Original Article

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Effect of Esmolol, Labetalol and Metoprolol for Attenuating the Cardiovascular Stress Response to Laryngoscopy and Intubation: A Comparative Study

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Abstract

Background: To compare esmolol, labetalol and metoprolol in attenuating the cardiovascular response of L&I. **Subjects and Methods:** It was a randomized prospective study in 120 patients of 18-60 years, of ASA grade I and II, of either sex, posted for elective surgery under GA. After approval from ethical committee and informed written consent, the patients were randomly allocated in four groups of 30 each. Group C (control) received 10 ml 0.9% saline, group E esmolol 0.5 mg/kg (both 2min prior to induction), Group L labetalol 0.25 mg/kg and Group M metoprolol 0.1 mg/kg (both 5min prior to induction). All patients were pre-medicated with inj. ondansetron 0.1 mg/kg, inj. glycopyrrolate 0.004 mg/kg, inj. pen-tazocine 0.6 mg/kg and inj. midazolam 1 mg. All patients were induced with inj. thiopentone 5 mg/kg and succinylcholine 2 mg/kg. Anaesthesia was maintained on isoflurane, O2:N2O and Atracurium. Heart rate and BP were recorded: pre-operative, after pre-medication, after induction, after L&I, after 1, 3, 5, 10, 15 minutes following L&I. **Results:** All the study drugs significantly attenuated the HR, SBP, DBP, MBP and RPP following L&I compared to control. Metoprolol attenuated the heart rate and RPP compared to esmolol and labetalol. Esmolol attenuated the heart rate immediately following L&I better than labetalol and significantly attenuated the SBP at 5min and 10 min following L&I. All readings of RPP were lower in esmolol in comparison to labetalol. Esmolol, was better than labetalol in attenuating the hemodynamic response. Sinus tachycardia and hypotension were the common side effects. Three patients in control and one in labetalol group developed ectopic beats following L&I. One patient in esmolol had pain on i.v injection. **Conclusion:** Metoprolol attenuated the cardiovascular stress response to L & I in comparison to esmolol and labetalol. Esmolol was comparably better than labetalol. Metoprolol can be used as alternative to esmolol and labetalol.

Keywords: Esmolol, Labetalol, Metoprolol.

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Introduction

Laryngoscopy and endotracheal intubation is an indispensable part of prac-tice for an anaesthesiologists career despite the advent of technological advances in airway equipment. L&I causes cardiovascular changes which are largely ignored or taken for granted.

These responses were initially described as reflex in nature [King BD],[18] but were stated to be vasovagal type or as being the result of reflex sympatho-adrenal stimulation [Bruder N],[2] caused by the efferent responses from the pharyngeal stimulation. There is increase in heart rate, blood pres-sure [Forbes AM, Prys Roberts C, Stoelting RK],[10,31,43] intracranial pressure and intraocular pressure. There is an average increase in blood pressure by 40-50% and 20% increase in heart rate.[2]

It is believed that the increase in the arterial blood pressure during L&I is predominantly due to an increase in cardiac output and less predominantly due to increase in SVR. There is an associated increase in CVP and some-times arrhythmias.

These cardiovascular stress responses can be detrimental in patients of cardiovascular diseases like hypertension, coronary artery diseses, and in CNS conditons of raised ICP-EDH, SDH, aneurysms, intracranial tumors etc.[10]

LVF, MI, cerebral haemorrhage can occur in susceptible patients. Convul-sions can occur in parturients with pre-eclampsia.

Esmolol is an ultrashort acting beta-blocker with rapid onset of action. Its elimination half life is 9.2 min. It is metabolized by red cell esterases into methanol and other inactive metabolites. Esmolol achieves peak effect on heart rate within one minute and on blood pressure within two minute of i.v injection [Miller Donald R].[28]

Labetalol is a combined alpha 1 and beta blocker. It has on onset of action of 5 min. Its average duration of action is 6 hrs. The i.v dose is 10-20 mg given over 2 min, followed by

repeat dose every 10 min till the clinically desired BP is attained.

Metoprolol is a beta-1 selective adrenoreceptor blocker. It decreases heart rate and contractility leading to decrease in cardiac output. Given in a dose of 0.1mg/kg, the maximum response is obtained in 20 min on iv injection and the duration of action is about 4 hours.

We did a study to assess and compare esmolol, labetalol and metoprolol in attenuating the cardiovascular response of L&I.

Aims and objectives

The Aims and objectives of the study is to assess and compare the effects of esmolol, labetalol and metoprolol in attenuating the haemodynamic cardi-ovascular pressor response in L&I and to evaluate for any side effects intra or perioperatively.

Subjects and Methods

The present study was conducted in the Department of Anaesthesiology and Critical Care, Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital Raipur, Chhattisgarh after approval from ethical committee.

It was a prospective, randomised controlled study. We compared esmolol, labetalol and metoprolol in decreasing the cardiovascular stress response during rigid laryngoscopy and intubation.

The study included 120 normotensive patients (30 in each group)belonging to ASA grade I and II of either sex undergoing elective surgery requiring gen-eral anaesthesia and intubation in general surgery, ENT, orthopaedics and gynaecological procedures.

All the patients were randomly allocated into four groups of 30 each to re-ceive the study drugs:-

1. Group C: 0.9% saline 10ml given as control
2. Group E: iv esmolol 0.5 mg/kg
3. Group L: slow iv labetalol 0.25 mg/kg
4. Group M: slow iv metoprolol 0.1 mg/kg

All the study drugs were diluted to 10 ml 0.9% NS.

Criteria for selection of patients

Inclusion criteria

i. ASA physical status I and II adult patients
ii. Age 18-45 years
iii. Either sex
iv. Normotensive patient

Exclusion criteria

i. Cardiovascular diseases
   a. Hypertension
   b. Ischemic heart disease
   c. Recent myocardial infarction
   d. Cardiac failure
   e. Sinus bradycardia(<60/min or heart block)
   f. Current treatment with β-blockers, verapamil, diltiazem and amiodarone
ii. Pulmonary diseases: Chronic obstructive airway disease or asthma
iii. Hepatic diseases
iv. Renal diseases
v. Patients with anticipated difficult airway; laryngoscopy and intubation time more than 30 seconds or requiring more than two attempts
vi. Poor general condition
vii. Fever(temp.>99 deg. F)
viii. Diabetes mellitus
ix. Anaemia with Hb<10g/dl.

Pre-operative Assessment

A detailed pre-operative assessment of the patient was done after taking complete history, clinical examination and recording of vital parameters.

Informed written consent was taken from all the patients.

Following investigations were carried out in all patients:-

1. Hb, TLC, DLC, ESR
2. Urine examination routine and microscopy
3. Blood glucose level fasting and post prandial
4. Blood urea
5. Chest X-ray PA view
6. ECG
7. Other investigations were carried out if indicated

Protocol

1. All the patients were kept fasting 6 hours preoperatively.
2. In the operation theatre, on day of surgery the patients were again ex-amined. Pre-induction (baseline) HR, SBP, DBP and MBP were noted. ECG monitoring was done with Multipara monitors.
3. Intravenous access was secured with18 G i.v cannula with RL.
4. Pre-anaesthetic medication was done15 minutes prior to induction with:
   a. Inj. Ondansetron ~4mg (0.1 mg/kg)
   b. Inj. Glycopyrrolate ~0.2mg (0.004 mg/kg)
   c. Inj. Pentazocine 0.6 mg/kg
   d. Inj. Midazolam 1 mg
5. Injection of the study drugs and saline:-
   i. In group C, received 10 ml of 0.9% saline 2 min before L&I.
   ii. In group E, 0.5 mg/kg of esmolol was given 2 min prior to L&I
   iii. In group L, 0.25 mg/kg of labetalol was given 5 min prior to L&I.
   iv. In group M, 0.1 mg/kg of metoprolol was given 5 min prior to L&I.

