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Research Article

A comparative study of efficacy of intravenous dexmedetomidine and intravenous esmolol for attenuation of stress response during laryngoscopy and endotracheal intubation

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ABSTRACT

Background: The present study compares the effects of I.V. dexmedetomidine and I.V. esmolol on hemodynamic response occurring due to laryngoscopy and endotracheal intubation in elective general surgery.
Methods: A total of 60 patients aged 18-60 years, American Society of Anesthesiologists physical status I or II, either sex, scheduled for elective surgical procedures were included in this study. Patients were randomly allocated by chit method into two equal groups of 30 each, comprising of group dexmedetomidine (group D) 1 µg/kg diluted with 0.9% saline to 10 ml I.V. over 10min and group esmolol (group E) 1 mg/kg diluted with 0.9% saline to 10 ml I.V. given just before induction. Heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were recorded at baseline, after 5 min of infusion, after induction and at 1, 3, 5 and 10 min after endotracheal intubation.
Results: In group D, there was no statistically significant increase in HR and blood pressure after intubation at any time intervals, where as in group E, there was a statistically significant increase in blood pressure and heart rate after intubation at 1, 3, 5 and 10 min.
Conclusions: Dexmedetomidine 1 µg/kg is more effective than esmolol for attenuating the hemodynamic response to laryngoscopy and intubation in elective surgical patients.

Keywords: Dexmedetomidine, Endotracheal intubation, Esmolol, Hemodynamic response

INTRODUCTION

Laryngoscopy and tracheal intubation are noxious stimuli that evoke transient but marked sympathetic response manifesting as an increase in the heart rate, blood pressure, intraocular and intracranial pressure. These changes are seen maximum immediately after intubation and last for 5 to 10 minutes.[1] Topical or intravenous (I.V.) lidocaine, opioids, inhaled anesthetics, vasodilators, calcium channel blockers or adrenergic blockers have been used successfully for decreasing the hemodynamic response to laryngoscopy.[2-7] Esmolol is a water soluble, rapid onset, ultra-short-acting, selective β adrenergic receptor antagonist with proven efficacy to provide hemodynamic stability during laryngoscopy and tracheal intubation.[2] It has a half-life of nine minutes.

Dexmedetomidine is an imidazole derivative and selective alpha α2 adrenergic receptor agonist.[8] α2-agonists produce hyperpolarization of noradrenergic neurons and suppression of neuronal firing in the locus ceruleus which leads to decreased systemic noradrenaline release resulting in attenuation of sympathoadrenal responses and hemodynamic stability during laryngoscopy and tracheal intubation.[9]

We conducted this study to compare the efficacy of esmolol and dexmedetomidine for attenuation of the

sympathomimetic response during laryngoscopy and intubation in patients undergoing elective procedures under general anaesthesia.

METHODS

After permission from institutional ethics committee, the prospective comparative randomized study was carried out in 60 patients, aged between 18 years and 60 years, of either gender, belonging to ASA class I or class II, posted for elective surgeries which were planned under general anaesthesia. The study was conducted from January 2013 to June 2014. Patients with anticipated difficult airway, laryngoscopy time more than 20 seconds, on preoperative β blockers, with history of asthma, hypertension diabetes, hepatic failure and renal failure, pregnant and lactating women were excluded from the study.

On the day prior to surgery a thorough clinical examination of the patient was performed including general physical examination and systemic examination. All patients were explained about the anaesthesia technique and written informed consent was taken. Patients were kept fasting for 8 hours prior to surgery.

Patients were randomly divided into 2 groups by chit method, each group consisted of 30 patients.

Group D (Dexmedetomidine group)

Group E (Esmolol group)

An I.V. line was secured with an appropriate sized cannula in all patients inside operation theatre & fluid was started @10-15ml/kg/hour. Patients was connected to multi-channel monitor and basal systolic blood pressure(SBP), diastolic blood pressure (DBP), Mean arterial pressure (MAP), heart rate, electrocardiography (ECG) and SpO_2 were recorded. Continuous monitoring of the vital parameters was done and injection glycopyrrolate 0.004 mg/kg I.V. was administered. The study drugs were premixed to a volume of 10ml and were presented by an anaesthesiologist not involved in the study.

