

## Comparison of Effect of IV Esmolol and I.V. Metoprolol For Attenuation of Pressor Response to Laryngoscopy And Intubation During Elective General Surgical Procedures Under General Anaesthesia

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**Abstract:** A randomized placebo controlled single blind study was conducted to compare the effects of bolus doses of metoprolol and esmolol heart rate ,systolic blood pressure and rate pressure product during laryngoscopy and intubation.60 patients of ASA I and II randomly received placebo or study group(1 mg/kg of esmolol) or 80 µg/kg of metoprolol in 20 ml normal saline.Heart rate,systolic b.p were recorded serially after study drug , before induction,during laryngoscopy and intubation and 1/2min,1min,1 1/2 min ,2 min each minute till parameters reach baseline or 20 minutes whichever is earlier. Rate pressure product was calculated and statistically evaluated in all 3 groups.Statistically significant fall in heart rate blood pressure and rate pressure product obtained in group II and III compared to control. While comparing between study drugs esmolol appears better attenuator of peak rise of blood pressure and metoprolol appears better attenuator of heart rate.Rate pressure product never reached above 15000 in any group at which myocardial ischemia may set in.

**Keywords:** (esmolol metoprolol,laryngoscopy ,intubation,rate pressure product)

### I. Introduction

Laryngoscopy and intubation are integral parts of anaesthesiology. Sir Ivan Magills endotracheal intubation technique which he developed with Sir Horolad Gillis at Sidcup hospital, Kent was one of the most significant advances made in the field of anaesthesiology during first world war. Reid and Brane (1940) were first to recognize that cardiovascular stability may be affected by laryngoscopy and intubation. Circulatory changes are mediated by reflex sympathetic discharge due to epipharyngeal and laryngopharyngeal stimulation and are marked tachycardia, hypertension and cardiac arrhythmias . The rise in the pulse rate and blood pressure is usually transitory, unpredictable and variable. In young healthy and normotensive patients these changes are well tolerated but in patients with hypertension heart disease, coronary artery disease, the pressor response can result in increase in cardiac workload .Most of the neurosurgical patients suffer from decrease intracranial compliance due to presence of tumor or intracranial haemorrhage. Here a steep rise in blood pressure which accompanies laryngoscopy and intubation can result in rise of intracranial pressure leading to herniation of brain tissue . Over a period of time various methods are used to attenuate the pressure response .These are

- Sufficient depth of anaesthesia .
- Duration of laryngoscopy < 15 seconds .
- Vasodilator e.g. i.v. sodium nitroprusside.
- Calcium channel blocker e.g. Nifedipine
- Lignocaine
- Beta blockers.

#### Beta blockers

Prys Roberts in 1971 suggested that beta blockers may attenuate the pressor response to laryngoscopy and endotracheal intubation. In 1973,he studied the effect of proctolol pressor response in hypertensive patients.He demonstrated significant attenuation pressor response along with decreased incidence of arrhythmia in patients receiving beta blockers. Magnusson J et al in 1986 studied pretreatment with metoprolol in hypertensive patients undergoing surgery and concluded that it was more effective than nonselective beta blocker like propranolol. In present study we have attempted to evaluate and compare the effectiveness of bolus doses of esmolol and metoprolol for attenuation of pressor response to laryngoscopy and intubation.

#### Aim

- 1) To study the hemodynamic effect of laryngoscopy and intubation in a normotensive patient using following parameters.
  - a) Pulse rate
  - b) systolic and diastolic blood pressure
  - c) Rate pressure product

- d) Mean arterial blood pressure  
 2) To compare the effectiveness of i.v. injection esmolol and metoprolol to attenuate the haemodynamic response to laryngoscopy and intubation.

## II. Material And Methods

After obtaining permission from institutional ethics committee and written informed consent from all patients were 60 patients of either sex divided into three groups 20 patients each. Patient were randomly allocated to one of the three groups .20 patients in group one received normal saline i.v. 20 patients in group two received i.v. esmolol hydrochloride .20 patient in group three received i.v. metoprolol tartarate .

