Attenuation of Hemodynamic Response to Tracheal Extubation: A Comparative Study between Esmolol and Labetalol

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Abstract

Background and Aims: Cardiovascular stress response to extubation can result in elevated heart rate (HR) and mean arterial blood pressures which can be detrimental in high-risk patients. Settings and Design: The objective of this study is to compare the esmolol and labetalol efficacy in attenuating hemodynamic response to tracheal extubation. Materials and Methods: Sixty patients scheduled for elective surgical procedures were selected randomly and divided into two groups of thirty each. Group I - esmolol 1.5 mg/kg and Group II - labetalol 0.25 mg/kg were administered 2 min before extubation after following a standard perioperative anesthetic management. Hemodynamic parameters recorded include HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) at baseline, reversal, study drug, 1 min after study drug, extubation, and at 1, 2, 3, 4, 5, and 15 min postextubation. Statistical Analysis: Student’s t-test and analysis of variance have been used to find the significance of study parameters between groups of patients. P < 0.05 was considered statistically significant. Results: Both esmolol and labetalol attenuated extubation response throughout the extubation and postextubation period. At extubation and immediately postextubation at 1st and 2nd min, there was statistical significance (P < 0.05) in SBP, DBP, and MAP which showed esmolol was better than labetalol. Whereas labetalol was more efficient in controlling HR at 5th and 15th min postextubation having statistical significance. Conclusions: Both esmolol and labetalol attenuated hemodynamic response. Esmolol was more efficient than labetalol at extubation and immediately postextubation. If patient has tachycardia at extubation, labetalol is preferred. If patient has raised blood pressure, then esmolol is a good option in blunting the response.

Keywords: Attenuation, esmolol, extubation, labetalol, stress response

INTRODUCTION

Endotracheal extubation is one of the frequently performed procedures in the practice of anesthesiology. Complications after extubation are more prominent than complications occurring during the intubation and induction of anesthesia. Hypertension and tachycardia are well-documented events during extubation. These hemodynamic responses reflect sympathoadrenal reflex stimulation (epipharyngeal and laryngopharyngeal stimulation) with a concomitant increase in plasma level of catecholamine and activation of alpha and beta adrenergic receptors. This increase in blood pressure and heart rate (HR) is usually transitory, variable, and unpredictable. The development of postoperative hypertension warrants immediate assessment and treatment to reduce the risks of myocardial infarction, arrhythmias, congestive heart failure, stroke, bleeding, and other end-organ damages.

Tracheal extubation is associated with a 10%–30% increase in arterial pressure and HR lasting 5–15 min. Patient with coronary artery disease experiencing 40%–50% decrease in ejection fraction.

The response may be attenuated by pharmacological interventions including esmolol (1.5 mg/kg intravenous [i.v.] 2–5 min before extubation), glyceryl trinitrate, magnesium, propofol infusion, remifentanil/alfentanil infusion, i.v. lidocaine (1.5 mg/kg over 2 min), topical lidocaine 10%, and perioperative oral nimodipine with labetalol.

Since there are very few studies showing comparison of esmolol with 1.5 mg/kg and labetalol 0.25 mg/kg, this study was conceptualized to find the efficacy of each of these drugs in attenuating hemodynamic stress response postextubation.
**M A T E R I A L S  a n d M E T H O D S**

After obtaining clearance from the Institutional Ethical Committee and informed written consent, a prospective randomized double-blinded study was conducted on sixty patients scheduled for various elective surgical procedures belonging to patients physical status American Society of Anesthesiologists (ASA) Classes I and II were included in the study. The study population was divided into two groups of thirty patients each.

- **Group I** - the patients who received 1.5 mg/kg esmolol i.v. 2 min before extubation (*n* = 30)
- **Group II** - the patients who received 0.25 mg/kg labetalol i.v. 2 min before extubation (*n* = 30)

Patients who refused, posted for emergency surgery, with physical status ASA class III or more, having any significant systemic disorder, or comorbid diseases were excluded from the study.

Double-blinded randomization was accomplished by means of a computer-generated randomization list. The drug was given by one anesthesiologist whereas the observations were made by the second one who did not know what drugs were being used.

