

## To Study the Hemodynamic Response of Two Different Doses of Labetalol in Controlled Hypertensive Patients during Laryngoscopy and Endotracheal Intubation

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Conflict of interest: Nil

### Abstract:

**Background:** The purpose of this study was to evaluate the effectiveness of two different Labetalol dosages in managing the hemodynamic responses to tracheal intubation and laryngoscopy in controlled hypertensive patients while using the same anesthetic techniques.

**Methods:** Over the course of a year, from 1 September 2021 to 31 August 2022, 96 patients who presented for a pre-anaesthetic check-up at the Department of Anaesthesiology and Critical Care at Gauhati Medical College and Hospital participated in this hospital-based prospective, randomized, double-blinded study with written informed consent from study participants and approval from the institutional ethics committee.

**Results:** A statistically significant difference was observed in the mean SBP between patients receiving IV Labetalol 0.15 mg/kg and IV Labetalol 0.3 mg/kg within the same group. At five and ten minutes, there was a significant intragroup difference in the mean DBP of patients receiving IV Labetalol 0.15 mg/kg. It was statistically significant to compare changes in DBP and MAP at different predefined time intervals, such as at intubation. After ten minutes, there was a significant difference between the mean RPP of patients receiving IV Labetalol (0.3 mg/kg) and the baseline.

**Conclusions:** In patients with controlled hypertension, both IV dosages of labetalol (0.15 mg/kg and 0.3 mg/kg), administered five minutes prior to endotracheal intubation, are useful in reducing the hemodynamic reaction to laryngoscopy and intubation. The hemodynamic response to laryngoscopy and endotracheal intubation was more attenuated by IV Labetalol (0.3 mg/Kg) than by the 0.15 mg/Kg dose.

**Keywords:** Hemodynamic, Laryngoscopy, Endotracheal Intubation, Labetalol, Hypertensive.

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### Introduction

An alpha-1 and nonselective b1- and b2-adrenergic antagonist, labetalol is a novel oral and parenteral antihypertensive medication. It rapidly redistributes (5.9 min redistribution half-life) and reaches its peak effect 5–15 min after intravenous (IV) injection.[1] While simultaneous  $\beta$ -blockade attenuates reflex tachycardia induced by vasodilatation, it lowers blood pressure by decreasing systemic vascular resistance ( $\alpha$ 1-blockade).[1-4,6-7,9-16] Cardiac output does not alter.[14,16]

The current study's objective was to examine the effects of two distinct Labetalol dosages on the hemodynamic response during laryngoscopy and endotracheal intubation in patients with controlled

hypertension while using the same anesthetic techniques.

### Methods

96 patients who came to the Department of Anaesthesiology and Critical Care at Gauhati Medical College and Hospital for a pre-anaesthetic check-up between September 1, 2021, and August 31, 2022, participated in this hospital-based prospective, randomized, double-blinded study.

The study was approved by the institutional ethics committee, and participants provided written informed consent. The study took place over the course of a year. Data was gathered using study proforma that satisfied the study's goals and objectives. The study included 96 patients with

ASA physical status II who were between the ages of 18 and 60 and undergoing elective surgical procedures that required endotracheal intubation and general anesthesia. Patients with hypertension were identified during the pre-anesthetic evaluation, but antihypertensive medications like renin-angiotensin inhibitors and calcium channel blockers were controlling their hypertension. None had an aberrant ECG or a history of myocardial ischemia or infarction. The study excluded patients with concomitant conditions such as cardiovascular, pulmonary, or renal disease; beta blocker use; difficult airway; laryngoscopy; and intubation times greater than 20 seconds or more than two attempts. Two groups of patients were randomly selected using a computer-generated sequence.

The sealed envelope technique was used to conceal the allocation.

Labetalol 0.15 mg/kg intravenously was given to Group A (n=48) five minutes prior to endotracheal intubation.

Group B (n=48): Five minutes prior to endotracheal intubation, a dose of labetalol (0.3 mg/Kg) was administered.

Heart rate, diastolic and diastolic blood pressure were measured before induction, during intubation, and one, three, five, and ten minutes after intubation. For the same time intervals, the mean arterial pressure and rate pressure product were computed.

**Statistical Methods**

With SPSS, the statistical analysis was carried out. A paired "t" test was used to analyze the study data (for intragroup values at various intervals of time) and an independent "t" test (for values between groups). The mean plus SD was used to express all values. A statistically significant result was defined as P < 0.05, and a non-significant result as P > 0.05.

