-significantly at post intubation and finally settled down non-significantly at 2 and 5 minutes. Esmolol had caused a highly significant fall in HR at all the intervals of the study, except at 2 minutes past intubation when the decline was just significant. RPP had a highly significant decrease in its mean value at prior to laryngoscopy, post intubation, 2 and 5 minutes after intubation. The present study with diltiazem, administered as an intravenous bolus dose of 0.2mg /kg 60 seconds prior to laryngoscopy, demonstrated a highly significant fall in SBP just prior to laryngoscopy. There was an increase in SBP mean on intubation but to an insignicant value. **Conclusion:** With diltiazem, RPP after a highly significant decline prior to laryngoscopy surged to a significant extent on intubation. The RPP declined at 2 and 5 minutes of intubation, the fall at 2 minutes being highly significant. On the other hand, with esmolol RPP had a highly significant decrease in its mean value at prior to laryngoscopy, post intubation, 2 and 5 minutes after intubation.

Keywords: Laryngoscopy, endotracheal intubation, esmolol, diltiazem, cardiovascular responses, elective craniotomy

*Correspondence
Dr.Sayantan Mukhopadhyay
Assistant Professor, Department of Anaesthesiology, Calcutta National Medical College & Hospital, Beniapukur, Kolkata,West Bengal
E-mail: sayantandoc@gmail.com

Introduction

Patients with intracranial pathology are in a compromised state of cerebral haemodynamics, intracranial pressure and cerebral perfusion. The CBF autoregulates with respect to blood pressure changes [1]. As the cerebral autoregulation is disturbed and Blood Brain Barrier (BBB) disrupted in patients with intracranial lesions [2], slight change in MAP increases the cerebral blood volume (CBV), ICP and may cause gross reduction in CPP resulting in neuronal damage. Increased ICP may also cause presurgery brain herniation. Maintenance of an optimal CPP during anaesthetic procedures is a key factor in the management of these patients undergoing operation for intracranial lesions.Laryngoscopy and tracheal intubation may cause undesirable increases in BP and/or heart rate in anaesthetized patients [3]. Those with chronic hypertension, even if controlled have the most exaggerated presssor responses [4, 5]. Among the recommended methods to control the pressor response, are increase depth of anesthesia with fentanyl [6], lidocaine, esmolol [6], nitroprusside, verapamil, diltiazem [7] or nicardipine. In modern anaesthesia practice, laryngoscopy and endotracheal intubation are mandatory for most patients undergoing operation under general anaesthesia, more so in neurosurgical procedures. These haemodynamic responses arise as a form of sympathoadrenal reflex [8]. This reflex is initiated by stimulation of upper airway during laryngoscopy and tracheal intubation, which in turn leads to increased plasma norepinephrine concentration. This adrenergic stress response is extremely harmful in patients with intracranial pathology, e.g. aneurismal rupture, intratumour haemorrhage etc. resulting in severe intracranial hypertension, brain herniation and thereby increased mortality in neuroanaesthesia.In 1986, Cucchiara RF et al [9] studied the effect of esmolol in controlling the increase of heart rate and blood pressure during endotracheal intubation. Esmolol is an water soluble, cardio selective beta adrenergic blockade of rapid onset and ultra short duration of action, and half life of 9 minutes. They found that esmolol blunted both the increase in blood pressure and heart rate in response to laryngoscopy and intubation. Esmolol is effective in a dose dependent manner, in the attenuation of the adrenergic response to laryngoscopy and endotracheal intubation. Diltiazem, a slow channel calcium ion antagonist inhibits the transmembrane influx of calcium ion into cardiac and vascular smooth muscle, and such inhibition reduces heart rate, depresses contractility, decrease conduction velocity and dilates coronary, cerebral and systemic arterioles [10]. Calcium ions exert a major role in the release of from the adrenal glands and adrenergic nerve endings which affects plasma concentration of catecholamines in response to sympathetic stimulation [11]. Animal experiments have shown that calcium channel blocker inhibited catecholamine release from the sympathetic nerve ending by electrical stimulation these observation suggest that calcium channel blockers interferes with catecholamine release after tracheal intubation [12, 13]. Calcium channel blocker have been shown to reduce the pressure effect of circulating nor adrenaline on resistance vessels, resulting in inhibition of the calcium influx that accompanies stimulation of α2 receptors, leading to attenuation of the increase in arterial pressure after elevated conc. of noradrenaline [14].Present study was done to evaluate and compare esmolol and diltiazem for attenuation of pressor response to direct laryngoscopy and endotracheal intubation in patients undergoing elective craniotomy.