A routine preanesthetic examination was conducted assessing the general condition of the patients on the evening before surgery. From all patients, informed consent was obtained. All patients were kept nil per oral for 8 h. On arrival in the operating room, i.v. line was established, and fluid dextrose with normal saline was started. Patients were connected to multichannel monitor which records HR, noninvasive blood pressure, end-tidal carbon dioxide, and oxygen saturation.

The baseline blood pressure and HR were recorded from the same noninvasive monitor, and cardiac rate and rhythm were also monitored from a continuous display from lead II. After premedication, patients were induced with injection thiopentone 5 mg/kg and endotracheal intubation was facilitated with injection succinylcholine 1.5 mg/kg. After confirming bilateral equal air entry, the endotracheal tube was secured. Anesthesia was maintained using 5 ml/min nitrous oxide and 3 ml/min oxygen, isoflurane 0.2%–1% concentration, and injection vecuronium 0.1 mg/kg.

At the end of the surgery, HR, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded. These served as baseline values. Then, the patients received injection neostigmine 0.05 mg/kg i.v. and glycopyrrolate 0.01 mg/kg i.v.

Then, after 3 min of giving reversal and 2 min before extubation drugs were given:

- **Group I** received injection esmolol 1.5 mg/kg i.v.
- **Group II** received injection labetalol 0.25 mg/kg i.v.

**Monitoring**

The following cardiovascular parameters were recorded in all the patients:

- HR in beats per min (bpm), systolic blood pressure (SBP) in mmHg, DBP in mmHg, and mean arterial pressure (MAP) in mmHg.

The above cardiovascular parameters were noted as below.

1. At the end of surgery served as baseline (BASAL)
2. Then after giving reversal (REV)
3. At the end of administration of study drug (DRUG)
4. 1 min after administration of study drug (DRUG1)
5. At the time of extubation (EXT)
6. After extubation at 1, 2, 3, 4, 5, and 15 min (E1, E2, E3, E4, E5, and E15, respectively).

**Statistical analysis**

Data were entered into MS Excel 2016 and analysis was done using SPSS version 20.0 (IBM SPSS Statistics for windows, Armonk, NY: IBM Corp, NY, USA) and data were expressed in percentages. To compare quantitative variables, Student’s t-test was used. The changes in quantitative findings throughout the study in groups were evaluated using repeated measure of analysis of variance (ANOVA). A *P* < 0.05 was considered statistically significant.

**RESULTS**

The purpose of this study was to compare efficacy between esmolol 1.5 mg/kg and labetalol 0.25 mg/kg given intravenously have on hemodynamic response to extubation.

This prospective randomized to compare efficacy between esmolol and labetalol study was done with sixty patients divided into two groups consisting of thirty patients each (*n* = 30).

- **Group I** - Esmolol group (1.5 mg/kg)
- **Group II** - Labetalol group (0.25 mg/kg).

No statistical significance was found in demographic profile of age, sex, and weight, thereby making the two groups similar and comparable.

In esmolol group, the basal HR was 97.8 bpm. After reversal, HR increased to 102.7 bpm. During drug administration and subsequently, HR decreased as shown in Table 1. At 15th min postextubation, HR was 84.6 bpm which was less than basal.

In labetalol group, the basal HR was 97.5 bpm. During reversal, HR increased to 103.1 bpm. During drug injection and subsequently, HR decreased as shown in Table 1. At 15th min postextubation, HR was 69.9 bpm which was very much less than basal.

Statistical evaluation between the esmolol and labetalol group showed that there was no significance between them at basal, extubation, and postextubation up to 4th min (*P* > 0.05). At 5th (*P* < 0.034) and 15th min (*P* < 0.000) postextubation, statistical significance noted, especially at 15th min. Tables 1 and 2 show both attenuated hemodynamic response, which was proved by ANOVA results, *P* < 0.000. Both behaved differently during the course (ANOVA, *P* < 0.001) which is also evident [Table 2].
at 5th and 15th min. The HR decrease was more in labetalol group when compared to esmolol group, but it was statistically insignificant except at E5 and E15.

In esmolol group, the basal SBP was 130.96 mmHg. During reversal, systolic blood pressure increased to 135.8 mmHg. During drug administration and subsequently, systolic pressure decreased [Table 3]. At 15th min post extubation, pressure was 119.8 mmHg which was less than basal.

