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A Comparative Study of The Effect of I.V. Esmolol And Diltiazem In Attenuating Haemodynamic Response To Laryngoscopy and endotracheal intubation

Authors
Dr Hansraj Charan[1], Dr. Chiranji Lal Khedia[2], Dr. Manoj Singhal[3]
[1,2,3]Assistant professor, Govt. Medical College Kota (Raj)

Abstract

Introduction: *Laryngoscopy and tracheal intubation are noxious stimuli that evoke a transient but marked sympathetic response manifesting as hypertension and tachycardia.*
They are particularly detrimental to patient with cardiovascular and intracranial diseases.

Aims and Objectives

1. *To study the effect of intravenous Esmolol (B-selective blocker) and Diltiazem (Calcium channel blocker) on hemodynamic change to laryngoscopy and intubation in comparison to control group Normal saline.*
2. *To study the side effect and complications, if any.*

Methodology: *Randomized double-blind controlled study was conducted in the Department of Anesthesia, Govt. Medical College, KOTA including 111 patients.*
Patients were divided in three groups of 37 each.

- *Group A (Control)- (n=37) - Normal saline was given (Volume = 10ml)*
- *Group B (Esmolol) (n=37) - Injection Esmolol 1 mg/kg I.V. bolus (diluted to 10 ml with Normal Saline)*
- *Group C (Diltiazem) (n=37) - Injection Diltiazem 0.2 mg/kg I.V. bolus (diluted to 10 ml with Normal Saline)*

Results: *In control group there was significant rise in heart rate just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol group there was small rise in HR after intubation that was significant ($p<0.05$) but value touched the baseline within 5 min after intubation that was insignificant ($p>0.05$) there after there was fall in HR till 10 min. in diltiazem group there was significant. In control group there was significant rise in SBP just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol and diltiazem group there was significant rise in SBP after intubation but value touched the baseline within 3 min in diltiazem group and within 5 min.post intubation in esmolol group($p>0.05$).no incidence of hypotension was observed in any of the study group.*
In control group there was significant rise in MBP just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol and diltiazem group there was significant rise in MBP after intubation but value touched the baseline within 3 min in diltiazem group and within 5 min.post intubation in esmolol group($p>0.05$).no incidence of hypotension was observed in any of the study group.
It was observed that mean baseline variables (HR, SBP, DBP and MBP) were similar in the three groups and no statistically significant difference was present (P value>0.05).

Conclusion: *Highly significant hemodynamic response was observed just after laryngoscopy and intubation in control group which lasted for the entire 10 min of the study period after intubation. Esmolol was the most effective in controlling the heart rate but ineffective in attenuating the pressure response. Diltiazem was quite effective in controlling the pressure response but it failed to achieve any control over the heart rate. No ECG abnormality and hypotension was observed in any patients in any group.*

Introduction

Endotracheal intubation is an integral part of anesthesiologist's contribution to patient care. Laryngoscopy and Tracheal intubation are one of the essential components of general anesthesia.

Besides the technical difficulty inherent to the procedure, laryngoscopy and tracheal intubation are noxious stimuli that evoke a transient but marked sympathetic response manifesting as hypertension and tachycardia.

Although these cardiovascular responses are not of great clinical significance in healthy normotensive patients but they are undesirable and may be particularly detrimental to patient with cardiovascular and intracranial diseases. The response is associated with acute left ventricular failure (Foxe et al; 1977[1]), ischaemic ECG changes (Prys Robert et al, 1971[2]) and ruptured cerebral aneurysm (Fox et al; 1977[1]).

Various drugs and techniques have been used in the past from time to time to attenuate these haemodynamic response. these include deepening of anesthesia (King at al; 1951[3]), Lidocaine Spray by Dehlinger et al (1976)[4] opioids by Dahlgaren et al (1981)[5], Nitroglycerine by Dich Neilson J et al (1986)[6], Droperidol by curron et al (1980)[7] propanolol by Kopriva CJ et al (1978)[8], NTG ointment by Elkayam et al (1982)[9] and Calcium channel blockers (Mikawa et al, 1996)[10], Fentanyl, Magnesium sulfate etc.

As today more and more patients with cardiovascular disorders are presenting themselves for surgery, anesthesiologists are in search of safest and the most efficient drug which can prevent cardiovascular response to the laryngoscopy and tracheal intubation.

