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

Deepak R¹, Jaya Lalwani², Prathibha Jain Shah², K P Dubey²
¹Assistant Professor, Department of Anaesthesia, ESIC Medical College & PGIMSR, K K Nagar, Chennai 600078, India, ²Professor, Department of Anaesthesia, Pt.Jawaharlal Nehru Memorial Medical College, Raipur, Chhattisgarh, India.

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 10min 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.

Corresponding Author: Dr Deepak R, D26, ESIC Staff Quarters, 143 Sterling Road, Next to ES-IC Regional Office, Tamilnadu Nungambakkam, Chennai 600034

Received: June 2019
Accepted: July 2019

Introduction

Laryngoscopy and endotracheal intubation is an indispensable part of practice for an anaesthesiologist 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 effenter responses from the pharyngeal stimulation. There is increase in heart rate, blood pressure [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 conditions of raised ICP-EDH, SDH, aneurysms, intracranial tumors etc.[10] LVF, MI, cerebral haemorrhage can occur in susceptible patients. Convulsions 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...
All the patients were randomly allocated into four groups of 30 each to receive 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.

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.

The study included 120 normotensive patients (30 in each group) belonging to ASA grade I and II of either sex undergoing elective surgery requiring general anaesthesia and intubation.

The study recruited 120 normotensive patients (30 in each group) belonging to ASA grade I and II of either sex undergoing elective surgery requiring general anaesthesia and intubation. In the operation theatre, on day of surgery the patients were induced with:

i. Hypertension
ii. Ischemic heart disease
iii. Recent myocardial infarction
iv. Cardiac failure
v. Sinus bradycardia (<60/min or heart block)
vi. Current treatment with β-blockers, verapamil, diltiazem and amiodarone
vii. Pulmonary diseases: Chronic obstructive airway disease or asthma

The study included 120 normotensive patients (30 in each group) belonging to ASA grade I and II of either sex undergoing elective surgery requiring general anaesthesia and intubation. The study recruited 120 normotensive patients (30 in each group) belonging to ASA grade I and II of either sex undergoing elective surgery requiring general anaesthesia and intubation.

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

Followings 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 given pre-induction (baseline) HR, SBP, DBP and MBP were noted. ECG monitoring was done with Multipara monitors.
3. Intravenous access was secured with 18 G i.v cannula with RL.
4. Pre-anesthetic medication was done 15 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 10 ml 0.9% normal saline (Q.S)
6. Pre-oxygenation was done with 100% for 3-5 minutes.
7. Induction:
   a. All patients were induced with inj. thiopentone 5 mg/kg followed by suc-cinylcholine 2 mg/kg to facilitate intubation.
   b. 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 attempts required for intubation were noted.
8. Maintenance: Anaesthesia was maintained on isoflurane;
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 tachycardia.
iii. Systolic Blood Pressure below 90mmHg was considered as hypotension.
iv. Fall in SpO2 below 90% and any signs of respiratory distress were considered 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     |
| Metoprol | 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.

[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 metoprolol 0.1mg/kg. Labetalol and metoprolol was given 5 minutes before induction whereas saline and esmolol was given 2 min prior to induction. All the study drugs were diluted to 10 ml N.S (Q.S)

[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, 54.27±10.23 and 56.23±12.51 respectively. The youngest patient in all the groups was 18 years. The oldest patient in
Deepak et al: Attenuating the Cardiovascular Stress Response to Laryngoscopy and Intubation

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

Table 3b: Demographic 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 distribution [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.

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              |
| 1 min 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               | < 0.01               | < 0.001              |
| 10 min after L & I                | > 0.05               | < 0.01               | < 0.001              |

(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 1 min and at 10 min (P<0.01) and in comparison to esmolol just after L&I, at 3 min, 5 min and 10 min (P<0.0001). Labetalol significantly attenuated (P<0.05) the HR rise, 3 min after L&I in comparison to esmolol.
Deepak et al: Attenuating the Cardiovascular Stress Response to Laryngoscopy and Intubation

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

| SBP (mm Hg) | 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             | > 0.05               | > 0.05               |
| 1 min 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 6b: Changes In Diastolic Blood Pressure: Comparison among the Study Drug Groups

| DBP (mm Hg) | 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             | > 0.05               | > 0.05               |
| 1 min 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 10 minutes following L&I (P<0.05).

Figure 6: Changes in Diastolic Blood Pressure.

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

| MBP (mm Hg) | 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             | > 0.05               | > 0.05               |
| 1 min 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 comparison in MBP between the study drug groups, except a statistically significant fall in esmolol compared to metoprolol 10 minutes following L&I (P<0.05).