   All the study drugs were diluted to 10ml 0.9% normal saline (Q.S)
6. Pre-oxygenation was done with 100% for 3-5 minutes.
7. Induction:
   i. All patients were induced with inj. thiopentone 5 mg/kg followed by suc-cinylcholine 2 mg/kg to facilitate intubation.
   ii. After maximal relaxation and IPPV, laryngoscopy was carried out by Ma-cintosh laryngoscope and intubation was achieved with appropriate size cuffed orotracheal tube. Duration of laryngoscopy and number of at-tempts required for intubation were noted.
8. Maintenance: Anaesthesia was maintained on isoflurane;

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O2, N2O: 40:60 and inj Atracurium and IPPV.

9. Reversal: At the end of surgery, reversal was done with inj. neostigmine (40µg/kg) and inj. glycopyrrolate (0.008 mg/kg).

Monitoring

Haemodynamic monitoring: Heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, respiratory rate and oxygen saturation (SpO2) and ECG changes were monitored at various time intervals.

i. Pre-operative
ii. After pre-medication
iii. After induction
iv. Just after laryngoscopy and intubation
v. After 1 min, 3 min, 5 min, 10 min, 15 min following L&I

Rate pressure product was derived and recorded at the same time intervals.

Haemodynamic changes:

i. Heart rate below 50 beats per minute was considered as bradycardia.
ii. Heart rate above 120 beats per minute was considered as sinus tachy-cardia.
iii. Systolic Blood Pressure below 90mmHg was considered as hypotension.
iv. Fall in SpO2 below 90% and any signs of respiratory distress were con-sidered significant and treated.

Analysis of results and statistical methods:

The results were analyzed by various statistical techniques-percentage, mean and standard deviation

Probability value (P value):-

1. Significance of difference between means within a group i.e comparison of the haemodynamic variations with their respective baseline values was calculated by paired t-test.
2. Significance of difference between means of the groups was found out by ANOVA test (analysis of variance).

A 'p' value < 0.05 was taken as significant.

All the data were compiled in masterchart, tabulated, calculated and ana-lysed with the help of Figure-pad prism software.

Results

The observations recorded in each group are shown in the following tables and Figures:

Table 1: Drug Distribution

Drug	No. of Cases	Group
Control	30	C
Esmolol	30	E
Labetalol	30	L
Metoprolol	30	M

[Table 1] shows the distribution of cases according to the drug used [Figure 1]. Patients were randomly divided into four groups with 30 patients in each group.

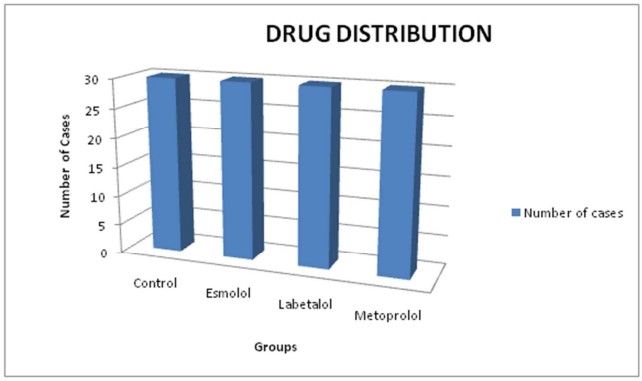

Figure 1: Drug Distribution

Table 2: Doses of Drug Received

	Group C	Group E	Group L	Group M
Dose of the drug recieved	0.9% NS	0.5mg/kg	0.25mg/kg	0.1mg/kg

[Table 2] shows the doses of the drug received (mg/kg) by the cases [Figure 2] Group C received 0.9% normal saline 10 ml, group E received esmolol 0.5mg/kg, group L received labetalol 0.25mg/kg and group M received meto-prolol 0.1mg/kg. Labetalol and metoprolol was given 5 minutes before induc-tion whereas saline and esmolol was given 2 min prior to induction. All the study drugs were diluted to 10 ml N.S (Q.S)

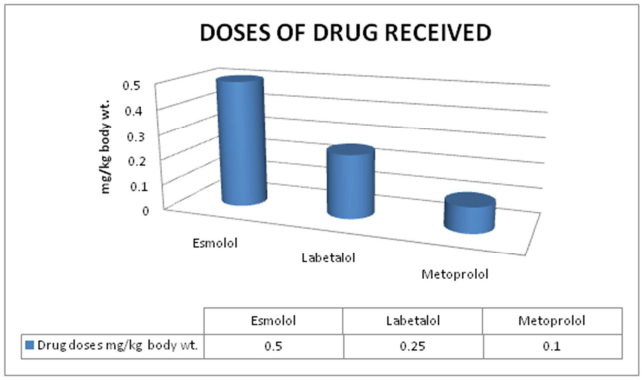

Figure 2: Doses of Drug Received

Table 3a: DemoFigureic Profile: Age And Body Weight Distri-Bution

S.No.	Variables	Groupc (Mean± Sd)	Group E (Mean± Sd)	Group L (Mean± Sd)	Group M (Mean ± Sd)
1.	Age (years)	37.57±9.67	35.53±11.41	36.87±14.59	35.87±12.22
2.	Weight (kg)	54.64±9.94	55.37±11.56	54.27±10.23	56.23±12.51

[Table 3a] shows that the four groups are comparable with respect to age and weight [Figure 3a (i) and (ii)]. The groups were comparable with respect to age and weight. The mean age (in years) was 37±9.67, 35.53±11.41, 36.87±14.59 and 35.87±12.22 in the groups C, E, L and M respectively. The mean weight (in kg) was 54.64±9.94, 55.37±11.56, 54.37±10.23 and 56.23±12.51 respectively. The youngest patient in all the groups was 18 years. The oldest patient in

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groups E, L and M was 60 years while that in group C was 57 years.

Table 3b: DemoFigureic Profile: Sex Distribution

Sex	Group C	Group E	Group L	Group M
Male	15	14	16	14
Female	15	16	14	16

[Table 3b] shows that the four groups are comparable with respect to sex dis-tribution [Figure 3b]. The male to female ratios were 15:15, 14:16, 16:14 and 14:16 in groups C, E, L and M respectively.