The present study is set out to compare the efficacy of two different classes of drugs in attenuating the haemodynamic responses related to laryngosopy and tracheal intubation. These drugs are Esmolol (B-selective blocker) and diltiazem (calcium channel blocker).

Aims and Objectives

The present study is planned

1. To study the effect of intravenous Esmolol and Diltiazem on haemodynamic response to laryngoscopy and intubation.
2. To study the effect of intravenous Esmolol and Diltiazem on haemodynamic chang to laryngoscopy and intubation in comparison to control group Normal saline.
3. To study the side effect and complications, if any.

Methodology

- The study was conducted in the Department of Anesthesia, Govt. Medical College Kota. This randomized double-blind controlled study included 111 patients (age 20-50 years) undergoing elective surgery. Due permission from the Institutional Ethics Committee and review board and written informed patient consent was obtained.
- Study design- It's a Randomized, Double blind, Controlled study.
- The study was conducted in following three groups of the patients. Patients were divided in three groups of 37 each.
  1. **Group A (Control)** (n=37)- Injection Normal saline 10 ml I.V. 1 minute before layngoscopy and intubation.
  2. **Group B (Esmolol)** (n=37) - Injection Esmolol 1 mg/kg I.V. bolus (diluted to 10 ml with Normal Saline) 1 minute before layngoscopy and intubation.
  3. **Group C (Diltiazem)** (n=37) - Injection Diltiazem 0.2 mg/kg I.V. bolus (diluted to 10 ml with Normal Saline) 1 minute before laryngoscopy and intubation.

Statistical Analysis

- Analysis was done by applying parametric T-test and Anova test as applicable.
- A '*P*' value of <0.05 was considered significant and >0.05 Non significant.

Inclusion criteria

1. Patients aged 20-50 yrs

2. ASA grade I-II
3. Patients willing to give written and informed consent.
4. Patient's Weight 30 – 70 kg.

Exclusion criteria

1. History of chronic disease like hypertension, varying degree of heart blocks, diabetes mellitus, respiratory disease, myopathy, neurological disorders.
2. Patients with impaired renal or hepatic function.
3. Any absolute or relative contraindication to study drug.
4. Patients on medications like hypnotics, narcotic analgesics, α_2 agonists, calcium channel blockers, β blockers.
5. Patients with anticipated difficult intubation.
6. Patients intubated after more than 1 attempt or more than 20 seconds.

Pre Anaesthetic Check Up

All patients were visited on the day prior to surgery and will be explained about the anaesthetic technique and perioperative course. Each patient had a pre anaesthetic check up which includes –

1. Any significant present and past medical/surgical history
2. Physical examination
3. Vital parameters like BP, pulse ,Temperature & respiratory rate
4. All routine and specific investigations required for major surgeries will be obtained

Procedure

After taking informed consent and confirming overnight fasting, patient was taken on the recovery room and baseline vitals like B.P., pulse rate, respiratory rate were recorded. After an 18 gauge intravenous (IV) cannula have been inserted at the forearm level.

Randomization was done using chit in box method. Medication preparation was done by another assistant for double blinding.

All the patients were premedicated with five minutes prior to induction of anaesthesia. Heart rate, systolic and diastolic blood pressure were recorded as baseline value.

After preoxygenation induction was done by inj. thiopentone sodium 5mg/kg followed by inj. rocuronium 0.6mg/kg in intubating dose. Study drugs given slow I.V. 1 minute after rocuronium. Endotracheal intubation was done 2 minutes after rocuronium.

Anaesthesia was maintained with halothane, oxygen and N2O through Bain's circuit on controlled ventilation. Muscle relaxation was done with intermittent dose of rocuronium. At the end of surgery reversal was done with neostigmine 0.05mg/kg and glycopyrrolate 0.01 mg/kg.

Hamodynamic data were collected at baseline, just after premedication, just after injecting the drug under study, just after intubation, 1min, 3min, 5min and10 min after intubation.

Observations And Results

Table 1 Demographic Profile

Demographic Factors	A (Control)	B (Esmolol)	C (Esmolol)	P Value
AGE: (Mean ± S.D.) of age in years	38.8 ± 09.5	36.4 ± 10.1	34.9 ± 10.6	P>0.05
SEX: (F/M RATIO IN %)	64.9/35.1	54.1/45.9	45.9/54.1	
WEIGHT: (Mean ± S.D.) of Weight in kg	54.1± 09.2	54.5 ± 11.3	55.6 ± 10.0	

From table 1, it was observed that there was no significant difference in the mean age of patients, sex distribution and weight of patients (p>0.05) in all the groups.