In labetalol group, the SBP was 125.5 mmHg. During reversal, SBP increased to 140.7 mmHg. During drug injection and subsequently, SBP decreased [Table 3]. At 15 min postextubation, SBP was 113.6 mmHg which was again less than basal.

Statistical evaluation between the groups esmolol and labetalol showed no significance between them at basal, extubation, and up to 1st min postextubation (P > 0.05). Significance was observed at 2nd (P < 0.034), 3rd (P < 0.023), and 15th min (P < 0.024) postextubation, with esmolol performing better than labetalol at 2nd and 3rd min and labetalol being better esmolol at 15th min. From Table 4, it is evident that both attenuated hemodynamic response, which is again proved by ANOVA results, P < 0.000. Moreover, both behaved differently during the course (ANOVA P < 0.000) which can be seen in graphs and table at 2nd, 3rd, and 15th min. Pressure decrease in esmolol is more than labetalol but statistically insignificant except at E2 and E3.

In esmolol group, the basal DBP was 86.9 mmHg. During reversal, diastolic pressure increased to 97.8 mmHg. During drug injection and subsequently, diastolic decreased as seen in Table 5. At 15 min postextubation, pressure was 74.1 mmHg which was less than basal.

In labetalol group, the DBP was 83.7 mmHg. During reversal, DBP increased to 94.36 mmHg. During drug injection and subsequently, DBP decreased as shown in Table 5. At 15 min postextubation, DBP was 72.9 mmHg which was again less than basal.

Statistical evaluation between the groups showed that there was no significance between them at basal and extubation (P > 0.05). At 1st (P = 0.024), 2nd (P < 0.002), and 3rd min (P < 0.005), postextubation significance noted. Table 6 summarizes that both attenuates hemodynamic response, which was proven by ANOVA results, P < 0.000. Moreover, both behaved differently during the course (ANOVA P < 0.000) also seen in graph and table at 2nd, 3rd, and 15th min. Pressure decrease in esmolol is more than labetalol but statistically insignificant except at E1, E2, and E3.

In esmolol group, the basal mean arterial pressure was 98.6 mmHg. During reversal, mean arterial pressure increased to 110.4 mmHg. During drug injection and subsequently, mean arterial decreased [Table 7]. At 15 min postextubation, pressure was 89.3 mmHg which was less than basal.

In labetalol group, the mean arterial blood pressure was 99.56 mmHg. During reversal, mean arterial blood pressure increased to 107.07 mmHg. During drug injection and subsequently, mean arterial blood pressure decreased [Table 7]. At 15 min postextubation, mean arterial blood pressure was 84.47 mmHg which was again less than basal.

Statistical evaluation between the groups showed that there was no significance between them at basal and

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**Table 1: Change in heart rates between esmolol and labetalol**

| Source | Mean±SD | Mean | P |
|--------|---------|------|---|
| **Esmolol** | **Labetalol** | **Esmolol** | **Labetalol** | **Esmolol** | **Labetalol** | **Esmolol** | **Labetalol** | **Esmolol** | **Labetalol** |
| BASAL | 97.86±14.6 | 97.50±14.5 | 0.3667 | 0.923 |
| REV | 102.73±16.4 | 103.1±15.6 | 0.930 |
| DRUG | 99.86±16.9 | 95.5±16.3 | 4.3000 | 0.322 |
| DRUG 1 | 94.7±19.0 | 92.3±14.7 | 2.3667 | 0.592 |
| EXT | 90.83±15.8 | 90.66±14.3 | 0.1667 | 0.966 |
| E1 | 88.86±12.8 | 87.46±14.2 | 1.0000 | 0.690 |
| E2 | 84.96±13.2 | 85.13±13.8 | 0.1667 | 0.962 |
| E3 | 83.73±12.6 | 81.83±13.6 | 1.9000 | 0.577 |
| E4 | 81.96±11.2 | 78.43±13.4 | 3.5333 | 0.274 |
| E5 | 80.86±10.7 | 74.96±10.3 | 5.9000 | 0.034 |
| E15 | 84.56±10.7 | 69.96±8.6 | 14.6000 | <0.001 |