Patient of either sex in age group of 18 to 50 years undergoing different elective surgical procedures under general anaesthesia were taken up for study

- Patient selected were ASA group 1 and 2 patients
- Patients with predicted difficult intubations pulse less than 60 beats/min systolic blood pressure less than 100 mm of hg were excluded.Patient with any medical illness like D.M., Hypertension, IHD, Renal disease were excluded from the study.
- patients were investigated with all routine investigations including complete hemogram ,serum electrolytes ,random blood sugar, renal and liver function test,radiograph of chest (PA view) and ECG.

On arriving to operating room,B.P.cuff tied, pulseoximeter and ECG monitors attached. Baseline pulse, B.P.(systolic ,diastolic and mean),ECG noted. I.V. cannula taken and intravenous fluid ringer's lactate started at the rate of 4ml/Kg/hr.

Patients were premedicated with injection glycopyrrolate 4µg/Kg and pre oxygenated with 100% O<sub>2</sub> for three minutes.

Patients in group 1 received normal saline i.v. 20 ml bolus .Group 2 patients received injections esmolol 1 mg /Kg in 20cc normal saline. Group 3 patient received injection Metoprolol 80µg/Kg in 20 ml normal saline.

Study drugs was given three minutes prior to induction Patients were anaesthetized with inj propofol 1.5-2 mg/kg iv. Endotracheal intubation was facilitated by inj.suxamethonium 1.5 mg/kg iv. 60 seconds after inj. suxamethonium laryngoscopy and intubation was carried out by single operator who was blinded to premedication and study drug.

Non depolarizing muscle relaxant given was injection vecuronium bromide 0.1 mg/Kg intravenous after confirming the endotracheal tube position by auscultation and ET CO<sub>2</sub> .Patient were maintained on oxygen 40% and N<sub>2</sub>O 60% with IPPV on Bain's circuit .Injection Pethidine 0.5 mg -1 mg/Kg and injection Phenargan 0.25 -0.5 mg/Kg was given for sedation and analgesia 25 minutes after intubation .Injection diclofenac sodium 1 mg/Kg I.M., given half hour prior to the end of procedure.Following parameters were noted heart rate, systolic blood pressure ,diastolic blood pressure, ECG, SpO<sub>2</sub> noted as basal awake immediately after premedication immediately after induction at laryngoscopy and intubation ½min,1min,2min,3min each minute till parameters reach baseline or for 20 minutes whichever is earlier .Duration of laryngoscopy was noted .

Intubation score calculated based on jaw relaxation, is of laryngoscopy position of vocal cord ,coughing and limb movement .In all the groups mean and standard deviation , paired student's t test ,unpaired student's t test and chi-square test were calculated using statistical package SPSS version 10-01.

## III. Results

Table 1

Metoprolol	Esmolol	Control		
11	8	9	male	Sex
9	12	11	female	
32.75 ± 9.464 NS	33.70 ± 12.04 <sup>NS</sup>	33.9 ± 8.83		Mean Age ±SD
19.71 ± 1.81 <sup>NS</sup>	21.21 ± 2.42 <sup>NS</sup>	20.38 ± 1.99		BMI
2.145 ± 0.114 NS	2.105 ± 0.105 NS	2.095 ± 1.05		Dose of propofol
13.90 ± 1.210 <sup>NS</sup>	14.00 ± 1.77 <sup>NS</sup>	13.95 ± 1.57		Intubation Time

NS: Not significant

Table 2: Variations in mean heart rate in esmolol and metoprolol against control group at Various time intervals.

	Control	Esmolol	Metoprolol
Basal	81 + 3.86	80.1 + 4.02 <sup>NS</sup>	79.80 + 5.54 <sup>NS</sup>
After premedication	84 + 4.27	82.8 + 3.98 <sup>NS</sup>	82.3 + 5.24 <sup>NS</sup>
After study drug	84 + 4.21	77 + 4.02 <sup>***</sup>	77.6 + 4.96 <sup>***</sup>
After propofol	84 + 5.77	75 + 4.17 <sup>***</sup>	76.60 + 4.69 <sup>***</sup>
After scoline	84.4 + 4.6	76.4 + 4.35 <sup>***</sup>	77.4 + 5.01 <sup>***</sup>
During	93.0 + 5.1	79.8 + 3.87 <sup>***</sup>	80.5 + 4.61 <sup>***</sup>