Table 2 Mean Heart Rate in various groups (Mean ± S.D.)

Observation Time	Control			Esmolol			Diltiazem		
	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.
Base Line	82.7 ± 13.8			83.4 ± 15.2			81.0 ± 12.8		
After premedication	95.4 ± 15.0	0.0000	S	86.9 ± 15.5	0.0017	S	83.9 ±= 14.0	0.0990	NS
After administration of Drug	94.2 ± 15.7	0.0000	S	84.5 ± 15.5	0.5738	NS	90.8 ± 14.3	0.0000	S
Just after intubation	115.5 ± 19.1	0.0000	S	90.3 ± 15.5	0.0025	S	104.8 ± 16.7	0.0000	S
1 Minute after intubation	113.1 ± 15.8	0.0000	S	89.8 ± 16.0	0.0050	S	101.2 ± 15.5	0.0000	S
3 Minutes after intubation	107.6 ± 15.7	0.0000	S	86.3 ± 17.4	0.1882	NS	95.0 ± 15.3	0.0000	S
5 Minutes after intubation	99.0 ± 13.7	0.0000	S	82.3 ± 19.0	0.6363	NS	90.2 ± 10.7	0.0000	S
10 Minutes after intubation	97.0 ± 13.7	0.0000	S	78.3 ± 19.0	0.0411	S	88.2 ± 10.7	0.0001	S

The above table depicts the mean heart rate (Mean ± S.D.**)** from the baseline in all three groups at various study intervals. In control group there was significant rise in heart rate just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol group there was small rise in HR after intubation that was significant ($p<0.05$) but value touched the baseline within 5 min after intubation that was insignificant ($p>0.05$) there after there was fall in HR till 10 min. in diltiazem group there was significant increase in HR after intubation ($p<0.05$) but this rise was significantly less than the control group.

