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# Efficacy of intravenous dexmedetomidine (0.5µg/kg) versus intravenous esmolol (1.5mg/kg) given before extubation on stress response to extubation

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**Abstract**
Hypertension and tachycardia are well documented events during extubation[3]. These hemodynamic reflexes reflect sympatho-adrenal reflex stimulation (Epipharyngeal and laryngopharyngeal stimulation) with concomitant increase in plasma levels of catecholamines and activation of α and β adrenergic receptors. All patients included in the study were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally at bed time the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night. Ten patients in the dexmedetomidine group and 4 patients in esmolol group had hypotension which was transient and responded to intravenous fluid administration was statistically significant compared to control group. The incidence of hypotension was statistically insignificant between esmolol and dexmedetomidine group.

**Keywords:** Dexmedetomidine, esmolol, extubation on stress response

## Introduction
Endotracheal extubation is one of the frequently performed procedures in the practice of anaesthesia. Endotracheal extubation is the translaryngeal removal of a tube from trachea via mouth or nose. Complications that occur during and after extubation are three times more common than that occurring during tracheal intubation.

Critical component of airway management is the process of extubation and extubation may be far more treacherous than that of intubation. Increased incidence of complications has been correlated with the preoperative physical status, depth of anaesthesia at extubation, increasing age and gender with a male preponderance. These complications remain consistent regardless of the type of surgery [1]. Hypertension and tachycardia are well documented events during extubation. These hemodynamic reflexes reflect sympatho-adrenal reflex stimulation (Epipharyngeal and laryngopharyngeal stimulation) with concomitant increase in plasma levels of catecholamines and activation of α and β adrenergic receptors. This increase in blood pressure and heart rate are transitory, variable and unpredictable. This development of postoperative hypertension warrants immediate assessment and treatment to reduce the risks of myocardial infarction, arrhythmias, congestive heart failure, cerebrovascular accidents, bleeding and other end organ damage. Tracheal extubation is associated with a 10-30 % increase in arterial pressure and heart rate lasting for 5-15 minutes. Patients with coronary artery disease experiencing 40-50 % decrease in ejection fraction [2, 3]. Respiratory complications associated with tracheal extubation are coughing and sore throat (ranges from 38-96%), laryngospasm, bronchospasm which leads to hypoxemia. Laryngospasm is the commonest cause for post extubation upper airway obstruction. These reflexes may be attenuated by pharmacological interventions including opioids, calcium channel blockers, β blockers, lidocaine, propofol, clonidine and others [4]. Esmolol is a selective β1 antagonist with a very short duration of action. It has a very little if any sympathomimetic action and it lacks membrane stabilizing action. Esmolol is administered IV and used when β blockade of short duration is desired or in critically ill patient in whom adverse effects of bradycardia heart failure or hypotension may necessitate rapid withdrawal of the drug. Many authors used different doses of Esmolol(1,1.5,and 2mg/kg) and observed that all three doses (1, 1.5, 2mg/kg) were effective in controlling heart rate but 1mg/kg was insufficient to control increase in systolic blood pressure, higher doses controlled both systolic blood pressure and heart rate.

It is also found that 2mg/kg body weight had produced significant decrease in heart rate [5].

Dexmedetomidine is a highly selective α2 adrenoreceptor agonist (α1:α21:1600). α2 agonists decrease the sympathetic outflow and noradrenergic activity thereby counteracting hemodynamic fluctuations occurring at the time of extubation. Many authors have conducted studies using 0.5µg/kg Dexmedetomidine intravenously and observed that it was effective in controlling stress response to extubation [6].

## Methodology

All patients included in the study were premeditated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally at bed time the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night.

On arrival of the patient in the operating room, Intravenous line was obtained with 18G cannula and preloaded with ringer lactate 10ml/kg body weight before anaesthesia. The patients were connected to multi-parameter monitor which records heart rate, non-invasive measurements of SBP, DBP, MAP, EtCO2 and continuous ECG monitoring and oxygen saturation. The baseline systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were recorded (basal parameters). The cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II.

All patients were premedicated with injection midazolam-0.02mg/kg body weight, inj. ondansetron 4mg and inj. glycopyrrolatte 0.2mg and injection fentanyl 1µg/kg body weight. Then patients were preoxygenated for 3 minutes via a face mask with closed circuit. Anaesthesia was induced with injection Propofol 2mg/kg body weight and endotracheal intubation was facilitated with 1.5mg/kg IV Succinylcholine one minute prior to laryngoscopy and intubation. Laryngoscopy and intubation were performed using Macintosh no.3 blade and after confirmation of bilateral equal air entry and capnograph, the endotracheal tube was fixed.