Materials & methods

Inclusion Criteria

- Patients within 20-60 yrs of age
- Either sex
- ASA Grade I & II undergoing supratentorial craniotomies

Exclusion Criteria

- Patients who are allergic to the study drugs
- Patients with heart block, severe hypotension etc
- Patients with known COPD, bronchial asthma etc
- Patients with underlying renal & hepatic diseases
- Pregnancy, morbid obesity, diabetes mellitus
- Known neuromuscular disorders

- Severe intracranial hypertension
- Dyselectrolytemia
- Anticipated difficult airway

A total of 60 patients who had fulfilled selection criteria were included in the study. Patients were divided into two groups. Group A (n=30) received esmolol 1mg/kg i.v. bolus 2 minutes before direct laryngoscopy and intubation; Group B (n=30) received inj. Diltiazem 0.2mg/kg i.v. bolus 60 sec before direct laryngoscopy and intubation. Equipments required were penlon anaesthesia machine, invasive blood pressure monitoring system, pulse oximetry, ECG, EtCO2 Monitor and peripheral nerve stimulator.The study was carried out in the department of Neuroanesthesiology & Critical Care at Bangur Institute of Neurosciences, IPGME&R, Kolkata, after approval of the institutional Ethics Committee in 60 adult patients according to above stated selection criteria. They were randomly allocated into two groups – Group A (n=30) & Group B (n=30). Informed written consent was obtained from the potential subjects prior to including them in the study during pre-anesthetic check up.Thorough pre-anesthetic check up & counseling was done prior to anaesthesia. Standard of heart rate, mean arterial pressure, SpO2, ECG was performed before induction of anaesthesia. Group A or esmolol group received esmolol 1mg/kg administered as an i.v. bolus 2 minutes before direct laryngoscopy and intubation, and Group B (n=30) received inj. diltiazem 0.2mg/kg iv bolus 60sec before direct laryngoscopy and intubation. After pre-oxygenation of at least 3 minutes, anaesthesia was induced with fentanyl 2µg/kg and inj. thiopentone sodium in increments of 50mg every 5 seconds until eye abolition of eyelash reflex. Inj. Rocuronium 0.9mg/kg was administered by i.v. route to facilitate endotracheal intubation by appropriate sized non kinkable cuffed endotracheal tube. The study drug was administered by intravenous route in the above mentioned dose and schedule in two groups by a person, who remained blind to the study. Neither the observer and nor the patient were aware of the chemical nature of the study agent and thus blinding was ensured in the study. The tube was connected to capnometer and invasive intra-arterial pressure monitoring access was secured. Anaesthesia was maintained by N_20/O_2/Propofol and intermittent fentanyl injection. Muscle relaxation was maintained by continuous atracurium infusion. Hypoxia and hypercarbia was avoided throughout the procedure. Reversal from neuromuscular blockade was done with inj neostigmine 0.05 mg/kg and inj glycopyrrolate 0.2 mg per mg of inj neostigmine. Extubation was done when the patient was fully awake, obeying commands, haemodynamically stable and after complete recovery from neuromuscular block. Thorough oropharyngeal suction was done before extubation. The following parameters were recorded and studied like systolic blood pressure, mean arterial pressure and heart rate. All the readings were divided in the following time schedule.