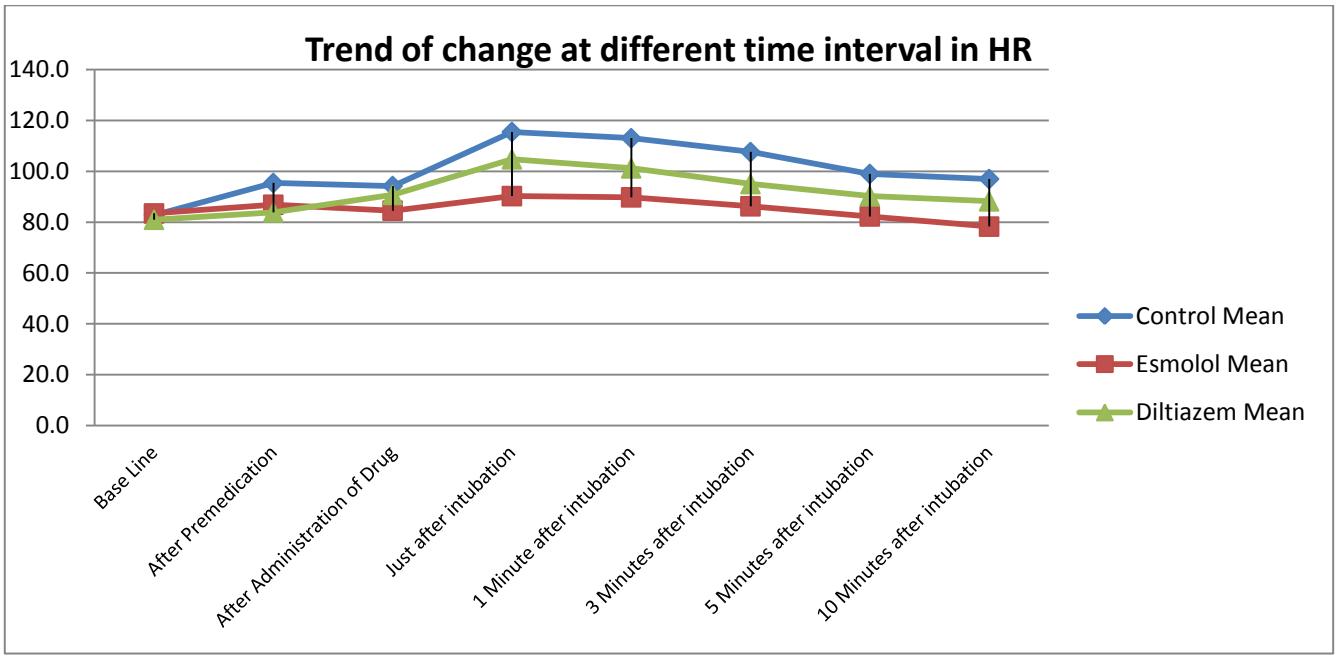

Table 3 Mean Systolic B.P. in various groups (Mean ± S.D.)

Observation Time	Control			Esmolol			Diltiazem		
	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.
Base Line	124.0 ± 11.5			122.6 ± 13.3			123.6 ± 9.9		
After premedication	128.6 ± 12.2	0.0011	S	121.9 ± 10.1	0.6674	NS	131.8 ± 12.2	0.0000	S
After administration of Drug	125.2 ± 15.6	0.5673	NS	116.9 ± 10.8	0.0173	S	115.9 ± 20.1	0.0492	S
Just after intubation	161.8 ± 24.7	0.0000	S	143.9 ± 15.4	0.0000	S	141.2 ± 8.6	0.0000	S
1 Minute after intubation	149.1 ± 21.6	0.0000	S	141.2 ± 14.5	0.0000	S	135.7 ± 14.0	0.0000	S
3 Minutes after intubation	139.8 ± 21.4	0.0000	S	133.9 ± 14.7	0.0003	S	123.8 ± 18.1	0.9546	NS
5 Minutes after intubation	130.0 ± 18.0	0.0307	S	122.9 ± 12.6	0.8815	NS	120.5 ± 15.5	0.3168	NS
10 Minutes after intubation	128.0 ± 18.0	0.1417	NS	118.9 ± 12.6	0.1592	NS	118.1 ± 15.4	0.0812	NS

The above table 3 depicts the mean SBP (Mean ± S.D.**)** from the baseline in all three groups at various study intervals. In control group there was significant rise in SBP just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol and diltiazem group there was significant rise in SBP after intubation but value touched the baseline within 3 min in diltiazem group and within 5 min.post intubation in esmolol group($p>0.05$).no incidence of hypotension was observed in any of the study group.

