Comparison of Esmolol and Dexmedetomidine for Suppression of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation in Adult Patients Undergoing Elective General Surgery: A Prospective, Randomized Controlled Double-blinded Study

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Abstract

Context: Laryngoscopy and endotracheal intubation lead to strong sympathetic response which may precipitate arrhythmias, myocardial ischemia and cerebrovascular accidents in patients with preexisting cardiovascular disease. Aims: This study was aimed to compare the effect of dexmedetomidine and esmolol on hemodynamic response to laryngoscopy and endotracheal intubation in patients undergoing elective surgery under general anesthesia. Settings and Design: This was a prospective, randomized controlled double-blinded study. Materials and Methods: A total of ninety patients were selected and randomized into three groups of thirty patients each: Group C received infusion of 20 mL 0.9% normal saline (NS) over 10 min, Group D received infusion of dexmedetomidine 1 µg/kg diluted in 20 mL NS over 10 min, and Group E received infusion of esmolol 1.5 mg/kg diluted in 20 mL NS over 10 min. Three minutes after the completion of infusion, patients were induced with general anesthesia. Baseline parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and rate pressure product (RPP) were recorded before administration of study drugs and at 1, 3, 5, 7, and 10 min after intubation. Statistical Analysis Used: One-way ANOVA was used for comparison among the groups and unpaired t-test was used for comparison within the groups along with Tukey’s test for post test analysis. Results: Mean HR, SBP, DBP, MAP, and RPP values remained significantly lower in Group D than that of Group C and Group E at all time intervals up to 10 min after intubation. Conclusions: Both dexmedetomidine and esmolol suppressed the hemodynamic response to intubation when compared to control group, but dexmedetomidine is more effective than esmolol in maintaining hemodynamic stability following laryngoscopy and intubation.

Keywords: Dexmedetomidine, endotracheal intubation, esmolol, hemodynamic response, laryngoscopy

Introduction

Laryngoscopy and endotracheal intubation lead to strong sympathetic response which manifests as transient but marked tachycardia and hypertension.[1] This response is maximum immediately following intubation and lasts for 5–10 min. The response may be tolerated by healthy individuals but may precipitate arrhythmias, myocardial ischemia, and cerebrovascular accidents in patients with preexisting cardiovascular disease.[2-3]

Different methods have been used to suppress these responses such as use of topical lignocaine spray, maintenance of deep Plane of anesthesia by intravenous (IV) opioids, calcium channel blockers, and vasodilators, but none of the approaches were perfect and the search for a perfect agent is continuing.[4-7] Esmolol is a rapid-onset, ultrashort-acting (half-life 9 min), selective β-1 adrenergic receptor antagonist and proved to be effective in the prevention of transient and sustained hypertension and tachycardia associated with laryngoscopy and tracheal intubation in patients undergoing elective surgery under general anesthesia.[8-10]

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an efficient agent to provide hemodynamic stability during laryngoscopy and intubation.\cite{8-10} Dexmedetomidine is a selective $\alpha_2$-agonist which produces hyperpolarization of noradrenergic neurons and suppresses neuronal firing in the locus coeruleus, which decreases sympathoadrenal response and maintains hemodynamic stability during laryngoscopy and endotracheal intubation.\cite{11-14}

The primary outcome observed in the study was to compare the efficacy of dexmedetomidine and esmolol to suppress hemodynamic response during laryngoscopy and endotracheal intubation. The side effects of either drug were studied as the secondary outcome.

Materials and Methods

The study plan was approved by the Institutional Ethical Committee (Letter No.F.1/Acad/MC/JU/12/6283 in Dr. S N Medical College, Jodhpur). A total of ninety patients of either sex with inclusion criteria aged between 20 and 50 years and American Society of Anesthesiologists (ASA) physical status Classes I and II posted for elective surgery under general anesthesia were enrolled in this prospective, randomized controlled double-blinded study.

All the patients were included after obtaining written informed consent and after thorough preanesthetic checkup including general, physical, and systemic examinations. Routine investigations (complete blood count, renal function tests, liver function tests, electrocardiogram (ECG), and chest X-ray) were carried out in all patients. Patients were kept fasting for 8 h prior to surgery.

Patients with anticipated difficult airway, laryngoscopy time more than 20 s, a history of hypertension, diabetes, hepatic disease or renal disease, or on preoperative beta blockers, and pregnant or lactating women were excluded from the study.

