European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 02, 2022

# A study on heart rate and side effects between esmolol and labetalol during tracheal extubation

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## Abstract

Electrophysiological studies revealed that Esmolol causes an increase in sinus cycle length and sinus node recovery time. Electrocardiographic parameters like 'PR' 'QRS' and 'QT' intervals were not prolonged. In contrast to other beta blockers, electrophysiological values return to baseline values within a period of 30 minutes after withdrawing the drug. When infused at a dose of 200 micrograms/kg/minute, Esmolol can significantly reduce the namely, resting heart rate, Systolic blood pressure, rate pressure product, cardiac index. Esmolol can also attenuate isoprenaline induced tachycardia. 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. In esmolol group the basal heart rate was 97.8bpm. During reversal heart rate increased to 102.7bpm. During drug injection and subsequently heart rate decreased as shown in table. At 15min post extubation heart rate was 84.6bpm which was less than basal.
In labetalol group the basal heart rate was 97.5bpm. During reversal heart rate increased to 103.1bpm. During drug injection and subsequently heart rate decreased as shown in table. At 15min post extubation heart rate was 69.9bpm which was much less than basal.

**Keywords:** Heart rate, esmolol, labetalol

## Introduction

Esmolol Hydrochloride is a beta-selective (cardio selective) adrenergic receptor blocking agent with a very short duration of action (ultra short acting). Elimination half- life is approximately 9 minutes. Esmolol is available for intravenous administration only. The product is available in two strengths, namely, 10 mg/ml vial for bolus injection and 250 mg/ml ampoule for infusion. The solution is buffered to pH 4.5-5.5. Molecular weight is 331.8. Esmolol HCL is a white to off white crystalline powder. It is a relatively hydrophilic compound, which is very soluble in water and freely soluble in alcohol. Its partition coefficient (Octanol/water) at pH 7.0 is 0.42 compared to 17.0 for propranolol Esmolol Hcl is a beta-selective (cardio selective) adrenergic receptor-blocking agent with rapid onset, short duration of action and no significant intrinsic sympathomimetic or membrane stabilizing

ISSN 2515-8260 Volume 09, Issue 02, 2022

activity at therapeutic dosage. Esmolol inhibits the beta receptors located chiefly in cardiac muscle, but this preferential effect is not absolute and at higher doses it begins to inhibit beta-2 receptors located chiefly in the bronchial and vascular musculature Esmolol is a beta adrenergic receptor blocking drug. It is a relatively cardioselective drug (40: I for beta-I to beta-2 receptors). It has a clinical advantage of shortest duration of action among the available beta blockers. Thus, the effects of Esmolol may be rapidly discontinued in clinical situations when necessary [1, 2].

Electrophysiological studies revealed that Esmolol causes an increase in sinus cycle length and sinus node recovery time. Electrocardiographic parameters like 'PR' 'QRS' and 'QT' intervals were not prolonged. In contrast to other beta blockers, electrophysiological values return to baseline values within a period of 30 minutes after withdrawing the drug. When infused at a dose of 200 micrograms/kg/minute, Esmolol can significantly reduce the namely, resting heart rate, Systolic blood pressure, rate pressure product, cardiac index. Esmolol can also attenuate isoprenaline induced tachycardia.

Labetalol is an adrenergic receptor blocking agent that has both selective alpha1-and non-selective beta-adrenergic receptor blocking actions in a single substance [3].

The pharmacological effects of labetalol have become clearer since the four isomers were separated and tested individually. The R,R isomer is about four times more potent as a alpha receptor antagonist than is racemic labetalol, and it accounts for much of the alpha blockade produced by the mixture of isomers, although it no longer is in development as a separate drug (dilevalol). As an $alpha_1$ antagonist, this isomer is less than 20% as potent as the racemic mixture. The RS isomer is almost devoid of both alpha and beta blocking effects. The SR isomer has almost no alpha blocking activity, yet is about five times more potent as an $alpha_1$ blocker than is racemic labetalol. The SS isomer is devoid of alpha blocking activity and has a potency similar to that of racemic labetalol as an $alpha_1$ receptor antagonist. The RR isomer has some intrinsic sympathomimetic activity at $beta_2$ adrenergic receptors; this may contribute to vasodilation. Labetalol also may have some direct vasodilation capacity [4]. The actions of labetalol on both alpha [1]. And beta receptors contribute to the fall in blood pressure observed in patients with hypertension. Alpha [1]. Receptor blockade leads to relaxation of arterial smooth muscle and vasodilation, particularly in the upright position. The alpha [1]. blockade also contributes to a fall in blood pressure, in part by blocking reflex sympathetic stimulation of the heart. In addition, the intrinsic sympathomimetic activity of labetalol at beta [2]. receptors may contribute to vasodilation [5].

