Original Research Article

Comparative study between intravenous clonidine versus intravenous dexmedetomidine for attenuation of pressor response during endotracheal intubation

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Abstract

Background: Laryngoscopy and tracheal intubation are noxious stimuli which evoke a transient but marked sympathetic response manifesting as increase in heart rate (HR) and blood pressure (BP). These changes can lead to life-threatening complications such as acute heart failure, myocardial ischemia, and cerebrovascular accidents. The present study was designed to compare the effects of IV dexmedetomidine and clonidine in attenuating the pressor response to laryngoscopy and endotracheal intubation. **Material and Methods:** Present study was single-center, pprospective randomized double blinded study, conducted in patients of 18-60 years age, either gender, with ASA physical status I/II, posted for surgery under general anaesthesia. 100 patients were selected and randomization was done by computer generated table. The anaesthesiologist administering drug and evaluating the patient was blinded to the drug injected. Group C [Clonidine group]: 1 microgram/kg iv in 100 ml normal saline over 10 mins. Group D [Dexmedetomidine group]: 1 microgram/kg iv in 100 ml normal saline over 10 mins. **Results: M**ean age, gender and mean weight between two groups was comparable, the difference was found to be statistically not significant. Mean baseline SBP, SBP/ DBP/HR/MAP/sPO_2 at the start of infusion, at 1 min, at 5 min, were comparable between two groups, the difference was not statistically significant ($p>0.05$). Mean SBP, DBP, MAP and HR in Group D was significantly lower as compared Group C. Mean HR, DBP and MAP at 10 minutes, after induction, at induction, at 1 minute after intubation between two groups, the difference was statistically significant ($p<0.05$). SBP and HR at after 3 minutes after intubation between two groups, the difference was statistically significant ($p<0.05$). **Conclusion:** IV Dexmedetomidine is superior and better drug compared to IV Clonidine to reduce hemodynamic response i.e. attenuation of pressure response to laryngoscopy and tracheal intubation with single premedication dose.

Keywords: Dexmedetomidine, Clonidine, attenuation of pressure response, laryngoscopy, tracheal intubation.

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INTRODUCTION

Laryngoscopy and tracheal intubation are noxious stimuli which evoke a transient but marked sympathetic response manifesting as increase in heart rate (HR) and blood pressure (BP). These changes are maximum immediately after intubation and last for 5–10 min. In patients with cardiovascular disease, these hemodynamic changes can lead to life-threatening complications such as acute heart failure, myocardial ischemia, and cerebrovascular accidents.[1] Conventional treatment methods include topical lignocaine sprays, deeper planes of anaesthesia by inhalational/intravenous (IV) agents or opioids, calcium

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channel blockers, and vasodilators such as sodium nitroprusside and nitroglycerine.[2] Premedication with clonidine, an α2-adrenergic agonist, has been recently shown to blunt the stress response to the surgical stimuli and reduce the narcotic and anesthetic requirements.[3] In addition, clonidine increases the cardiac baroreceptor reflex sensitivity to an increase in the systolic BP (SBP), and hence stabilizes the BP.[4,5] However, its mild selectivity to α2 adrenoceptors and long half- life has limited its use. Dexmedetomidine is a newer imidazole derivative which is a highly selective α2-adrenergic receptor agonist. [6] α2-agonists produce hyperpolarization of noradrenergic neurons and suppression of neuronal firing in the locus ceruleus leading to decreased systemic noradrenaline release. This results in attenuation of sympathoadrenal responses and hemodynamic stability during laryngoscopy and tracheal intubation.[7] The present study was designed to evaluate and compare the effects of IV dexmedetomidine and clonidine in attenuating the pressor response to laryngoscopy and endotracheal intubation.

MATERIAL AND METHODS

Present study was single-center, prospective randomized double blinded study, conducted in Department of Anaesthesiology, Vilasrao Deshmukh Government Medical College, Latur,, India. Study duration was of 18 months. Study was approved by institutional ethical committee.

Inclusion criteria: Patients of 18-60 years age, either gender, with ASA physical status I/II, posted for surgery under general anaesthesia

Exclusion criteria: Known to drug allergy. Patients with difficult intubation. Pregnant and nursing females. Not willing to participate.

All patients routine laboratory investigations like CBC, LFT, KFT, RBSL, ECG and CHEST XRAY done. Patients were explained the procedure of general anaesthesia and drugs profile during preanesthetic evaluation and informed consent obtained. All patients fasted for at least six hours before the procedure. Once the patient shifted to OT, IV access was secured with an 18G cannula and approximately 10 ml/kg of crystalloids were infused. Monitors ECG, NIBP and Spo2 probe were to be connected. Baseline Heart rate, SBP, DBF, and Spo2 were measured.

100 patients were selected and randomization was done by computer generated table. The anaesthesiologist administering drug and evaluating the patient was blinded to the drug injected.

Group C [Clonidine group]: 1 microgram/kg iv in 100 ml normal saline over 10 mins.

Group D [Dexmedetomidine group]: 1 microgram/kg iv in 100 ml normal saline over 10 mins.