**Results**

The mean heart rate (HR) in Group A was compared within the group and found to have significantly increased during intubation and decreased at 3, 5, and 10 minutes (83.81±9.49, 83±9.39, 81.6±9.13). Values were non-significant at three, five-, and ten-minutes relative to the baseline, and significant at ten minutes.

When comparing the mean heart rate within groups, Group B reveals that there was a non-significant increase in heart rate during intubation and a decrease in heart rate at 1, 3, 5, and 10 minutes (81, 63±7.99, 80, 96±8.07, 79, 65±7.97, 78, 92±7.78). Values were non-significant at one minute and significant at three, five-, and ten-minutes relative to the baseline.

When comparing the mean heart rate changes between Group A and Group B at different time intervals, the intergroup comparison p-values were found to be >0.05, indicating that there was no statistically significant difference in the heart rate changes between the groups.

**Table 1: Intergroup comparison of mean systolic blood pressure (mean SBP)**

Intervals	mean (mmHg)	SD (mm Hg)	Change from baseline (mmHg)	% change from baseline	P value
Baseline	131.77	4.5			-
At intubation	139.69	4.88	7.92	1.27%	0.0001
1 minute after intubation	137.96	5.91	6.19	1.10%	0.0001
3 minutes after intubation	134.58	4.87	2.81	3.44%	0.0001
5 minutes after intubation	131.42	4.65	-0.35	27.04%	0.331
10 minutes after intubation	127.44	5.73	-4.33	24.27%	0.0001
T6 SBP	148.94	10.298	26.7	21.84%	P<0.0001
T7 SBP	143.03	10.08	20.79	17.01%	P<0.0001
T8 SBP	139.79	9.396	17.55	14.36%	P<0.0001
T9 SBP	134.24	8.763	12	9.82%	P<0.0001
<b>Intragroup comparison of mean systolic blood pressure of Group A</b>					
Intervals	mean (mmHg)	SD (mmHg)	Change from baseline(mmHg)	% change from baseline	P value
Baseline	132.88	4.66			-
At intubation	131.6	5.45	-1.28	1.27%	0.062
1 minute after intubation	128.5	5.93	-4.38	1.10%	0.0001
3 minutes after intubation	123.31	5.75	-9.57	3.44%	0.0001
5 minutes after intubation	117.08	5.84	-15.8	27.04%	0.0001
10 minutes after intubation	110	6.74	-22.88	24.27%	0.0001
<b>Intragroup comparison of mean systolic blood pressure of Group B</b>					
	<b>Mean systolic blood pressure (mmHg)</b>				
<b>Time</b>	<b>Group A</b>	<b>Group B</b>	<b>p Value</b>		

	Mean + SD	Mean + SD	
Baseline	131.77+4.88	132.88+4.66	0.24
At intubation	139.69+4.50	131.60+5.45	0.0001
1 min after intubation	137.96+5.91	128.50+5.93	0.0001
3 min after intubation	134.58+4.87	123.31+5.75	0.0001
5 min after intubation	131.42+4.65	117.08+5.84	0.0001
10 min after intubation	127.44+5.73	110.00+6.74	0.0001

Group A's mean systolic blood pressure (SBP) was compared intragroup, and the results indicate a significant increase during intubation, at 1 and 3 minutes after intubation, and a decrease at 5 and 10 minutes (131.42+4.65, 127.44+5.73). Values were non-significant at five minutes and significant at ten minutes when compared to the baseline.

The mean SBP in Group B was compared within the group and it was found to be significantly

higher during intubation, to be lower at 1 and 3 minutes after intubation, and to be lower at 5 and 10 minutes (131.42+4.65, 127.44+5.73). Values were non-significant at five minutes and significant at ten minutes with respect to the baseline.

When comparing the two groups, statistical analysis revealed p values of 0.0001 (<0.05), suggesting a statistically significant difference in the variations in SBP between the groups.