SD=Standard deviation

**Table 2: Results of repeated measure analysis of variance - heart rate changes between esmolol and labetalol**

| Source | Type III sum of squares | df | Mean square | F | Significance |
|--------|-------------------------|----|-------------|---|-------------|
| Change | 45,546.545 | 10 | 4554.655 | 52.307 | 0.000 |
| Change × GRP | 2780.236 | 10 | 278.024 | 3.193 | 0.001 |

**Table 3: Change in systolic blood pressure between esmolol and labetalol**

| Source | Mean±SD | Mean | P |
|--------|---------|------|---|
| **Esmolol** | **Labetalol** | **Esmolol** | **Labetalol** |
| BASAL | 130.96±13.5 | 125.5±6.9 | 5.4667 | 0.054 |
| REV | 135.86±19.0 | 140.7±8.4 | 4.8333 | 0.209 |
| DRUG | 130.46±10.9 | 135.46±6.8 | 5.0000 | 0.037 |
| DRUG 1 | 125.96±8.3 | 127.80±7.6 | 1.8333 | 0.375 |
| EXT | 125.10±8.2 | 124.53±7.5 | 0.5667 | 0.781 |
| E1 | 118.73±7.6 | 121.73±8.7 | 3.0000 | 0.160 |
| E2 | 114.40±8.7 | 119.53±8.4 | 5.1333 | 0.024 |
| E3 | 112.76±8.9 | 118.36±9.6 | 5.6000 | 0.023 |
| E4 | 113.23±7.8 | 116.58±8.9 | 3.2667 | 0.135 |
| E5 | 113.8±7.9 | 114.6±8.5 | 0.8333 | 0.694 |
| E15 | 119.8±10.5 | 113.6±10.1 | 6.2000 | 0.024 |

SD=Standard deviation

**Table 4: Repeated measure analysis of variance study of systolic blood pressure**

| Source | df | Mean square | F | Significance |
|--------|----|-------------|---|-------------|
| Change | 10 | 3961.073 | 62.174 | 0.000 |
| Change × GRP | 10 | 257.012 | 4.034 | 0.000 |

subsequently, mean arterial blood pressure decreased [Table 7]. At 15 min postextubation, mean arterial blood pressure was 84.47 mmHg which was again less than basal.

Statistical evaluation between the groups showed that there was no significance between them at basal and
extubation \((P > 0.05)\). At 1\(^{st}\) \((P < 0.022)\), 2\(^{nd}\) \((P < 0.001)\), and 3\(^{rd}\) \((P < 0.001)\) postextubation, there was significance. Table 8 showed that both attenuated hemodynamic response which was proven by ANOVA results, \(P < 0.000\). Moreover, both behaved differently during the course (ANOVA \(P < 0.000\)) also evident in Table 8 at E1, E2, and E3. Pressure decrease in esmolol is more than labetalol but statistically insignificant except at E1, E2, and E3. In esmolol group, no complications were observed in labetalol group. Two incidence of bradycardia \(< 60\) bpm after 15\(^{th}\) min postextubation in recovery room treated with atropine and one episode of hypotension SBP < 90 mmHg also after 15\(^{th}\) min treated with fluids and 6 mg of mephentermine i.v. Complications observed were statistically insignificant \(P > 0.05\).

### DISCUSSION

Emergence from general anesthesia and especially postextubation phase are the stages associated with cardiovascular hyperdynamic status leading to increase in oxygen consumption and catecholamine release. This phase lasting 5–15 min could frequently be accompanied by tachycardia and hypertension. Most patients, however, endure this temporary situation appropriately. On the other hand, patients having preoperative hypertension and cardiovascular and cerebrovascular diseases and patients with increased intracranial pressure could be affected by severe cardiac and/or cerebral complications. Therefore, it is of great importance to prevent postoperative and postintubation sympathetic excitations in high-risk patients as maintaining stability in the dynamic status reduces mortality and morbidity rates in these patients. Most of the clinicians use adjuncts to attenuate the sympathetic response associated with laryngoscopy and intubation in high-risk patients. Beta blockers have been compared with fentanyl, nitroprusside, nitroglycerin, calcium channel blockers, etc. However, studies comparing esmolol (cardioselective beta blocker) and labetalol (nonselective adrenergic blocker) are lacking.

