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Blood pressure response to tracheal extubation: Comparative study between esmolol and labetalol

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Abstract

Complications after trachea extubation are three times more common than complications occurring during tracheal intubation and induction of anaesthesia. Hypertension and tachycardia are well documented events during extubation. These hemodynamic responses reflects sympatho-adrenal reflex stimulation (epipharyngeal and laryngo pharyngeal stimulation) with concomitant increase in plasma level of catecholamines and activation of alpha and beta adrenergic receptors. 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. Statistical evaluation between the group showed there was no significance of SBP between the group at basal, extubation upto 1th minute post extubation (p>0.05). At 2th min (p=0.034), 3rd min (p-0.023) and 15th min (p=0.024) post extubation there was significance esmolol> labetalol at 2nd and 3rd, labetalol >esmolol at 15th min.

Keywords: Blood pressure response, esmolol, labetalol

Introduction

Endotracheal extubation is one of the frequently performed procedure in the practice of anaesthesia. Endotracheal extubation is the translaryngeal removal of a tube from trachea via the nose or mouth [1].
Complications after trachea extubation are three times more common than complications occurring during tracheal intubation and induction of anaesthesia. Hypertension and tachycardia are well documented events during extubation. These hemodynamic responses reflects sympatho-adrenal reflex stimulation (epipharyngeal and laryngo pharyngeal stimulation) with concomitant increase in plasma level of catecholamines and activation of alpha and beta adrenergic receptors. This increase in blood pressure and heart rate are usually transitory, variable and unpredictable. The development of postoperative hypertension warrants immediate assessment and treatment to reduce the risks of myocardial infraction, arrhythmias, congestive heart failure, stroke, bleeding, and other end-organ damage [2, 3].
Tracheal extubation is associated with a 10-30% increase in arterial pressure and heart rate 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 (1.5mg/Kg IV 2-5 min before extubation), glyceryl trinitrate, magnesium, propofol infusion, remifentanil/alfentanil infusion, IV lidocaine (1.5mg/Kg over 2 min), topical lidocaine 10% and perioperative oral nimodipine with labetalol [4].

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).

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.

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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

Table 1: Change in systolic blood pressure between esmolol and labetalol

	Mean ± sd		Mean difference	P value
	Esmolol	Labetalol		
Basal	130.96±13.5	125.50±6.9	5.4667	.054
Rev	135.86±19.0	140.70±8.4	-4.8333	.209
Drug	130.46±10.9	135.46±6.8	-5.0000	.037
Drug 1	125.96±8.3	127.80±7.6	-1.8333	.375
Ext	125.10±8.2	124.53±7.5	.5667	.781
E 1	118.73±7.6	121.73±8.7	-3.0000	.160
E2	114.40±8.7	119.53±8.4	-5.1333	.024
E3	112.76±8.9	118.36±9.6	-5.6000	.023
E4	113.23±7.8	116.5±8.9	-3.2667	.135
E5	113.8±7.9	114.6±8.5	-.8333	.694
E15	119.8±10.5	113.6±10.1	6.2000	.024

Table 2: Repeated measure ANOVA study of systolic blood pressure

Source	Df	Mean square	F	Significance
Change	10	3961.073	62.174	.000
Change*GRP	10	257.012	4.034	.000

In esmolol group the basal systolic blood pressure was 130.96mmHg. During reversal systolic pressure increased to 135.8mmHg. During drug injection and subsequently systolic decreased. At 15min post extubation pressure was 119.8mmHg which was less than basal.
In labetalol group the systolic blood pressure was 125.5mmHg. During reversal systolic blood pressure increased to 140.7mmHg. During drug injection and subsequently systolic blood pressure decreased. At 15min post extubation systolic blood pressure was 113.6mmHg which was again less than basal.
Statistical evaluation between the group showed there was no significance between the group at basal, extubation upto 1^{th} minute post extubation ($p>0.05$). At 2^{th} min ($p=0.034$), 3^{rd} min (p-0.023) and 15^{th} min ($p=0.024$) post extubation there was significance esmolol> labetalol at 2^{nd} and 3^{rd}, labetalol >esmolol at 15^{th} min. Both attenuated hemodynamic response, which was proved by ANOVA results $p=0.000$. And both behaved differently during course ANOVA $p=0.000$ at 2^{nd} 3^{rd} and 15^{th} min. Pressure decrease in esmolol is more than labetalol but statistically insignificant except at E2and E3.

