Original Article

The comparison of the effects of dexmedetomidine versus esmolol to attenuate the hemodynamic response to endotracheal intubation

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Abstract

Background and Objectives: Laryngoscopy and intubation can cause hemodynamic response like tachycardia and hypertension. The objective of this study is to compare the effects of dexmedetomidine and esmolol on hemodynamic response during laryngoscopy and intubation. **Settings and Design:** A prospective, randomized, double-blind, comparative study. **Methods:** Sixty elective surgical patients of either sex who needed endotracheal intubation who were in American Society of Anesthesiology I–II group and ages between 20 and 60 years were included in this study. The patients were randomized into two groups: Group D (n = 30) 1 µg/kg dexmedetomidine with intravenously over 10 min, Group E (n =30) received 1mg/kg esmolol with intravenously over 10 mins and 3 min before induction. All patients were uniformly pre-medicated, induced and intubated using thiopentone and succinylcholine as per standard protocol. Systolic, diastolic, mean arterial pressures and heart rates were measured baseline, before induction, before intubation and 1, 3, 5, 10 min after intubation **Statistical analysis:** Analysis of variance and t-test as appropriate. **Results**: In group D, there was no statistically significant increase in HR and blood pressure after intubation at any time intervals when compared with the group E ($P < 0.001$) ,whereas in group E, there was a statistical significant increase in blood pressure after intubation at 1 and 3 min only and HR upto 5 min. **Conclusion:** Dexmedetomidine 1 µg/kg is more effective than esmolol 1mg/kg for attenuating the hemodynamic response to laryngoscopy and intubation.

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

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INTRODUCTION

Laryngoscopy and tracheal intubation are noxious stimuli that evoke a transient but marked sympathetic response manifesting as tachycardia, increase in blood pressure these response reaches its maximum level within 1 min and lasts for 5-10 mins. In patients with cardiovascular disease the hemodynamic changes may lead to life threatening complications including myocardial ischaemia, acute heart failure and cerebrovascular accidents[1] The degree of the reflex response of laryngoscopy and intubation is related with the deepness of anesthesia, patient's age and the presence of diabetes or heart disease. Narcotic analgesics, local anesthetics, beta-blockers, calcium canal blockers and vasodilators are employed in order to control that response.[2] Dexmedetomidine is a selective α2 adrenergic agonist. Its effects on cardiovascular system are particularly prominent.[3,4] α2- agonist produce hyperpolarization of noradrenergic neurons and suppression of neuronal firings in the locus cerelous leads to decreased systemic noradrenaline release results in attentuation of sympathoadrenal response and hemodynamic stability during laryngoscopy and tracheal intubation.[5] Esmolol is a ultrashort acting, beta-adrenergic receptor antagonist.[6] While it inhibits β1 receptors of myocardium, it also inhibits β2 receptors of smooth muscles of bronchial and vascular walls at higher doses.[7] In this study, we aimed to compare the effects of dexmedetomidine and esmolol on

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control of hemodynamic response due to laryngoscopy and endotracheal intubation.