First Reading: Before induction/base line value
Second Reading: Just prior to laryngoscopy and intubation
Third Reading: Immediately after laryngoscopy and intubation
Fourth Reading: Two minutes after intubation
Fifth Reading: Five minutes after intubation

The parametric variables were compared between the two groups by Student's unpaired t-test. Within each group, changes in haemodynamic parameters was assessed by repeated measures of analysis of variance (ANOVA) followed by Student's paired t-test for comparison between two individual time points. A categorical variable was compared between the groups by Chi-square test or Fisher's exact test, whichever is appropriate. The analysis was conducted on an intention to treat basis. A two tailed 'p' value<0.05 was considered statistically significant.

Results

Table 1: Sex distribution in the two groups

Group	Sex		Row
	Male	Female	Totals
A	20	10	30
Row %	66.67%	33.33%	100%
B	19	11	30
Row %	63.33%	36.61%	100%

This distribution is NS by Chi-square test (p = 0.846) [Table 1].

The table 1 shows that among 30 patients under study in each group, Group A (Esmolol), 20 were male (66.67%and 10 were female (33.33%). Out of 30 in group B (Diltiazem) 19 were male (63.33%) and 11 (36.61%)

were female. It was found that males outnumbered females in the two groups. This distribution is not significant as p > 0.05 by chi-square test. The age distribution in all three groups was even and the patients were in the age range of 18-60 years [Table 2].

Table 2: Comparison of age between the 2 group by one-way ANOVA

AGE	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	39.562	2	19.781	.233	.792
Within Groups	8650.686	102	84.811		
Total	8690.248	104			

Table 3: Lesion distribution in the two groups

Group	Lesion Meningioma	Lesion Glioma	Lesion Parietal	Lesion Frontal Sol	Lesion Suprasellar Sol	Lesion Parietal Sol	Lesion Parasellar Sol	Lesion Cystic Sol	Lesion Astrocytoma	Lesion Pineal Tumour	Lesion Temporal	Row Totals
A	12	8	0	4	0	2	0	3	4	1	1	35
Row %	34.29%	22.86%	0.00%	11.43%	0.00%	5.71 %	0.00%	8.57%	11.43%	2.86%	2.86 %	
B	14	10	1	4	1	3	2	0	0	0	0	35
Row %	40.00%	28.57%	2.86%	11.43%	2.86%	8.57 %	5.71%	0.00%	0.00%	0.00%	0.00 %	

Table 4: Descriptive statistics for sbp (systolic blood pressure)

Group	Statistical Value	Base line	Pre	Post	2 Min	5 Min
A	Mean	129.00	118.00	142.00	133.00	136.00
	S.D	6.70	9.60	9.16	5.60	5.47
	Minimum	118.00	99.00	126.00	122.00	122.00
	Maximum	142.00	146.00	176.00	144.00	148.00
B	Mean	133.00	119.00	138.00	125.00	119.00
	S.D	11.73	13.16	11.88	11.37	9.49
	Minimum	110.00	83.00	104.00	90.00	100.00
	Maximum	160.00	153.00	158.00	144.00	140.00

The table shows the mean values of SBP in mmHg at different time intervals in two groups [Table 4].

Table 5: Descriptive statistics for MAP (mean arterial pressure)

Group	Statistical Value	Base line	Pre	Post	2 Min	5 Min
A	Mean	90.37	82.94	96.74	90.91	92.66
	S.D	5.69	7.79	10.84	6.07	5.89
	Minimum	80.00	56.00	68.00	70.00	80.00
	Maximum	102.00	99.00	134.00	98.00	102.00
B	Mean	88.97	80.57	91.74	86.00	81.74
	S.D	8.77	8.58	8.85	10.29	9.49
	Minimum	74.00	62.00	72.00	51.00	70.00
	Maximum	110.00	96.00	108.00	112.00	98.00

The table shows the mean values of MAP in mmHg at different time intervals in two groups [Table 5].