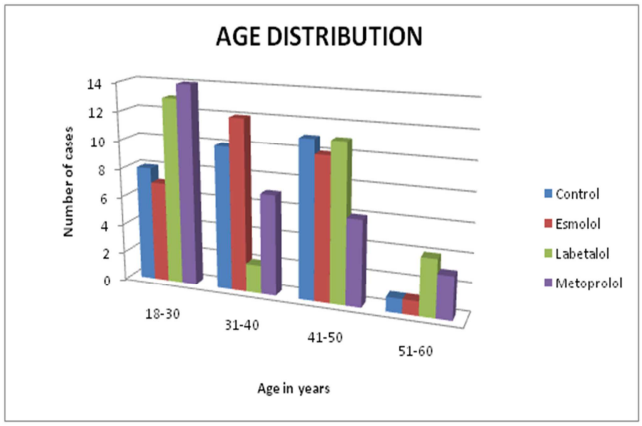

Figure 3a (i): Age Distribution

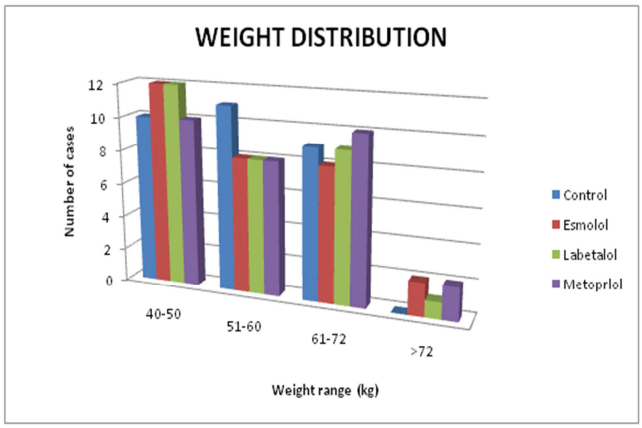

Figure 3a (ii): Weight Distribution

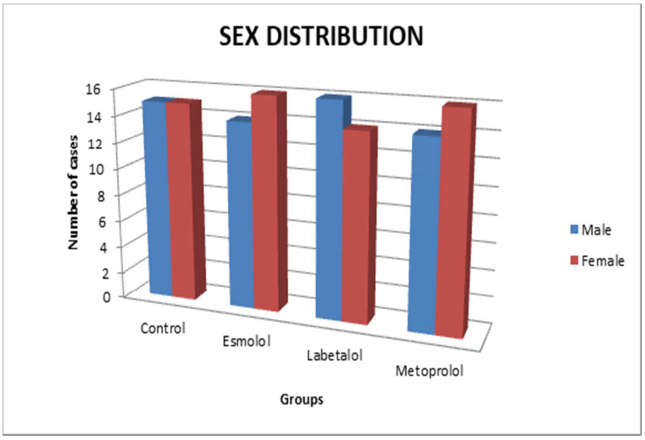

Figure 3b: Sex Distribution.

TABLE-4a

CHANGES IN HEART RATE: Comparison with Baseline and Control

	GROUP C MEAN± SD p compared to pre-indn values	GROUP E MEAN ± SD p compared to pre-indn.values	'P' (compared with control)	GROUP L MEAN± SD p compared to pre-indn values	'P' (compared with control)	GROUP M MEAN± SD p compared to pre-indn values	'P' (compared with control)
Pre-induction	84.43 ± 5.367	87.77 ± 7.267	> 0.05	86.2 ± 9.707	> 0.05	88 ± 8.94	> 0.05
After induction	84.4 ± 5.096 p< 0.0001	87.43 ± 7.704 p< 0.0001	> 0.05	86.38 ± 11.54 p< 0.0001	> 0.05	86.33 ± 7.009 p=0.2925	> 0.05
Just after L & I	111.5 ± 7.031 p< 0.0001	103 ± 7.531 p< 0.0001	< 0.01	101.6 ± 13.11 p< 0.0001	< 0.0001	92.87 ± 7.352 p=0.0041	< 0.0001
1 min after L & I	108.7 ± 6.215 p< 0.0001	95.33 ± 7.88 p< 0.0001	< 0.0001	101 ± 11.7 p=0.0002	< 0.01	92.37 ± 7.266 p=0.0055	< 0.0001
3 min after L&I	102.8 ± 4.942 p< 0.0001	103.5 ± 7.361 p< 0.0001	> 0.05	95.83 ± 10.96 p=0.0002	< 0.05	91.93 ± 6.4 p=0.0173	< 0.0001
5 min after L &I	101.4 ± 4.582 p< 0.0001	101.2 ± 8.779 p< 0.0001	> 0.05	95.57 ± 11.96 p=0.0005	> 0.05	90.5 ± 5.993 p=0.0988	< 0.0001
10 min after L&I	94.83 ± 5.286 p< 0.0001	95.23 ± 7.496 p< 0.0001	> 0.05	91.9 ± 10 p=0.0245	> 0.05	91.9 ± 10 83.73 ± 8.851	< 0.0001

Table 4 shows changes in the heart rate and comparison with baseline and control(Graph 4).

Table 4b: Changes In Heart Rate: Comparison among the Study Drug Groups

Heart Rate (beats/min) w.r.t time	Group E vs L P value	Group L vs M P value	Group M vs E P value
Pre-induction	> 0.05	> 0.05	> 0.05
After induction	> 0.05	> 0.05	> 0.05
Just after L & I	> 0.05	< 0.01	< 0.001
1min after L & I	> 0.05	< 0.01	> 0.05
3 min after L&I	< 0.05	> 0.05	< 0.0001
5 min after L &I	> 0.05	> 0.05	< 0.0001
10 min after L&I	> 0.05	< 0.01	< 0.0001

[Table 4b] shows comparison in heart rate among the study drug groups [Figure 4]. Metoprolol significantly attenuated the HR rise in comparison to labetalol just after L&I, at 1min and at 10 min (P<0.01) and in comparison to esmolol just after L&I, at 3 min, 5min and 10 min (P<0.0001). Labetalol significantly attenuated (P<0.05) the HR rise, 3 min after L&I in comparison to esmolol.

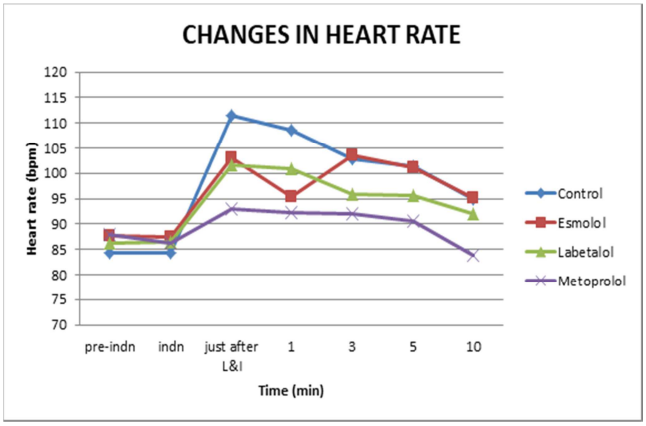

Figure 4: Changes in Heart Rate

TABLE-5a

CHANGES IN SYSTOLIC BLOOD PRESSURE: Comparison with Baseline and Control

	GROUP C MEAN± SD p compared to pre-indn values	GROUP E MEAN ± SD p compared to pre-indn.values	'P' (compared with control)	GROUP L MEAN± SD p compared to pre-indn values	'P' (compared with control)	GROUP M MEAN± SD p compared to pre-indn values	'P' (compared with control)
Pre-induction	116.2 ±4.213	114.6 ± 7.346	> 0.05	118.2 ± 9.966	> 0.05	119.4 ± 8.897	> 0.05
After induction	116.3 ±4.571 p>0.05	113.2 ± 7.202 p>0.05	> 0.05	116.5 ± 9.818 p>0.05	> 0.05	116.3 ± 8.903 p>0.05	> 0.05
Just after L & I	156.8 ±5.054 p< 0.001	135.9 ± 9.573 p< 0.001	< 0.0001	140.6 ± 13.4 p< 0.001	< 0.0001	136 ± 8.552 p< 0.001	< 0.0001
1 min after L & I	145 ±2.665 p< 0.001	126.5 ± 9.024 p< 0.001	< 0.0001	129.3 ± 13.08 p=0.001 to 0.01	< 0.0001	129.7 ± 11.03 p< 0.001	< 0.0001
3 min after L&I	135.8 ±3.727 p< 0.001	115.2 ± 4.506 ns	< 0.0001	114.9 ± 13.91 p>0.05	< 0.0001	113.6 ± 12.11 p>0.05	< 0.0001
5 min after L &I	127.9 ±3.695 p< 0.001	103.9 ± 6.266 p< 0.001	< 0.0001	113.2 ± 11.13 p>0.05	< 0.0001	106 ± 11.04 p< 0.001	< 0.0001
10 min after L&I	121.8 ±3.295 p< 0.001	97.53 ± 4.133 p< 0.001	< 0.0001	107 ± 13.48 p=0.001 to 0.01	< 0.0001	103.9 ± 7.021 p< 0.001	

