

ATTENUATION OF CARDIOVASULAR RESPONSES TO LARYNGOSCOPY AND INTUBATION BY INTRAVENOUS METOPROLOLGurudatta K. N¹, Kumara A. B²**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: The cardiovascular responses to laryngoscopy and intubation may become hazardous in patients with compromised cardiovascular system, such as hypertension, ischemic heart diseases or cerebrovascular diseases. Attenuation of this response is extremely important. Intravenous Metoprolol 4mg was given 5 minutes before induction of Anesthesia for the attenuation of cardiovascular responses. **AIM:** To observe the occurrence of tachycardia hypertensive (pressor) responses that occurs at the time of laryngoscopy and intubation. In the present study an attempt was made to attenuate these responses by I.V. Metoprolol 4mg. **METHODS:** One hundred patients of ASA physical status 1 or 2 divided into 2 groups – study and control. The study group received intravenous metoprolol 4 mg before laryngoscopy and intubation and the control group did not receive the metoprolol injection. The changes in heart rate, mean arterial pressures and rate pressure product before, during and after laryngoscopy and intubation were evaluated and compared between the two groups. The statistical analysis done using Chi-square test and two samples 't' test. **RESULTS:** The cardiovascular responses laryngoscopy and intubation were significantly attenuated ($P > 0.001$) by intravenous Metoprolol.

KEYWORDS: Cardiovascular responses, intubation response, Laryngoscopy and intubation, intravenous Metoprolol.

INTRODUCTION: Induction of anesthesia is a hazardous phase in the management of patients during surgery. The frequent occurrence of cardiovascular responses to laryngoscopy and tracheal intubation has attracted the attention of anesthesiologists since 1940's. The cardiovascular responses to laryngoscopy and intubation^{1,2} may be less harmful in an otherwise normal individual. But in a patient with compromised cardiovascular system such as hypertension,³ ischemic heart disease or cerebrovascular disease, these pressor responses may be of disastrous consequences.^{4,5} Attenuation of this response, at least in such patients is extremely important.

Many studies have been conducted to attenuate the cardiovascular responses to laryngoscopy and intubation using, deeper plane of Anesthesia, β -blockers,^{6,7} α_2 agonist clonidine,⁸ opioids⁹ like fentanyl, alfentanil, buprenorphine; calcium channel blockers (sublingual nifedipine),¹⁰ vasodilators¹¹ (nitroglycerine), topical anesthesia with lignocaine and intravenous lignocaine,¹² etc.

Administration of intravenous metoprolol (selective β -blocker) as a method to attenuate the cardiovascular responses has been studied by many researchers and is found to be useful in this regard.⁶ So, we decided to study effect of intravenous use of metoprolol on induction of anesthesia and effect on cardiovascular responses during laryngoscopy and endotracheal intubation.

METHODS: After approval from hospital administration and written informed consent, this prospective study done on 100 patients of either sex, aged between 20 to 70 years belonged to ASA

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physical status 1 or 2, admitted for various elective surgical procedures under general anesthesia were included in our study. Patients excluded from study were those with uncontrolled hypertension, diabetes mellitus, bronchial asthma, cardiac arrhythmias, atrio-ventricular conduction block, anticipated difficult airway, and patients on vasoactive drugs.

All patients were explained about the surgical procedure and anesthesia and about drug being used and were given tab diazepam 5 mg orally at bed time the day before surgery.

On arrival inside the operation theatre, patients were connected to continuous electrocardiography, non-invasive blood pressure, and pulse-oximetry on operation table and basal parameters noted. An intravenous line secured and the study group (metoprolol group) received 4 mg metoprolol intravenously 5 minutes before induction of Anesthesia while the control group did not receive metoprolol. All the patients were pre-oxygenated. The analgesia was provided by inj. Pentazocine 0.5 mg/kg and was induced with inj.

Thiopentone sodium (2.5%) 5 mg/kg body weight given over 30 sec with loss of eyelash reflex being endpoint, followed by neuromuscular blockade with inj. Succinylcholine 1.5 mg/kg body weight. Once the patient was apneic, ventilation was accomplished manually. Direct laryngoscopy was performed 90 seconds after inj. Succinylcholine, using Macintosh laryngoscope. Endotracheal intubation was done with a suitable cuffed endotracheal tube in shortest possible time. The time taken for laryngoscopy and intubation was kept to a minimum (less than 15 sec.).