MATERIAL AND METHODS

After approval of the study protocol by the Institutional Ethical Committee, written informed consent was obtained from each patient. 60 normotensive, ASA physical status I and II patients of either sex, aged 20-60 years, who were scheduled for elective non-cardiac surgery under general anesthesia (GA) requiring endotracheal intubation, were included in this study. All patients were thoroughly examined and routine investigations were carried out. The patients who refuses to consent, patients whose physical characteristics suggested difficulties in intubation (Mallampati grades III and IV), who had hypertension or cardiovascular, respiratory, neurological, psychological, endocrinal, hepatic, renal disease and who were using any cardiovascular medication, having history of alcohol abuse or drug allergies, pregnant and lactating patients were excluded from the study. Baseline (average of three readings) vital parameter of patients including HR, systolic arterial pressure (SAP), diastolic arterial pressure (DAP); mean arterial pressure (MAP) and oxygen saturation were recorded in the pre-operative ward. patients were taken to the operation theatre . In the operating room an IV line was secured with 18-G venous cannula and Ringer's lactate infusion (10 ml/kg/hr) was started. Routine standard monitors such as pulse oxymetry, electrocardiography (ECG) and non-invasive blood pressure were applied and monitoring started. All the patients were uniformly pre-medicated with IV ondansetron 0.08 mg/kg, glycopyrrolate 0.004 mg/kg and midazolam 0,02mg/kg iv 10 min before induction. The patients were randomized into two groups. These groups were determined with closed envelopes. The subjects were blinded to the treatment they received. The anaesthesiologists who prepared and administered the medications were provided to be different. group D (n=30) received 1 µg/kg dexmedetomidine diluted with 0.9% saline to 10 ml intravenously over 10 mins ,group E (n=30) received 1mg/kg esmolol diluted with 0.9% saline to 10 ml intravenously over 10 mins and 3min before induction. Then 6mg/kg thiopental and succinylcholine 2.0mg/kg was administered iv as per standard protocol .the patients were ventilated manually with 100% oxygen. Laryngoscopy was attempted 1min after the administration of succinylcholine with Macintosh curved blade number 4 ny an anaesthesiologist. The trachea was intubated with appropriate size-cuffed disposable ETtube. laryngoscopy and intubation was limited to 15-20sec in all patients, failure to intubate within this period was excluded from this study. After confirming the position and fixing the ET tube anaesthesia was maintained with 50% N2O (3L/min), 50% O2(3L/min) 1.5 MAC sevoflurane. Bolus iv dose of 0.08mg/kg followed by intermittent dose of 0.02mg/kg vecuronium was used for muscle relaxation. These parameters were measured and recorded before induction (*t*0), after induction (*t*1) before intubation (*t*2) and 1 (*t*3), 3(*t*4), 5 (*t*5) and 10 min (*t*6) after intubation in all patients. The measurements before induction (*t*0) were considered as basal levels. Surgical incisions were started following completion of the data collection process. The patients were ventilated in orderto maintain end tidal CO2 levels between 30-35 mmHg. at the end of surgery all patients were reversed with neostigmine 0.05mg/kg and glycopyrolate 0.008 mg/kg iv .patients were extubated after adequate recovery and then shifted to anaesthesia recovery room for 60 min following awakening and then were transferred to inpatient clinics.

Statistical Analysis

After the initial pilot observations, it was decided that a 20% of difference should be the minimum detectable difference of means in all groups. The standard deviation (SD) of residual was also kept same (20% of average difference between the groups). The α value was 0.05 and the power (1-a) of the study was 0.80. Thus, the calculated sample size for each group was 23 patients. Preserving the designing effect it was decided to include 30 patients in each group. Groups were compared for demographic data (age, weight) and hemodynamic parameters (HR, blood pressure) by one way analysis of variance and paired t-test was used for comparison among the groups, while for comparison within the groups unpaired t test was used. Probability was considered to be significant if less than 0.05. Data are represented as mean and SD.

RESULTS

All Cases were selected from general surgery only; all the 60 patients completed the study. The demographic profile of the patients in terms of age, body weight, male: female ratio, ASA status, Mallampati Class were comparable and there were no significant differences among the two groups ($P > 0.05$) [Table 1].