Table 6: Descriptive statistics for HR (heart rate)

Group	Statistical Value	Base line	Pre	Post	2 Min	5 Min
A	Mean	80.29	74.97	89.09	84.97	87.06
	S.D	10.21	9.57	11.16	8.65	7.03
	Minimum	60.00	58.00	66.00	70.00	76.00
	Maximum	100.00	100.00	120.00	104.00	104.00
B	Mean	83.40	82.14	94.17	88.74	82.17
	S.D	13.37	15.14	11.44	10.26	9.44
	Minimum	60.00	60.00	64.00	68.00	68.00
	Maximum	120.00	118.00	122.00	116.00	102.00

The table shows the mean values of HR in beats per minute at different time intervals in two groups [Table 6].

Table 7: Comparison of study variables – at baseline – between the 2 groups by one-way ANOVA

Variable		F	p Value
SBP0	Between Group	1.784	0.173
MAP0	Between Group	0.925	0.400
HR0	Between Group	2.080	0.130
RPP0	Between Group	2.578	0.081

Table 8: Comparison of study variables – pre-intubation – between the 2 groups by one-way ANOVA

Variable		F	p Value
SBPPRE	Between Group	6.336	0.003
MAPPRE	Between Group	2.468	0.090
HRPRE	Between Group	3.833	0.025
RPPPRE	Between Group	2.799	0.066

Table 9: Comparison of study variables – post-intubation – between the 2 groups by one-way ANOVA

Variable		F	p Value
SBPPOST	Between Groups	12.377	0.000
MAPPOST	Between Groups	14.828	0.000
HRPOST	Between Groups	7.492	0.001
RPPPOST	Between Groups	10.616	0.000

Table 10: Comparison of study variables – 2 minutes following intubation – between the 2 groups by one-way ANOVA

Variable		F	p Value
SBP2	Between Groups	39.995	0.000
MAP2	Between Groups	25.319	0.000
HR2	Between Groups	13.150	0.000
RPP2	Between Groups	29.403	0.000

Table 11: Comparison of study variables – 5 minutes following intubation – between the 2 groups by one-way ANOVA

Variable		F	p Value
SBP5	Between Groups	72.914	0.000
MAP5	Between Groups	46.590	0.000
HR5	Between Groups	17.710	0.000
RPP5	Between Groups	46.635	0.000

Discussion

The challenge of any anaesthetic for neurosurgery is to provide good intracranial operating conditions, with a slack brain and low intracranial pressure (ICP). When a patient has an intra-cranial space occupying lesion (SOL), the achievement of allow ICP during surgery demands a careful choice of the most appropriate anaesthetic and an attention to detail.Patients present for craniotomy for a supratentorial SOL most often because of a tumour but space occupation may also be caused by subdural, extradural or intracerebral haematomas or an intracerebral abscess. Even when a tumour is histologically benign, the processes set in train by intracranial space occupation can be fatal if the tumour is not treated. A badly administered or inappropriate anaesthetic may add to the intracranial problems generated by the space occupation, increasing ICP [15]. The dangers of intraoperative high ICP in the presence of a SOL mean that the anaesthetist must be especially careful to choose anaesthetic agents and techniques which lower ICP. In particular, it is important to avoid a rise in cerebral venous pressure, cerebral vasodilatation, hypercapnia and hypertension. All these circumstances can be provoked during the induction and maintenance of anaesathesia [16].The presser response to laryngoscopy and intubation will cause an increase in the size of vascular tumours in particular, because the tumour blood supply will not be under autoregulatory control [17]. At the same time, laryngoscopy tends to kink the jugular veins, so that cerebral venous outflow is impaired. The result is a greater tendency for a dangerous rise in ICP. As the process continues the ICP can rise to very high levels and the brain can become displaced from its normal position. High intracranial pressure can force the medulla out of the posterior fossa into the narrow confines of the foramen magnum, where compression of the vital centres is associated with bradycardia, hypertension and respiratory irregularity followed by aponea [18]. The pressor response should therefore, be controlled. A second dose of the induction agent or the use of IV lignocaine 1.5 mg/kg 90s before intubation is well established, as is the use of agents such as esmolol.In contrast to other organs the brain is protected by stiff skull. An increase in ICP may therefore impede cerebral blood flow (CBF) and cause ischaemia. Raised ICP is an important secondary insult in supratentorial lesions and a predictor of poor outcome after operation. It is used as a target in many treatment algorithms [19]. ICP is also used to calculate CPP, which is the difference between MAP and ICP. CPP = MAP – ICP. CPP represents the pressure gradient across the cerebral vascular bed and is used as a therapeutic target for intracranial lesions during intra-operative and post-operative period [20].The rationale of any CPP augmentation is to increase CBF in brain regions which have critically low blood flow. However, an increase in CPP will only lead to an increase in CBF when autoregulation has failed or CPP is below the lower limit of autoregulation. In a normal brain CBF is constant in the CPP range of about 50-150 mmHg because of auto regulation and a shift to right of autoregulation the curve has been suggested after brain tumours. Autoregulation is frequently disturbed in brain lesions, nevertheless, the effects of CPP augmentation are difficult to predict and may be small despite large increase in CPP [21].Haemodynamic responses during laryngoscopy and tracheal intubation arise as a form of sympatho-adrenal reflex. The reflex is initiated by stimulation of upper airway during laryngoscopy and tracheal intubation which in turn leads to increased plasma norepinephrine concentration.Various agents have been studied for attenuating this surge associated with laryngoscopy and intubation in various types of patients [22].The present clinical study was undertaken to evaluate the effect of two drugs on the attenuation of haemodynamic surge at laryngoscopy and intubation in elective craniotomy patients. Study was conducted after dividing the study population in two groups- Group A patient received IV esmolol, Group B were given IV diltiazem. Findings of each group are discussed in comparison with their initial pre-operative values at