laryngoscopy intubation			
At 30 sec	98.6 + 4.5	81.65 + 3.93 <sup>***</sup>	82.55 + 4.54 <sup>***</sup>
At 1 min	103.2 + 4.4	83.70 + 4.25 <sup>***</sup>	85.0 + 4.37 <sup>***</sup>
At 1 ½ min	106.7 + 4.11	85.65 + 3.89 <sup>***</sup>	87.05 + 4.39 <sup>***</sup>
At 2 min	109.4 + 3.80	87.0 + 3.52 <sup>***</sup>	88.40 + 6.037 <sup>***</sup>
At 3 min	106 + 3.78	85.8 + 3.47 <sup>***</sup>	87.2 + 4.95 <sup>***</sup>
At 4 min	102.8 + 3.45	84.4 + 3.58 <sup>***</sup>	85.5 + 4.39 <sup>***</sup>
At 5 min	100.5 + 3.17	83.25 + 3.82 <sup>***</sup>	83.0 + 4.57 <sup>***</sup>
At 6 min	98.4 + 3.15	82.25 + 2.5 <sup>***</sup>	82.10 + 4.128 <sup>***</sup>
At 7 min	96.35 + 3.45	81.00 + 4.07 <sup>***</sup>	80.2 + 4.25 <sup>***</sup>
At 8 min	93.8 + 3.77	80.65 + 4.15 <sup>***</sup>	79.40 + 4.86 <sup>***</sup>
At 9 min	91.75 + 3.94	80.55 + 3.77 <sup>***</sup>	78.30 + 5.202 <sup>***</sup>
At 10 min	89.9 + 3.64	80.2 + 3.66 <sup>***</sup>	77.5 + 5.06 <sup>***</sup>
At 11 min	87.7 + 3.74	80.3 + 3.96 <sup>***</sup>	76.95 + 5.28 <sup>***</sup>
At 12 min	85.8 + 4.44	80.3 + 4.26 <sup>***</sup>	76.20 + 5.09 <sup>***</sup>
At 13 min	83.8 + 4.34	80.5 + 3.88 <sup>*</sup>	75.9 + 5.56 <sup>***</sup>
At 14 min	82.2 + 4.72	80.5 + 3.66 <sup>NS</sup>	76.05 + 4.09 <sup>***</sup>
At 15 min	81.2 + 4.37	80.5 + 3.88 <sup>NS</sup>	75.6 + 5.22 <sup>***</sup>
At 20 min	81.4 + 4.54	81.05 + 3.63 <sup>NS</sup>	75.5 + 5.22 <sup>***</sup>

\* P < 0.05, \*\* P < 0.01, \*\*\* P < 0.001  
NS: Not significant

**Table 3:** Variation in mean systolic blood pressure in esmolol and metoprolol against control group at various time intervals

	Control	Esmolol	Metoprolol
Basal	121.7+7.84	119.80+9.79 <sup>NS</sup>	118+9.613 <sup>NS</sup>
After premedication	122.4+7.33	120.7+9.52 <sup>NS</sup>	188+8.61 <sup>NS</sup>
After study drug	122.8+7.48	116.6+10.05*	116.3+8.21*
After propofol	114.90+9.41	109.7+9.782*	109.2+7.74*
After scoline	116.00+6.87	112.0+8.75*	110.9+7.152*
At laryngoscopy & intubation	125.8+6.89	117.7+6.937** *	117.3+8.163***
At 30secs	135+7.004	122.10+6.601* **	123+7.776***
At 1min	142+7.421	126+6.159***	130+7.338***
At 1 ½ mins	148+8.91	131.4+6.32***	136+5.94***
At 2mins	153.4+10.56	135.6+6.57***	141.8+5.57***
At 3mins	150.7+9.67	133.1+6.632** *	139.2+5.709***
At 4mins	145.7+9.357	130.4+6.27***	135+5.315***
At 5mins	141.9+9.61	127.8+6.67***	133+4.87***
At 6mins	138+9.42	125.9+7.09***	131+5.44***
At 7mins	135+9.677	123.5+6.95***	128.5+5.18***
At 8mins	132.8+9.254	122.1+7.355** *	124.9+5.44***
At 9mins	130.2+9.128	120.9+8.322** *	121.3+6.626***
At 10mins	127.70+8.56	119.7+9.319**	119+8.143**
At 11mins	126+8.182	119.7+9.229*	118.2+9.40**
At 12mins	124.2+7.164	120+9.798 <sup>NS</sup>	118.7+9.251 <sup>NS</sup>
At 13mins	122.9+7.509	119.7+9.609 <sup>NS</sup>	118.6+9.064 <sup>NS</sup>
At 14mins	122.2+7.509	120.1+9.27 <sup>NS</sup>	118.8+9.001 <sup>NS</sup>
At 15mins	121.8+7.537	120.1+9.75 <sup>NS</sup>	118.4+9.075 <sup>NS</sup>
At 20mins	121.6+7.72	120+9.60 <sup>NS</sup>	118+9.16 <sup>NS</sup>