In the operating room, an 18G IV cannula was secured and infusion of Ringer lactate was started at 10 mL/kg/h. Standard monitoring including pulse oximetry (SpO$_2$), ECG, and noninvasive blood pressure was instituted and baseline vitals such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and rate pressure product (RPP) were recorded. All patients received premedication with IV midazolam 0.03 mg/kg and IV fentanyl 1 $\mu$g/kg. The patients were randomly allocated to three groups of thirty patients each. Randomization was performed by computer-generated random numbers. This was done by an anesthesiologist who was unaware of the study protocol and was not involved in administering the drugs or observing results. The patients were blinded to the treatment group and all recordings were performed by a separate anesthesiologist blinded to the group allocation.

The drugs were infused in the following manner over 10 min: Group C patients received an infusion of 20 mL 0.9% normal saline (NS), Group D patients received infusion of dexmedetomidine 1 $\mu$g/kg diluted in 20 mL 0.9% NS, and Group E patients received infusion of esmolol 1.5 mg/kg diluted in 20 mL 0.9% NS.

After completion of the study drug infusion, all patients were preoxygenated with 100% oxygen for 3 min and general anesthesia was induced with IV propofol 2.5 mg/kg. After loss of response to verbal commands, IV succinylcholine 2 mg/kg was given as per standard protocol. Laryngoscopy was done by an expert anesthesiologist using McIntosh curved blade of appropriate size, and intubation was done with cuffed endotracheal tube of appropriate size and confirmed using capnography. Laryngoscopy time was considered as time from the introduction of laryngoscope blade into the oropharynx to the appearance of the capnography curve on the monitor and this time was limited to <20 s. Bilateral equal air entry was confirmed by auscultation, the tube was secured, and the patients were put on controlled ventilation using closed circuit with circle absorber system. All patients received IV vecuronium 0.08 mg/kg for muscle relaxation and maintained on intermittent bolus doses of vecuronium 0.02 mg/kg as per requirement along with oxygen and isoflurane 1%–1.5%.

During the study period of 10 min following intubation, no stimulus such as any surgical intervention, nasogastric tube insertion, surgical incision, or any drug administration was given.

Vital parameters including HR, SBP, DBP, MAP, and RPP were recorded at 1, 3, 5, 7, and 10 min after intubation. Patients were observed for any episode of bradycardia (HR <50 beats/min), hypotension (SBP <20% baseline), and any other adverse events during the surgery.

After completion of surgery, residual neuromuscular blockade was reversed with IV neostigmine 0.05 mg/kg and IV glycopyrrolate 0.01 mg/kg. Patients were extubated after complete clinical recovery and were shifted to postanesthesia care unit.

Statistical analysis

An initial pilot study was done and 20% of difference was decided as the minimum detectable difference of means in all groups. Standard deviation (SD) was considered 20% of average difference between the groups. The $\alpha$ value was 0.05 and the power of the study ($1-\beta$) was 0.90. The calculated sample size for each group was 23 patients considering 10% dropout. Preserving the designating effect, thirty patients were included in each group. Mean and SD for HR, SBP, DBP, MAP, and RPP were calculated and compared with the baseline value. One-way ANOVA was used for comparison among the groups while unpaired t-test was used for comparison within the groups along with Tukey’s test for post test analysis. Chi-square test was used for categorical data. $P$ value > 0.05 was considered non significant.

Results

All the patients who were enrolled completed the study. There was no significant difference with regard to demographic
profile (age, sex, height, weight, and ASA physical status) among the groups \((P < 0.05)\) [Table 1].

Mean HR at baseline was comparable in all the three groups \((P = 0.8250)\). After completion of study drug infusion and just before intubation, there was a significant fall in mean HR in both Group D (16.72%) and Group E (7.31%), but there was a rise in Group C (2.53%). After intubation, mean HR remained significantly lower \((P < 0.001)\) in Group D compared to Group C and Group E at all time intervals up to 10 min [Table 2].

Mean values of SBP, DBP, and MAP at baseline were comparable in all the three groups \((P < 0.05)\) [Figure 1]. After completion of study drug infusion and just before intubation, there was a significant fall in mean SBP, DBP, and MAP in both Group D and Group E compared to Group C. Mean SBP, DBP, and MAP values increased in all the three groups at 1 min after intubation. The values in Group D were significantly lower than that of Group C and Group E \((P < 0.001)\). In addition, the values in Group E were significantly lower than that of Group C \((P < 0.05)\) at this time. Whereas the mean SBP, DBP, and MAP values remained significantly lower in Group D than Group C and Group E at all time intervals up to 10 min after intubation; the difference between the esmolol and control groups was not significant after 3 min and these two groups remained comparable thereafter.