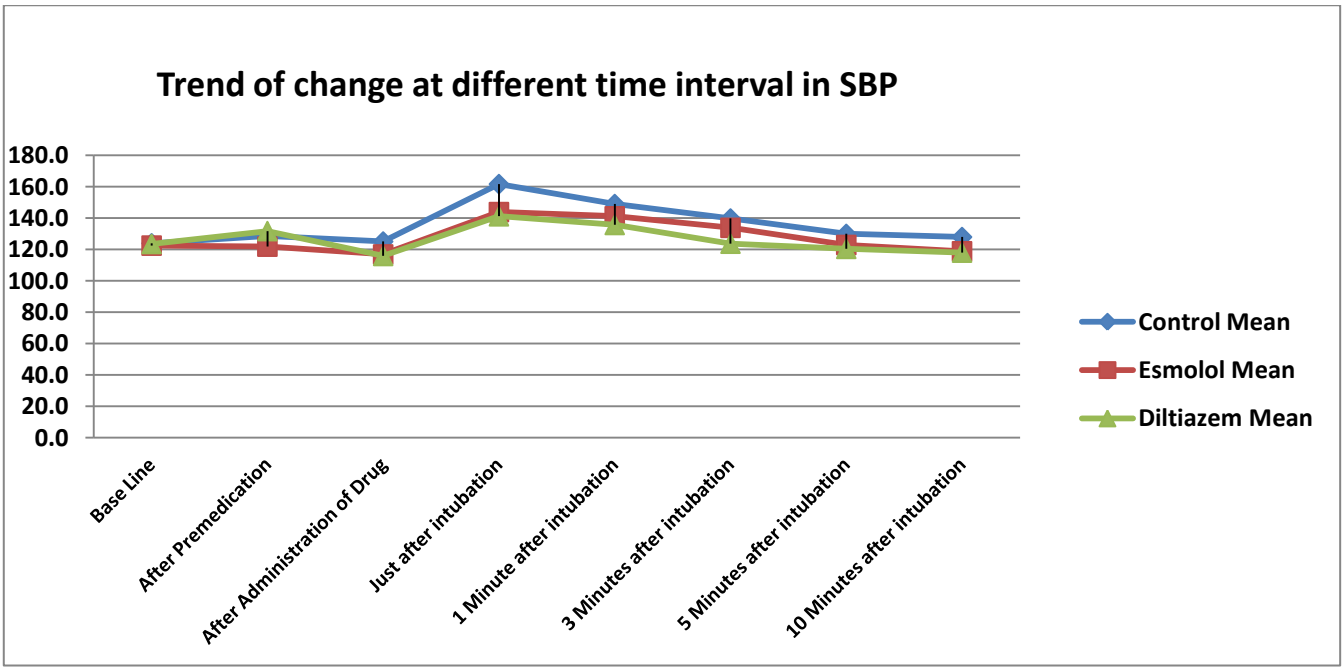

Table 4 Mean Diastolic B.P. in various groups (Mean ± S.D.)

Observation Time	Control			Esmolol			Diltiazem		
	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.
Base Line	81.6 ± 8.7			80.8 ± 7.6			**81.9 ± 6.5**		
After premedication	84.2 ± 7.5	0.0155	S	81.2 ± 7.3	0.2176	NS	86.8 ± 6.5	0.0000	S
After administration of Drug	82.8 ± 8.3	0.3654	NS	79.5 ± 7.6	0.2734	NS	77.7 ± 12.9	0.0339	S
Just after intubation	104.3 ± 17.4	0.0000	S	95.8 ± 12.5	0.0000	S	93.4 ± 9.8	0.0000	S
1 Minute after intubation	99.8 ± 14.6	0.0000	S	95.5 ± 8.9	0.0000	S	90.3 ± 7.8	0.0000	S
3 Minutes after intubation	94.7 ± 16.1	0.0000	S	87.9 ± 8.7	0.0000	S	82.8 ± 10.4	0.6293	NS
5 Minutes after intubation	88.2 ± 12.9	0.0042	S	83.0 ± 8.1	0.1441	NS	82.0 ± 9.8	0.9635	NS
10 Minutes after intubation	86.2 ± 12.9	0.0400	S	81.0 ± 8.1	0.9115	NS	80.2 ± 9.9	0.3182	NS

The above table depicts the mean DBP (Mean ± S.D.**)** from the baseline in all three groups at various study intervals. In control group there was significant rise in DBP just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol and diltiazem group there was significant rise in DBP after intubation but value touched the baseline within 3 min in diltiazem group and within 5 min.post intubation in esmolol group($p>0.05$). No incidence of hypotension was observed in any of the study group.