ISSN 2515-8260 Volume 09, Issue 02, 2022

Table 3: Change in diastolic blood pressure between esmolol and labetalol

	Mean ± sd		Mean difference	P value
	Esmolol	Labetalol		
Basal	86.9667±9.01	83.7000±5.8	3.2667	.112
Rev	97.8000±11.7	94.2667±6.32	3.5333	.113
Drug	89.0333±14.2	88.2667±8.2	.7667	.799
Drug 1	86.3333±10.13	83.3667±8.5	2.9667	.226
Ext	80.1333±12.21	80.4333±7.3	-.3000	.909
E 1	71.6333±14.9	78.5333±6.6	-6.9000	.024
E2	69.9333±10.04	77.3667±7.4	-7.4333	.002
E3	69.3000±10.26	75.7333±6.6	-6.4333	.005
E4	70.6667±11.8	73.4000±4.9	-2.7333	.245
E5	71.9667±11.5	72.3000±4.0	-.3333	.881
E15	74.1667±11.7	72.9000±5.8	1.2667	.597

Table 4: Repeated measure ANOVA study of diastolic blood pressure

Source	Df	Mean square	F	Significance
Change	10	3538.127	105.382	.000
Change*GRP	10	384.531	11.453	.000

In esmolol group the basal diastolic blood pressure was 86.9mmHg. During reversal diastolic pressure increased to 97.8mmHg. During drug injection and subsequently diastolic decreased. At 15min post extubation pressure was 74.1mmHg which was less than basal.

In labetalol group the diastolic blood pressure was 83.7mmHg. During reversal diastolic blood pressure increased to 94.36mmHg. During drug injection and subsequently diastolic blood pressure decreased. At 15min post extubation diastolic blood pressure was 72.9mmHg which was again less than basal.

Statistical evaluation between the group showed there was no significance between the group at basal and extubation ($p>0.05$. At 1^{th} min ($p=0.024$), 2nd min ($p=0.002$) and 3rd min (p-0.005) post extubation there was significance. Both attenuated hemodynamic response especially at E2 and E3, which was proved by ANOVA results $p=0.000$. And both behaved differently during course ANOVA $p=0.000$ also at 2^{nd} 3^{rd} and 15^{th} min. Pressure decrease in esmolol is more than labetalol but statistically insignificant except at E1, E2 and E3.

Table 5: Change in mean arterial pressure between esmolol and labetalol

	Mean ± sd		Mean difference	P value
	Esmolol	Labetalol		
Basal	98.6333±7.3	95.6333±4.7	3.0000	.100
Rev	110.4889±12.1	107.077±6.1	3.4111	.175
Drug	102.8444±12.1	104.000±7.01	-1.1556	.653
Drug 1	99.5444±8.5	98.1778±6.6	1.3667	.493
Ext	95.1222±10	95.1333±6.7	-.0111	.996
E 1	87.3333±11.2	92.9333±6.4	-5.6000	.022
E2	84.7556±7.7	91.4222±6.9	-6.6667	.001
E3	83.7889±7.5	89.9444±6.6	-6.1556	.001
E4	84.8556±8.2	87.7667±4.9	-2.9111	.101
E5	85.9000±8.2	86.3778±4.07	-.4778	.776
E15	89.3889±9.0	86.4778±6.6	2.9111	.162

Table 6: Repeated measure ANOVA study of mean arterial pressure

Source	Df	Mean square	F	Significance
Change	10	3665.688	142.284	.000
Change*GRP	10	260.801	10.123	.000

In esmolol group the basal mean arterial blood pressure was 98.6mmHg. During reversal mean arterial pressure increased to 110.4mmHg. During drug injection and subsequently mean arterial. At 15min post extubation pressure was 89.3mmHg which was less than basal.
In labetalol group the mean arterial blood pressure was 995.6mmHg. During reversal mean arterial blood pressure increased to 107.07mmHg. During drug injection and subsequently mean arterial blood pressure decrease. At 15min post extubation mean arterial blood pressure was 84.47mmHg which was again less than basal.
Statistical evaluation between the group showed there was no significance between the group at basal and extubation ($p>0.05$). At 1^{th} min ($p=0.022$), 2nd min ($p=0.001$) and 3rd min (p-0.001) post extubation there was significance. Both attenuated hemodynamic response which was proved by ANOVA results $p=0.000$. And both behaved differently during course ANOVA $p=0.000$ at E1, E2 and E3. Pressure decrease in esmolol is more than labetalol but statistically insignificant except at E1, E2 and E3.

Discussion

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 post anaesthetic care. This study showed both esmolol 1.5mg/kg and labetalol 0.25mg/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 post-extubation 1^{st} and 2^{nd} minute. Labetalol was more effective in control of heart rate which was statistically insignificant upto 4^{th} min post extubation.
Emergence from general anaesthesia and especially post-extubation phase are the stages associated with cardiovascular hyperdynamic status leading to increase in oxygen consumption, and catecholamine release. This phase lasting 15 to 5 minutes could frequently be accompanied by tachycardia and hypertension. Most patients, however, endure this temporary situation appropriately. On the other hand, patients having pre-operative hypertension and cardiovascular and cerebrovascular diseases and patients with increased intracranial pressure (ICP) could be affected by severe cardiac and or cerebral complications. Therefore, it is of great importance to prevent post-operative 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, nitroglycerine, calcium channel blockers, etc.; however, studies comparing esmolol (cardio selective beta blocker) and labetalol (nonselective adrenergic blocker) are lacking.
Esmolol hydrochloride is an ultra-short acting, beta-one selective adrenergic receptor blocker with a distribution half-life of 2 min and an elimination half-life of 9 min. Esmolol appears quite suitable for use during a short-lived stress such as tracheal intubation, extubation or ECT.
Esmolol 1.0 mg kg-1, 1.5 mg kg-1, and 2.0 mg kg-1 were used in patients before extubation in a study by Dyson *et al*. (22), which showed that the increase in systolic blood pressure could be prevented with 1.5 mg kg-1 and 2.0 mg kg-1 esmolol, but 1 mg kg-1 esmolol was found to be ineffective. Since distinct hypotension was observed with 2.0 mg kg-1 esmolol, 1.5 mg kg-1 esmolol was reported as the optimal dose for the prevention of haemodynamic response due to tracheal extubation. Alkaya, *et al.* [5] used 2mg/kg esmolol over 10 min 5min before extubation to attenuate hemodynamic response to