One-way ANOVA showed no significant difference in RPP among the three groups at baseline \((P > 0.05)\) [Figure 2]. RPP increased from baseline 1 min after intubation in all the groups. The values in Group D were significantly lower compared to Group C and Group E and this trend was observed up to 10 min after intubation. Similarly, RPP values in Group E were significantly lower than that of Group C up to 7 min after intubation.

Monitoring of HR, BP, and ECG has shown no evidence of myocardial insult, bradycardia, or hypotension in any of the patients in any group in our study.

**Discussion**

In our study, we found that dexmedetomidine infusion 1.0 \(\mu g/kg\) before induction of anesthesia was more effective than esmolol infusion 1.5 \(mg/kg\) to attenuation in hemodynamic responses to laryngoscopy and tracheal intubation in normotensive patients.

Laryngoscopy and endotracheal intubation are considered as the most critical events in conducting general anesthesia.\(^1\) They provoke a transient and marked sympathoadrenal response resulting in tachycardia and hypertension.\(^2,3\) Various methods have been used to blunt these responses including inhalational anesthetic agents, lignocaine, opioids, calcium channel blockers, and direct-acting vasodilators.\(^4-6\) These methods have got side effects such as bradycardia, hypotension,

### Table 1: Distribution of study population by patients’ characteristics

| Parameters          | Group C  | Group D  | Group E  | P      |
|---------------------|----------|----------|----------|--------|
| Age (years)         | 31.46±9.0| 33.1±9.52| 30.86±8.65| >0.05  |
| Height (cm)         | 152.32±6.8| 152.80±4.4| 152.83±6.43| >0.05  |
| ASA status (I:II)   | 10:20    | 9:21     | 11:19     | -      |
| Weight (kg)         | 66.6±5.43| 64.26±5.43| 65.43±5.83| >0.05  |
| Sex (male:female)   | 21:9     | 16:14    | 18:12     | -      |
| MPG Class (I:II)    | 21:9     | 11:19    | 12:18     | -      |

ASA=American Society of Anesthesiologists, MPG=Mallampati Grading

### Table 2: Comparison of mean heart rate among three groups

| Time interval             | Mean HR (beats/min)±SD | P       | Difference between groups |
|---------------------------|------------------------|---------|--------------------------|
|                           | Group C                | Group D | Group E                  | C–D | C–E | D–E |
| Baseline                  | 89.53±10.6             | 88.5±10.75| 90.2±10.7 | 0.8250 | >0.5 | >0.5 | >0.5 |
| 5 min after starting infusion | 91.01±10.73           | 81.3±9.92 | 85.3±9.30 | <0.05  | <0.001| <0.05| >0.05 |
| Just before intubation    | 91.8±11.01             | 73.7±11.08| 83.6±11.03 | <0.001 | <0.001| <0.05| <0.05 |
| 1 min after intubation    | 109.06±13.17           | 78.8±13.20| 95.0±11.8 | <0.001 | <0.001| <0.001| <0.001 |
| 3 min after intubation    | 111.5±13.20           | 79.2±12.82| 93.3±13.5 | <0.001 | <0.001| <0.001| <0.001 |
| 5 min after intubation    | 106.3±11.82           | 75.4±11.06| 90.3±11.43 | <0.001 | <0.001| <0.001| <0.001 |
| 7 min after intubation    | 102.43±11.06          | 72.5±11.0 | 87.8±11.1 | <0.001 | <0.001| <0.001| <0.001 |
| 10 min after intubation   | 93.42±10.45           | 70.01±10.7 | 86.6±10.38 | <0.001 | <0.001| <0.001| <0.001 |

HR=Heart rate, SD=Standard deviation
sedation, and respiratory depression. Thus, the search for an ideal agent is continuing.

We compared the effect of dexmedetomidine 1 µg/kg IV and esmolol 1.5 mg/kg IV given as infusion over 10 min and observed the changes in HR, SBP, DBP, MAP, and RPP at 1, 3, 5, 7, and 10 min in these groups and also control group. All the three groups were comparable with regard to the demographic profile (age, weight, sex, etc.). All the patients enrolled belonged to ASA physical status Classes I and II, had Mallampati Class I and II, and were posted for routine noncardiac surgeries requiring general anesthesia. The three groups were also comparable (P > 0.05) regarding the time to laryngoscopy and intubation and baseline HR, SBP, DBP, and MAP values.

HR variability decreases with increasing age. Keeping it in view, patients between 20 and 55 years were considered in this study. Laryngoscopy has a linear relation with presser response during the first 48 s, and with further prolongation has little effect. Keeping it as a guide, laryngoscopy and intubation were limited to <20 s in this study.