The ventilation was continued manually in all cases using Bain's circuit. Anesthesia was maintained with oxygen, halothane and nitrous oxide. Further muscle relaxation was achieved by inj. Pancuronium bromide (0.08mg/kg-initial dose and intermittent supplements).

Laryngoscopy and intubation were done by the same individual in all cases and parameters were recorded. Surgical stimulation was avoided during the study period. The heart rate and noninvasive blood pressure recordings were done at the following intervals.

T _b	Basal value at time of injecting metoprolol
T _{pi}	Just before induction
T _{pl}	Just before laryngoscopy (post induction)
T _{1i}	1 minute after intubation
T _{3i}	3 minutes after intubation
T _{5i}	5 minutes after intubation
T _{10i}	10 minutes after intubation

At the end of the surgery the residual neuromuscular blockade was reversed with inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.01 mg/kg. Extubation was done when the patient was conscious and responding to oral commands with all other parameters within acceptable limits.

Statistical analysis was done using two-samples't' test and Mann-Whitney test for parametric data and Chi-square test for non-parametric data with p value <0.05 being significant.

RESULTS: Patients in the both groups are comparable in age, gender distribution and weight and were statistically insignificant.

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	Control group	Study group	n = 100, p - Value
Age (in years)	39.04±12.51	40.26±12.50	t=0.488, p > 0.05
Sex (Male/Female)	29/21	28/22	x ² = 0.0815, p > 0.05
Weight (in kg)	52.08±7.48	53.68±6.44	t=1.23, p > 0.05

Table 1: Demographic profile

	Control group	Study group	Total
General surgical procedures	44	48	92
Orthopedic surgeries	4	1	5
ENT surgeries	2	1	3
Total	50	50	100

Table 2: Number of surgical procedures

The tables 3, 4, 5, 6 and 7 depict comparative changes in Heart Rate (HR), Systolic Blood Pressure (SBP), Mean Arterial Pressure (MAP) and Rate Pressure Product (RPP) between the two study groups from T_b (basal value), T_{pi} (prior induction), T_{pl} (prior laryngoscopy) T_{1i} (1 minute after intubation) to T_{10i} (10 minutes after intubation).

Timing	Control group	Study group	t - value	p - value
T _b	83.5±6.42	83.38±6.46	0.093	>0.05
T _{pi}	85.3±6.17	76.44±7.11	6.66	<0.001
T _{pl}	88.94±6.88	68.24±6.025	17.25	0.001
T _{1i}	121.46±8.25	87.62±5.91	23.66	<0.001
T _{3i}	111.44±7.72	83.6±6.57	19.46	<0.001
T _{5i}	101.98±8.85	79.98±5.38	15.06	<0.001
T _{10i}	88.6±5.41	82.58±4.99	0.175	>0.05

Table 3: Heart rate changes (beats/min) at different intervals

Timings	Control group	Study group
T _{pi}	↑ 1.8 (2.15%)	↓ 7.44 (8.86%)
T _{pl}	↑ 5.44(6.5%)	↓ 15.14(18.15%)
T _{1i}	↑ 37.96 (45.46%)	↑ 4.24 (5.08%)
T _{3i}	↑ 27.94 (33.46%)	↑ 0.22 (0.26%)
T _{5i}	↑ 18.48 (22.13%)	↓ 3.4 (4.07%)
T _{10i}	↑ 15.1 (6.10%)	↓ 0.7 (0.83%)

Table 4: Showing the mean heart rate changes at specified time intervals from the mean basal level at T_b

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Timing	Control group	Study group	t - value	p - value
T _b	120.6±11.13	122.96±11.76	1.03	>0.05
T _{pi}	121.68±11.78	119.28±11.36	1.037	>0.05
T _{pl}	118.2±10.87	111.6±9.85	3.18	<0.001
T _{1i}	166.6±26.34	136.04±10.83	7.58	<0.001
T _{3i}	151.96±11.67	129.28±11.68	9.71	<0.001
T _{5i}	139.32±12.95	122.76±15.11	5.88	<0.001
T _{10i}	127.62±9.66	122.04±11.04	2.68	<0.01

Table 5: Showing mean Systolic blood pressure (in mm Hg) at different intervals.