Table 1: Patient's characteristics

Variables Age (years)	Group D 45.73±8.79	Group E 45.13± 7.62	P value 0.7457
Weight (kg)	52.73±4.87	53.2±4.22	0.9345
Height (cm)	153.83±7.43	153.80±4.40	0.7547
BMI (kg/m2)	22.7±2.0	21.9±1.6	>0.05
Sex (male: female)	12:18	10:20	-
ASA status I/II	10/20	7/23	-
MP grade I/II	8/22	9/21	-
Baseline spo2	98.23±0.57	98.33±0.60	0.6481

Values are Mean±SD and numbers, BMI: body mass index; ASA: American society of anaesthesiologists; MP: Mallampati; SpO2: oxygen saturation; SD: standard deviation. The increase in mean HR after intubation was seen in all the two groups. But the mean increase was minimal 5.83% in Group D (4 beats, P= 0.0848), when compared with Group E 14% (9.81beats; P = 0.0152). Also, only in the Group D, there was no significant rise of HR at any time interval [Figure 1]

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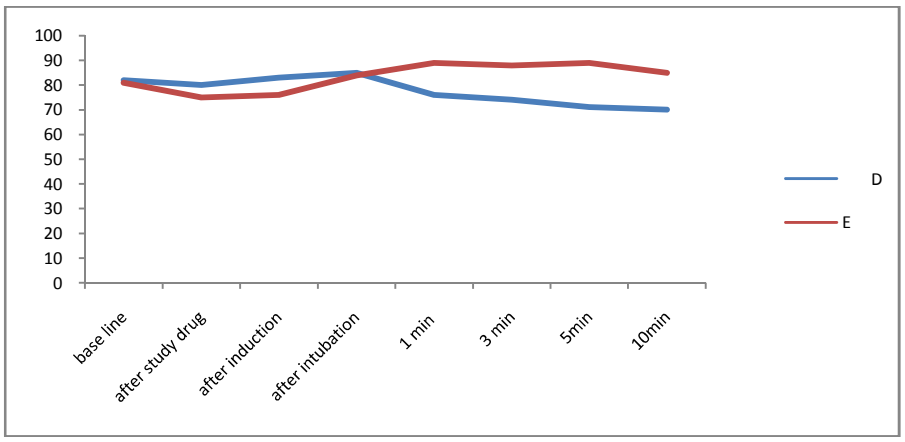

Figure 1: Mean heart rate of patients

The mean SAP levels in Group D were significantly lower than Group E immediately after intubation (P > 0.001) and until the end of surgery. Esmolol does not prevented the raise in SAP following intubation [Table 2].

Table 2: Comparison of SAP (mm of Hg) in the two groups

Variables	Group D	Group E	P value
Baseline	121.27±4.4	121.50±11.00	0.95
After study drug	127.43±15.09	130.60±17.42	0.57
After induction	123.80±13.80	115.03±12.37	0.0019
After intubation			
Immediately	125.27±18.59	158.00±12.15	0.0001***
1st min	116.90±12.68	147.83±21.90	0.0001***
3rd min	111.00±11.73	132.33±22.11	0.0001***
5th min	111.13±12.06	124.23±18.29	0.0005**
10th min	114.00±14.21	120.50±18.40	0.12

Values are mean±SD. *significant, **highly significant, ***extremely significant. SD: standard deviation; SAP: systolic arterial pressure

The DAP levels in Group D were significantly lower than Group E at all times after intubation. In esmolol group, there is a transient raise 21.4% (16.63 mm Hg) in DAP following intubation (P < 0.0001) at other times it remained below the baseline level [Table 3].

Table 3: Comparison of diastolic arterial pressure (mm of Hg) in the two groups

Variables	Group D	Group E	P value
Baseline	79.17±8.75	77.77±8.61	0.80
After study drug	81.40±13.90	77.50±8.36	0.13
After induction	78.10±13.44	72.33±10.48	0.048*
Immediately	80.37±16.22	94.40±10.82	<0.0001***
1st min	76.33±12.91	84.73±13.65	0.0023**
3rd min	71.73±12.19	76.77±8.92	0.003**
5th min	71.57±10.34	71.73±10.00	0.029*
10th min	70.67±11.85	70.70±9.68	0.14

Values are mean±SD. *significant, **highly significant, ***extremely significant. SD: standard deviation

The MAP was comparable in all the two groups at baseline level. The MAP decreased following induction, which was not significant in Group E (P = 0.088) and Group D (P = 0.3145). The MAP rose 26% (24.00 mm Hg) in Group E and only 2% (1.67 mm Hg) in Group D at intubation. The rise in MAP was significant after intubation in Group E (P < 0.05) which was not significant in Group D (P > 0.05) [Table 4].