\* P<0.05, \*\*P<0.01, \*\*\*P<0.001

**Table 4:** variation in mean rate pressure product in esmolol and metoprolol against control groups at various time intervals:

	Control	Esmolol	Metaprolol
Basal	9867.2±8.95	9590.2±870.8 <sup>NS</sup>	9397±720.210 <sup>***</sup>
After premedication	10239.3±880.25	9992.4±916.66 <sup>NS</sup>	9742.6±603.412 <sup>***</sup>
After study drug	10319.2±851.2	8981.0±823.1 <sup>***</sup>	9006±632.199 <sup>***</sup>
After propofol	9689.8±1056.5	8255.1±933.4 <sup>***</sup>	8351.7±623.199 <sup>***</sup>
After scoline	9797.2±856	8562.7±900.9 <sup>***</sup>	8577.5±633.65 <sup>***</sup>
At laryngoscopy & intubation	11730.2±1122.8	9397.9±795.837 <sup>***</sup>	9430.1±678.72 <sup>***</sup>

At 30 sces	13349.2±1122.8	9973.5±787.4***	10192.8±706.98***
At 1 mins	14670.8±1231.5	10598±771.75***	11080.4±656.44***
At 1 ½ mins	15829.4±1360	11257±797***	11870.7±577.814***
At 2 mins	16814.9±1591.7	11798.8±773.23***	12534.2±969.94***
At 3 mins	15990±1389.24	11418.70±716.69***	12139±860.39***
At 4 mins	14995±1322.1	11004.8±701***	11580±796.93***
At 5 mins	14272.6±1224	10639.3±753***	11123±796.51***
At 6 mins	13589.0±1158.23	10351.2±736.09***	10760±766.2***
At 7 mins	13036.9±1186.73	10001.4±728.96***	10307.4±704.2***
At 8 mins	12472.6±1193	9841.4±707.45***	99915.8±727.49***
At 9 mins	11958.0±1144.03	9736.2±791.28***	9486±678.26**
At 10 mins	11495.2±1089.8	9601.2±891***	9204.6±658***
At 11 mins	11064.6±1036.9	9611.±883.8***	9077±774.39***
At 12 mins	10670.80±1005.9	9634.4±941.06***	9026.8±739.887***
At 13 mins	10312.8±998.17	9630±851.0***	8982.8±763.7***
At 14 mins	10057.4±989.62	9666.8±861***	9015.6 ± 691.87***
At 15 mins	9903.4±963	9656.2±890 <sup>NS</sup>	8932.8 ± 734.02**
At 20 mins	9910.6±965.85	9763±869.39 <sup>NS</sup>	8942.80 ± 733.236**