Group D (dexmedetomidine group) patients were given I.V. dexmedetomidine 1µg per kg in 10ml normal saline infused over 10 mins before intubation and 10ml normal saline bolus over 30 sec just before induction. Group E (esmolol group) patients were given 10 ml normal saline infused over 10mins before intubation and I.V. esmolol 1mg per kg bolus over 30 sec just before induction. After 5 mins of stabilizing period SBP, DBP, MAP, Heart rate, SpO_2 were recorded.

Inj. fentanyl 1µg/kg IV was given in both the groups just before induction. All patients were pre-oxygenated with 100% O_2 for 3 min. Anesthesia was induced by inj. thiopentone 5 mg/kg I.V. in graded dose till loss of eye lash reflex, and after confirming ventilation, inj. vecuronium 0.1mg/kg was given to facilitate laryngoscopy and intubation. Each patient was ventilated with 40% O_2 and 60% N_2O and sevoflurane for 2 min, 30 secs and with 100% O_2 for 30 sec. At 2 mins after induction, SBP, DBP, MAP, heart rate, SpO_2 was recorded. Patients were intubated with appropriate size endotracheal tube within 20 sec, after conforming air entry bilateral equal, tube was fixed and secured.

Anesthesia was maintained with O_2 40% and N_2O 60% and intermittent boluses of inj. vecuronium as per requirement and addition of propofol infusion @ 2.5-5.5 mg/kg/hr which was started 10 min after intubation on controlled ventilation with closed circuit with circle absorber system. Heart rate, SBP, DBP, MAP, SpO_2 were measured at 1, 3, 5 and 10 minutes after intubation.

Any surgical interventions like catheterization, nasogastric tube insertion, incision was done 10 minutes after intubation to avoid disturbances in data recording. Patient was observed for any episode of bradycardia, hypotension and any other adverse events during surgery. Bradycardia (HR <50 beat/min) was treated with inj. atropine 0.6mg I.V. Any hypotension (SBP <20% baseline) was managed initially with a fluid bolus. If unresponsive inj. ephedrine 0.5-0.6 mg/kg I.V. in graded doses was given. At the end of surgery, when patients regained respiratory attempts, residual neuromuscular blockade was reversed with inj. neostigmine and inj. glycopyrolate. Recovery was assessed and extubation was carried out. After complete clinical recovery patients were shifted to post anesthesia care unit.

Statistical analysis

Mean and standard deviation for all values were calculated and compared within the group, with the base line values as well as inter group comparison were done. Paired and unpaired t- tests and chi square test were used for statistical analysis.

P-value < 0.05 was considered statistically significant. P value <0.001 was considered statistically highly significant.

RESULTS

Demographic data

There was no significant difference in demographic characteristics such as age, weight and sex and both the groups were comparable (Table 1).

Comparison of heart rate (beats/min) between esmolol and dexmedetomidine

Mean heart rate at baseline was 79.53 beats/min in group E which was comparable to 80.26 beats/min in group D and difference was not statistically significant. Same trend

was observed till the end of induction. After that the heart rate at 1 min, 3 min, 5min and 10 min after intubation was significantly lesser in the dexmedetomidine group as compared to the esmolol group and difference was statistically significant (Table 2).

Comparison of SBP (mmHg) between esmolol and dexmedetomidine

The mean SBP at baseline was 120.13 mmHg in group E which was comparable with 119.40 mmHg in group D and the difference was not statistically significant. Same trend was observed at 5 min of infusion and at induction. One minute after intubation mean SBP was 128 mmHg in group D which was significantly less as compared mean SBP of 155.80 mmHg in group E. This difference was statistically significant observed at 1 min. Similar differences were noted at 3 min, 5 min and 10 min after intubation (Table 3).

Comparison of DBP (mm Hg) between esmolol and dexmedetomidine

The mean DBP at baseline was 79.13 mmHg in group E which was comparable with 79.53 mmHg in group D and the difference was not statistically significant. Same trend was observed at 5 min of infusion and at induction.

At 1 min after intubation mean DBP was 82.06 mmHg in group D which was significantly less as compared to mean DBP 89.33 mmHg in group E. This difference in mean DBP was statistically significant at 1 min and 3 min. after intubation. However, mean DBP at 5 min and 10 min after intubation was comparable between group E and group D and the difference was statistically insignificant (Table 4).

Table 1: Demographic data.