Table 6 shows changes in the systolic blood pressure and comparison with baseline and control (Graph 5).

Table 5b: Changes In Systolic Blood Pressure: Comparison among the Study Drug Groups

SBP (mm Hg) w.r.t time	Group E vs L P value	Group L vs M P value	GroupM vs E P value
Pre-induction	> 0.05	> 0.05	> 0.05
After induction	> 0.05	> 0.05	> 0.05
Just after L & I	> 0.05	> 0.05	> 0.05
1min after L & I	> 0.05	> 0.05	> 0.05
3 min after L&I	> 0.05	> 0.05	> 0.05
5 min after L &I	< 0.01	> 0.05	> 0.05
10 min after L&I	< 0.01	> 0.05	> 0.05

[Table 5b] shows the comparison in SBP among the study drug groups [Figure 5]. Esmolol significantly attenuated (P<0.01) the SBP rise, 3 min and 5 min after L&I in comparison to labetalol.

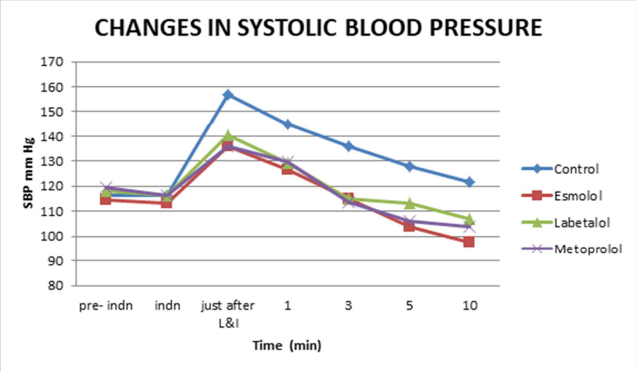

Figure 5: Changes in Systolic Blood Pressure.

TABLE-6a

CHANGES IN DIASTOLIC BLOOD PRESSURE: Comparison with Baseline and Control

	GROUP C MEAN± SD p compared to pre-indn values	GROUP E MEAN ± SD p compared to pre-indn.values	'P' (compared with control)	GROUP L MEAN± SD p compared to pre-indn values	'P' (compared with control)	GROUP M MEAN± SD p compared to pre-indn values	'P' (compared with control)
Pre-induction	78.83 ±5.16	74.2 ± 6.054	> 0.05	74.3 ± 7.949	P > 0.05	73.8 ± 6.451	P > 0.05
After induction	79.93 ± 5.265 p>0.05	81.47 ± 5.998 p< 0.001	> 0.05	77.3 ± 7.835 p>0.05	P > 0.05	82.83 ± 5.82 p< 0.001	P > 0.05
Just after L & I	94.33 ± 2.354 p< 0.001	92.1 ± 5.616 p< 0.001	> 0.05	93.07 ± 7.625 p< 0.001	P > 0.05	89.3 ± 6.487 p< 0.001	P > 0.05
1min after L & I	92.67 ± 3.871 p< 0.001	85.67 ± 6.92 p< 0.001	< 0.001	84.8 ± 5.762 p< 0.001	< 0.0001	85.27 ± 6.068 p< 0.001	P < 0.001
3min after L&I	84.93 ± 2.392 p< 0.001	75.63 ± 4.131 p>0.05	< 0.0001	73.63 ± 5.768 p>0.05	< 0.0001	75.47 ± 8.186 p>0.05	P < 0.0001
5min after L &I	83.2 ± 3.585 p< 0.001	71.13 ± 4.305 p>0.05	< 0.0001	70.83 ± 8.367 p>0.05	< 0.0001	70.77 ± 6.463 p>0.05	P < 0.0001
10min after L&I	75.6 ± 6.268 p=0.01 to 0.05	64.03 ± 4.951 p< 0.001	< 0.0001	64.6 ± 10.93 p< 0.001	< 0.0001	69.63 ± 4.351 p>0.05	P < 0.01

Table 6 shows changes in the diastolic blood pressure and comparison with baseline and control (Graph 6).

Table 6b: Changes In Diastolic Blood Pressure: Comparison among the Study Drug Groups

DBP (mm Hg) w.r.t time	Group E vs L P value	Group L vs M P value	GroupM vs E P value
Pre-induction	> 0.05	> 0.05	> 0.05
After induction	> 0.05	> 0.05	> 0.05
Just after L & I	> 0.05	> 0.05	> 0.05
1min after L & I	> 0.05	> 0.05	> 0.05
3 min after L&I	> 0.05	> 0.05	> 0.05
5 min after L &I	> 0.05	> 0.05	> 0.05
10 min after L&I	> 0.05	> 0.05	< 0.05

[Table 6b] shows comparison of DBP among the study drug groups [Figure 6]. No statistically significant difference was seen among the comparison in DBP between the study drug groups, except a statistically significant fall in esmolol compared to metoprolol at 10 minute following L&I (P<0.05).

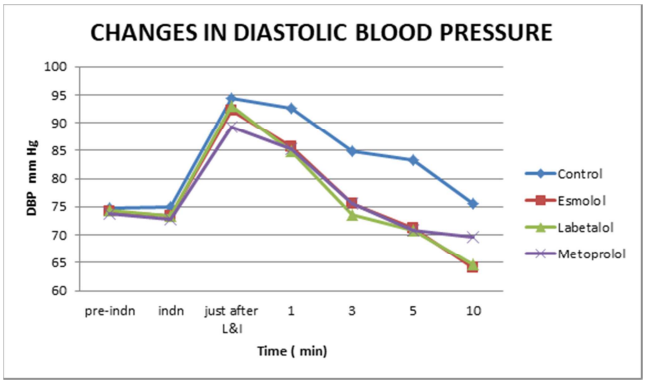

Figure 6: Changes in Diastolic Blood Pressure.