Time interval	Control group	Study group	t - value	p - value
T _b	93.72±8.76	94.34±7.40	0.382	>0.05
T _{pi}	93.98±9.08	92.05±6.93	1.195	>0.05
T _{pl}	92.32±8.91	86.79±6.28	3.587	<0.001
T _{1i}	128.32±7.2	105.44±15.02	9.715	<0.001
T _{3i}	117.93±7.36	99.25±7.02	12.99	<0.001
T _{5i}	108.68±8.24	94.68±7.11	9.096	<0.001
T _{10i}	98.96±6.25	94.15±9.42	3.01	<0.01

Table 6: Showing Mean Arterial Pressure (MAP) in mmHg at different intervals

Time interval	Control group	Study group	p - value
T _b	9972.12±1228.28	10287.04±1463.50	>0.05
T _{pi}	10349.8±1312.42	9142.56±1386.3	<0.001
T _{pl}	10505.6±1256.1	7596.44±956.74	0.001
T _{1i}	20279.20±2121.5	11937.16±1383.28	<0.001
T _{3i}	16984.28±1870.36	10826.92±1474.21	0.001
T _{5i}	14227.88±1902.83	9840.64±1271.4	<0.001

Table 7: Showing rate pressure products (RPP) at various intervals as mean ±SD

"On comparison of haemodynamic parameters basal values of heart rate (HR), blood pressures (SBP, MBP and DBP) and rate pressure product (RPP = SBP x HR) between the control and the study group were statistically not significant (p-value >0.05). At T_{pi} (just after induction) there was a small increase in the values of all the parameters in case of control group compared to significant reduction of parameter values in the study group. At T_{pl} (just before laryngoscopy) there was a significant increase in the values of all the parameters in case of control group, while all these parameters significantly reduced further in the study group."

Maximal increase in the values of parameters was seen in both the groups at T_{1i} (1 min. after intubation). Increase in the mean HR was 36.56% over the previous value (T_{pi}) in the control group whereas it was 28.39% over the previous value in the study group. But this increase at T_{1i} was

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45.46% from the basal value (T_b) in the control group while it was 5.08% from the basal value in case of study group. Similarly mean SBP raised by 19.44% over the previous value & 10.63% over the basal value in the study group.

The corresponding increases in SBP were 48.4% and 38.14% in the control group. The mean DBP increased by 21.24% over the previous value and this increase was only 12.69% over the basal value in the study group. The corresponding increases in mean DBP of control group at T_{1i} were 36.76% and 35.87% respectively. Similarly increase in mean MAP was 21.48% over the previous value and this was only 11.76% from the basal value in the study group.

The corresponding increases in the mean MAP in the control group were 38.98% and 36.9% respectively. Similar changes were noticed in mean RPP also. Increase in mean RPP at T_{1i} was 57.14% over the previous value and it was only 16% over the basal value in the study group. The corresponding increases in the mean RPP of the control group were 93% and 103% respectively.

All the above hemodynamic parameters were found to reduce gradually over next 5-10 minutes after intubation. At T_{10i} , (10 mins. after intubation) the values observed in control group considerably decreased but were still slightly above the basal mean values whereas values in the study group had reached their respective basal values. "Within the group" and "Between the group" comparison of the observations showed that intravenous metoprolol (4mg) given 5mins before induction, effectively attenuated (but not abolished) the cardiovascular responses to laryngoscopy and intubation.

DISCUSSION: Attenuation of cardiovascular responses during laryngoscopy has been one of the most researched topics in anesthesiology. Numerous drugs have been tried in this regard. In the present study, Metoprolol, a selective β -blocker was intravenously administered for the purpose.