Table 4: Comparison mean arterial pressure (mm Hg) level in two groups The rate pressure product (RPP) was calculated as the product of HR and SAP (RPP = HR × SAP)

Variables	Group D	Group E	P value
Baseline	93.70±6.66	92.63±7.82	0.8703
After study drug	96.57±13.72	94.87±11.80	0.2913
After induction	96.57±13.99	87.57±13.94	<0.0001***
After intubation			
Immediately	95.57±17.64	116.63±10.20	<0.0001***
1st min	90.90±11.81	105.83±15.14	<0.0001***
3rd min	84.77±12.27	95.30±12.52	<0.0002***
5th min	84.17±11.00	89.50±11.29	0.0091**
10th min	85.23±11.65	87.80±11.50	0.2693

Values are mean±SD. *significant, **highly significant, ***extremely significant. SD: standard deviation

In our study the RPP during intubation revealed a significant increase in Group E (49%, $P < 0.001$), whereas the increase was insignificant in Group D (16%, $P > 0.0666$). These changes were highly significant up to 10 min post-intubation. Although comparing Group E to Group D the increase in RPP in Group E at the time of intubation ($P < 0.001$) was statistically significant. The rise in mean RPP was least in Group D.

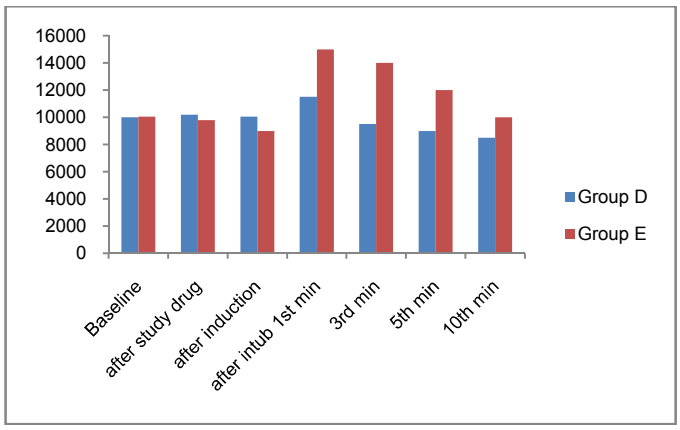

Figure 2: The comprehensive changes in rate pressure product of patients

DISCUSSION

In this study infusion of dexmedetomidine 1.0 µg/kg prior to induction of anesthesia suppressed the hemodynamic response to tracheal intubation in normotensive patients was found to be greater than that resulted from infusion of esmolol 1.0 mg/kg. The most frequent effects are cardiovascular hemodynamic responses characterized with hypertension, tachycardia, arrhythmia. cardiovascular hemodynamic responses carry risk for all patients who receive anesthesia that risk is more prominent in those who have cerebrovascular or coronary artery disease. Thus preventing the increase in sympathoadrenergic activity due to endotracheal intubation is an important aspect.[8] prophylaxis include topical lignocaine sprays, deeper planes of anaesthesia by inhalation agents; narcotics, calcium channel blockers, vasodilators such as sodium nitroprusside; nitroglycerine etc.[9] Dexmedetomidine is a selective α2 adrenergic agonist has sedative, anxiolytic, analgesic and sympatholytic effects that may blunt the cardiovascular response in the perioperative period without causing significant respiratory depression. Dexmedetomidine decreases arterial blood pressure and heart rate by reducing serum noradrenalin levels. Talke el al.[10] performed a placebo controlled study in vascular surgery and showed that dexmedetomidine caused less increase in heart rates and noradrenalin levels when administered at a dose of 0.8 µg/kg via intravenous infusion. Hall *et al.*[11] Yildiz *et al.*[12] found that a single dose of 1 µg/kg dexmedetomidine prevented cardiovascular hemodynamic response and decreased the need for additional opioid during laryngoscopy and endotracheal intubation in elective minor surgery patients. Scheinin *et al*[13] reported that 0.6 µg/kg dexmedetomidine decreased ,but not totally suppressed, the hemodynamic response to tracheal intubation in healthy individual. Keniya *et al* . stated that the pre treatment with dexmedetomidine 1.0 µg/kg attenuated ,but not totally obtuneded the cardiovascular response to tracheal intubation after induction of anaesthesia.[14] Ozkose *et al.