Figure 7: Changes in Mean Blood Pressure.
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 compared to labetalol group just after L&I (P<0.0001), at 5min and at 10min after 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.

Table 9: Incidence of Side Effects

| S. No. | Complications | Group C | Group E | Group L | Group M |
|--------|---------------|---------|---------|---------|---------|
| 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 3 patients (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.
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.

**Discussion**

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

**Changes in heart rate:**

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 < 0.0001) 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 esmolol 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), Rathore Arti et al (2002), Taner Tasyuz et al (2007), and Sarvesh P Singh et al (2010).

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), Maharaj RJ et al (1983), Leslie John B et al (1989), and Castelli I et al (1995).

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

**Changes In Systolic Blood Pressure:**

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...
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 1 min following L&I (p<0.001). At 3 min, 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 up to 1 min following L&I. SBP remained statistically insignificant at 3 min and 5 min. 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 3 min 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
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
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.

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, was 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 up to 5 min following L&I (p<0.001) compared to pre-induction values. In esmolol group, the increase in MBP was statistically significant up to one minute following L&I (p<0.001). MBP at 3 min 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) up to 1 min 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 up to 1 min following L&I (p<0.001). MBP at 5 min and 10 min following L&I, was found to be statistically significant (p<0.001). The reading at 3 rd 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:

In our study, the pre-induction rate pressure product values 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 up to three minute following L&I (p<0.001). In labetalol group, the increase in RPP was statistically significant (p<0.001) up to 1 min following L&I. In metoprolol group, the increase in RPP was statistically significant (p<0.0001) up to 1 min 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 3 min 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:

In our study, the pre-induction respiratory rate values in all the groups were comparable. The pre-induction readings of RPP of the groups C, E, L and M were 120±3, 122±3, 121±3 and 125±4 respectively. RPP crossed the critical mark of 22000 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].

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:

Sinus tachycardia was seen in 6 patients (20%), 3 patients (10%), 5 patients (16.6%) and 3 patients (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 ectopies 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),[43] 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 Tanyer 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 and undesirable reduction in myocardial performance.

Academia Anesthesiologica International | Volume 4 | Issue 2 | July-December 2019
Maharaj RJ et al (1983), 241 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), 250 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), 252 noted that the incidence of bradycardia had no statistic difference between metoprolol group and placebo. Coleman AJ et al (2007), 257 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.