Parameter	Esmolol (30)	Dexmedetomidine(30)	P value
Age (years)	41.71±5.42	43.45± 5.27	0.99.
Weight (kg)	53.46± 5.35	54.44 ± 4.51	0.99.
Gender	M:17 ; F:13	M:18 ; F:12	0.79

Table 2: Comparison of heart rate (beats/min) between esmolol and dexmedetomidine.

Parameter	Esmolol (30)	Dexmedetomidine (30)	P-value.
HR at baseline	79.53±3.39	80.26±2.44	0.38. (NS)
HR after 5 min of infusion	79.66±2.97	79.13±2.66	0.53. (NS)
HR at induction	77.60±2.64	76.80±2.75	0.22. (NS)
HR at 1 min after intubation	86.93±4.44	81.33±3.33	<0.0001. *
HR at 3 min after intubation	85.86±3.99	79.33±3.37	<0.0001. *
HR at 5 min after intubation	83.66±4.003	76.13±3.14	<0.0001. *
HR at 10 min after intubation	80.53±3.52	74.73±2.94	<0.0001. *

NS=Non significant *=Significant

Table 3: Comparison of SBP (mmHg) between esmolol and dexmedetomidine.

Parameter	Esmolol (30)	Dexmedetomidine (30)	P value.
SBP at Baseline	120.13 ± 4.03	119.40 ± 4.52	0.51. (NS)
SBP after 5 min of infusion	120.27 ± 3.92	119.80 ± 4.58	0.67. (NS)
SBP at induction	116.20 ± 3.29	116.07 ± 3.25	0.73. (NS)
SBP at 1 min after intubation	155.80 ± 9.53	128 ± 7.33	<0.0001. *
SBP at 3 min after intubation	146.80 ± 9.09	124.20 ± 6.33	<0.0001. *
SBP at 5 min after intubation	133.80 ± 7.88	119 ± 4.48	<0.0001. *
SBP at 10 min after intubation	120.27 ± 5.29	114.73 ± 3.61	<0.0001. *

NS = Non Significant * = Significant

Comparison of MAP (mmHg) between esmolol and dexmedetomidine

The mean MAP at baseline was 92.80 mmHg in group E which was comparable with 92.53 mmHg for group D and the difference was not statistically significant. Same trend was observed at 5min of infusion and at induction.

At 1 min after intubation mean MAP was 92.27 mmHg in group D which was significantly less as compared to mean MAP 111.49 mmHg in group E. The difference was statistically significant at 1 min, 3 min, 5 min and 10 min after intubation (Table 5).No patients in either group required treatment for bradycardia and hypotension. No other adverse effects were noted in any patient.

Table 4: Comparison of DBP (mmHg) between esmolol and dexmedetomidine.

Parameter	Esmolol (30)	Dexmedetomidine (30)	P value.
DBP at Baseline	79.13 ± 5.88	79.53 ± 4.59	0.5517. (NS)
DBP after 5 min of infusion	78.66 ± 5.39	79.33 ± 5.66	0.64. (NS)
DBP at induction	73.60 ± 5.13	76.53 ± 7.51	0.17. (NS)
DBP at 1 min after intubation	89.33 ± 6.65	82.06 ± 8.008	<0.0006. *
DBP at 3 min after intubation	80.26 ± 7.67	74.86 ± 8.26	<0.0081. *
DBP at 5 min after intubation	74.66 ± 5.68	71.86 ± 7.12	0.59. (NS)
DBP at 10 min after intubation	71.60 ± 5.71	69.26 ± 6.203	0.12. (NS)

NS = Non Significant * = Significant

Table 5:Comparison of MAP (mm Hg) between esmolol and dexmedetomidine.

Parameter	Esmolol (30)	Dexmedetomidine (30)	P value.
MAP at Baseline	92.80 ± 5.108	92.53 ± 4.62	0.79. (NS)
MAP after 5 min of infusion	92.53 ± 4.62	92.82 ± 4.60	0.80. (NS)
MAP at induction	87.80 ± 4.19	89.71 ± 5.25	0.12. (NS)
MAP at 1 min after intubation	111.49 ± 7.26	97.27 ± 5.41	<0.0001. *
MAP at 3 min after intubation	102.44 ± 7.76	91.31 ± 5.38	<0.0001. *
MAP at 5 min after intubation	94.37 ± 5.99	87.57 ± 4.88	<0.0001. *
MAP at 10 min after intubation	87.82 ± 5.39	84.42 ± 4.38	0.0127. *

NS = Non Significant * = Significant

DISCUSSION

The pressor response to laryngoscopy and endotracheal intubation in the form of tachycardia, hypertension and arrhythmias, though transient, may be potentially dangerous.[10] This response is due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. Transient hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular disease. These changes are the maximal at 1 minute after intubation and last for 5-10 minutes. Prophylaxis include topical lignocaine sprays, deeper planes of anaesthesia by inhalational agents; narcotics, calcium channel blockers, vasodilators such as sodium nitroprusside; nitroglycerin etc, but they have got side effects such as sedation, respiratory depression, hypotension and bradycardia.