different time intervals with regard to SBP, MAP, HR, and RPP.

Systolic Blood Pressure

In the group A or esmolol group, the initial mean SBP of 129 ± 6.7 mmHg decreased to a highly significant value of 118 ± 9.9 (p- 0.000; p < 0.001) mmHg just prior to laryngoscopy. Immediately post intubation mean SBP there was a significant rise (p - 0.000; p < 0.001) to 142 ± 9.16 mmHg, compared to baseline. At 2 and 5 minutes post intubation the mean SBP had a significant (p - 0.001 and p - 0.000; p < 0.001) fall to 133 ± 5.6 mmHg and 136 ± 5.47 mmHg respectively, compared to baseline.

In the diltiazem group or group B, the baseline mean SBP of 133 ± 11.3 decreased to a highly significant (p < 0.001) value of 119 ± 13.16 mmHg prior to laryngoscopy. Then it increased non-significantly (p - 0.126; p < 0.05) to 138 ± 11.88 mmHg immediately after intubation. There was a highly significant (p- 0.0003; p < 0.001) fall at 2 minutes post intubation to 125 ± 11.37 mmHg, compared to baseline. At 5 minute after intubation the mean SBP had a highly significant decline (p- 0.000; p < 0.001) to 119 ± 9.49 mmHg, compared to baseline. One patient in group 1, three patients in group 2 had an increase in SBP greater than 20 % from their baseline value. As the baseline mean SBP in two groups did not show statistically significant difference, so SBP was comparable in three groups. At time point-just prior to, 1 minutes, 2 minutes and 5 minutes after intubation the mean SBP of the patients in group 1 was lower than group 2, and the difference between the two groups was highly statistically significant (p < 0.001) at each of these points of time.

Mean Arterial Pressure

In the group A or esmolol group the baseline mean MAP of 90.37 ± 5.69 mm ± Hg had a highly significant (p - 0.000; p < 0.001) decline to 82.94 ± 7.79 mmHg; then it had a non-significant (p - 0.647, p - 0.078; p > 0.05) surge to 96.74 ± 10.84 mmHg just after intubation. At 2 minutes post intubation there was a non-significant (p - 0.647, p - 0.078; p > 0.05) decrease to 90.91 ± 6.70 mmHg and to 92.65 ± 5.89 mmHg at 5 minute interval, compared to baseline. In the diltiazem group or group B, the initial mean baseline of MAP 88.97 ± 8.77 mmHg, decreased to highly significant (p - 0.000; p < 0.001) value of 80.57 ± 8.57 mmHg prior to laryngoscopy. Just after laryngoscopy there was a non-significant surge (p - 0.094; p > 0.05) to 91.74 ± 8.85 mmHg and again a non-significant (p - 0.075; p > 0.05) fall at 2 minutes interval to 86 ± 10.29 mmHg, compared to baseline. After 5 minutes of intubation the mean MAP had a highly significant (p - 0.0.000; p < 0.001) fall to 81.74 ± 9.49 mmHg..