TABLE-7a

CHANGES IN MEAN BLOOD PRESSURE: Comparison with Baseline and Control

	MEAN± SD GROUP C p compared to pre-indn values	MEAN± SD GROUP E p compared to pre-indn values	'P' (compared with control)	MEAN± SD GROUP L p compared to pre-indn values	'P' (compared with control)	MEAN± SD GROUP M p compared to pre-indn values	'P' (compared with control)
Pre-induction	91.29 ± 3.835	87.68 ± 6.1	P > 0.05	88.92 ± 7.454	P > 0.05	89.01± 5.2	P > 0.05
After induction	92.04 ± 3.915 p>0.05	92.03 ± 5.605 p=0.01 to 0.05	P > 0.05	90.36 ± 7.615 p>0.05	P > 0.05	94 ± 5.981 p=0.01 to 0.05	P > 0.05
Just after L & I	115.2 ± 2.482 p< 0.001	106.7 ± 6.215 p< 0.001	P < 0.0001	108.9 ± 8.239 p< 0.001	P < 0.01	104.9 ± 6.104 p< 0.001	P < 0.0001
1min after L & I	110.1 ± 2.556 p< 0.001	99.28 ± 7.297 p< 0.001	P < 0.0001	99.62 ± 7.452 p< 0.001	P < 0.0001	100.1 ± 7.349 p< 0.001	P < 0.0001
3min after L&I	101.9 ± 2.283 p< 0.001	88.82 ± 3.776 p>0.05	P < 0.0001	87.4 ± 7.44 p>0.05	P < 0.0001	88.18 ± 9.039 p>0.05	P < 0.0001
5min after L &I	98.11 ± 2.495 p< 0.001	82.06 ± 4.454 p< 0.001	P < 0.0001	84.97 ± 9.013 ns	P < 0.0001	82.51 ± 7.356 p=0.001 to 0.01	P < 0.0001
10min after L&I	91 ± 4.03 p>0.05	75.2 ± 4.348 p< 0.001	P < 0.0001	78.73 ± 11.17 p< 0.001	P < 0.0001	81.04 ± 4.662 p< 0.001	P < 0.0001

Table 6 shows changes in the Mean blood pressure and comparison with baseline and control (Graph 7).

Table 7b: Changes in Mean Blood Pressure: Comparison among the Study Drug Groups

MBP (mm Hg) w.r.t time	Group E vs L P value	Group L vs M P value	GroupM vs E P value
Pre-induction	> 0.05	> 0.05	> 0.05
After induction	> 0.05	>0.05	> 0.05
Just after L & I	> 0.05	> 0.05	> 0.05
1min after L & I	> 0.05	> 0.05	> 0.05
3 min after L&I	> 0.05	> 0.05	> 0.05
5 min after L &I	> 0.05	> 0.05	> 0.05
10 min after L&I	> 0.05	> 0.05	< 0.05

[Table 7b] shows comparison in MBP among the study drug groups [Figure 7]. No statistically significant difference was seen among the com-parison in MBP between the study drug groups, except a statistically signifi-cant fall in esmolol compared to metoprolol 10 minutes following L&I (P<0.05).

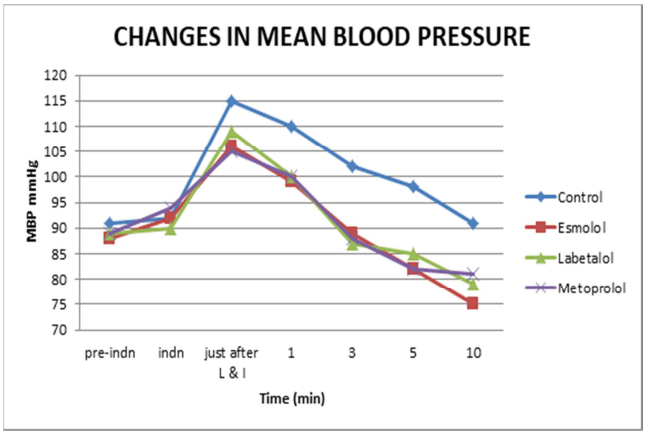

Figure 7: Changes in Mean Blood Pressure.

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TABLE-8a

CHANGES IN RATE PRESSURE PRODUCT: Comparison with Baseline and Control

	MEAN± SD			MEAN± SD		MEAN± SD	
	GROUP C p compared to pre-indn values	GROUP E p compared to pre-indn values	'P' (compared with control)	GROUP L p compared to pre-indn values	'P' (compared with control)	GROUP M p compared to pre-indn values	'P' (compared with control)
Pre-induction	9811 ± 710.7	10048 ± 980.7	P > 0.05	10191 ± 1421	P > 0.05	10516 ± 1380	P > 0.05
After induction	9816 ± 752.5 p>0.05	9907 ± 1247 p>0.05	P > 0.05	10044 ± 1404 p>0.05	P > 0.05	10047 ± 1185 p>0.05	P > 0.05
Just after L & I	17479 ± 1181 p< 0.001	13978 ± 1300 p< 0.001	P < 0.0001	14282 ± 2306 p< 0.001	P < 0.0001	12649 ± 1525 p< 0.001	P < 0.0001
1min after L & I	15761 ± 934.6 p< 0.001	12048 ± 1236 p< 0.001	P < 0.0001	13029 ± 1802 p< 0.001	P < 0.0001	11989 ± 1501 p< 0.001	P < 0.0001
3min after L&I	13959 ± 657 p< 0.001	11929 ± 983.4 p< 0.001	P < 0.0001	10992 ± 1656 p>0.05	P < 0.0001	10423 ± 1140 p>0.05	P < 0.0001
5min after L &I	12972 ± 765.4 p< 0.001	10537 ± 1284 p>0.05	P < 0.0001	10793 ± 1516 p>0.05	P < 0.0001	9600 ± 1216 p=0.01 to 0.05	P < 0.0001
10min afterL&I	11551 ± 730.1 p< 0.001	9310 ± 996.4 p>0.05	P < 0.0001	9830 ± 1569 p>0.05	P < 0.0001	8717 ± 1296 p< 0.001	P < 0.0001

Table 10 shows changes in the Rate pressure product and comparison with baseline and control (Graph 8).

Table 8b: Changes In Rate Pressure Product: Comparison among the Study Drug Groups

RPP w.r.t time	Group E vs L P value	Group L vs M P value	Group M vs E P value
Pre-induction	> 0.05	> 0.05	> 0.05
After induction	> 0.05	> 0.05	> 0.05
Just after L & I	> 0.05	< 0.0001	< 0.01
1min after L & I	> 0.05	> 0.05	> 0.05
3 min after L&I	> 0.05	> 0.05	< 0.001
5 min after L &I	> 0.05	< 0.05	> 0.05
10 min after L&I	> 0.05	< 0.05	> 0.05

[Table 8b] shows comparison in RPP among the study drug groups [Figure 8]. Statistically significant lesser RPP was seen in metoprolol group com-pared to labetalol group just after L&I (P<0.0001), at 5min and at 10min af-ter L&I (P<0.5). Statistically significant lesser RPP was seen in metoprolol group compared to esmolol group just after L&I (P<0.01) and at 3min (P<0.01) following L&I.

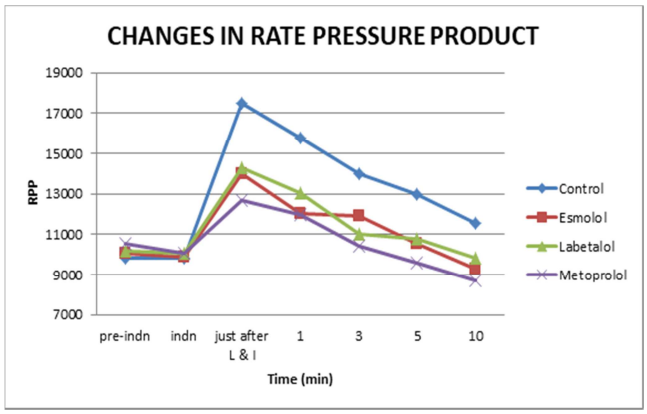


Figure 8: Changes in Rate Pressure Product.