**Table 2: Intergroup comparison of mean diastolic blood pressure (mean DBP)**

Intervals	mean (mmHg)	SD (mmHg)	Change from baseline(mmHg)	% change from baseline	P value
Baseline	79.17	6.65			-
At intubation	84.31	6.85	5.14	1.27%	0.0001
1 minute after intubation	84	7.05	4.83	1.10%	0.0001
3 minutes after intubation	81.04	6.59	1.87	3.44%	0.0001
5 minutes after intubation	78.46	6.54	-0.71	27.04%	0.045
10 minutes after intubation	75.33	6.3	-3.84	24.27%	0.0001
<b>Intragroup comparison of mean diastolic blood pressure from baseline of Group A</b>					
Intervals	mean (mmHg)	SD (mmHg)	Change from baseline(mmHg)	% change from baseline	P value
Baseline	79.58	6.3			-
At intubation	79.02	6.52	-0.56	1.27%	0.07
1 minute after intubation	74.35	6.43	-5.23	1.10%	0.0001
3 minutes after intubation	71.06	5.59	-8.52	3.44%	0.0001
5 minutes after intubation	67.63	5.14	-11.95	27.04%	0.0001
10 minutes after intubation	62.85	4.94	-16.73	24.27%	0.0001
<b>Intragroup comparison of mean diastolic blood pressure from baseline of Group B</b>					
<b>Mean systolic blood pressure (mmHg)</b>					
Time	Group A		Group B		p Value
	Mean±SD		Mean±SD		
Baseline	79.17+6.65		79.58+6.30		0.753
At intubation	84.31+6.85		79.02+6.52		0.0001
1 min after intubation	84.00+7.05		74.35+6.43		0.0001
3 min after intubation	81.04+6.59		71.06+5.59		0.0001
5 min after intubation	78.46+6.54		67.63+5.14		0.0001
10 min after intubation	75.33+6.30		62.85+4.94		0.0001

The mean diastolic blood pressure in Group A was compared intragroup, and the results indicate a significant increase during intubation, a decrease at 1 and 3 minutes after intubation, and a decrease at 5 and 10 minutes (78.46+6.54, 75.33+6.30). Values at 5 and 10 minutes were significantly different from the baseline, and data from Group B indicates that DBP decreased at intubation, 1, 3, 5, and 10 minutes after intubation (79.02+6.52, 74.35+6.43, 71.06+5.59, 67.63+5.14, 62.85+4.94). Values were non-significant at intubation and significant at 1, 3, 5, and 10 minutes after

intubation relative to the baseline. When the two groups were compared using statistical analysis, the p values resulted in 0.0001 (<0.05), indicating that there was a statistically significant difference in the DBP changes between the groups. A notable increase in mean MAP was observed during intubation, at 1- and 3-minutes post-intubation, and a decrease was observed at 5 and 10 minutes (95.88+5.50, 92.46+5.45), according to the intragroup comparison of mean MAP in Group A. Values were non-significant at five minutes and significant at ten, and Group B indicates a decrease

in mean arterial pressure at intubation, one, three, five, and ten minutes after intubation (96. 27+5. 72, 92. 1+5. 78, 88. 21+5.17, 83. 81+4. 67, 78. 27+4. 9). Values were non-significant at intubation and significant at 1, 3, 5, and 10 minutes after

intubation relative to the baseline. When comparing the two groups, statistical analysis revealed p values of 0. 0001(<0.05), suggesting a statistically significant difference in the MAP changes between the groups.

**Table 3: Intergroup comparison of the mean map between Group A and Group B**

Intervals	mean (mmHg)	SD (mmHg)	Change from baseline (mmHg)	% change from baseline	P value
Baseline	96.38	5.6			-
At intubation	102.46	5.62	6.08	1.27%	0.0001
1 minute after intubation	101.58	6.26	5.2	1.10%	0.0001
3 minutes after intubation	98.60	5.5	2.22	3.44%	0.0001
5 minutes after intubation	95.88	5.5	-0.5	27.04%	0.075
10 minutes after intubation	92.46	5.45	-3.92	24.27%	0.0001
<b>Intragroup comparison of the mean map from the baseline of Group A</b>					
Intervals	mean (mmHg)	SD (mmHg)	Change from baseline (mmHg)	% change from baseline	P value
Baseline	97	5.62			-
At intubation	96.27	5.72	-0.73	1.27%	0.07
1 minute after intubation	92.1	5.78	-4.9	1.10%	0.0001
3 minutes after intubation	88.21	5.17	-8.79	3.44%	0.0001
5 minutes after intubation	83.81	4.67	-13.19	27.04%	0.0001
10 minutes after intubation	78.27	4.9	-18.73	24.27%	0.0001
<b>Intragroup comparison of the mean map from the baseline of Group B</b>					
	Mean arterial blood pressure (mmHg)				
Time	Group A		Group B		P Value
	Mean±SD		Mean±SD		
Baseline	96.38+5.60		97.00+5.62		0.587
At intubation	102.46+5.62		96.27+5.72		0.0001
1 min after intubation	101.58+6.26		92.10+5.78		0.0001
3 min after intubation	98.60+5.50		88.21+5.17		0.0001
5 min after intubation	95.88+5.50		83.81+4.67		0.0001
10 min after intubation	92.46+5.45		78.27+4.90		0.0001

