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Original Research Article

Study of Attenuation of Hemodynamic Response to Endotraceal Intubation with the Use of Intravenous Labetalol

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Abstract:

Background: Endotracheal intubation, a common procedure in anesthesia and critical care, often triggers a significant hemodynamic response characterized by increased heart rate and blood pressure. This response can lead to complications, particularly in patients with cardiovascular comorbidities. Labetalol, a combined alpha and beta-adrenergic blocker, has been proposed as an effective agent to attenuate these hemodynamic changes.

Objective: To evaluate the efficacy of intravenous labetalol in attenuating the hemodynamic response to endotracheal intubation.

Material and Methods: A prospective, randomized, controlled clinical trial conducted at Mamata Medical College, Khamam, from March 2023 to March 2024. Patients scheduled for elective surgery requiring endotracheal intubation were enrolled. Inclusion criteria included adults aged 18-65 years, ASA physical status I or II. Exclusion criteria were significant cardiovascular, hepatic, or renal disease, pregnancy, and known hypersensitivity to labetalol. Participants were randomized into two groups: the labetalol group (Group L) and the placebo group. Group L received intravenous labetalol (0.30 mg/kg) five minutes before intubation. Group p received a placebo (normal saline).

Results: The study included 96 patients, with 48 in each group. Baseline demographic and clinical characteristics were comparable between the groups. Group L exhibited a significantly lower increase in HR post-intubation compared to Group C ($p < 0.05$). SBP was significantly lower in Group L at all-time points post-intubation ($p < 0.05$). Both DBP and MAP were attenuated in Group L compared to Group p.

Conclusion: Intravenous labetalol effectively attenuates the hemodynamic response to endotracheal intubation, making it a valuable agent in managing perioperative hemodynamics, particularly in patients at risk of cardiovascular complications.

Keywords: Endotracheal Intubation, Hemodynamic Response, Labetalol, Heart Rate, Blood Pressure, Anesthesia, Cardiovascular Stability.

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Introduction

Endotracheal intubation is a common and essential procedure in anesthesia and emergency medicine, aimed at securing the airway and ensuring adequate ventilation. Despite its routine nature, endotracheal intubation can provoke significant hemodynamic changes, including increases in blood pressure and heart rate. These hemodynamic responses are primarily due to the stress of intubation, which triggers sympathetic stimulation and the subsequent release of catecholamines.

In patients with pre-existing cardiovascular conditions or those undergoing major surgeries, these responses can be particularly concerning and may lead to adverse outcomes.[1] The hemodynamic response to endotracheal intubation typically involves a transient but pronounced increase in systolic blood pressure, diastolic blood pressure, and heart rate. This response is a result of the sympathetic nervous system's activation, which causes vasoconstriction and increased cardiac output. For patients with compromised cardiovascular systems or those at higher risk for perioperative cardiovascular events, these fluctuations can pose significant risks.[2]

Studies have demonstrated that the magnitude of this hemodynamic response can be influenced by various factors, including the technique of intubation, the use of analgesics and anesthetics, and the patient's underlying health condition. Therefore, effective management of these hemodynamic changes is crucial for minimizing perioperative risks and improving patient outcomes.[3]

To mitigate the hemodynamic responses associated with intubation, several pharmacological agents have been investigated. Among these, intravenous (IV) labetalol, a non-selective beta-adrenergic blocker with additional alpha-1 receptor antagonistic properties, has garnered interest. Labetalol is known for its ability to attenuate sympathetic outflow and reduce cardiovascular stress, making it a potential candidate for blunting the hemodynamic response during intubation.[4]

Labetalol works by blocking both beta-1 and beta-2 adrenergic receptors, which reduces cardiac output and myocardial oxygen demand. Additionally, its alpha-1 antagonism leads to vasodilation, further contributing to the reduction in blood pressure. The combination of these effects can potentially moderate the hemodynamic changes induced by intubation.

Rationale for the Study

The use of labetalol to attenuate the hemodynamic response to intubation represents a promising approach to enhance patient safety during the perioperative period. While labetalol has been utilized in various clinical settings for blood pressure management, its specific role in reducing the cardiovascular stress associated with intubation has not been comprehensively studied. Given the potential benefits, investigating the efficacy of intravenous labetalol in this context could provide valuable insights into its utility as part of the pre-intubation preparation. By exploring the impact of labetalol on blood pressure and heart rate during intubation, this study aims to assess whether it effectively mitigates the hemodynamic changes typically observed.