Metoprolol reduces sinus rate, decreases the spontaneous rate of depolarization of ectopic pace makers, and slows the conduction in atria and in the AV node. It also increases the functional recovery period of AV node. Metoprolol reduces blood pressure in hypertensive patients. The release of renin from juxta-glomerular apparatus stimulated by sympathetic system is blocked by metoprolol.¹³ Metoprolol improves the relationship between cardiac oxygen supply and demand.

CHANGES IN MEAN HEART RATE EXPRESSED AS DIFFERENCE FROM THE BASELINE VALUES			
STUDY		POST INDUCTION	AT 1 MINUTE AFTER INTUBATION
OUR STUDY	CONTROL	+5.4	+37.96 (45.46%)
	METOPROLOL(4mg)	-15.14	+4.24 (5.08%)
COLEMAN & JORDAN	CONTROL	+27	+37
	METOPROLOL(2mg)	-7.6	+23.7
	METOPROLOL(4mg)	-12.9	+20.6
SINGH ET AL	CONTROL		+21.7 (24.8%)
	METOPROLOL		+14.9 (17.6%)
KUMAR & TIKLE	METOPROLOL	-6.7	+10.26

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SYSTOLIC BP CHANGES (in mmHg) EXPRESSED AS DIFFERENCE FROM BASELINE			
		POST INDUCTION	AT 1 MINUTE AFTER INTUBATION
OUR STUDY	CONTROL	+1.4	+34.59
	METOPROLOL	-7.6	+11.1
KUMAR & TIKLE	CONTROL	+1.2	+21.4
	METOPROLOL	-11.14	+13.8
COLEMAN & JORDAN	METOPROLOL (4mg)	-8.1	BELOW BASELINE
MEAN BP (MAP) CHANGES (in mmHg) EXPRESSED AS DIFFERENCE FROM BASELINE			
OUR STUDY	CONTROL	+1.4	+34.59 (36%)
	METOPROLOL	-7.6(8%)	+11.1 (11.6%)
SINGH ET AL	CONTROL	-1	+34.8
	METOPROLOL	-5.3	+18.9
MEAN RPP CHANGES			
STUDY		BASELINE	AT 1 MINUTE AFTER INTUBATION
OUR STUDY	CONTROL	9972	20279 (103%↑)
	METOPROLOL	10287	11938 (16%↑)
KUMAR & TIKLE	CONTROL	9988	15603 (56% ↑)
	METOPROLOL	10311.4	11734.9 (13%↑)
SINGH ET AL	CONTROL	10866	15839 (57% ↑)
	METOPROLOL	10287	11938 (16%↑)

Table 8: Comparison of studies

+: indicates increase from the baseline. -: indicates increase from the baseline.

Heart Rate (HR): Study by Coleman and Jordan, ⁶ observed a mean rise in heart rate by 27 beats after induction and a mean increase of 37 beats per minute (bpm) from basal value after intubation in the control group compared to their study groups (metoprolol 2mg and 4mg respectively) HR reduced first following metoprolol injection by 7.6 and 12.9 bpm respectively and maximum rises in HR after intubation was 23.7 and 20.6 bpm respectively, which were much below those in the control group. In our study we observed a similar trend with mean HR reduced in metoprolol group by 8.86% following induction and increased by 5.08% (4.24 bpm) following intubation at 1 minute which was significant reduction in intubation response in comparison to our control group which had a rise of 45.46% (37.96 bpm) at the same time.

Singh et al,¹⁴ observed an increase in HR by 17% from the pre-induction value in the metoprolol group (82.9±14 to 97.8±11.5 bpm) at one minute after intubation, while corresponding increase in the control group was 24.85% (87.3±114.3 to 109±110.8 bpm) and concluded that metoprolol significantly attenuated HR response to laryngoscopy and intubation. Similarly, in study by Kumar and Tikle, ¹⁵ they found that the mean HR decreased by 6.7 bpm following intravenous metoprolol and later increased by 10.26 bpm following intubation from basal value, which was

significantly less as compared to the control group with maximum rise in HR after intubation of 27.53 bpm.

Magnusson et al,⁷ have reported an incidence of bradycardia in one patient which was effectively reversed with I.V. atropine. Kumar and Tikle also have reported one such incidence. But in our study, we didn't have such incidence of bradycardia in any of patients in both the groups.