**Table 4: Intragroup comparison of mean rate pressure product of Group B**

Intervals	Mean (bpm) (mmHg) x10 <sup>-3</sup>	SD (bpm) (mmHg) x 10 <sup>-3</sup>	Change from baseline (bpm) (mmHg) x10 <sup>-3</sup>	% change from baseline	P value
Baseline	11.01	1.45			-
At intubation	11.93	1.4	0.92	1.27%	0.0001
1 minute after intubation	11.71	1.52	0.7	1.10%	0.0001
3 minutes after intubation	11.23	1.31	0.22	3.44%	0.033
5 minutes after intubation	10.79	1.33	-0.22	27.04%	0.119
10 minutes after intubation	10.35	1.26	-0.66	24.27%	0.0001
<b>Intragroup comparison of mean rate pressure product of Group A</b>					
Intervals	mean (bpm) (mmHg) x 10 <sup>-3</sup>	SD (bpm) (mmHg) x10 <sup>-3</sup>	change from baseline (bpm) (mmHg) x10 <sup>-3</sup>	% change from baseline	p-value
baseline	10.89	1.17			-
at intubation	10.79	1.02	-0.1	1.27%	0.389
1 minute after intubation	10.42	0.96	-0.47	1.10%	0.0001
3 minutes after intubation	9.91	0.9	-0.98	3.44%	0.0001
5 minutes after intubation	9.25	0.84	-1.64	27.04%	0.0001
10 minutes after intubation	8.62	0.87	-2.27	24.27%	0.0001

The mean RPP in Group A was compared intragroup, and the results indicate a significant increase during intubation, at 1 and 3 minutes after intubation, and a decrease at 5 and 10 minutes (10.

79+1. 33, 10. 35+1. 26). Values were non-significant at five minutes and significant at ten, and in Group B, RPP decreased at intubation, one, three, five, and ten minutes after intubation (10.

79+1.02, 10.42+0.96, 9.91+0.90, 9.25+0.84, 8.62+0.87). Values were non-significant at intubation and significant at 1, 3, 5, and 10 minutes after intubation relative to the baseline.

## Discussion

### Hemodynamic Parameters

**Heart Rate:** In our investigation, we observed that there was no difference between the two groups and that both dosages of Labetalol were successful in reducing the HR response to laryngoscopy and intubation. The results of our investigation are consistent with a study conducted by Kumar Rajender, Gandhi Ritika, Mallick Indira, et al. [1] which demonstrated that heart rates increased in Group L1 (inj. Labetalol 0.15 mg/Kg) 16% and Group B (inj. Labetalol 0.3 mg/Kg) 11% following intubation. The results of our investigation also agreed with Singh SP, Quadi A, Malhotra P, et al.'s study [13], which found that labetalol significantly ( $p < 0.05$ ) reduced heart rate.

**Systolic Blood Pressure:** The SBP response to laryngoscopy and intubation was effectively attenuated by both doses of Labetalol in this study, and an intergroup comparison of the mean SBP revealed a significant difference ( $p < 0.05$ ) at every point during the study period, including intubation and 1, 3, 5, and 10 minutes after intubation. Our study's results were in line with those of Kumar Rajender, Gandhi Ritika, Mallick Indira, et al.'s study [1], which similarly examined two doses of intravenous labetalol (Group A = 0.15 mg/Kg and Group B = 0.3 mg/Kg) for attenuating hemodynamic responses to laryngoscopy and intubation in hypertensive patients. The researchers found that there was a statistically significant difference in SBP between the groups at 3, 5, and 10 minutes after intubation. In our study, we discovered that Group B (0.3 mg/Kg IV) had more attenuated SBP than Group A (0.15 mg/Kg iv).

**Diastolic Blood Pressure:** The DBP response to laryngoscopy and intubation was effectively attenuated by both doses of Labetalol, as we observed. An intergroup comparison of the mean DBP of the two groups revealed a significant difference ( $p < 0.05$ ) at every point during the study period, including at intubation and 1, 3, 5, and 10 minutes after intubation. The results of our investigation were in agreement with those of a study conducted by Kumar Rajender, Gandhi Ritika, Mallick Indira, et al. [1] which also examined two injection doses of labetalol (Group A = 0.15 mg/Kg and Group B = 0.3 mg/Kg) for the purpose of attenuating hemodynamic responses to laryngoscopy and intubation in hypertensive patients. The study also showed a statistically significant difference in DBP between the groups at 3, 5, and 10 minutes after intubation. When compared to fentanyl 2mcg/kg IV, a single dose of