Aim and objectives

Aim: To evaluate the effectiveness of intravenous labetalol in attenuating the hemodynamic response—specifically blood pressure and heart rate changes—associated with endotracheal intubation.

Objectives:

- To assess the impact of intravenous labetalol on systolic, diastolic, and mean arterial blood pressure during and immediately after endotracheal intubation.
- To Compare the Hemodynamic Effects of Labetalol with Placebo

Material and Methods

This study is a prospective, randomized, controlled trial designed to evaluate the effectiveness of intravenous labetalol in attenuating the hemodynamic response to endotracheal intubation. The study was conducted at Mamta Medical College, Khamam, from March 2023 to March 2024.

Inclusion Criteria:

- Adult patients aged 18-65 years
- Scheduled for elective surgical procedures requiring general anesthesia and endotracheal intubation
- ASA (American Society of Anesthesiologists) physical status I or II

Exclusion Criteria:

- History of significant cardiovascular disease (e.g., congestive heart failure, severe coronary artery disease)
- Known hypersensitivity to labetalol or other beta-blockers
- Pregnant or lactating women
- Patients with contraindications to beta-blockers (e.g., asthma, bradycardia)
- Patients with a history of severe reactions to anesthesia

Randomization and Group Allocation

Eligible patients were randomly assigned to one of two groups:

Labetalol Group: Patients in this group received intravenous labetalol.

Control Group: Patients in this group received a placebo.

Randomization was achieved using a computer-generated randomization sequence. The study personnel were blinded to group assignment to reduce bias.

Intervention

Labetalol Group: Patients received intravenous labetalol (dose: 0.30 mg/kg) administered over 2 minutes prior to intubation.

Control Group: Patients received an equivalent volume of normal saline as placebo, administered in the same manner and timing as the labetalol group.

Anesthesia and Intubation Protocol: General anesthesia was induced with a standard regimen including intravenous induction agents (e.g., propofol) and muscle relaxants (e.g., succinylcholine or rocuronium).

Endotracheal intubation was performed by experienced anesthesiologists using a standardized technique.

Hemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR), were continuously monitored using standard intraoperative monitoring equipment.

Data Collection

Pre-Intubation Measurements: Baseline hemodynamic parameters were recorded immediately before the administration of the intervention (labetalol or placebo).

Intubation and Post-Intubation Measurements: Hemodynamic parameters were recorded at the following time points:

- Immediately after intubation (T0)
- 1 minute after intubation (T1)
- 2 minutes after intubation (T2)
- 4 minutes after intubation (T3)
- 6 minutes after intubation (T3)
- 8 minutes after intubation (T3)
- 10 minutes after intubation (T3)
- 15 minutes after intubation (T3)
- 20 minutes after intubation (T3)

Any adverse effects or complications related to labetalol administration were documented. Post-intubation recovery parameters, including the time to stabilization of hemodynamic parameters and need for additional interventions, were recorded.

Statistical Analysis

Primary Outcome: The primary outcome was the change in SBP, DBP, MAP, and HR from baseline to each post-intubation time point.

Secondary Outcomes: Secondary outcomes included the incidence of adverse effects, time to stabilization, and need for additional interventions.

Statistical analysis was performed using appropriate tests (e.g., independent t-tests for continuous variables, chi-square tests for categorical variables) to compare hemodynamic responses between the labetalol and control groups. A p-value of <0.05 was considered statistically significant.

Result

In the present study Both groups consist of 45 subjects each. The mean age for the Labetalol group is 31.42 years with a standard deviation of 7.5 years, while the Control group has a mean age of 30.2 years and a standard deviation of 7.16 years. The ages in both groups range from 21 to 48 years. The p-value of 0.431 indicates that the difference in mean ages between the two groups is not statistically significant. The Labetalol group has a mean weight of 58.82 kg with a standard deviation of 6.62 kg, while the Placebo group has a mean weight of 58.58 kg and a standard deviation of 6.28 kg. Weights range from 48 to 72 kg in the Labetalol group and from 48 to 70 kg in the Placebo group. The p-value of 0.8578 indicates that the difference in mean weights between the two groups is not statistically significant.