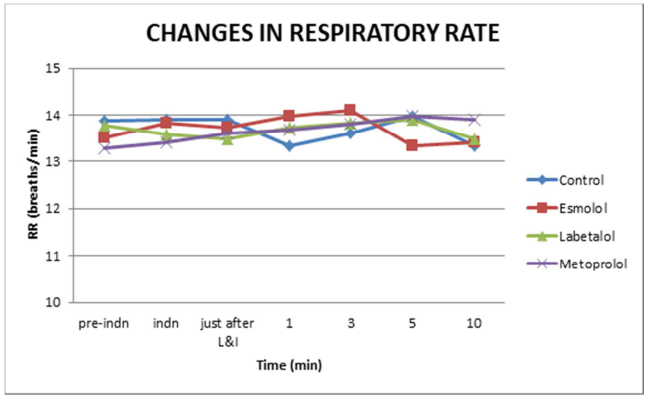


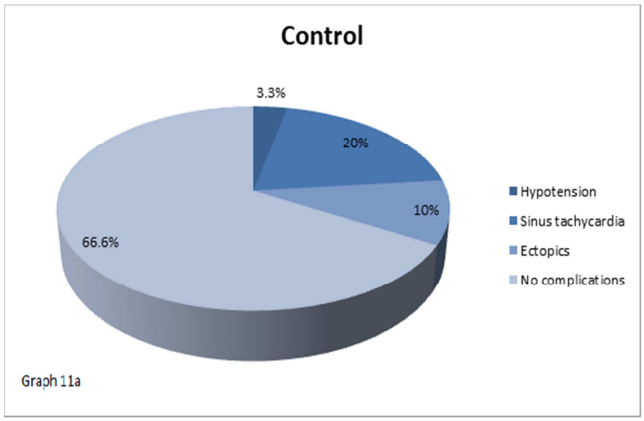
Figure 9: Changes in Respiratory Rate.

Figure 10: Changes in SpO_2

Table 9: Incidence of Side Effects

S. No.	Complications	Group C	Group E	Group L	Group m
		No. (%)	No. (%)	No. (%)	No. (%)
1	Hypotension (SBP<90mmHg)	1 (3.3%)	4 (13.3%)	3 (10%)	5 (16.6%)
2	Bradycardia (HR<50bpm)	-	-	-	-
3	Sinus tachycardia (HR>120bpm)	6 (20%)	3 (10%)	5 (16.6%)	3 (10%)
4	Pain on injection	-	1 (3.3%)	-	-
5	Ectopics	3 (10%)	-	1 (3.3%)	-
6	Bronchospasm	-	-	-	-
7	Miscellaneous	-	-	-	-

[Table 9] shows the incidence of complications in all the groups. Sinus tachycardia (HR>120bpm) was seen in 6 patients (20%), 3 patients (10%), 5 patients (16.6%) and 3patients (10%) following L&I in groups C, E, L and M respectively. Hypotension (SBP<90mmHg) was seen in one patient (3.3%), 4 patients (13.3%), 3 patients (10%) and 5 patients (16.6 %) in groups C, E, L and M respectively. One patient developed pain on esmolol injection (3.3%). No incidence of pain on injection was seen in other groups (C, L & M). Three patients in control and one patient in labetalol group developed ectopic beats following L&I which lasted for less than a minute and subsided without any intervention. No cases of ectopics were seen in esmolol and metoprolol groups. No other side effects attributable to the drug such as bronchospasm or bradycardia (HR<50bpm) were noted.



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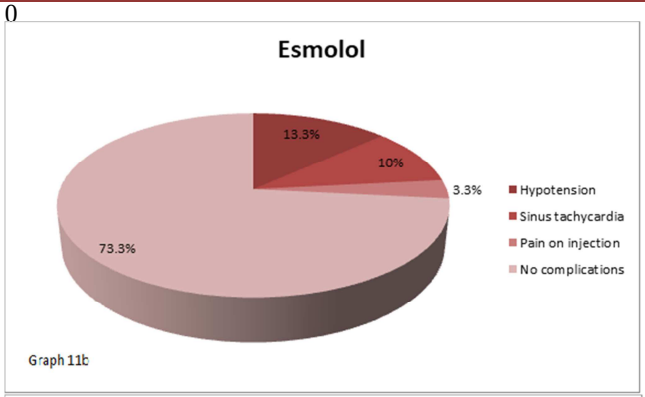

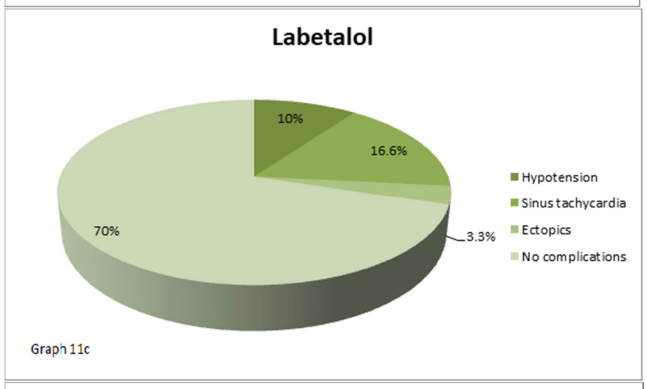

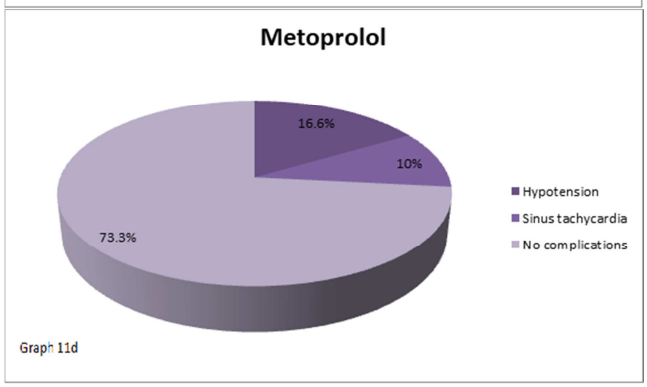

Figures 11a, 11b, 11c, 11d: Incidence of side effects.

Discussion

Each of the haemodynamic parameters were analysed by application of the significance of difference between means of groups.

1. Comparison with the baseline values was done by paired t test within each group.
2. Comparison of each of the study drug group with the control group at their respective time intervals was done by ANOVA test (analysis of variance)
3. Comparison among the study drug groups at their respective time intervals was done by ANOVA test.

Demofigureic profile:

[Table 3a & 3b; Figure -3a (i), 3a (ii) & 3b]

The groups were comparable with respect to age, sex and weight.