Systolic Blood Pressure (SBP): In our study, mean SBP decreased by 9.23% (11.36 mmHg) following induction and then increased by 10.63% (13.08 mmHg) at 1 min. after intubation from the basal value in the study group, whereas the corresponding changes in the control group were -1.99% (\downarrow 2.4mmHg.) and +38.14% (\downarrow 46mmHg) following induction and intubation respectively. SBP changes in this study are thus in comparison with the changes observed by Kumar and Tikle, as they observed reduction of mean SBP by 11.14mmHg at induction and then increased by 13.8 mmHg soon after intubation in the study group.

Coleman and Jordan⁶ noted the mean increase of 9.8mm Hg which occurred at intubation in control group where as in metoprolol groups (2mg and 4mg) there were significant mean reduction in blood pressure by 7.1 mmHg and 8.1 mmHg following metoprolol 1.V. respectively, this persisted following induction and thereafter, there was a small increase in systolic arterial pressure with intubation. They observed mean increase in systolic arterial pressure with intubation in metoprolol 4mg group was still below the basal level compared to slight increase in SBP in metoprolol 2 mg group.

Singh et al reported 5.5% reduction in mean MAP following induction (95.5 \pm 8.3 to 90.1 \pm 12.6 mm Hg) and they noticed 18% increases in MAP (113 \pm 12 mm Hg) following intubation in metoprolol group compared to increase in mean MAP by 34.8% following intubation (from 95.2 \pm 10.1 to 128.4 \pm 17.3 mm Hg in their study. Similarly, in our study in the metoprolol group mean MAP decreased by 8% following induction (94.34 \pm 7.40 to 86.79 \pm 6.28 mm Hg), and mean MAP increased by 11.6% from the basal value at 1 min after intubation (105.44 \pm 15.02 mm Hg). Thereafter it returned to basal level by next 5 minutes which was in comparison with study by Singh et al.

Rate Pressure Product (RPP): Rate pressure product is a derived parameter and is the product of heart rate and systolic blood pressure at any given moment. According to Marey's law heart rate rises with fall in blood pressure and vice-versa and this keeps rate pressure product fairly constant. Any condition which increases heart rate and systolic blood pressure multiplies the rate pressure product, which may cross critical limits of ischemia.

Roy et al,¹⁶ found that RPP of above 22000 was associated with ischemic changes in ECG in healthy volunteers. It was found that in patients with ischemic heart disease coming for tread mill test, the critical limit of RPP for angina to develop was 12, 000. But Bedford² observed RPP values of 20000 without appearance of ischemic changes in mild hypertensives. Anyhow, RPP is said to correlate well with myocardial oxygen consumption and it is a simple and useful means of clinically assessing the work load of heart.

In our study, the mean RPP rose from the basal value of 9972.12 \pm 1228.28 to a value of 10565.6 \pm 1256.10 following induction (\uparrow 5.34%) and reached a peak of 20279.2 \pm 2121.5 (\uparrow 103.35%) at T₄ i.e. one minute after intubation in the control group, whereas in metoprolol group the mean RPP decreased from basal value of 10287.01 \pm 1046.35 to 7596.44 \pm 956.74 (\downarrow 26%) following induction

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and then reached a peak of 11938.16 ± 1386.28 ($\uparrow 16\%$) following intubation (T_4). At the end of 5mins it was 9840.64 ± 1271.4 ($\downarrow 4.3\%$).

Study by Singh et al found that their study group had 25% increase in mean RPP (10448 ± 591 to 13072 ± 734) at 1 minute after intubation, while there was 57% increase in mean RPP in the control group (10866 ± 716 to 15839 ± 832). Similarly, Kumar and Tikle (1995), found in the study group 13% increase in mean RPP (10311.4 to 11734.9) following intubation, while it was 56% in the control group (9988.1 to 15603.3).

We concluded from this study that intravenous metoprolol 4 mg given 5 minutes before induction of anesthesia significantly attenuates the cardiovascular responses to laryngoscopy and intubation.

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