On using paired t test in group 2 different time interval values in MAP revealed a statistically highly significant difference. Two patients in group B, three patients in group A had increase in MAP greater than 20 % from their initial value. There was statistical significance between the groups. As the baseline mean MAP in two groups did not show statistically significant difference in the two groups, so MAP was comparable in three groups. At the time point –just prior to, immediately after, 2 minutes and 5 minutes after intubation mean MAP of the patient in group B was lower than the mean MAP of group B. This difference between the two groups was highly statistically significant (p < 0.001) at each of these points of time.

Heart Rate

The table shows statistical values of heart rate in beats per minute at different time interval.In the esmolol group, group B, the mean heart rate of 80.29 ± 10.21 beats per minute decreased highly significantly (p - 0.000; p < 0.001) to 74.97 ± 9.57 beats / minute just prior to laryngoscopy. After intubation the highly significant (p - 0.000; p < 0.001) surge to 89.09 ± 11.16 beats per minute, then a significant (p - 0.004; p < 0.0010) decrease to 84.97 ± 8.65 beats per minute at 2 minutes, compared to baseline. At 5 minutes it again increased to a highly significant (p - 0.000).In the diltiazem group or group B, the baseline mean heart rate of 83.4 ± 13.36 beats per minute decreased non-significantly (p - 0.327; p > 0.05) to 82.14 ± 15.14 beats per minute just prior to laryngoscopy. Mean heart rate increased highly significantly (p - 0.000; p < 0.001) to 94.17 ± 11.44 beats /minute at post intubation. Then there was a highly significant (p - 0.000; p < 0.001) decline after 2 minutes of intubation to 88.74 ± 10.26 beats per minute and finally a nonsignificant (p - 0.434; p > 0.05) decline to 82.17 ± 9.43 beats per minute at 5 minutes. As the baseline mean HR in two groups did not show statistically significant difference, so HR was comparable in two groups. At the time point –just prior to induction the mean HR in group B was slightly higher than mean HR in group A. Just post intubation and at 2 minute interval the mean HR was higher in group B compared to group A. At 5 minute after intubation the mean HR in group B was lower than that of mean HR in group A at that time point. These variations in HR in two groups were compared at different time points and the difference was significant (p < 0.05).In 2003, Santosh Kumar et al [23], underwent

a study on 100 patients undergoing various elective surgical procedures to compare the efficacy of IV esmolol, diltiazem and magnesium sulphate for attenuating the haemodynamic response to laryngoscopy and tracheal intubation. It was foundthat esmolol proved to be most effective in attenuating rise in heart rate following laryngoscopy and intubation while the rise in bloodpressure was suppressed but not prevented by bolus dose of esmolol (2 mg/kg). Study showed an average rise in SBP of 30 mm Hg and DBP of 32 mm Hg immediately after intubation in control group (Table 4). Esmolol group shows significant fall in SBP and DBP after giving the study drug and also there was significantly less rise in both SBP and DBP soon after intubation, at 3 minutes and at 5 minutes. Findings in diltiazem group (group III), shows insignificant rise in heart rate after giving the study drugs, highly significant rise in heart rate immediately after intubation, at 1 min and at 3 minutes after intubation.5 minutes after intubation the rise was insignificant. These findings are consistent with that of Mikawa et al (1990) [24]who said that IV diltiazem (0.2 and 0.3 mg/kg) given 1 minute before laryngoscopy failed to protect against the increase in heart rate after laryngoscopy.[12]This was due to that, diltiazem causes sympatho-adrenal reflex stimulation by hypotension.