Anaesthesia was maintained using 66% nitrous oxide and 33% of oxygen with 1% Isoflurane. After the patients recovered from succinylcholine, further neuromuscular blockade was maintained with vecuronium 0.05 mg/kg body weight initially and1mg increments as and when required.

At the beginning of skin suturing Isoflurane is discontinued and Group D will receive Dexmedetomidine 0.5µg/kg body weight diluted in 10 ml normal saline as infusion over 10 minutes using an infusion pump whereas Group C and Group E will receive 10ml normal saline over ten minutes. Nitrous Oxide will be discontinued at the end of infusion.

At the end of surgery heart rate, systolic and diastolic blood pressure recorded serve as baseline values. The residual neuromuscular blockade will be reversed using Inj Neostigmine 0.05mg/kg and Inj Glycopyrrolate 0.01mg/kg intravenously. After 2 minutes of reversal, Group E will receive Esmolol 1.5mg/kg intravenously diluted to 10ml with normal saline and Group C and Group D will receive 10ml normal saline.

The test drugs were prepared by an anaesthesiologist not involved with the study in 10ml syringes and thus the observer and the patients will be blinded for the study drugs.

## Results

**Table 1:** Showing the age distribution

| | | Drug | | | |
|---|---|---|---|---|---|
| | | **Group C** | **Group D** | **Group E** | **Total** |
| Age (in years) | 18 to 20 | 3(10) | 1(3) | 2(7) | 6(7) |
| | 21 to 30 | 9(30) | 12(40) | 7(23) | 28(30) |
| Group | 31 to 40 | 11(37) | 9(30) | 5(17) | 25(28) |
| | 41 to 50 | 6(20) | 8(27) | 11 (36) | 25(28) |
| | 51 to 60 | 1(3) | 0(0) | 5(17) | 6(7) |
| | Total | 30(100) | 30(100) | 30(100) | 90(100) |
| Mean age in years | | 34.30±9.24 | 33.87±9.32 | 36.83±9.51 | 35.24±10.2 |
| | P value | | 0.1(NS) | | |
| NS–Not significant | | | | | |

**Table 2:** Comparison of Ramsay Sedation Scale in three groups of patients

| | **Group C** | **Group D** | **Group E** | **P** |
|---|---|---|---|---|
| At extubation | 1.59±0.38 | 2.51±0.53 | 1.45±0.41 | <0.001 |
| Post extubation 5 min | 1.97±0.25 | 2.40±0.32 | 1.78±0.38 | <0.001 |
| Post extubation 10 min | 1.90±0.30 | 2.24±0.38 | 1.90±0.49 | <0.001 |
| Post extubation 15 min | 2.01±0.38 | 2.13±0.19 | 1.96±0.13 | 0.004 |
| Post extubation 30 min | 2.02±0.50 | 2.10±0.20 | 2.01±0.41 | 0.045 |
| Post extubation 60 min | 2.00±0.49 | 2.08±0.41 | 2.00±0.15 | 0.156 |
| Post extubation 90 min | 2.00±0.00 | 2.00±0.00 | 2.00±0.00 | ----- |
| Post extubation 120 min | 2.00±0.00 | 2.00±0.00 | 2.00±0.00 | ----- |

Patients in the Dexmedetomidine group had higher score compared to the control group and esmolol group which was statistically significant at extubation ($p$<0.001), 5$^{th}$ minute ($p$<0.001), 10$^{th}$ minute ($p$<0.001), 15$^{th}$ minute ($p$<0.001), 30$^{th}$ minute post Extubation (p=0.045).

Post hoc analysis showed no significant differences between the mean sedation scores of esmolol and control group. The patients in dexmedetomidine group were more sedated compared to the patients in control and esmolol group.