References

1. Alexander R, Binns J,Hetreed M. A controlled trial of the effects of esmol-lol on cardiac function. Br. J. Anaesth 1994; May 72(5):594-5.
2. Bruder N, Granthil C, Ortega D. Consequences and prevention methods of hemodynamic changes during laryngoscopy and intubation. Ann Fr Anaesth Reanim 1992; 11(1):57-71
3. Bikiye U, Ogurlu M, Gezer E. Effects of esmolol, lidocaine and fentanyl on haemodynamic responses to endotracheal intubation: A comparative study. Clinical Drug Investigation 2007;27:269-77
4. Castelli I, Steiner A, Kaufmann MA, Afille H, Schouten et al. Comparative study of esmolol and labetalol to attenuate dynamic stress states after Elec-troconvulsive therapy. Anaesth Analg. 1995; 80:557-61
5. Chia YY, Chan MH, Ko NH, Liu K. Role of β-blockade in anaesthesia and post operative pain management after hysterec-tomy. Br J Anaesth. 2004; 93(6):796-805
6. Chung KS, Sinatrah RS, Haley JD, Paige D, Silverman DG. A Comparison of fentanyl,esmolol and their combination for blunting the haemodynamic responses during rapid sequence induction. Canadian Journal of Anaesthesia 1992; 39:774-9
7. Coleman AJ, Jordan C. Cardiovascular responses to Anaesthesia. Influence of β-adrenoreceptor blockade with metoprolol. Anaesthesia 1980;2:398-402
8. Cope DHP. Use of labetalol during halothane anaesthesia.Br J Clin.Pharmac. 1979; 8:223S-227S
9. Ebert TJ, Bernstein JS, Stowe DF, Roerig D, Kampine JP. Attenuation of hemodynamic responses to rapid sequence induction and intubation in healthy patients with a single bolus dose of esmolol.J Clin Anesth. 1990;2:243-52
10. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia-sia and endotracheal intubation in normotensive man. Br. J.Anesthesi. 1970; 42:618-624
11. Gobel FL, Nordstrom LA, Nelson RR, Jorgensen CR, Wang Y. The rate-pressure product is an index of myocardial oxygen consumption during ex-exerice in patients with angi na pectoris. Circulation 1978; 57: 549-56
12. Helfman SM, Gold MJ, DeLisser EA, Herrington CA. Which drug pre-vents tachycardia and hypertension associated with tracheal intubation: Li-docaine, fentanyl or esmolol? Anaesthesia and Analgesia 1991; Apr;72(4):482-6
13. Helfman SM,Herrington CA and Gold MI. Bolus esmolol treatment for intraoperative tachycardia. Anaesthesia Anal 1991; Mar(3):229-3
14. Inada E, Cullen DJ, Nemeskal R, Toplick R. Effect of labetalol on the hemodynamic response to intubation. J Clin Anesth. 1989;4:11-5
15. Kasey P,Bensky, Linda Donahue Spencer, G Erik Hertz, Martha T An-derson, Robert James. The dose related effects of bolus esmolol on heart rate and BP following L&I. ANA Journaal October 2000; Vol68 No5 :437-441
16. Kamra S, Wig J, Sapru RP. Topical nitroglycerine:A safeguard against pressor response to tracheal intubation. Anaesthesia 1986;41:1087-91
17. Kindler CH, Schumacher PG, Schneider MC, Uwrley A. Effect of intra-venous lidocaine and/or esmolol on hemodynamic responses to laryngoscopy-and tracheal intubation: a double blind controlled clinical trial. Journal of Clinical Anaesthesia 1996; Sept; 8(6): 491-6
18. King BD, Harris LC, Griefenstein FE, Elder JD, Drripps RD. Reflex cir-culatory response to direct laryngoscopy and intubation performed during general anaesthesia. Anaesthesiology 1951; 12:556
19. Kim HY, Chung CW, Lee HY, Yim. The effect of labetalol on the hemo-dynamic response to endotracheal intubation. Korean J Anesthesiol 1994; 27:161-9
20. Kissin I, Reves JG, Mardis M. Is the rate pressure product a misleading guide? Anaesthesiology 1980; 52: 373-4
21. Leslie John B, Kalayjian RW, Mc Loughlin TM, Plachetka JR. Attenua-tion of hemodynamic response to endotracheal intubation with pre-in-duction intravenous labetalol. J Clinical Anaesthesia 1989;1:194-200
22. Liu Y, Huang CL, Zhang LN, Cai HW, He M, Guo QL. Influences of peri-operative metoprolol on hemodynamics and myocardial ischaemia in elderly patients undergoing non-cardiac surgery. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2006 Apr;31(2):249-53
23. Liu Philips et al. Esmolol for control of increase in heart rate and blood pressure during tracheal intubation after thiopentone and succinylcholine. Can J. Soc. 3; 5:556-62
24. Maharaj RJ, Thompson M, Brock JG, Williamson R, Drowing JW. Treatment of hypertension following endotracheal intubation.A study comparing the efficacy of labetalol, proctolol and placebo. S Afr Med J 1983;63:691-4
25. Magnusson J, Werner O, Carlsson C, Pettersson KI, Norden N. Metoprolol, fentanyl and stess response to microlyography. Effect on arterial pres ure, heart rate and plasma concentration of catecholamine, ACTH and corti-sol. Br J Anaesth 1983;55:405-14