Changes in heart rate:

[Table 4a & 4b; Figure 4]

The pre-induction heart rate of the groups C, E, L and M were 84.43±5.37, 87.77±7.27, 86.2±9.71 and 88±8.94 (bpm) respectively and were comparable. In control, labetalol and metoprolol groups, the peak value of heart rate, seen just after L&I, were 111.5± 7.03, 101.6±13.11, 92.87±7.35 respectively. In esmolol group, the peak value was seen at 3 min following L&I (103.5±7.36). In all the study drug groups, the rise in heart rate just after L&I were significantly attenuated in comparison to control (P<0.01, P<0.0001)

Comparison with baseline

In control, esmolol and labetalol groups, the increase in the HR was statistically significant throughout the 10 minute study period compared to the pre-induction values (p<0.001). In metoprolol group, the increase in the HR was statistically significant only up to three min following L&I (p<0.01 and p<0.05) after which, the rise in HR was statistically insignificant (p>0.05) compared to the pre-induction values.

Comparison with control

In the esmolol and labetalol group, the increase in HR was statistically significant upto 1 minute (P<0.01) and 5 minute (P<0.05) respectively following L&I as compared to control. In metoprolol group, the increase in HR after L&I, were significantly less than those in the control group (P < 0•001) at all times following L&I.

Comparison among the study drugs

Statistically significant lesser HR rise was seen in esmolol group compared to labetalol group, at 1min following L&I (P<0.05). Statistically significant less HR rise was seen in metoprolol group compared to labetalol group just after L&I (P<0.01), 1min (P<0.01) and 10 min (P<0.01) following L&I. Statistically significant less HR rise was seen in metoprolol group compared to esmolol group, just after L&I (P<0.001), 3min (P<0.0001), 5min (P<0.0001) and 10min (P<0.0001) following L&I.

The, the findings of our study in esmolol group are similar to those of Kasey P Bensky et al (2000),[15] Rathore Arti et al (2002),[35] Taner Tasyuz et al (2007),[47] and Sarvesh P Singh et al (2010).[38]

The differences in our studies and other studies done on esmolol are likely due to the higher doses of esmolol used in their studies. We preferred lower doses of the study drugs so as to prevent any side effects.

The findings of our study in labetalol group are similar to those of Cope DHP et al (1979),[8] Maharaj RJ et al (1983),[24] Leslie John B et al (1989),[21] and Castelli I et al (1995).[4]

Thus, the findings of our study in metoprolol group are similar to those of Zargar JA et al (2002),[50] Liu Y et al (2006),[22] and Coleman AJ et al (2007).[7]

Changes In Systolic Blood Pressure:

[Table 5a & 5b; Figure 5].

In our study, the pre-induction SBP in all the groups were comparable. The pre-induction SBP of the groups C, E, L and M were 116.2±4.21, 114.6±7.35, 118.2 ±9.97 and 119.4±8.89 mmHg respectively. In all groups, the peak values of SBP seen just after intubation (L&I) were 156.8±5.05, 135.9±9.57, 140.6±13.4 and 136±8.55 mmHg respectively. In all the study drug groups, the rise in SBP, just after laryngoscopy and intubation, was significantly

attenuated in comparison to control (P<0.001).

Comparison with baseline

In control group, the increase in SBP was statistically significant throughout the 10 minute study period compared to the pre-induction values (p<0.001). In esmolol group, there was a statistically significant increase in SBP for 1min following L&I (p<0.001). At 3min, it was statistically insignificant (p>0.05). The SBP decreased further below the pre-induction values at 5 min and 10 min and this decrease was statistically significant (p<0.001). In labetalol group, the increase in SBP was statistically significant upto 1min following L&I. SBP remained statistically insignificant at 3min and 5min. Thereafter, a statistically significant fall (p<0.001), was noted at 10 min following L&I. In metoprolol group, the increase in SBP was statistically significant (p<0.001) one minute following L&I compared to the pre-induction values. SBP decreased to values below the baseline at 3min following L&I, though the value was statistically insignificant. Thereafter, statistically significant fall (p<0.001) was noted at 5 min and 10 min.

Comparison with control

Statistically significant fall in SBP (P<0.0001) was noted in all the study drug groups compared to control group at all times following L&I.

Comparison among the study drugs

Statistically significant fall in SBP was noted in esmolol group compared to labetalol at 5 min and 10 minute following L&I (P<0.01). All other comparison between the study drug groups were statistically insignificant (P>0.05).

The findings of our study in esmolol group are similar to those of Sheppard Shane et al (1990),[41] Santosh Kumar et al (2003),[37] and Taner Tasyuz et al (2007).[47]

The findings of our study in labetalol group are similar to those of Cope DHP et al (1979),[8] Scott DB et al (1982),[39] Castelli I et al (1995),[4] and Sarvesh P Singh et al (2010).[38]

The findings of our study in metoprolol group are similar to those of Magnusson J et al (1986),[26] Zargar JA et al (2002),[50] Liu Y et al (2006),[22] and Coleman A.J et al (2007).[7]

Changes In Diastolic Blood Pressure:

[Table 6a & 6b; Figure 6].

In our study, the pre-induction diastolic blood pressures in all the groups were comparable. The pre-induction DBP of the groups C, E, L and M were 74.983±5.16, 74.2±6.05, 74.3±7.95 and 73.8±6.45 mmHg respectively. The peak values of DBP, seen just after L&I in all groups, were 94.33±2.35, 92.1±5.61, 93.07±7.63, 89.3±6.49 in groups C, E, L and M respectively.

Comparison with baseline

In control group, the increase in DBP was statistically significant upto 5min following L&I (p<0.001) compared to pre-induction values. At the 10th minute a fall in DBP was noted which was statistically significant (p<0.05). In esmolol and labetalol group, the increase in DBP was statistically significant only upto one minute following L&I (p<0.001) after which, a fall in DBP was noted. DBP at 3min and 5min was statistically insignificant (p>0.05). DBP at 10 minute following L&I, in both the groups (E&L), showed a statistically significant fall compared to pre-induction value (p<0.0001). In metoprolol group, the rise in DBP was statistically significant upto 1minute following L&I (p<0.0001). The values at 3 and 5 minutes were statistically insignificant (p>0.05). A fall in DBP was noted at the 10th minute following L&I, though it was statistically insignificant (p>0.05).

Comparison with control

DBP values of all the study drug groups compared to control group showed statistically significant attenuation at all times following L&I (P<0.01; P<0.0001).

Comparison among the study drugs

No statistically significant difference was seen among the comparison in DBP between the study drugs, except a statistically significant fall in esmolol compared to metoprolol at 10 minute following L&I (P<0.05).

The findings of our study in esmolol group are similar to those Santosh Kumar et al (2003),[37] Taner Tasyuz et al (2007),[47] and Sarvesh P Singh et al (2010).[38]

The findings of our study in labetalol group are similar to those of Maharaj RJ et al (1983),[24] and Sarvesh P Singh et al (2010).[38]

Changes in Mean Blood Pressure:

[Table 7a & 7b Figure 7]

In our study, the pre-induction mean blood pressures in all the groups were comparable. The pre-induction MBP readings of the groups C, E, L and M were 88.62±3.84, 87.68±6.1, 88.92 ±7.45 and 89.01±5.2 mmHg respectively. The peak value of MBP, seen just after L&I in all groups, were 115.2±2.48, 106.7±6.22, 108.9±8.24, 104.9±6.10 in groups C, E, L and M respectively.