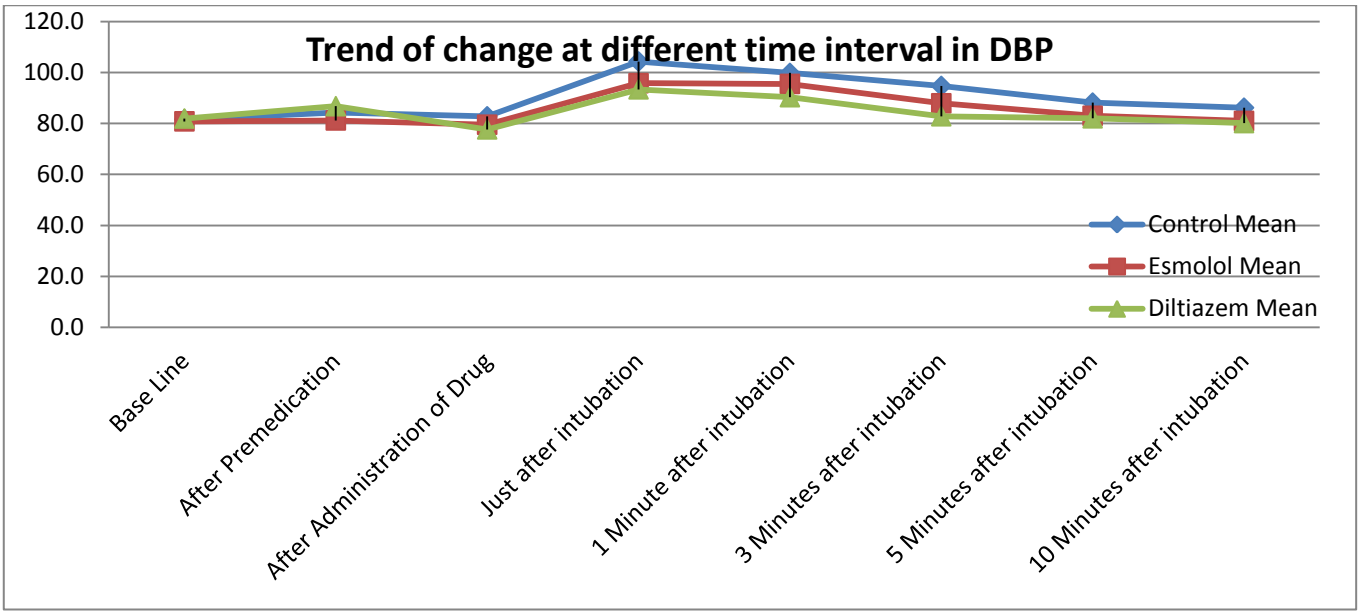

Table 5 Mean B.P. in various groups (Mean ± S.D.)

Observation Time	Control			Esmolol			Diltiazem		
	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.	Mean ± S.D.	P value	Sig.
Base Line	95.7 ± 8.9			94.8 ± 8.1			95.8 ± 6.8		
After premedication	99.0 ± 8.4	0.0037	S	94.8 ± 7.2	1.0000	NS	101.8 ± 8.0	0.0000	S
After administration of Drug	96.9 ± 10.2	0.4248	NS	92.0 ± 7.9	0.0602	NS	90.4 ± 14.7	0.0329	S
Just after intubation	123.5 ± 18.9	0.0000	S	111.8 ± 12.9	0.0000	S	109.4 ± 8.3	0.0000	S
1 Minute after intubation	116.2 ± 16.4	0.0000	S	110.7 ± 9.1	0.0000	S	105.5 ± 8.8	0.0000	S
3 Minutes after intubation	109.8 ± 17.3	0.0000	S	103.3 ± 9.6	0.0000	S	96.5 ± 12.3	0.7688	NS
5 Minutes after intubation	102.1 ± 14.2	0.0075	S	96.3 ± 9.0	0.3589	NS	94.8 ± 10.9	0.6395	NS
10 Minutes after intubation	100.1 ± 14.2	0.0590	NS	93.9 ± 9.2	0.5998	NS	92.8 ± 10.9	0.1541	NS

The above table depicts the mean MBP (Mean ± S.D.**)** from the baseline in all three groups at various study intervals. In control group there was significant rise in MBP just after intubation ($p<0.05$). The value remained significantly raised during whole study period. In the esmolol and diltiazem group there was significant rise in MBP after intubation but value touched the baseline within 3 min in diltiazem group and within 5 min.post intubation in esmolol group($p>0.05$).no incidence of hypotension was observed in any of the study group.