26. Magnusson J, Thulin T, Werner O, Jarhult J, Thomson D. Haemodynamic Effects Of Pretreatment With Metoprolol In Hypertensive Patients Undergoing Surgery.Br J Anaesthesia 1986;58(3) : 251-260
27. Menigaux C, Guimard B, Adam F et al. Esmolol prevents movement and attenuates the BIS response to orotracheal intubation. Br J Anaesth 2002;89:852-62
28. Miller Donald R, Martineau R.J., et al: Bolus administration of esmolol in controlling the hemodynamic response to tracheal intubation. The Can-dian Multicentre Trial. Can J. Anaesthesia 1991.
29. Moffitt E, Sethna D, Bussell J, Raymond M, Matloff J, Gray R. Hemo-dynamics and myocardial metabolism after acute β-adrenergic blockade in coronary patients. Anesth Analg 1984; 63):540-1
30. Nahid Aghdaii, Azarfarin R,Yazdanian F, Faritus S Z. Cardiovascular re- sponse to orotracheal intubation in patients undergoing coronary artery bypass grafting surgery. MEJ Anesth 2010;20(6):833-837
31. Prys Roberts, Can-dian Multicentre Trial. Can J. Anaesthesia 1991.
32. Prys Roberts, Can-dian Multicentre Trial. Can J. Anaesthesia 1991.
33. Prys Roberts, Can-dian Multicentre Trial. Can J. Anaesthesia 1991.
34. Prys Roberts, Can-dian Multicentre Trial. Can J. Anaesthesia 1991.
35. Robinson BF, Relation of heart rate and systolic blood pressure to the onset of pain in angina pectoris. Circulation 1967;35:1073-83
36. Ramanathan J, Sibai BM, Madic WE, Chauhan D, Ruz AG. The use of labetalol for attenuation of hypertensive responses to endotracheal intubation on pre-eclampsia. AM J Obstet Gynecol 1988; 159:650-4
37. Rathore A, Gupta HK, Tanwar GL. Attenuation of the pressor response to laryngoscopy and endotracheal intubation with different doses of esmolol. Indian J Anaesth 2002;46(2):449-52
38. Saif Ghaus,M, Vinitha Singh, Kumar A, Wahal R, Bhatia VK, Agrawal J. A study of cardiovascular response during laryngoscopy and intubation by ultra-short acting b-blocker Esmolol. Indian J Anaesth 2002; 46(2):104-106
37. Santosh Kumar, Mishra MN, Mishra LS, Sapna Bathla. Comparative study of efficacy of i.v esmolol, diltiazem and magnesium sulphate in attenuating haemodynamic response to laryngoscopy and intubation. Indian J. Anaesth 2003;47(1):41-44
38. Sarvesh P Singh, Abdul Quadir, Poonam Malhotra. Comparison of esmolol and labetalol, in low doses, for attenuation of sympathomimetic re-sponse to laryngoscopy and intubation. Saudi J. Anaesth 2010; Vol4;issue3:163-168
39. Scott DB, Buckley, F.P., Littlewood, D.G.,Macrae,W.R., Arthur, G.B. Circulatory effects of labetalol during halothane anaesthesia. Anaesthesia 1982;33:145-156
40. Sharma Suman, Mitra S, Grover VK, Kalra R. Esmolol blunts the haemodynamic responses to tracheal intubation in treated hypertensive patients. Canadian Journal of Anaesthesia 1996 Aug; 43 (8): 778-82
41. Sheppard Shane, Eagle CJ, Strunon L. A bolus dose of esmolol attenuates tachycardia and hypertension after tracheal intubation. Canadian Journal of Anaesthesia 1990;37:202-205
42. Singh H, Vichitvejpaisal P, Gaines GY, White PF. Comparative effects of lidocaine, esmolol and nitroglycerin in modifying the haemodynamic re sponses to laryngoscopy and intubation. Journal of Clinical Anaesthesia 1995; Feb 7(1):5-8
43. Stoelting RK, Peterson C. Circulatory changes during anesthetic induction: impact of d subcurarine pre-treatment, thia-mylal, succinylcholine, laryngoscopy and tracheal lidocaine. Anesth Analg (Cleve) 1976; 55:77-81
44. Stoelting RK. Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation. Influence of viscous or intrave nous lidocaine. Anesth Analg. 1978; 57:197
45. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. Anesth Analg 1979;58:116-9
46. Tan P H, Yang HC, Lin CR, Lan KC, Chen CS: Combined use of esmolol and nicardipine to blunt the haemodynamic changes following laryngoscopy and tracheal intubation: Anaesthesia 2002. 57, 1207-1211
47. Taner Tasyuz, Ismet Topcu, Sabri Ozaslan, Melk Sakarya: Effects of esmolol on hemodynamic responses to L&I in diabetic vs Non-Diabetic patients. Turk J Med Sci 2007;37(5):289-296
48. Yuan L, Chia YY, Jan KT et al. The effect of single bolus dose of esmolol for controlling the tachycardia and hypertension during laryngoscopy and tracheal intubation. Acta Analgesiologica Sinica 1994; Sep; 32(3): 147-52
49. Yutaka Oda, Kiyonobu Nishikawa, Ichiro Hase, Akira Asada. The short acting β1 adrenoreceptor antagonists Esmolol and landiolol suppress the bispectral index response to tracheal intubation during sevoflurane anaesthesia. Anaesth Analg 2005;100:733-7
50. Zargar JA, Nagash IA, Gurcoo SA, Mehrj ud din. Effect of metoprolol and esmolol on rate pressure product and ECG changes during laryngoscopy and tracheal intubation in controlled hypertensive patients. Indian J. Anaesth 2002; 46:365-8