In this study, we aimed to compare pure beta blocker esmolol with alpha and beta blocker labetalol regarding their use during extubation to obtund hemodynamic response and safe postanesthetic care.\(^7\) This study showed that both esmolol 1.5 mg/kg and labetalol 0.25 mg/kg administered before extubation decreased hemodynamic response to extubation. Esmolol was more effective than labetalol in decreasing SBP, DBP, and MAP response which was statistically significant at extubation and 1\(^{st}\) and 2\(^{nd}\) min postextubation. Labetalol was more effective in controlling the HR which was statistically insignificant till 4\(^{th}\) min postextubation. At 5\(^{th}\) and 5\(^{th}\) min, HR decrease was significant in labetalol group.

Esmolol 1.0 mg/kg, 1.5 mg/kg, and 2.0 mg/kg were used in patients before extubation in a study by Dyson et al.,\(^8\) which showed that 1.5 mg/kg esmolol was reported as the optimal dose for the prevention of hemodynamic response due to tracheal extubation. In Alkaya et al.‘s\(^9\) study, no complications were noted even though esmolol was used at 2 mg/kg, probably because infusion was started 5 min before extubation as compared to 2–5 min before extubation in Dyson et al.‘s\(^9\) study. In our study, we used esmolol 1.5 mg/kg slow bolus

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**Table 5:** Change in diastolic blood pressure between esmolol and labetalol

| Source | Mean±SD Esmolol | Mean±SD Labetalol | Mean | \(P\) |
|--------|-----------------|------------------|------|------|
| BASAL  | 86.9667±9.01    | 83.7000±5.8      | 3.2667 | 0.112 |
| REV    | 97.8000±11.7    | 94.2667±6.32     | 3.5333 | 0.113 |
| DRUG   | 89.0333±14.2    | 88.2667±8.2      | 0.7667 | 0.799 |
| DRUG 1 | 86.3333±10.13   | 83.3667±8.5      | 2.9667 | 0.226 |
| EXT    | 80.1333±12.21   | 80.4333±7.3      | −0.3000 | 0.909 |
| E1     | 71.6333±14.9    | 75.3333±6.2      | −6.9000 | 0.024 |
| E2     | 69.9333±10.04   | 77.3667±7.4      | −7.4333 | 0.002 |
| E3     | 69.3000±10.26   | 75.7333±6.6      | −6.4333 | 0.005 |
| E4     | 70.6667±11.8    | 73.4000±4.9      | −2.7333 | 0.245 |
| E5     | 71.9667±11.5    | 72.3000±4.0      | −0.3333 | 0.881 |
| E15    | 74.1667±11.7    | 72.9000±5.8      | 1.2667  | 0.597 |

\(SD=\)Standard deviation

**Table 6:** Repeated measure analysis of variance study of diastolic blood pressure

| Source          | df  | Mean square | \(F\) | Significance |
|-----------------|-----|-------------|------|-------------|
| Change          | 10  | 3538.127    | 105.382 | 0.000       |
| Change × GRP    | 10  | 384.531     | 11.453 | 0.000       |

**Table 7:** Change in mean arterial pressure between esmolol and labetalol

| Source | Mean±SD Esmolol | Mean±SD Labetalol | Mean | \(P\) |
|--------|-----------------|------------------|------|------|
| BASAL  | 98.6333±7.3     | 95.6333±4.7      | 3.0000 | 0.100 |
| REV    | 110.4889±12.1   | 107.077±6.1      | 3.4111 | 0.175 |
| DRUG   | 102.8444±12.1   | 104.0007±7.01    | −1.1556 | 0.653 |
| DRUG 1 | 99.5444±8.5     | 98.1778±6.6      | 1.3667 | 0.493 |
| EXT    | 95.122±10       | 95.1333±6.7      | −0.0111 | 0.996 |
| E1     | 87.3333±11.2    | 92.9333±6.4      | −5.6000 | 0.022 |
| E2     | 84.7556±7.7     | 91.4222±6.9      | −6.6667 | 0.001 |
| E3     | 83.7889±7.5     | 89.9444±6.6      | −6.1556 | 0.001 |
| E4     | 84.8556±8.2     | 87.7667±4.9      | −2.9111 | 0.101 |
| E5     | 85.9000±8.2     | 86.3778±4.07     | −0.4778 | 0.776 |
| E15    | 89.3889±9.0     | 86.4778±6.6      | 2.9111  | 0.162 |