Comparison with baseline

In control group, the increase in MBP was statistically significant upto 5min following L&I (p<0.001) compared to pre-induction values. In esmolol group, the increase in MBP was statistically significant upto one minute following L&I (p<0.001). MBP at 3min was also found to be statistically insignificant (p>0.05). Subsequently, a fall in MBP noted at 5 min and 10 min following L&I, was found to be statistically significant (p<0.001). In labetalol group, the increase in MBP was statistically significant (p<0.0001) upto 1min following L&I. Later on the values at 3 min and 5 min were found to be statistically insignificant. Subsequently, the fall in MBP noted at 10th minute was found to be statistically significant (p<0.001). In metoprolol group, the MBP rise was statistically significant upto 1min following L&I (p<0.001). The reading at 3rd minute was statistically insignificant. The fall in MBP noted, thereafter at 5th min and 10th min was found to be statistically significant (p<0.01) compared to baseline.

Comparison with control

MBP values of all the study drug groups compared to control group showed statistically significant attenuation at all times following L&I (P<0.0001).

Comparison among the study drugs

No statistically significant differences were seen among the comparison in MBP between the study drug groups, except a statistically significant fall in esmolol compared to metoprolol at 10th minute following L&I (P<0.05).

The findings of our study in esmolol group are similar to those of Menigaux C et al (2002),[27] and Sarvesh P Singh et al (2010).[38]

The findings of our study in labetalol group are similar to those of Maharaj RJ et al (1983),[24] and Sarvesh P Singh et al (2010).[38]

Liu Y et al (2006),[22] and Coleman AJ et al (2007),[7] found metoprolol effective in controlling the arterial pressure during L&I. The findings in our study correlate these studies.

Changes In Rate Pressure Product:

[Table 8a & 8b, Figure 8]

Rate Pressure Product is an index of myocardial oxygen consumption [Gobel FL11]. It is a product of systolic blood pressure and the heart.[11] Rate pressure product exceeding 22,000 is commonly associated with myocardial ischaemia and angina [Robinson BF33]. Although RPP does not predict regional myocardial supply demand relationships, examination of the individual components (heart rate and SBP) is useful in the management of ischaemic heart disease [Kissin I20]. An increase in blood pressure without a change in heart rate appears to be better for myocardial oxygenation than an increase in HR along with increase in blood pressure [Moffitt E e29]

In our study, the pre-induction rate pressure products in all the groups were comparable. The pre-induction readings of RPP of the groups C, E, L and M were 9811±710.7, 10048±980.7, 10191±1421 and 10516±1380 respectively. The peak value of RPP seen just after laryngoscopy and intubation in all groups were 17479±1181, 13978±1300, 14282±2306, 112649±1525 in groups C, E, L and M respectively. RPP crossed the critical mark of 15000 in control group just after L&I and at 1 min following L&I. RPP in the study drug groups never crossed this value.

Comparison with baseline

In control group, the increase in RPP was statistically significant at all times following L&I (p<0.001) compared to pre-induction values. In esmolol group, the increase in RPP was statistically significant upto three minute following L&I (p<0.001). In labetalol group, the increase in RPP was statistically significant (p<0.001) upto 1min following L&I. In metoprolol group, the increase in RPP was statistically significant (p<0.0001) upto 1min following L&I. RPP at 3rd min was statistically insignificant. A statistically significant (p<0.05) fall in RPP from the baseline was noted at 5 min and 10 min following L&I.

Comparison with control

RPP values of all the study drugs compared to control showed statistically significant attenuation at all times following L&I (P<0.0001).

Comparison among the study drugs

Statistically significant lesser RPP was seen in metoprolol group compared to labetalol group just after L&I (P<0.0001), at 5min and 10min after L&I. Statistically significant lesser RPP was seen in metoprolol group compared to esmolol group just after L&I and at 3min following L&I.

The findings of our study in esmolol, labetalol and metoprolol group are similar to those of Rathore Arti et al (2002)35, Sarvesh P Singh et al (2010)38 and Zargar JA et al (2002)50 respectively.

Changes In Respiratory Rate:

[Table 9, Figure 9]

Comparison in the respiratory rate within a group and that among the study groups at their respective time intervals was statistically insignificant throughout the study period (p>0.05, P>0.05).

Changes in SpO2:

[Table 10, Figure 10]

Comparison in the SpO2 within a group and that among the study groups at their respective time intervals was statistically insignificant throughout the study period (p>0.05, P>0.05)

Incidence of Side Effects/Complications:

[Table 11; Figure 11a, 11b, 11c & 11d]

Sinus tachycardia was seen in 6 patients (20%), 3 patients (10%), 5 patients (16.6%) and 3patients (10%) following L&I in groups C, E, L and M respectively. Hypotension (SBP<90mmHg) was seen in one patient (3.3%), 4 patients (13.3%), 3 patients (10%) and 5 patients (16.6 %) in groups C, E, L and M respectively. One patient developed pain on esmolol injection (3.3%). No incidence of pain on injection was seen in other groups (C, L & M). Three patients in control and one patient in labetalol group developed ectopic beats following L&I which lasted for less than a minute and subsided without any intervention. No cases of ectopics were seen in esmolol and metoprolol groups. No other side effects attributable to the drug such as bronchospasm or bradycardia were noted.

Sheppard Shane et al (1990),[41] noted pain on inj. in 1 patient (n=15) in both placebo and esmolol 100mg.

Miller Donald R et al (1991),[28] found hypotension the most common side effect. In E100 group, 25% developed hypotension and 16% in placebo. Bradycardia in 1% patients and pain on inj. 1.6% in both esmolol and in placebo were noted.

Rathore Arti et al (2002),[35] One patient (4%) in esmolol 150 mg group developed bradycardia.

Sarvesh P Singh et al (2010),[38] noted atrial ectopics in 1 patient in control (4%) and one in esmolol (4%) post intubation. 7 patients (28%) in labetalol 0.25mg/kg group developed bradycardia after study period. No cases of bradycardia were noted in our study.

Sharma Suman et al (1996),[40] Kasey P Bensky et al (2000),[15] Menigaux C et al (2002),[27] Saif Ghaus M et al (2002),[36] Tan PH et al (2002),[46] Yutaka Oda et al (2005),[49] and Taner Tasyuz et al (2007),[47] did not notice any adverse reactions attributable to esmolol.

Scott DB et al (1982),[39] noted that high doses of halothane (3%) with labetalol predisposes to myocardial depressant effects of halothane and undesirable reduction in myocardial performance.

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Maharaj RJ et al (1983),[24] No cardiac dysrhythmias were noted in the study with labetalol (0.25mg/kg and 0.5mg/kg). We noted premature ventricular contraction in one patient in labetalol group just after L&I which persisted for less than 1min and subsided without treatment.

Zargar JA et al (2002),[50] noted sinus tachycardia of 55% in control and 20% in metoprolol 4mg group. PVC in 10% patients in control was seen 1min after L&I.

Liu Y et al (2006),[22] noted that the incidence of bradycardia had no statistic difference between metoprolol group and placebo.

Coleman AJ et al (2007),[7] noted cardiac rhythm disturbance of short duration of no apparent consequence in metoprolol group.

Conclusion

Our study demonstrates that metoprolol appreciably and remarkably atten-uated the cardiovascular stress response to laryngoscopy and intubation in comparison to esmolol and labetalol. Esmolol was comparably better than labetalol in attenuating this hemodynamic response.

Metoprolol can thus, be used as a safe and better alternative to esmolol and labetalol considering the favourable protective cardiovascular effects during laryngoscopy and intubation. Being a longer acting β-blocker in comparison to esmolol, it can also provide its protective effects even in the intra-operative period.

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