\* P<0.05, \*\*P<0.01, \*\*\*P<0.001

**Table 5:** Comparison of Heart rate at various time intervals between - Esmolol and Metoprolol group

Time interval	Esmolol	Metoprolol
Basal	80.1 ± 4.02	79.80 ± 5.54 <sup>NS</sup>
After premedication	82.8 ± 3.98	82.3 ± 5.24 <sup>NS</sup>
After study drug	77 ± 4.02	77.6 ± 4.96 <sup>NS</sup>
After propofol	75 ± 4.17	76.6 ± 4.69 <sup>NS</sup>
After scoline	76.4 ± 4.35	77.4 ± 5.01 <sup>NS</sup>
At laryngoscopy & intubation	79.8 ± 3.87	80.5 ± 4.61 <sup>NS</sup>
At 30secs.	81.65 ± 3.93	82.5 ± 4.54 <sup>NS</sup>
At 1mins	83.7 ± 4.25	85.0 ± 4.37 <sup>NS</sup>
At 1 ½ mins	85.65 ± 3.89	87.0 ± 4.39 <sup>NS</sup>
At 2 mins	87.0 ± 3.52	88.0 ± 6.07 <sup>NS</sup>
At 3 mins	85.8 ± 3.47	87.2 ± 4.95 <sup>NS</sup>
At 4 mins	84.4 ± 3.58	85.5 ± 4.39 <sup>NS</sup>
At 5 mins	83.25 ± 3.82	83.6 ± 4.57 <sup>NS</sup>
At 6 mins	82.25 ± 25	82.1 ± 4.12 <sup>NS</sup>
At 7 mins	81.0 ± 4.02	80.2 ± 4.25 <sup>NS</sup>
At 8 mins	80.5 ± 4.15	79.4 ± 4.86 <sup>NS</sup>
At 9 mins	80.55 ± 3.77	78.3 ± 5.20 <sup>NS</sup>
At 10mins	80.2 ± 3.66	77.5 ± 5.06*
At 11 mins	80.3 ± 3.96	76.95 ± 5.28*
At 12mins	80.3 ± 4.26	76.2 ± 5.09**
At 13mins	80.5 ± 3.88	75.95 ± 5.56**
At 14mins	80.5 ± 3.66	76.05 ± 5.90**
At 15mins	80.5 ± 3.88	75.6 ± 5.22**
At 20mins	81.05 ± 3.63	75.5 ± 5.22**

< 0.05, \* P < 0.01, \* P < 0.001

NS - Not Significant.

**Table 6:** Comparison of Mean systolic blood pressure at various time intervals between esmolol and metoprolol group.

Time interval	Esmolol	Metoprolol
Basal	119.80 ± 9.79	118 ± 9.613 <sup>NS</sup>
After premedication	120.7 ± 9.52	118 ± 8.61 <sup>NS</sup>
After study drug	116.6 ± 10.05	116 ± 8.21 <sup>NS</sup>
After propofol	109.7 ± 9.782	109.2 ± 7.74 <sup>NS</sup>
After scoline	112.0 ± 8.75	119.9 ± 7.152 <sup>NS</sup>
At laryngoscopy & intubation	117.7 ± 6.937	117.3 ± 8.163 <sup>NS</sup>
At 30secs.	122.10 ± 6.601	123 ± 7.776 <sup>NS</sup>
At 1mins	126 ± 6.159	130 ± 7.338 <sup>NS</sup>
At 1 1/2mins	131.4 ± 6.32	136 ± 5.54*
At 2mins	135.6 ± 6.57	141.8 ± 5.57*
At 3mins	133.1 ± 6.637	139.2 ± 5.709*
At 4mins	130.4 ± 6.27	135 ± 5.315*
At 5mins	127.8 ± 6.67	133 ± 4.87*

At 6mins	125.9 ± 7.09	131 ± 5.44*
At 7mins	123.5 ± 6.95	128.5 ± 5.18*
At 8mins	122.1 ± 7.355	124.9 ± 5.44*
At 9mins	120.9 ± 8.322	121.3 ± 6.26 <sup>NS</sup>
At 10mins	119.7 ± 9.319	119 ± 8.143 <sup>NS</sup>
At 11mins	119.7 ± 9.229	118.2 ± 9.401 <sup>NS</sup>
At 12mins	120 ± 9.798	118.7 ± 9.251 <sup>NS</sup>
At 13mins	119.7 ± 9.609	118.6 ± 9.064 <sup>NS</sup>
At 14mins	120.1 ± 9.27	118.8 ± 9.001 <sup>NS</sup>
At 15mins	120 ± 9.75	118.4 ± 9.075 <sup>NS</sup>
At 20mins	120 ± 9.60	118 9.16 <sup>NS</sup>