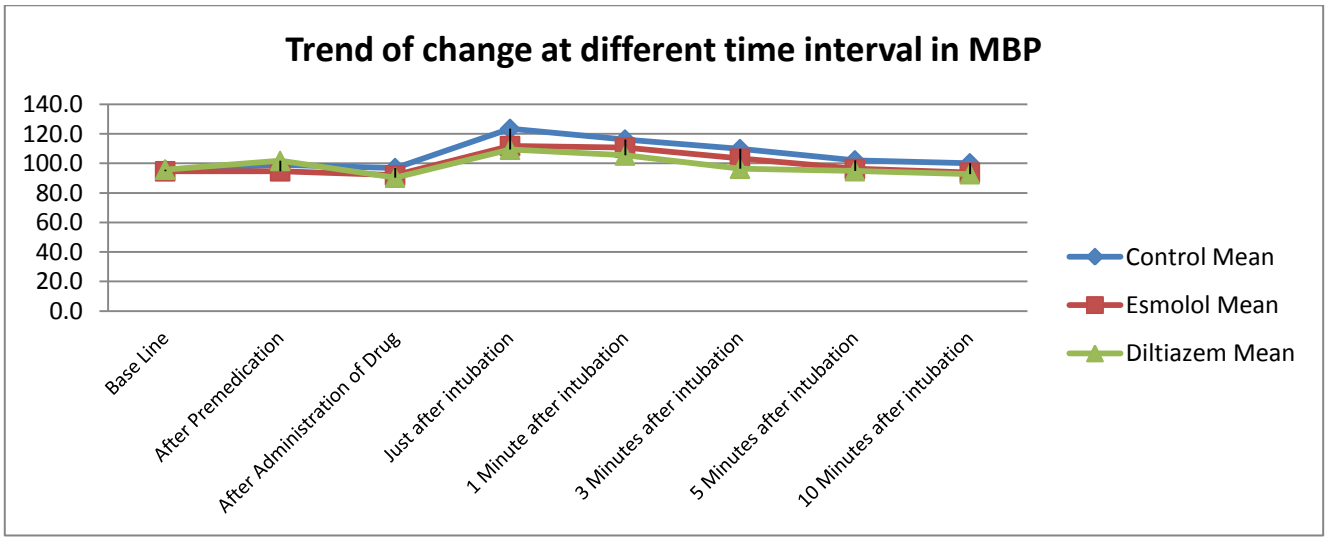

Table 6 Comparison of Mean Baseline Variables in the three groups

	Baseline			
	HR	**SBP**	**DBP**	**MBP**
Control	82.7 ± 13.8	124.0 ± 11.5	81.6 ± 8.7	95.7 ± 8.9
Esmolol	83.4 ± 15.2	122.6 ± 13.3	80.8 ± 7.6	94.8 ± 8.1
Diltiazem	81.0 ± 12.8	123.6 ± 9.9	81.9 ± 6.5	95.8 ± 6.8
P value	>0.05	>0.05	>0.05	>0.05
Significance	NS	NS	NS	NS

NS = Non Significant (P value >0.05); S = Significant (P value <0.05).

It was observed that mean baseline variables (HR, SBP, DBP and MBP) were similar in the three groups and no statistically significant difference was present (P value>0.05).

Discussion

The haemodynamic responses to laryngoscopy and intubation comprising elevation in HR, systolic and diastolic pressure are well known. The potential for life threatening complication associated with these responses especially in patients with preexisting cardiovascular and intracranial disorders is also well documented.

All the three study groups were statistically similar with regards to age and body weight. There was no statically significant difference between the basal value of heart rate, systolic and diastolic blood pressure and mean blood pressure between the three groups in the study.

Heart Rate

The heart rate was significantly raised after induction in control group and diltiazem group while no rise or rather decrease in heart rate was seen in the esmolol group. This rise in heart rate in control group might be due to glycopyrolate and vasodilatation caused by thiopentone. The additional rise in heart rate in diltiazem group might be due to diltiazem induced peripheral vasodilatation leading to the reflex tachycardia.

Immediately after intubation, there was a significant increase in heart rate in control group (p>0.05) and diltiazem group. In esmolol group the heart rate was increased but it was not statistically significant.

The diltiazem group was also found to be inefficient in controlling tachycardia due to this symphathatic stimulation. The significant increase in heart rate in control group and diltiazem group may be associated with\ critical increase in myocardial oxygen consumption yet ischemic changes did not appear in any patient probably because the myocardial perfusion pressure was maintained.

The esmolol group were however very effective in controlling tachycardia response associated with laryngoscopy and intubation. Mean heart rate was just minimally raised above the basal value in esmolol group.

Three minutes after intubation significant increase in heart rate in control group(p>0.05).the same was observed at 5 min.(p>0.05).

In diltiazem group tachycardia was found to be almost similar to the control group at all the time intervals. Increase in HR slightly lesser than the control group.

Thus diltiazem proved to be ineffective in controlling heart rate response associated with laryngoscopy and intubation.

Individual study on diltiazem was done by santosh kumar et al (2003)[11]. They also found that diltiazem was ineffective in controlling the heart rate.

These finding are consistent with that of Mikawa et al (1990)[10] who said i.v. diltiazem given 1 min. before laryngoscopy failed to protect against increase in heart rate after laryngoscopy and intubation.

In esmolol group the heart rate showed a very insignificant rise immediately after intubation but at 1 min. It started decreasing and almost touched the baseline value within 5 min. in esmolol group ,the heart rate remained closer to the basal value at all the time intervals and rise in heart rate observed after intubation was significantly lower

than what observed in other group. So the heart was most effectively controlled by esmolol group.