*[15] administered a single dose of 1 µg/kg dexmedetomidine 10 min before induction. They reported that when compared with control measurements, mean arterial pressures decreased up to 20% and heart rates decreased up to 15% 1 and 3 min following intubation. They observed bradycardia that necessitated atropin administration in four of their 20 patients. The most common side effects of dexmedetomidine are hypotension and bradycardia that occur more frequently during loading period. We suggest that reducing loading dose and slowing infusion rate may prevent cardiovascular side effects. We administered dexmedetomidine with slow infusion in our study and observed no bradycardia nor hypotension in the patients. Similarly Venn *et al.*16 reported that these side effects were not observed when 2.5 µg/kg loading dose of dexmedetomidine was administered in 10 min and followed by an infusion rate of 0.2–0.5 µg/kg/min. In this study, we did not observe any significant differences in HR and arterial BP values between the baseline and post intubation values in the dexmedetomidine group, suggesting dexmedetomidine as an effective agent for blunting the hemodynamic response to laryngoscopy and intubation. Among the β2 adrenergic blocking drugs ,esmolol seems to be an appropriate selection for attenuating the hemodynamic response to laryngoscopy and tracheal intubation ,because of its cardioselectivity ,rapid onset of action and short elimination half-life.[17] Ugur *et al.*[18] used 1.5 mg/kg esmolol, 1 µg/kg fentanyl and 1.5 mg/kg lidocain 2 min before intubation and found that esmolol prevented the increase in heart rate. Hussain *et al.*[7] compared the effects of 2 µg/kg fentanyl and 2 mg/kg esmolol that were administered 2 min before laryngoscopy and intubation and also showed that esmolol prevented the increase in heart rate, but did not have any effect on blood pressure. Gupta *et al.*19 compared the effects of 2 mg/kg esmolol and 2 µg/kg fentanyl that were administered 3 min before anesthesia induction in order to prevent hemodynamic response in patients in whom elective surgical procedures were planned. They reported that a single dose of esmolol prevented the increase in blood pressure. Although esmolol is consider to have significant effect on both

tachycardia and hypertensive response following ET intubation, Oxorn *et al*[20]**.** Concluded that esmolol in bolus doses of 100mg and 200mg affects solely the chronotropic response in a significant manner. Kindler *et al*. found that esmolol administration before laryngoscopy was sufficient to control HR after intubation but it did not affect SAP[21]. Figueredo *et al*.[22] performed a meta-analysis of different esmolol doses and reported that infusion was more effective than single dose administration to prevent cardiovascular stress response. We used esmolol at a dose of 1 mg/kg in this study. We observed that this level was not adequate to prevent the hypertensive response as it was on attenuating the chronotropic response to tracheal intubation. In fact, a significant increase SAP and a transient raise in DAP was observed after intubation compared to the baseline values and when compared with dexmedetomidine the increase in SAP was greater and more significant in this study.

CONCLUSION

Evaluation of baseline and immediately after intubation values**,** revealed a greater percentage variation in MAP in the esmolol group as compared to the dexmedetomidine group. Therefore, within the constraints of this study we demonstrated that administration of a single dose of dexmedetomidine before GA induction was an effective method for attenuating the hemodynamic response to tracheal intubation.

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