Table 1: Mean endoscopy time in both the study Group

	group	N	Mean	Std. Deviation	Std. Error Mean	P value
endoscopy time	Labetolol	45	2.820(2 min 49 sec)	0.5599	0.0835	<0.01, significant
	Placebo	45	3.251(3 min 15 sec)	0.4465	0.0666	

Table-1 displays the mean endoscopy times for the Labetalol and Placebo groups. The Labetalol group has a mean endoscopy time of 2.820 minutes (2 minutes 49 seconds) with a standard deviation of 0.5599 minutes. The Placebo group has a mean endoscopy time of 3.251 minutes (3 minutes 15 seconds) with a standard deviation of 0.4465 minutes. The p-value is less than 0.01, indicating that the difference in endoscopy times between the two groups is statistically significant, with the Labetalol group having a shorter mean endoscopy time.

Table 2: Mean Onset Time (Time taken to reach RSS>-2) in both the study Group

	group	N	Mean	Std. Deviation	Std. Error Mean	P value
Onset Time (sec)	Labetolol	45	170.89(2 min 51 sec)	23.167	3.453	0.002
	Placebo	45	188.11(3 minutes 8 sec)	27.079	4.037	

Table-2 shows the mean onset time for reaching an RSS score of >-2 in both the Labetalol and Placebo groups.

The Labetalol group has a mean onset time of 170.89 seconds (2 minutes 51 seconds) with a standard deviation of 23.167 seconds. The Placebo group has a mean onset time of 188.11 seconds (3 minutes 8 seconds) with a standard deviation of 27.079 seconds. The p-value of 0.002 indicates a statistically significant difference between the two groups, with the Labetalol group reaching the desired RSS score faster.

Table 3: Distribution of subjects by cough score in both Group

	group	N	Mean	Std. Deviation	Std. Error Mean	P value
cough score	Labetolol	45	1.98	1.196	0.178	0.002, significant
	Placebo	45	2.73	1.053	0.157	

Table-3 presents the distribution of cough scores for subjects in the Labetalol and Placebo groups. The Labetalol group has a mean cough score of 1.98 with a standard deviation of 1.196, while the Placebo group has a mean score of 2.73 with a standard deviation of 1.053. The p-value of 0.002 indicates that the difference in mean cough scores between the two groups is statistically significant, with the Labetalol group experiencing a lower average cough score.