\* P < 0.05, \*\* P < 0.01, \*\*\* P < 0.001

NS - Not Significant

**Table 7:** Comparison of Mean Rate pressure product at various time intervals between esmolol and metoprolol group:

Time interval	Esmolol	Metoprolol
Basal	9520.2 ± 870.8	9397 ± 720.21 <sup>NS</sup>
After premedication	9992.4 ± 916.66	9742.6 ± 603.412 <sup>NS</sup>
After study drug	8981.0 ± 823.1	9006 ± 632.199 <sup>NS</sup>
After propofol	8255.2 ± 933.4	8351.7 ± 623.19 <sup>NS</sup>
After scoline	8562.7 ± 900.9	8577.5 ± 633.65 <sup>NS</sup>
At DLI	9397.9 ± 795.837	9430.1 ± 678.7**
At 30secs.	9973.5 ± 787.4	10192.8 ± 706.98 <sup>NS</sup>
At 1mins	10598 ± 771.75	11080.4 ± 656.4 <sup>NS</sup>
At 1 ½ mins	11257 ± 797	11870.7 ± 577.81 <sup>NS</sup>
At 2mins	11798.8 ± 773.23	12534.2 ± 969.9 <sup>NS</sup>
At 3mins	11418.70 ± 716.69	12139 ± 860.39 <sup>NS</sup>
At 4mins	110048 ± 701	11580 ± 796.93 <sup>NS</sup>
At 5mins	10639.3 ± 753	11123 ± 796.051 <sup>NS</sup>
At 6mins	10351.2 ± 736.05	10760 ± 766.2 <sup>NS</sup>
At 7mins	10001.4 ± 728.96	10307.4 ± 704.2 <sup>NS</sup>
At 8mins	9841.4 ± 707.45	9915.8 ± 727.49 <sup>NS</sup>
At 9mins	9736.2 ± 791.28	9486 ± 678.26 <sup>NS</sup>
At 10mins	9601.2 ± 891	9204 ± 658 <sup>NS</sup>
At 11mins	9611 ± 883.8	9077 ± 774 <sup>NS</sup>
At 12mins	9634.4 ± 941.06	9026.8 ± 739*
At 13mins	9630 ± 851.0	8962.8 ± 763.7*
At 14mins	9666.8 ± 861	9015.6 ± 691.8*
At 15mins	9.565 ± 890	8932.8 ± 734*
At 20mins	9.763 ± 896.39	8942.8 ± 733.2**

P < 0.05, \*\* P < 0.01, \*\*\* P < 0.001

NS: Not significant

There was no statistically significant difference among the three groups in pre anaesthetic demographic data i.e. sex distribution ,age group, dose of propofol in milligram required for induction,intubation timeand intubation score in all three groups.

**Hemodynamic trends**

After study drug mean heart rate in esmolol and metoprolol has decreased over baseline heart rate and significantly lower than in control group (P<0.001) while comparing metoprolol and esmolol fall in heart rate is comparable (P>0.05).Upto 9 minutes mean heart rate in esmolol and metoprolol group is comparable and difference is not statistically significant. After 10 minutes there is gradual decline in heart rate in metoprolol group over baseline and difference in two study groups is statistically significant for 10 minutes (p<0.05)and 11 minutes(0.01).Mean heart rate reaches baseline at around 13 minutes after intubation in control group (p<0.05). But heart rate is lower in metoprolol group than control group ( P<0.01).After inj.of study group mean systolic B.P.was significantly lower in esmolol and metoprolol group (P< 0.001)but difference between two groups was not significant . after induction with propofol was there is much greater fall in systolic B.P. in esmolol and metoprolol group than control (P<0.001).

After the injection study drug and injection propofol fall in rate pressure product was much greater in esmolol and metoprolol group (P<0.001).During laryngoscopy and intubation rate pressure product increased in all three groups but two much greater extent in control group and maximum rise seen at two minutes after intubation which was much greater in control group than esmolol and metoprolol (p<0.001)

RPP remain elevated over base line for about fifteen minutes in control group while in esmolol and metoprolol group it reached baseline 8 minutes and 9minutea after intubation respectively . In metoprolol group RPP remain lower than control and no difference in esmolol and metoprolol group up to 11 minutes after intubation.