V.B. Rupakar et al (2009) [25], found attenuation of cardiovascular responses to laryngoscopy and endotracheal intubation with diltiazem-lignocaine combination. There was significant increased in heart rate, mean arterial pressure and rate pressure product during laryngoscopy and intubation in control group. Diltiazem–lignocaine combination produces more significant attenuation of rise in heart rate, mean arterial pressure and rate pressure product during laryngoscopy and intubationas compared to diltiazem or lignocaine alone.

Another study of Mikhawa et al (1996) [24] who found that increase in SBP and DBP was significantly less in diltiazem group (0.2 mg/kg). The study of Y. Fuji et al.[26], observed that diltiazem-lidocaine combination is more effective to attenuate the cardiovascular responses to laryngoscopy and tracheal intubation than lidocaine or diltiazem alone.

The present study with diltiazem, administered as an intravenous bolus dose of 0.2mg/kg 60 seconds prior to laryngoscopy, demonstrated a highly significant fall in SBP just prior to laryngoscopy. There was an increase in SBP mean on intubation but to an insignicant value. Then there was a highly significant fall in mean SBP at 2 and 5 minutes after intubation and at 5 minutes the mean SBP was around or less than the baseline mean. The MAP had a highly significant decline before laryngoscopy that had a non-significant surge on intubation. MAP decreased at 2 and 5 minutes of intubation. The insignificant decline in HR prior to laryngoscopy was observed with diltiazem that increased to a highly significant extent on intubation. HR declined at 2 and 5 minutes of intubation, the decline at 2 minutes of intubation being highly significant.

Conclusion

Both drug cause highly significant decrease in SBP prior to laryngoscopy and intubation. With diltiazem there is an increase in SBP mean on intubation but to an insignificant value. In comparison, esmolol causes a significant rise of mean SBP after intubation. There is a highly significant fall in mean SBP at 2 and 5 minutes after intubation with both drugs. With diltizem, at 5 minutes the mean SBP was around or less than the baseline mean. The MAP decreased highly significantly before laryngoscopy that surged non-significantly at post intubation with both drugs. With diltiazem, MAP decreased at 2 and 5 minutes of intubation. In comparison, with esmolol MAP finally settled down non-significantly at 2 and 5 minutes.

Few comparative study have been published between the drugs in respect to blood pressure reduction both drugs are comparable according to the present and previous studies. Heart rate variability is more with diltiazem. Further study is required to prove superiority of one drug with another.

References

1. Anaesthesia and neurosurgery, 4th eds. James E Cottrell; David S Smith. Intracerebral perfusion and cerebral blood flow. Chapter 15; page- 299.
2. Anaesthesia and neurosurgery, 4th eds. James E Cottrell; David S Smith. The blood brain barrier and edema. Chapter 15; page- 299.
3. Stehling LC. Management of airway. In: Barash P, Cullen B, Stoelting R, eds. Clinical Anaesthesia. 2nd ed. Phildelphia: JB Lippincott, 1992; 685-708.
4. Foex P, Prys-Roberts C. Anesthesia and hypertensive patients. Br J Anaesth 1974; 46:575-88.
5. Goldman L, Caldera DL. Risks of general anaesthesia and elective operation in hypertensive patient. Anaesthesiology 1979; 50;285-92.
6. Ebert JP, Pearson JD, Gelman S, et al. Circulatory responses to laryngoscopy: The comparative effects