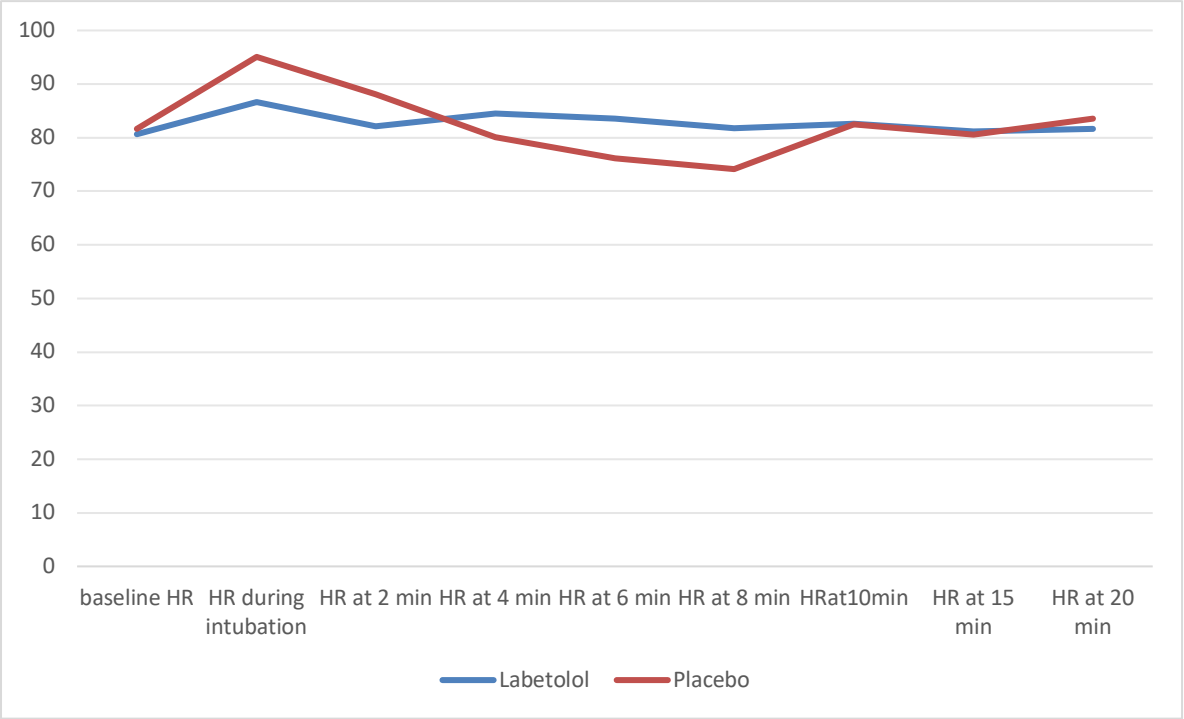

Figure 1: Line graph of subjects by Mean HR and group

Table 4: Distribution of subjects by Mean MAP in both Groups

	Group	N	Mean	Std. Deviation	P value
baseline MAP	Labetolol	45	89.62	5.399	0.93
	Placebo	45	89.53	4.257	
MAP during intubation	Labetolol	45	95.71	4.930	<0.001
	Placebo	45	103.53	4.257	
MAP at 2 min	Labetolol	45	89.47	4.516	0.41
	Placebo	45	88.76	3.675	
MAP at 4 min	Labetolol	45	96.09	4.161	0.31
	Placebo	45	95.27	3.570	
MAP at 6 min	Labetolol	45	90.00	3.778	0.76
	Placebo	45	89.76	3.850	
MAP at 8 min	Labetolol	45	89.7333	3.78033	0.38
	Placebo	45	89.0222	3.91088	
MAP at 10 min	Labetolol	45	89.49	3.565	0.43
	Placebo	45	90.11	4.013	
MAP at 15 min	Labetolol	45	88.84	4.067	0.49
	Placebo	45	89.47	4.615	
MAP at 20 min	Labetolol	45	89.00	3.405	0.41
	Placebo	45	89.58	3.173	

Table-4 shows the distribution of mean arterial pressure (MAP) at various time points for subjects in the Labetalol and Placebo groups. Baseline MAP values are similar between the groups, with Labetalol at 89.62 mmHg and Placebo at 89.53 mmHg. During intubation, the Labetalol group has a significantly lower MAP (95.71 mmHg) compared to the Placebo group (103.53 mmHg, $p<0.001$). At subsequent time points (2, 4, 6, 8, 10, 15, and 20 minutes), there are no significant differences between the groups. Overall, Labetalol is associated with a lower MAP during intubation but similar MAP values at later times compared to Placebo.

Table 5: Distribution of study subjects as per post intubation score for tolerance to intubation

			Group		Total
			Labetolol	Placebo	
post intubation score	1	Count	30	11	41
		% within group	66.7%	24.4%	45.6%
	2	Count	4	18	22
		% within group	8.9%	40.0%	24.4%
	3	Count	11	16	27
		% within group	24.4%	35.6%	30.0%
Total		Count	45	45	90
		% within group	100.0%	100.0%	100.0%
Chi-sq value- 18.64, p value- <0.001, significant					

Table-5 presents the distribution of post-intubation scores for tolerance to intubation between the Labetalol and Placebo groups. In the Labetalol group, 66.7% of subjects scored 1 (indicating good tolerance), compared to 24.4% in the Placebo group. For scores of 2, 8.9% of the Labetalol group and 40.0% of the Placebo group were observed. Scores of 3 were seen in 24.4% of the Labetalol group and 35.6% of the Placebo group. The chi-square value of 18.64 with a p-value of <0.001 indicates a statistically significant difference in post-intubation tolerance between the groups, with the Labetalol group showing better tolerance overall.

Table 6: Distribution of study subjects as per Rescue given

			Group		Total
			Labetolol	Placebo	
Rescue	No	Count	42	27	69
		% within group	93.3%	60.0%	76.7%
	yes	Count	3	18	21
		% within group	6.7%	40.0%	23.3%
Total		Count	45	45	90
		% within group	100.0%	100.0%	100.0%
Chi-sq value- 13.97, p value- <0.01, significant					

Table-6 shows the distribution of subjects based on whether they received rescue medication. In the Labetalol group, 93.3% did not require rescue medication, while 6.7% did. In contrast, 60.0% of the Placebo group did not need rescue medication, and 40.0% did. The chi-square value of 13.97 with a p-value of <0.01 indicates a statistically significant difference between the groups. This suggests that the Labetalol group required less rescue medication compared to the Placebo group.