The analgesic, sedation, anxiolytic, sympatholytic and blunting of exaggerated hemodynamic responses by administration of dexmedetomidine are being extensively studied and are mainly mediated by the activation of α-2 receptors located in the postsynaptic terminals in the central nervous system (CNS), which causes decreased neuronal activity and augmentation of the vagal activity. The role of α-2 agonists in regulating the autonomic and cardiovascular responses is well understood, whereby they inhibit release of catecholamines (norepinephrine) from the sympathetic nerve terminals by augmentation of a vasoconstrictive effect.[2,3]

Esmolol is water soluble, rapid onset, ultra-short-acting, selective beta adrenergic receptor antagonist with proven efficacy to provide hemodynamic stability during laryngoscopy and tracheal intubation.[2] It has a half-life of nine minutes and without severe side effects. It has been administered in various doses ranging from 0.5-2 mg/kg. Sharma et al in their study concluded that 1-1.5mg/kg is most effective in attenuating haemodynamic responses during laryngoscopy and intubation without major adverse effects.[11]

In this study infusion of dexmedetomidine 1.0 µg/kg prior to induction of anaesthesia suppressed the hemodynamic response to tracheal intubation in normotensive patients. This suppression in cardiovascular responses was found to be greater with dexmedetomidine infusion than with esmolol.

In the present study the haemodynamic response to laryngoscopy and intubation were studied for a period of 10 min as this is the average period for which haemodynamic changes are believed to last.[1] It was found that with this dose dexmedetomidine had better control over HR, SBP, DBP and MAP even after laryngoscopy and intubation. There was significant increase in heart rate and blood pressure from baseline after laryngoscopy and intubation in both groups, maximum rise in heart rate and blood pressure was noted at one minute after intubation but the rise in heart rate and blood pressure in dexmedetomidine group was significantly lower, less pronounced and shorter lasting as compared to esmolol group. On comparison between the two groups, the heart rate and blood pressure was better controlled with dexmedetomidine than esmolol after laryngoscopy and

intubation over period of 10 minutes. Similar result was seen in the Srivastava VK and Reddy SV et al.[12,13]

Similar result about dexmedetomidine to control HR and blood pressure after laryngoscopy observed in Lee JH et al, Bajwa SS et al and Efe EM et al study.[14-16]

Keniya VM et al study observed that bradycardia occurred in two patients in dexmedetomidine group intraoperatively.[17] Decrease in HR was observed in our study in permissible limit but none of our patients required treatment with atropine.

In contrast to present study result, Bajwa SS et al demonstrated that increase in HR and MAP for 3-5 min was observed after the start of dexmedetomidine infusion and was probably due to the vasoconstriction effect of dexmedetomidine appearing earlier than the central sympathetic action.[15]

Unlike HR and SBP, in DBP difference was statistically significant at 1 min and 3 min. after intubation and the groups were comparable at 5 min and 10 min. Similar result was seen in Reddy SV et al study.[13] In contrast, Dr Sagar Gandhi observed that DBP remain low in Dexmedetomidine group after intubation for period of 10 min.[18]

CONCLUSION

Thus we concluded that this randomized, observer blind study demonstrated that dexmedetomidine is an effective agent for blunting the hemodynamic response to laryngoscopy and tracheal intubation. There was significant less increase in hemodynamic parameter like HR, SBP, DBP and MAP from baseline after laryngoscopy and tracheal intubation in dexmedetomidine group as compared to esmolol. The difference was statistically significant and without any side effect. According to this study and various other study it is advisable and safe to use dexmedetomidine in patients to attenuate the hemodynamic responses of cardiovascular system during laryngoscopy and ET intubation. A study comparing dexmedetomidine with infusion of esmolol or esmolol bolus of 2 mg/kg which has been studied to be more effective than a bolus of 1mg/kg would be needed.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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