Beta blockers have been used for blunting hemodynamic response to laryngoscopy and intubation. However, they blunt the HR response better than blood pressure response. Esmolol is an ultrashort-acting cardioselective beta blocker with rapid onset of action and short elimination half-life; these properties make it a valuable agent to obtund the cardiovascular response. It decreases the force of contraction and HR by blocking the beta-adrenergic receptors, thereby attenuating tachycardia and hypertensive response to intubation. It has been used in doses ranging from 0.5 to 2 mg/kg IV to provide hemodynamic stability during laryngoscopy and intubation in previous studies. Kindler et al. observed that esmolol administration in the doses of 1 and 2 mg/kg before laryngoscopy was sufficient to control HR after intubation but did not affect SBP. Sharma et al. concluded that esmolol in the dose of 1–1.5 mg/kg is most effective in controlling the response to laryngoscopy and intubation. Based on the above studies, we decided to administer esmolol at a dose of 1.5 mg/kg. Mercanooglu Efe et al. found that esmolol infusion was more effective than esmolol bolus on controlling systolic arterial pressure during both intubation and sternotomy, so we used esmolol as an infusion.

Recently, α-2 agonists such as clonidine and dexmedetomidine have been tried for attenuating response to intubation without any of the side effects. Dexmedetomidine is a direct α-2 adrenergic agonist with sedative, anxiolytic, analgesic, and sympatholytic effects. It is better than clonidine for suppressing the hemodynamic response to laryngoscopy and intubation because of higher selectivity to α-2 receptors (α-1:α-2 = 1:1620) than clonidine (α-1:α-2 = 1:220).

Dexmedetomidine acts on the α-2 adrenergic receptors located on sympathetic presynaptic terminals where they inhibit epinephrine and norepinephrine release. It decreases central sympathetic outflow by acting on locus coeruleus. Thus, it attenuates the hemodynamic response to intubation and also reduces intraoperative anesthetic agents and opioid requirements. Scheinin et al. used dexmedetomidine 0.6 µg/kg for attenuating response to intubation and found that it decreased but not totally suppressed the response. Lee et al. used dexmedetomidine at a dose of 1 mcg/kg and found that it suppressed the response to intubation. Bajwa et al. used dexmedetomidine 1 µg/kg and found similar results. We used dexmedetomidine 1 µg/kg as higher doses have been associated with the risk of bradycardia and hypotension. At the same time, we infused the drug as slow IV infusion over 10 min as rapid administration of dexmedetomidine has been reported to produce tachycardia and hypertension.

In our study, we observed that both dexmedetomidine and esmolol significantly attenuated the rise in HR after intubation compared to control group and dexmedetomidine suppressed the response to intubation more than esmolol. While comparing SBP, DBP, and MAP, we found that dexmedetomidine attenuated the rise in these parameters significantly up to 10 min after intubation, but there were no significant differences in values between esmolol and control groups, showing that dexmedetomidine showed greater hemodynamic stability than esmolol. Our findings were in accordance to the study by Reddy et al. who compared dexmedetomidine 1 µg/kg and esmolol 0.5 mg/kg to suppress the response to intubation. Srivastava et al. conducted a similar study in neurosurgical patients and found dexmedetomidine better. Gupta and Vyas and Selvaraj and Manoharan also observed similar results.

We also observed variations in the RPP in our study. RPP is the product of HR and SBP and is a better determinant of myocardial oxygen demand. Our observations revealed that RPP increased from baseline after intubation in all the three groups, but both dexmedetomidine and esmolol attenuated the rise in RPP significantly compared to control. Dexmedetomidine was more effective in suppressing this response compared to esmolol. Thus, dexmedetomidine group was hemodynamically more stable than esmolol group.

Our study had some limitations. First, adequate depth of anesthesia and neuromuscular blockade were monitored...
only by clinical observations. Use of bispical index and neuromuscular monitoring could have been a better guide. Second, hemodynamic changes associated with two stages, i.e., direct laryngoscopy and passage of tracheal tube, were not studied separately. Furthermore, we included only normotensive patients. Thus, further studies are awaited in the future.