ISSN 2515-8260 Volume 09, Issue 02, 2022

extubation. He concluded esmolol infusion before extubation can prevent hypertension and tachycardia caused by extubation in patients undergoing elective craniotomy. In his study he dint have any complications though he used 2mg/kg probably because he started infusion 5min prior to extubation as compared to 2-5min before extubation in Dyson study [6].

Lim *et al.* [7] sought to find the optimal prophylactic esmolol dose for controlling hemodynamic responses in patients undergoing intracranial surgery. He observed 0.2 mg kg-1 min-1 to be more effective and 100 mg kg-1 min-1 was considered to be safe. J. P. O'Dwyer *et al.* (500 µg/kg over 1 min followed by 100 µg/kg/min), Tempe DK *et al.*, Grillo P(esmolol 0.3 mg · kg_1 · min_1) and Apostolos karavidas (50 µg/kg/min upto 150 µg/kg/min) all have studied and concluded esmolol is effective in blunting hemodynamic response with no complications. All have used ≤0.5mg/kg/min infusion throughout the extubation period. So complications not observed. In our study we used 1.5mg/kg esmolol slow bolus 2min prior extubation without any adverse effects.

Fuhrman TM *et al.* [8] (esmolol and alfentanil), Kovac *et al.* (nicardipine 0.03 mg/kg IV versus esmolol 1.5mg/kg IV) and Bostana *et al.* (Esmolol 1 mg kg-1, Lidocaine 1 mg kg-1) all found esmolol was more effective than others in suppressing the response. Hosseinzadeh et found both remifentany and esmolol in obtunding response though remifentanil was more effective which was statistically insignificant. Here they used esmolol 500µ/kg/min infusion which continued with 150µg/kg/min post extubation upto 10min. probably here timing and dosage might be the factor for reduced efficacy.

Labetalol is an adrenergic receptor blocking agent with mild alpha1-and predominant beta-adrenergic receptor blocking actions (alpha: beta blockade ratio of 1:7 for iv and 1:3 for PO administration). The onset of action of i.v. labetalol is 5 min.

The efficiency of labetalol in attenuating the rise in heart rate and blood pressure has been well documented as described in review of literature. In all studies labetalol was effective obtunding intubation response except in Indana study. 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 minutes prior to the stimulation.

In our study we observed labetalol 0.25mg/kg IV 2min before extubation was effective in obtunding hemodynamic response.

Donald A *et al.* [9] did Comparative study between esmolol (loading dose of 500 µg/kg followed by an infusion of50-300 µg.kg-'.min-,' mean= 160µg/kg/min) and labetalol (incremental doses of 0.25, 0.5, 0.75, and 1.00 mg/kg, mean=0.98mg/kg/min) in treating increase in blood pressure during emergence and recovery from anaesthesia after intracranial surgery and found both labetalol and esmolol were equally effective in controlling systolic blood pressure on emergence and in the recovery room. However, decreasing in heart rate was significantly more frequent in the immediate post-operative period in patients given labetalol as found in our study.

Singh *et al.* [10] compared esmolol 0.5mg/kg and labetalol 0.25mg/kg, 2min and 5min before intubation. He observed labetalol was more effective in controlling heart rate and systolic blood pressure than esmolol which was statistically significant $p<0.05$. Labetalol also controlled diastolic and mean pressure better than esmolol but statistically insignificant except one min post-intubation. The performance of esmolol was less than labetalol was probably because low dose 0.5mg/kg as compared to ours 1.5mg/kg. The author also commented about bradycardia being only the side effect in his study not hypotension this is probably because timings 5min before intubation as compared to 2 min before extubation. In our case hypotension and bradycardia was seen at 15min post extubation.

Conclusion

Both esmolol (1.5mg/kg) and labetalol (0.25mg/kg) given 2min prior was effective in controlling hemodynamic response to extubation. Esmolol more than labetalol at and immediately (1and2min) after extubation which was statistically significant. However, the incidence of hypotension was greater in patients treated with labetalol which was statistically insignificant. An increase in hemodynamic after extubation appears to be a transitory phenomenon adequately treated with a short-acting cardio

selective β blocker esmolol.

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