**Table 3:** Comparison of extubation parameters among three groups of patient studied

| | **Group C** | **Group D** | **Group E** | **P** |
|---|---|---|---|---|
| Time to extubation | 15.58±3.23 | 17.24± 2.89 | 15.8±3.66 | <0.001 |
| Time to eye opening | 13.84±3.67 | 16.15±3.12 | 14.23±2.95 | <0.001 |
| Extubation quality 5 pt. Scale | 1.57±0.81 | 1.03±0.20 | 1.60±0.70 | <0.001 |
| No. of bouts of cough per patient | 1.08±0.50 | 0.3±0.18 | 1.00±0.30 | 0.004 |

Time to extubation and time to eye opening is significantly prolonged in dexmedetomidine group (17.24± 2.89 and 16.15±3.12, $p$<0.001) compared to control group (15.58±3.23, 13.84±3.67) and esmolol group (15.8±3.66, 14.23±2.95). The number of cough bouts per patient was clinically and statistically significantly lesser in dexmedetomidine group (0.3±0.18, p=0.04) compared to control group (1.08±0.50) and esmolol group (1.00±0.30).

Extubation quality five point scale was lower in group dexmedetomidine (1.03±0.20) compared to control group (1.57±0.81) and esmolol group (1.60±0.70) which of statistically significant ($p$<0.001) implying that patients dexmedetomidine group had smoother extubation compared to the control and esmolol group.

**Table 4:** Comparison of extubation quality occurred in three groups

| | Group C | Group D | Group E |
|---|---|---|---|
| Scale 1 | 18(60) | 27(90) | 20(67) |
| Scale 2 | 6(20) | 3(10) | 5(17) |
| Scale 3 | 4(13) | 0(0) | 4(13) |
| Scale 4 | 2(7) | 0(0) | 1(3) |
| Scale 5 | 0(0) | 0(0) | 0(0) |
| Total | 30(100) | 30(100) | 30(100) |
| Inference | Lower score of Extubation quality is significantly associated with study group with $p$=0.001 | | |

**Table 5:** Comparison of complications occurred in three groups

| | Group C | Group D | Group E | P |
|---|---|---|---|---|
| Hypotension | 0 | 3 | 4 | 0.023 |
| Hypertension | 26 | 0 | 0 | <0.001 |
| Agitation | 9 | 0 | 8 | <0.001 |
| Tachycardia | 22 | 1 | 1 | <0.001 |
| Bradycardia | 0 | 0 | 0 | ---- |
| Coughing | 7 | 3 | 8 | 0.001 |
| Laryngospasm | - | - | - | - |
| Bronchospasm | - | - | - | - |
| Desaturation | - | - | - | - |

Ten patients in the dexmedetomidine group and 4 patients in esmolol group had hypotension which was transient and responded to intravenous fluid administration was statistically significant compared to control group. The incidence of hypotension was statistically insignificant between esmolol and dexmedetomidine group. Hypertension was observed in 26 patients in control group with none in dexmedetomidine or esmolol group which is highly significant. Tachycardia was observed in 26 patients in control group compared to1 each in dexmedetomidine and esmolol group which is statistically significant. Coughing post extubation was seen in 7, 3 and 8 patients each in control, dexmedetomidine and esmolol group respectively. Coughing incidence was significantly lower in dexmedetomidine group compared to other groups. Bradycardia, laryngospasm, bronchospasm and desaturation was not observed in any of the groups.

## Discussion

Endotracheal extubation is one of the frequently performed procedures in the practice of anaesthesia. Endotracheal extubation is the translaryngeal removal of a tube from trachea via mouth or nose. Critical component of airway management is the process of extubation and Period of extubation may be for more treacherous than that of intubation.

Complications that occur during and after extubation are three times more common than that occurring during tracheal intubation and induction of anaesthesia [2]. Hypertension and tachycardia are well documented events during Extubation [3]. These hemodynamic reflexes reflect sympatho-adrenal reflex stimulation (epipharyngeal and laryngopharyngeal stimulation) with concomitant increase in plasma levels of catecholamines and activation of α and β adrenergic receptors. This increase in blood pressure and heart rate are transitory, variable and unpredictable. This development of postoperative hypertension warrants immediate assessment and treatment to reduce the risks of myocardial infarction, arrhythmias, congestive heart failure, cerebrovascular accidents, bleeding and other end organ damage. Tracheal extubation is associated with a 10 – 30 % increase in arterial pressure and heart rate lasting for 5 – 15 minutes. Patients with coronary artery disease experiencing 40–50% decrease in ejection fraction [4]. Respiratory complications associated with tracheal extubation are local trauma, coughing, and sore throat (ranges from 38–96%), aspiration, laryngospasm, bronchospasm which leads to hypoxemia. Laryngospasm is the commonest cause for post extubation upper airway obstruction Endotracheal intubation and suctioning is associated with a rise in intracranial pressure (ICP). It is probable that extubation is associated with even more marked rises in ICP.