of placebo, fentanyl and esmolol. Can J Anaesth 1989; 36: 301-6.
7. Fujii Y, Tanaka H, Saitoh Y, Toyoka H. Effects of calcium channel blockers on circulatory response to tracheal intubation in hypertensive patients: Nicardipine vs Diltiazem. Can J Anaesth 1995; 42:785-8.
8. Mikawa K, Nishina K, Maekawa N, Obara H. Comparison of Nicardipine, diltiazem and verapamil for controlling the cardiovascular responses to tracheal intubation. Br J Anaesth 1996; 76:221-226.
9. Cucchiara RF, Benefiel DJ, Matteo RS, et al. evaluation of esmolol in controlling increases in heart rate and blood pressure during endotracheal intubation in patients undergoing carotid endarterectomy. Anaesthesiology 1986;65:528-31.
10. Roizen MF. Anaesthetic implications of concurrent diseases; In; Miller RD, ed. Anaesthesia. 5th ed.
11. Rasmussen H. The calcium messenger system. New England Journal of Medicine 1986; 314:1164-1170.
12. Pinto JEB, Trifaro JM. The different effects of D-600 (Methoxyverapamil) on the release of adrenal catecholamines induced by acetylcholine, high potassium or sodium deprivation. British journal of pharmacology 1976; 57:127-132.
13. Tsuda K, Hano T, Ueshima K, Kuchii M, Nishio I, Masuyama Y. Effects of Ca- antagonists on nonadrenaline from sympathetic nerve endings. Japanese Pharmacology and Therapeutics 1983; 11:315-316.
14. van Zwieten PA, van Meel JC, Timmermans PB. Calcium antagonists and alpha 2-adrenoceptors: possible role of extracellular calcium ions in alpha 2-adrenoceptor-mediated vasoconstriction. J Cardiovasc Pharmacol. 1982;4 Suppl 3:S273-9.
15. Bruner DI, Littlejohn L, Pritchard A. Subdural empyema presenting with seizure, confusion, and focal weakness. West J Emerg Med. 2012; 13(6): 509-511.
16. Rangel-Castilla L, Gopinath S, Robertson CS. Management of intracranial hypertension [published correction appears in Neurol Clin. 2008 Aug;26(3):xvii. Rangel-Castillo, Leonardo [corrected to Rangel-Castilla, Leonardo]]. Neurol Clin. 2008;26(2):521-x.
17. Nagy JA, Chang SH, Dvorak AM, Dvorak HF. Why are tumour blood vessels abnormal and why is it important to know?. Br J Cancer. 2009; 100 (6):865-869.
18. Tobias JD, Leder M. Procedural sedation: A review of sedative agents, monitoring, and management of complications. Saudi J Anaesth. 2011;5(4):395-410.
19. Pinto VL, Tadi P, Adeyinka A. Increased Intracranial Pressure. [Updated 2020 Jul 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482119/
20. Mount CA, M Das J. Cerebral Perfusion Pressure. [Updated 2020 May 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537271/
21. Steiner LA, Andrews PJ. Monitoring the injured brain: ICP and CBF. Br J Anaesth. 2006 ;97(1):26-38.
22. Sener EB, Ustun E, Ustun B, Sarihasan B. Hemodynamic responses and upper airway morbidity following tracheal intubation in patients with hypertension: conventional laryngoscopy versus an intubating laryngeal mask airway. Clinics (Sao Paulo). 2012;67(1):49-54.
23. Santosh Kumar, et al. Comparative study of the efficacy of I.V. Esmolol, Diltiazem and Magnesium Sulfate in attenuating hemodynamic response to laryngoscopy and tracheal intubation. Indian J Anaesth. 2003; 47 (1): 41-44.
24. Mikawa K, Ikegaki J, Maekawa N, Goto R, Kaetsu H, Obara H. The effect of diltiazem on the cardiovascular response to tracheal intubation. Anaesthesia. 1990;45(4):289-93.
25. Rupakar VB, Raval B, Chadha IA. Attenuation of Cardiovascular Responses to Laryngoscopyand Endotracheal Intubation with Diltiazem-Lignocaine Combination. J Anaesth Clin Pharmacol 2009; 25(3):341-344.
26. Fujii Y, Saitoh Y, Takahashi S, Toyooka H. Diltiazem-lidocaine combination for the attenuation of cardiovascular responses to tracheal intubation in hypertensive patients. Can J Anaesth. 1998 ;5(10): 933-7.

Source of Support:Nil
Conflict of Interest: Nil