\(SD=\)Standard deviation

**Table 8:** Repeated measure analysis of variance study of mean arterial pressure

| Source          | df  | Mean square | \(F\) | Significance |
|-----------------|-----|-------------|------|-------------|
| Change          | 10  | 3665.688    | 142.284 | 0.000       |
| Change × GRP    | 10  | 260.801     | 10.123 | 0.000       |
two min before extubation which was effective in blunting hemodynamic response with no side effects.

Tempe et al.\cite{10} has studied and concluded that esmolol is effective in blunting hemodynamic response with no complications. They have used different doses as infusion throughout the extubation period. In the present study, though we used 1.5 mg/kg esmolol which is more than the doses used, we did not observe any side effects. Reason can be, as we used bolus dose compared to infusion used by authors.

Roelofse et al.,\cite{11} Leslie et al.,\cite{12} and Chung et al.,\cite{13} studies showed that labetalol was effective in obtunding intubation response. The researchers concluded that, when small doses of labetalol were given, the optimal time the medication is administered should be closer to time of laryngeal stimulation. These researchers felt that this optimal time was between 3 and 5 min before the stimulation. In our study, we used labetalol 0.25 mg/kg, 2 min before extubation which fell short by 1 min for optimal time as told by the researcher. Although we administered the drug 2 min before extubation, we were able to observe the desired effect of blunting hemodynamic response, more toward the late postextubation period. The effect was less compared to esmolol.

Tempe et al.,\cite{14} did comparative study between esmolol (loading dose of 500 μg/kg followed by an infusion of 50–300 μg/kg/min, mean = 160 μg/kg/min) and labetalol (incremental doses of 0.25, 0.5, 0.75, and 1.00 mg/kg, mean = 0.98 mg/kg/min) in treating increase in blood pressure during emergence and recovery from anesthesia after intracranial surgery and found both labetalol and esmolol were equally effective in controlling SBP on emergence and in the recovery room. However, decreasing in HR was significantly more frequent in the immediate postoperative period in patients given labetalol as found in our study. We also observed that both labetalol and esmolol were effective in controlling hemodynamic response. Moreover, in labetalol group, a decrease in HR was significantly more frequent in immediate postoperative period.

Singh et al.,\cite{15} compared esmolol 0.5 mg/kg and labetalol 0.25 mg/kg, 2 min and 5 min before intubation. He observed that labetalol was more effective in controlling HR and SBP than esmolol which was statistically significant $P < 0.05$. Labetalol also controlled diastolic and mean arterial pressure better than esmolol but statistically insignificant except 1 min post intubation. The author also commented about bradycardia being only the side effect in his study not hypotension. In the current study, we observed esmolol being more effective in controlling hemodynamic response except for the HR than labetalol. In Singh et al.’s study, the performance of esmolol was less than labetalol probably because of low-dose esmolol 0.5 mg/kg compared to ours where we used 1.5 mg/kg. Furthermore, in our study, hypotension and bradycardia were seen at 15th min postextubation unlike in author’s study where bradycardia was the only side effect. This is probably due to timing of administration 5 min before intubation as compared to 2 min before extubation.

**Conclusions**

An increase in hemodynamics after extubation appears to be a transitory phenomenon; hence, short-acting cardioselective β blocker esmolol is adequate to obtund such response. Labetalol α, β, and β blocker is also effective in controlling such response though less compared to esmolol except for HR, the effect is prolonged >15 min. Hence, chance of complications which necessitates thorough vigilance extending in the recovery room also.

Inference from our study is that both esmolol and labetalol can be used to obtund hemodynamic response. At the time of extubation if patient has tachycardia, labetalol is preferred and if patient has raised blood pressure, then esmolol is a better choice.

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**Conflicts of interest**

There are no conflicts of interest.

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