Various attempts have been made to attenuate extubation response with various pharmacologic agents. Extubation in deeper planes of anaesthesia ordinarily would involve the prior reversal of neuromuscular blockade and resumption of spontaneous ventilation. Its purported advantage is the avoidance of the adverse reflexes associated with extubation, such as hypertension, dysrhythmias, coughing, laryngospasm, and increased IOP or ICP. The fundamental disadvantage of deep extubation is the patient‟s inability to protect the airway against obstruction, aspiration and also depression of the respiratory and cardiovascular system. Also, if it is improperly executed, laryngospasm is more likely to occur [7].

This study was conducted to compare the effectiveness of intravenous Esmolol (1.5mg/kg), a selective β1 adrenergic blocker with Dexmedetomidine (0.5µg/kg), a α 2-adrenergic receptor agonist in attenuation of hemodynamic stress response and airway reflexes to endotracheal extubation

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, 1.5 mg/kg, and 2.0 mg/kg were used in patients before extubation in a study by Dyson *et al.* [8], which showed that the increase in systolic blood pressure could be prevented with 1.5 mg/kg and 2.0 mg/kg esmolol, but 1 mg/kg esmolol was found to be ineffective. Since distinct hypotension was observed with 2.0 mg/kg esmolol, 1.5 mg/kg esmolol was reported as the optimal dose for the prevention of haemodynamic response due to tracheal extubation.

Murat Alp Alkaya *et al.* [9] used 2mg/kg esmolol over 10 min 5min before extubation to attenuate hemodynamic respose to extubation. He concluded esmolol infusion before extubation can prevent hypertension and tachycardia caused by extubation in patients undergoing elective craniotomy. In his study he didn‟t 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 [8].

In our study we used esmolol 1.5mg/kg slow bolus two min prior to extubation which was effective in blunting hemodynamic response with no side effects.

Lim *et al*. [10] sought to find the optimal prophylactic esmolol dose for controlling hemodynamic responses in patients undergoing intracranial surgery. He observed 0.2 mg/kg/min to be more effective and 0.1 mg/kg/min was considered to be safe. Park SH *et al.* [11] (250 µg/kg/min) all have studied and concluded that esmolol is effective in blunting hemodynamic response with no complications. All have used ≤0.5mg/kg/min as infusion throughout the extubation period.

In present study though we used 1.5mg/kg esmolol which is more than the doses used by above authors we dint observe any side effects. Reason can be, as we used bolus dose compared to infusion used by authors.

Different doses of dexmedetomidine have been used to attenuate the stress response to emergence from general anaesthesia.

Dose 0.5 µg/kg and above have been found to be effective in attenuating stress response to extubation. Kwon Hui Seo *et al*. conducted a study comparing the effectiveness of doses 0.5 µg/kg, 0.7 µg/kg,1 µg/kg of dexmedetomidine and concluded that 0.5 µg/kg is effective in attenuating stress response and with minimal side effects [12].

Hence we selected dose of 0.5 µg/kg dexmedetomidine which is the dose effective with minimal side effects. In the present study dexmedetomidine was diluted in 10 ml of normal saline and given intravenously over 10 minutes using syringe pump. Rapid administration of bolus dose of dexmedetomidine, initially results in transient increase in blood pressure and reflex decrease in HR. The initial reaction is due to peripheral α-2B adrenoceptors stimulation of vascular smooth muscle and can be attenuated by a slow infusion over 10 minutes. Hence in our study we administered the bolus dose over 10 minutes.

From the pharmacokinetic profile, it is seen that the distribution half-life of intravenous dexmedetomidine is approximately 6 minutes. Various authors Jain *et al*, Sriranga Rao *et al*., Bindu *et al*. have administered dexmedetomidine 10 minutes before extubation. Hence, in the present study dexmedetomidine was administered 10 minutes before extubation to prevent stress response to extubation.

Of the total 90 patients, 30 in each group, all three groups were comparable with respect to demographic characteristics like age, sex, body weight. All the patients completed the study.

## Conclusion

Dexmedetomidine also attenuates airway reflexes during emergence from general anaesthesia and facilitates smoother extubation without causing undue sedation.

Hence we conclude that single dose intravenous Dexmedetomidine is better in comparison with Esmolol not only in attenuating stress response but also airway reflexes to extubation without any adverse effects.

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