Labetalol 0.25mg/Kg IV given five minutes prior to intubation showed a statistically significant decrease in DBP ( $P < 0.05$ ), according to Babita, Singh B, Saiyed A, Meena R, Verma I, Vyas CK et al. Leslie JB, Kalayjian RW, McLoughlin TM, Plachetka JR, et al. [10] showed that DBP was significantly reduced by labetalol at different doses of 0.25, 0.5, 0.75, and 1 mg/kg. In comparison to the placebo and esmolol groups, Labetalol significantly prevented the increase in DBP throughout the study period, according to Singh SP, Quadi A, Malhotra P, et al. [13]; similarly, Nishee R Swami R, Vaishalee K Badhe, Vaishali V. Deshpande, Vijayanti K. Badhe, Shodhaye et al. [16] demonstrated that Labetalol significantly decreased DBP. In our study, it was found that attenuation of DBP was more in Group B (0.3mg/Kg IV) when compared to group A (0.15mg/Kg IV).

**Mean Arterial Pressure:** The MAP response to laryngoscopy and intubation was effectively attenuated by both doses of Labetalol in our study. An intergroup comparison of the mean MAP of the two groups revealed a significant difference ( $P < 0.05$ ) at every study time point, including at intubation and 1, 3, 5, and 10 minutes after intubation. Our study's results were in line with those of Kumar Rajender, Gandhi Ritika, Mallick Indira et al.'s study [1], which also examined two doses of intravenous labetalol (group A = 0.3 mg/Kg and group B = 15. mg/Kg) for the purpose of attenuating hemodynamic responses to laryngoscopy and intubation in hypertensive patients. The results showed that there was a statistically significant difference in mean arterial pressure (MAP) between the groups at 3, 5, and 10 minutes after intubation. When compared to fentanyl 2mcg/kg IV, a single dose of Labetalol 0.25mg/Kg IV given five minutes prior to intubation showed a statistically significant decrease in MAP ( $P < 0.05$ ), according to Babita, Singh B, Saiyed A, Meena R, Verma I, Vyas CK et al. D. Amar, W. H. Frishman, H. Shamoan, who administered 0.15-0.3mg/Kg of Labetalol, showed in placebo group C increase in MAP up to 52% compared to Labetalol group ( $P < 0.001$ ). In our study, Comparable outcomes were observed; Group A and B both decreased MAP ( $B > A$ ). Leslie JB, Kalayjian RW, McLoughlin TM, Plachetka JR, et al. [10] showed that MAP was significantly reduced by labetalol at different doses of 0.25, 0.5, 0.75, and 1 mg/kg. MAP was significantly lower in preeclamptic patients treated with Labetalol group 1mg/Kg IV, as demonstrated by Ramanathan J, Sibai BM, Mabie WC, Chauhan D, Ruiz AG et al. [11] Additionally, Singh SP, Quadi A, Malhotra P et al. [13] reported that Labetalol prevented the significant increase in MAP throughout the study period as compared to the placebo and esmolol groups, and Nishee R Swami R, Vaishalee K

Badhe, Vaishali V. Deshpande, Vaijayanti K. Badhe, Shodhaye et al. [16] demonstrated that Labetalol significantly reduced MAP. In our study, it was found that attenuation of MAP was more in Group B (0. 3mg/Kg IV) when compared to group A (0. 15mg/Kg IV).

**Rate Pressure Product:** In our study, The RPP response to laryngoscopy and intubation was found to be effectively attenuated by both doses of Labetalol. An intergroup comparison of the mean RPP of the two groups revealed a significant difference ( $P < 0.05$ ) at every point during the study period, including at intubation and 1, 3, 5, and 10 minutes after intubation. Our study's results were in line with those of Kumar Rajender, Gandhi Ritika, Mallick Indira et al.'s study [1], which also examined two doses of intravenous labetalol (Group A = 0. 15 mg/Kg and Group B = 0. 3 mg/Kg) to reduce hemodynamic responses to laryngoscopy and intubation in hypertensive patients. The results showed that the groups' RPPs differed statistically significantly at three, five-, and ten-minutes post intubation.

### Conclusions

In controlled hypertensive patients, both IV doses of labetalol (0. 15 mg/Kg and 0. 3 mg/Kg), administered five minutes prior to endotracheal intubation, and were successful in reducing the hemodynamic response to laryngoscopy and intubation. The hemodynamic response to laryngoscopy and endotracheal intubation was more attenuated by IV Labetalol (0. 3 mg/Kg) than by the 0. 15 mg/Kg dose.

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