**IV. Discussion**

Pressor response to laryngoscopy and intubation is recognized since 1940 .The most deleterious effects of pressor response are tachycardia ,hypertension, myocardial ischemia ,arrhythmias .The purpose of present study was to compare the effects of esmolol and metoprolol both cardioselective β blockers for attenuation of pressor response to laryngoscopy and endotracheal intubation .

Both study drugs have direct chronotropic action and cause equal fall in heart rate ( $P > 0.005$ ). Magnusson J et al studied stress response to microlaryngoscopy with metoprolol and fentanyl and have shown that metoprolol causes fall in heart rate after injection ( $p < 0.01$ ). Another study by Magnusson et al in hypertensive patients also shown decrease in heart rate after metoprolol injection ( $p < 0.05$ ). In both studies metoprolol was given 4 days and 2 weeks prior to surgery respectively and dose used before induction intravenously was also higher 10 mg and 15 mg iv compared to present study. Coleman et al studied  $\beta$  blockade with 2 mg and 4 mg of metoprolol and found dose dependant fall in heart rate. Dose used by Coleman parallels dose in our study.

Greater fall in mean heart rate following propofol in study drugs indicates combined effect of beta blockers and propofol on heart rate. Effect of baroreceptor reflex control of heart is known with propofol. Though the pain factor on inj. propofol would be same in all three groups, sympathetic response to pain is blocked by beta antagonist esmolol and metoprolol group. Therefore present study shows the greater fall in heart rate in group of study drug than control group. Better results ( $p < 0.001$ ) obtained than Magnusson et al ( $p < 0.01$ ) indicates probable role of propofol as induction agent and additive effect on heart rate. Studies by Coleman et al, R. Korpinen, Canadian multicenter study by D.R. Miller and Phillip Liu shown results in accordance with present study and results are statistically better ( $p < 0.001$ ) probably related to induction agent propofol as against thiopentone sodium in other studies. Javed et al compared esmolol and metoprolol (25mg and 4 mg respectively) in hypertensive patient and esmolol was found to be better in attenuating heart rate response ( $p < 0.001$ ). Present study utilizing similar doses found no statistically significant difference between esmolol and metoprolol. Pressor response is always appears exaggerated and unpredictable or variable in hypertensive patients. After 10 minutes heart rate in metoprolol group has decreased more compared to esmolol group ( $p < 0.05$ ). The reason for this difference in heart rate is most probably duration of action of esmolol and metoprolol. Elimination half life of esmolol is 9 minutes and action remains for 15 -20 minutes after injection whereas elimination  $\frac{1}{2}$  life of metoprolol is 3-7 hours. Mechanism of attenuation of blood pressure response by beta blockers is by negative chronotropic and ionotropic action. Other mechanisms are inhibiting the release of renin, thus decreasing the angiotensin and aldosterone, decreasing central vasomotor activity. But probably these mechanisms come into play after many hours of starting drug therapy. So in study by Magnusson et al they have used oral metoprolol 4 days and 2 weeks prior to surgery and got positive results.

Rate pressure product is product of heart rate and systolic blood pressure. It is indicator of myocardial work load. Esmolol and Metoprolol have significantly decreased rate pressure product compared to control group ( $p < 0.001$ ) which is due to negative chronotropic action of beta blockers. It is seen that mean RPP increase as soon as laryngoscopy begins and reaches peak at 2 minutes after intubation. At all time intervals RPP remains significantly higher in control group than study drugs ( $p < 0.001$ ). There was no significant difference between esmolol and metoprolol group ( $p > 0.05$ ). RPP never reached above 15000 in esmolol and metoprolol group at which myocardial ischemia sets in [ Javed et al ].

## V. Summery And Conclusion

Based on results of present study it may be concluded that intravenous esmolol and metoprolol prevent rise in heart rate and peak rise in blood pressure with resultant rise in rate pressure product. Clinically and statistically it can be concluded that metoprolol may be a better agent for attenuation of heart rate and esmolol is better choice to attenuate blood pressure. Propofol appears to have additive effect with beta blockers on heart rate and blood pressure at lower doses of esmolol and metoprolol. No adverse effects like severe hypotension or bradyarrhythmias requiring treatment were observed in any group.

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