**Conclusions**

We concluded that both dexmedetomidine and esmolol are effective in blunting the hemodynamic response to laryngoscopy and intubation when compared to control. Dexmedetomidine shows better hemodynamic stability when compared to esmolol.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970;42:618-24.
2. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth 1987;59:295-9.
3. Miller DR, Martinaeu RJ. Esmolol for control of haemodynamic responses during anaesthetic induction. Can J Anaesth 1989;36:S164-5.
4. Ebert JP, Pearson JD, Gelman S, Harris C, Bradley EL. Circulatory responses to laryngoscopy: The comparative effects of placebo, fentanyl, and esmolol. Can J Anaesth 1989;36:301-6.
5. Oxorn D, Knox JW, Hill J. Bolus doses of esmolol for the prevention of perioperative hypertension and tachycardia. Can J Anaesth 1990;37:206-9.
6. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and perioperative fentanyl. Br J Anaesth 1992;68:126-31.
7. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J Clin Anesth 1996;8:63-79.
8. Sharma S, Mitra S, Grover VK, Kalra R. Esmolol blunts the haemodynamic responses to tracheal intubation in treated hypertensive patients. Can J Anaesth 1996;43:778-82.
9. Kindler CH, Schumacher PG, Schneider MC, Urwyler A. Effects of intravenous lidocaine and/or esmolol on hemodynamic responses to laryngoscopy and intubation: A double-blind, controlled clinical trial. J Clin Anesth 1996;8:491-6.
10. Ghouse MS, Singh V, Kumar A, Wahal R, Bhatia VK, Agarwal J. A study of cardiovascular response during laryngoscopy and intubation and their attenuation by ultra-short acting β-blocker esmolol. Indian J Anaesth 2002;46:104-6.
11. Basar H, Akpinar S, Doganci N, Buyukkocak U, Kaymak C, Sert O, et al. The effects of preanesthetic, single-dose dexmedetomidine on induction, hemodynamic, and cardiovascular parameters. J Clin Anesth 2008;20:431-6.
12. Kunisawa T, Nagata O, Nagashima M, Mitamura S, Ueno M, Suzuki A, et al. Dexmedetomidine suppresses the decrease in blood pressure during anesthetic induction and blunts the cardiovascular response to tracheal intubation. J Clin Anesth 2009;21:194-9.
13. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011;55:352-7.
14. Bajwa SJ, Kaur J, Singh A, Parmar S, Singh G, Kulshreshtha A, et al. Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth 2012;56:123-8.
15. Jensen-Urstad K, Storek N, Bouvier F, Ericson M, Lindblad LE, Jensen-Urstad M, et al. Heart rate variability in healthy subjects is related to age and gender. Acta Physiol Scand 1997;160:235-41.
16. Bucx MJ, van Geel RT, Scheek PA, Sijstjn T. Cardiovascular effects of forces applied during laryngoscopy. The importance of tracheal intubation. Anaesthesia 1992;47:1029-33.
17. Moon YE, Lee SH, Lee J. The optimal dose of esmolol and nicardipine for maintaining cardiovascular stability during rapid-sequence induction. J Clin Anesth 2012;24:8-13.
18. Mercanooglu Efe E, Atabey Bilgin B, Alanoglu Z, Akbaba M, Denker C. Comparison of bolus and continuous infusion of esmolol on hemodynamic response to laryngoscopy, endotracheal intubation and sternotomy in coronary artery bypass graft. Rev Bras Anestesiol 2014;64:247-52.
19. Lee JH, Kim H, Kim HT, Kim MH, Cho K, Lim SH, et al. Comparison of dexmedetomidine and remifentanil for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation. Korean J Anaesthesiol 2012;63:124-9.
20. Reddy SV, Balaji D, Ahmed SN. Dexmedetomidine versus esmolol to attenuate the hemodynamic response to laryngoscopy and tracheal intubation: A randomized double-blind clinical study. Int J Appl Basic Med Res 2014;4:95-100.
21. Srivastava VK, Agrawal S, Gautam SK, Ahmed M, Sharma S, Kumar R, et al. Comparative evaluation of esmolol and dexmedetomidine for attenuation of sympathomimetic response to laryngoscopy and intubation in neurosurgical patients. J Anaesthesiol Clin Pharmacol 2015;31:186-90.
22. Gupta HB, Vyas S. A comparative study of efficacy of intravenous dexmedetomidine and intravenous esmolol for attenuation of stress response during laryngoscopy and endotracheal intubation. Int J Basic Clin Pharmacol 2016;5:1803-8.
23. Selvaraj V, Manoharan KR. Prospective randomized study to compare between intravenous dexmedetomidine and esmolol for attenuation of hemodynamic response to endotracheal intubation. Anesth Essays Res 2016;10:343-8.
24. Gobel FL, Norstrom LA, Nelson RR, Jorgensen CR, Wang Y. The rate-pressure product as an index of myocardial oxygen consumption during exercise in patients with angina pectoris. Circulation 1978;57:549-56.