Table 7: Adverse effect in both the study group

			Group		Total
			Labetolol	Placebo	
side effects	erythema	Count	0	1	1
		% within group	0.0%	2.2%	1.1%
	flushing	Count	1	1	2
		% within group	2.2%	2.2%	2.2%
	o2 desaturation	Count	2	8	10
		% within group	4.4%	17.8%	11.1%
	no	Count	42	35	77
		% within group	93.3%	77.8%	85.6%
Total		Count	45	45	90
		% within group	100.0%	100.0%	100.0%
Chi-sq value- 0.23, p value- 0.15, non-significant					

Table-7 presents the distribution of adverse effects between the Labetalol and Placebo groups. Erythema was observed in 2.2% of the Placebo group but none in the Labetalol group. Flushing occurred in 2.2% of both groups. Oxygen desaturation was seen in 4.4% of the Labetalol group and 17.8% of the Placebo group. The majority of subjects in both groups reported no adverse effects (93.3% in Labetalol and 77.8% in Placebo). The chi-square value of 0.23 and p-value of 0.15 indicate that there is no statistically

significant difference in the occurrence of adverse effects between the two groups.

Discussion

Hypertensive patients are particularly susceptible to significant cardiovascular responses during laryngoscopy and tracheal intubation, potentially leading to severe complications such as pulmonary edema, cardiac failure, and cerebrovascular hemorrhage, as noted by Fox et al. Although transient increases in arterial pressure (AP) and heart rate (HR) might not be concerning in healthy individuals, they pose substantial risks for those with hypertension, myocardial insufficiency, or cerebrovascular disease. Consequently, managing these hemodynamic changes during intubation is crucial for hypertensive patients. Hemodynamic responses typically peak within one minute of tracheal intubation, emphasizing the importance of timing in administering drugs designed to attenuate these responses. Labetalol, with an onset of action of 2–3 minutes and a peak effect at 5–15 minutes, is well-suited for this purpose. Our study monitored hemodynamic responses for 20 minutes post-intubation, the average duration these responses are believed to last.

The adverse cardiovascular effects and catecholamine release during laryngoscopy and intubation occur in two distinct phases. Shribman et al. [5] demonstrated that laryngoscopy alone, even without intubation, increases systolic and diastolic blood pressure (SBP and DBP) due to norepinephrine release, without significantly affecting HR. The second phase, triggered by tracheal intubation, induces a more pronounced cardiovascular response, increasing SBP and DBP by 36–40% and HR by over 20%, primarily due to epinephrine release.

In the present study, intravenous labetalol effectively attenuated the increase in mean arterial pressure (MAP) following tracheal intubation. Although tachycardia poses a greater stress on the heart than increased BP by raising myocardial oxygen demand, reducing diastolic filling time, and impairing coronary circulation, labetalol's ability to control HR and MAP is crucial. Our findings showed insignificant increases in HR and MAP at intubation in the labetalol group compared to the placebo group, where HR and MAP increased by 30% and 23%, respectively. These results align with Amar et al [6] who reported significantly lower increases in HR and MAP in patients receiving labetalol during anesthesia induction and maintenance. Similarly, Kim et al. [7] found that a single preoperative dose of labetalol significantly reduced HR up to 10 minutes post-intubation.

However, Roelofse et al [8]. noted that labetalol given as an IV bolus 1 minute before laryngoscopy was ineffective in attenuating HR, likely due to the timing of administration relative to labetalol's peak effect. This discrepancy underscores the importance of proper timing when administering labetalol to optimize its hemodynamic benefits. In our study, the main side effect observed with labetalol was bradycardia in the group receiving 0.3 mg/kg, affecting seven patients (28%) who responded well to atropine without recurrent episodes. Two patients in the placebo group experienced transient premature ventricular contractions post-intubation, which did not require treatment. Overall, labetalol was well-tolerated, with no serious complications, demonstrating its efficacy and safety in managing hemodynamic responses during laryngoscopy and tracheal intubation.

Conclusion

To conclude, Labetalol in dose of 0.3 mg/kg iv is effective in reducing the hemodynamic responses to direct laryngoscopy and tracheal intubation. However bradycardia is more common in patients who are receiving labetalol in dose of 0.3 mg/kg. Further studies are needed to elucidate the comparative effects of both doses of labetalol in large number of patients.

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