Labetalol combines both selective, competitive alpha1-adrenergic blocking and nonselective, competitive beta-adrenergic blocking activity in a single substance. In man, the ratios of alpha- to beta-blockade have been estimated to be approximately 1:3 and 1:7 following oral and intravenous administration, respectively. Beta2-agonist activity has been demonstrated in animals with minimal beta1-agonist (ISA) activity detected. In animals, at doses greater than those required for alpha-or beta-adrenergic blockade, a membrane-stabilizing effect has been demonstrated [6].

## Methodology

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).

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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.

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## Results

**Table 1:** Age distribution

| Age | Esmolol | Labetalol | Total |
|---|---|---|---|
| <20 | 4(13.3%) | 4(13.3%) | 8(13.3%) |
| 21-30 | 7(23.3%) | 10(33.3%) | 17(28.3%) |
| 31-40 | 11(36.7%) | 5(16.7%) | 16(26.7%) |
| 41-50 | 5(16.7%) | 8(26.7%) | 13(21.7%) |
| >50 | 3(10.0%) | 3(10.0%) | 3(10.0%) |

**Table 2:** Mean age

| | GRP | N | Mean | Std. Deviation | Std. Error Mean | P value |
|---|---|---|---|---|---|---|
| Age | Esmolol | 30 | 34.9000 | 10.86072 | 1.98289 | 0.644 |
| | Labetalol | 30 | 36.3667 | 13.44845 | 2.45534 | NS |

**Table 3:** Gender distribution

| Sex | Esmolol | Labetalol |
|---|---|---|
| Male | 16(53.3%) | 15(50%) |
| Female | 14(46.7) | 15(50%) |

**Table 4:** Mean weight

| | GRP | N | Mean | Std. Deviation | Std. Error mean | P value |
|---|---|---|---|---|---|---|
| Weight | Esmolol | 30 | 64.3333 | 6.49845 | 1.18645 | 0.05 |
| | Labetalol | 30 | 60.4000 | 9.03480 | 1.64952 | (ns) |

**Table 5:** Change in heart rate between esmolol and labetalol

| | MEAN±SD | | Mean Difference | p value |
|---|---|---|---|---|
| | Esmolol | Labetalol | | |
| Basal | 97.86±14.6 | 97.50±14.5 | .3667 | .923 |
| Rev | 102.73±16.4 | 103.1±15.6 | -.3667 | .930 |
| Drug | 99.86±16.9 | 95.56±16.3 | 4.3000 | .322 |
| Drug 1 | 94.70±19.0 | 92.33±14.7 | 2.3667 | .592 |
| Ext | 90.83±15.8 | 90.66±14.3 | .1667 | .966 |
| E 1 | 88.86±12.8 | 87.46±14.2 | 1.4000 | .690 |
| E2 | 84.96±13.2 | 85.13±13.8 | -.1667 | .962 |
| E3 | 83.73±12.6 | 81.83±13.6 | 1.9000 | .577 |
| E4 | 81.96±11.2 | 78.43±13.4 | 3.5333 | .274 |
| E5 | 80.86±10.7 | 74.96±10.3 | 5.9000 | .034 |
| E15 | 84.56±10.7 | 69.96±8.6 | 14.6000 | .000 |

**Table 6:** Results of repeated measure anova-heart rate changes between esmolol and labetalol

| Source | Type III Sum of Squares | Df | Mean Square | F | Significance |
|---|---|---|---|---|---|
| Change | 45546.545 | 10 | 4554.655 | 52.307 | .000 |
| Change*GRP | 2780.236 | 10 | 278.024 | 3.193 | .001 |

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at basal, extubation up to 4th minute post extubation (p>0.05). At 5th min (p=0.034) and 15th min post (p=.000) extubation there was significance, especially at 15th min. Graph and table shows both attenuated hemodynamic response, which was proved by ANOVA results p=0.000. And both behaved differently during course ANOVA p=0.001 also seen in graph and table at 5th and 15th min. Heart rate decrease in labetalol is more than esmolol but statistically insignificant except at E5 and E15.

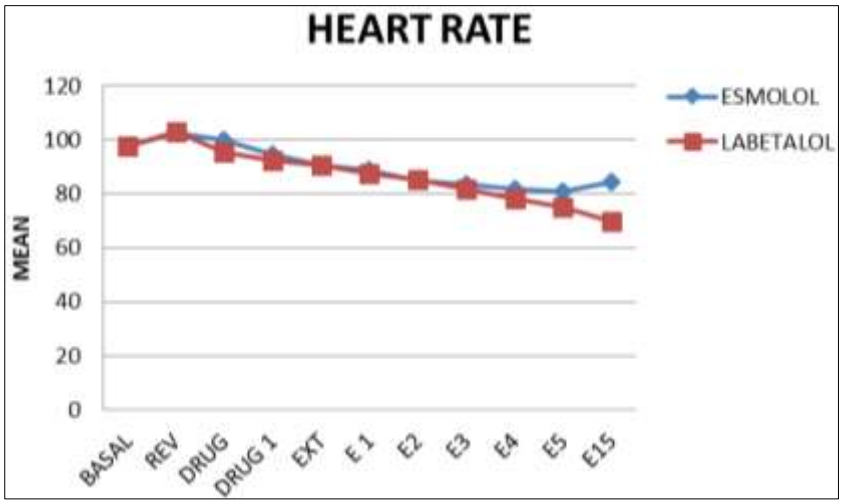


**Fig 1:** Change in heart rate between esmolol and labetalol

**Table 7:** Side effects

| IDE effects | Esmolol | Labetalol |
|---|---|---|
| Bradycardia | 0 | 2(3.3) |
| Hypotension | 0 | 1(1.1) |