Dr Santosh Kumar et al (2003)[11] compare the efficacy of I.V esmolol diltiazem and magnesium sulphate. It was found that esmolol proved to be the most effective in attenuating rise in heart rate following laryngoscopy and intubation.

Systolic Blood Pressure

After intubation the increase in SBP was observed in all the three groups. However,the increase in SBP in control,diltiazem and esmolol was 39%, 12% and 16% respectively.

The diltiazem and esmolol group provided significant protection($p<0.05$) compared to the control group in controlling the SBP response in relation to laryngoscopy and intubation.

In control group the SBP remained above the basal value during whole study period. In the diltiazem group, the SBP touched the basal value within 3 min of intubation. In esmolol group, the SBP came down to basal value within 5 min. of intubation.

These result are consistent with the study of Dr Santosh Kumar et al (2003)[11], who observed that i.v. diltiazem (0.2mg/kg) was quite effective in controlling the pressure response associated with laryngoscopy and intubation whereas esmolol (2mg/kg) was not that very effective in controlling the pressure response associated with laryngoscopy and intubation .

Diastolic Blood Pressure (DBP)

Following induction and just after intubation the DBP increased in all the three groups.

It was observed that DBP in the control group increased after intubation but it remained elevated to significant level above the basal value even at 5 min post intubation($P<0.05$).

In diltiazem group the DBP was significantly raised immediately after intubation ($p<0.05$) but it got settled down to basal value within 3 min of intubation.

In esmolol group also the elevation in DBP after intubation was highly significant ($p<0.05$) but it came down to baseline within 5 min post intubation

Our finding are also similar to the results of mikawa et al (1990)[10] who found that increase in SBP and DBP was significantly less in diltiazem group (0.2 mg/kg) compare to control group.

Mean Blood Pressure (MBP)

After induction and just after intubation the MBP increased in all the three groups.

It was observed that MBP in the control group increased after intubation but value remained significantly raised during whole study period ($P<0.05$). In diltiazem group the MBP was significantly raised immediately after intubation ($p<0.05$) but it got settled down to basal value within 3 min of intubation. In esmolol group also the elevation in MBP after intubation was highly significant ($p<0.05$) but it came down to baseline within 5 min post intubation.

Our finding are also similar to the results of mikawa et al (1990)[10] who found that increase in DBP and MBP was significantly less in diltiazem group (0.2 mg/kg) compare to control group.

Summary and Conclusion

1) Definitive haemodynamic response to laryngoscopy and intubation was observed in control group with highly significant increase in heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure occuring just after intubation compared to the preinduction basal value.
2) Diltiazem was found to be ineffective in controlling the heart rate response related with laryngoscopy and intubation. The intensity and duration of rise in heart rate was almost similar to the control group. Esmolol were very effective in attenuating this tachycardia. The heart rate at all the stages of the study period was significantly lesser in the esmolol group as compare to the placebo.thus esmolol achieved better control over the heart rate among all the study drugs.
3) The systolic blood pressure elevation after intubation in both diltiazem and esmolol

group was significantly less compared to the control. The value touched the baseline within 3 min in diltiazem group and within 5 min in esmolol group, however the rise in SBP was significantly lesser in diltiazem group then in esmolol group. Thus diltiazem achieved much better control on the systolic blood pressure rise related with laryngoscopy and intubation among all the three groups.

4) The diastolic blood pressure after intubation was significantly attenuated by both esmolol and diltiazem. The value touched the baseline within 3 min in diltiazem group and within 5 min in esmolol group. Thus diltiazem achieved better control on diastolic blood pressure among all the study drugs.
5) The mean blood pressure elevation after intubation in both diltiazem and esmolol group was significantly less compared to the control.the value touched the baseline within 3 min in diltiazem group and within 5 min in esmolol group. Thus diltiazem achieved much better control on the mean blood pressure rise related with laryngoscopy and intubation among all the three groups.
6) No ECG, abnormality was observed in any patients in any group.

Hence esmolol was the most effective in controlling the heart rate following laryngoscopy and intubation but it was not very effective in attenuating the pressure response related with laryngoscopy. Diltiazem was quite effective in controlling the pressure response but it failed to achieve any control over the heart rate response in relation to laryngoscopy and intubation.

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