In esmolol group no complications observed in labetalol group two incidence of bradycardia <60bpm after 15th min post extubation in recovery room treated with atropine and, one episode of hypotension systolic blood pressure <90mmHg also after 15th min treated with fluids and 6mg of mephentermine IV. Complications observed were statistically insignificant p>0.05.

## Discussion

Many investigators have documented that tracheal extubation causes modest (10% to 30%) and transient increases in blood pressure and heart rate, lasting 5-15min. Although such cardiovascular stimulation is usually inconsequential, certain patients may experience un favorable or undesirable sequela. Coriat *et al*., [3]. demonstrated that patients with coronary artery disease experience significant decreases in ejection fractions (from 55% ± 7% to 45% ± 7%) after extubation. The changes in ejection fraction occurred in the absence of electrocardiographic signs of myocardial ischemia. A study reported that patients with a cardiac index of less than 3.0 L / min/m did demonstrate an ischemic response to the stress of postoperative tracheal extubation after myocardial revascularization [5].

These patients experienced decreases in myocardial lactate extraction, Left ventricular compliance, and cardiac performance. Others, however, have failed to confirm electrocardiographic or enzymatic evidence of myocardial ischemia related to tracheal extubation in patients after coronary artery surgery. Tracheal extubation after caesarean section in parturient with gestational hypertension can cause significant increases of 45 and

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20 mm Hg in mean arterial and pulmonary artery pressures, respectively. It was concluded that tracheal extubation and related hemodynamic changes increased the risk of cerebral haemorrhage and pulmonary edema in in those parturient.

Coughing frequently occurs during tracheal extubation. Bucking is a more forceful and often protracted cough that physiologically mimics a Valsalva maneuver. Unlike a Valsalva maneuver, bucking occurs at variable lung volumes, which are often less than vital capacity. Coughing and bucking are not only aesthetically unpleasant, but can also be harmful.

They can cause abrupt increases in intracavitary pressures. For example, patients with an open eye injury or increased intracranial pressure can be placed at risk. Increased intraocular and intracranial pressures result from an increase in intrathoracic pressure that decreases venous return to the right atrium.

Abdominal wound separation, although rarely associated with emergence from anaesthesia, is another potential complication associated with an increase in intra-abdominal pressure secondary to bucking. Bucking also results in a decrease in FRC.

Coughing can lead to increases in intrathoracic pressure which can interfere with venous return to the heart. The effects of coughing on heart rate, systolic, diastolic, and arterial pulse pressure, and coronary flow velocity have been evaluated by Kern *et al*., [5-7].

Donegan and Bedford [8] reported that ICP increased by 12 ± 5 mm Hg in comatose patients whose tracheas were suctioned. White *et al.,* 18 also found ICP increased from 15 ±1 to 22 ± 3 mm Hg after endotracheal suctioning in fully resuscitated, comatose intensive care unit (ICU) patients. The ICP increases lasted for less than 3 min after suctioning. Both authors hypothesized that coughing associated with endotracheal suctioning causes ICP to increase by increasing intrathoracic pressure, cerebral venous pressure and cerebral blood volume. Thus tracheal extubation, especially when associated with suctioning and/or coughing or bucking, is also likely to increase ICP.

Increases in arterial blood pressure often result from tracheal extubation as mentioned above, and arterial hypertension can also lead to or be associated with intracranial haemorrhage or increases in ICP19. Possibly, associated hemodynamic changes, during and after extubation, can also negatively impact patients with intracranial pathology.

The endocrine response to tracheal extubation has received little attention. Lowrie *et al*., Evaluated the impact of tracheal extubation on changes in plasma concentrations of epinephrine and norepinephrine. Epinephrine levels were significantly increased from 0.9 to 1.4 pmol/mL only 5 min after extubation. Norepinephrine levels remained unchanged pressor response is a reflex phenomenon with the afferent stimuli carried over both glossopharyngeal and vagal pathways. Such stimuli activate suprasegmental and hypothalamic sympathetic centers to cause a peripheral sympathoadrenal response due release of adrenaline and noradrenaline.

## Conclusion

The incidence of bradycardia and hypotension was greater in patients treated with labetalol which was statistically insignificant. Labetalol is effective in controlling such response for prolong period >15min hence chance of complications which requires thorough vigilance in recovery room also.

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