Both the drugs were given in 100 ml ns infused over 10 minutes. Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), heart rate and SpO2 was noted after 5 mins of drug administration, and again at the completion of study drug infusion i.e., after 10 mins of drug administration. SBP, DBP, MAP, Heart rate, SpO2 were noted at 1st (Al 1st min), 3rd (Al 3rd min), 5th (Al 5th min), 7th (Al 7th min) and 10th minute after laryngoscopy and intubation. Anaesthesia was maintained on N20+ O2, Isoflurane, Vecuronium and analgesics. Data was collected by using a structure proforma. Data thus was entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of percentages and proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square/Fischer's exact test. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

RESULTS

Mean age of patients from Group C was 36.55±9.09 years and that of Group D was 38.82±10.45 years. When we compared the mean age between two groups, the difference was found to be statistically not significant (p>0.05) Proportion of males in Group C were 38% and that of Group D were 32% Proportion of females in Group C were 62% and that of Group D were 34%. Mean weight of patients from Group C was 56.98±7.97 kgs and that of Group D was 57.36±6.18 kgs, the difference was found to be statistically not significant (p>0.05)

Table 1: General characteristics

Characteristics	Group C		Group D		P value
	Frequency	Percent	Frequency	Percent	
Age group (years)					
20-30	13	26.0	14	28.0	
31-40	22	44.0	13	26.0	
41-50	12	24.0	17	34.0	
51-60	3	6.0	6	12.0	
Mean age (years)	36.55 ± 9.09		38.82 ± 10.45		0.252
Gender					

Male	19	38.0	16	32.0	
Female	31	62.0	34	68.0	
Mean weight (kgs)	56.98 ± 7.97		57.36 ± 6.18		0.790

Mean baseline SBP, SBP/ DBP/HR/MAP/sPO_2 at the start of infusion, at 1 min, at 5 min, were comparable between two groups, the difference was not statistically significant ($p>0.05$). Mean SBP, DBP, MAP and HR in Group D was significantly lower as compared Group C. Mean HR, DBP and MAP at 10 minutes between two groups, the difference was statistically significant ($p<0.05$).

Table 2: Comparison of parameters at 10 minutes

At 10 minutes	Group C	Group D	p value	Inference
SBP	119.12 ± 7.10	115.48 ± 10.42	0.044	Significant
DBP	75.40 ± 6.82	69.88 ± 6.73	0.0001	Highly significant
HR	85.72 ± 6.99	72.84 ± 9.27	0.0001	Highly significant
MAP	89.97 ± 5.77	85.28 ± 6.78	0.0001	Highly significant
SPO_2	100.00	100.00	0	Not Significant

SBP, DBP, MAP and HR was significantly lower in Group D as compared to Group C. Mean SBP, DBP, MAP and HR at after induction between two groups, the difference was statistically significant ($p<0.05$).

Table 3: Comparison of parameters after induction

after induction	Group C	Group D	p value	Inference
SBP	110.40 ± 7.89	105.92 ± 9.76	0.013	Significant
DBP	70.16 ± 7.56	61.68 ± 5.59	0.0001	Highly significant
HR	80.00 ± 7.03	66.16 ± 8.49	0.0001	Highly significant
MAP	83.57 ± 6.40	76.63 ± 5.36	0.0001	Highly significant
SPO_2	100.00	100.00	0	Not Significant

SBP, DBP, MAP and HR was significantly lower in Group D as compared to Group C immediately after intubation. When we compared the mean SBP, DBP, MAP and HR at after intubation between two groups, the difference was statistically significant ($p<0.05$).

Table 4: Comparison of parameters after intubation

after intubation	Group C	Group D	p value	Inference
SBP	147.36 ± 7.28	122.80 ± 7.84	0.0001	Highly significant
DBP	95.64 ± 3.44	74.00 ± 6.02	0.0001	Highly significant
HR	86.68 ± 6.84	81.76 ± 7.08	0.0001	Highly significant
MAP	112.92 ± 3.74	90.40 ± 5.71	0.0001	Highly significant
SPO_2	100.00	100.00	0	Not Significant

SBP, DBP, MAP and HR was significantly lower in Group D as compared to Group C. When we compared the mean SBP, DBP, MAP and HR at after 1 minute after intubation between two groups, the difference was statistically significant ($p<0.05$).

Table 5: Comparison of parameters after 1 minute after intubation

after 1 minute after intubation	Group C	Group D	p value	Inference
SBP	148.56 ± 7.02	124.60 ± 8.03	0.0001	Significant
DBP	96.72 ± 2.28	75.64 ± 6.16	0.0001	Highly significant
HR	89.16 ± 6.42	83.98 ± 6.40	0.0001	Highly significant
MAP	114.00 ± 3.10	92.09 ± 5.82	0.0001	Highly significant
SPO_2	100.00	100.00	0	Not Significant

SBP and HR was significantly lower in Group D as compared to Group C. When we compared the mean SBP and HR at after 3 minutes after intubation between two groups, the difference was statistically significant ($p<0.05$).

Table 6: Comparison of parameters after 3 minutes after intubation

after 3 minute after intubation	Group C	Group D	p value	Inference
SBP	123.04 ± 6.49	118.12 ± 7.42	0.0001	Highly significant
DBP	69.64 ± 6.37	70.20 ± 6.01	0.652	Not Significant
HR	87.88 ± 6.07	78.48 ± 6.41	0.0001	Highly significant
MAP	87.44 ± 5.45	86.31 ± 5.46	0.30	Not Significant
SPO_2	100.00	100.00	0	Not Significant

HR was significantly lower in Group D as compared to Group C. When we compared the HR at after 5 minutes after intubation between two groups, the difference was statistically significant ($p<0.05$).

Table 7: Comparison of parameters after 5 minutes after intubation

after 3 minute after intubation	Group C	Group D	p value	Inference
SBP	113.64 ± 6.61	113.16 ± 6.40	0.713	Not Significant
DBP	65.28 ± 6.22	65.92 ± 5.21	0.578	Not Significant
HR	87.64 ± 6.38	73.86 ± 6.06	0.0001	Highly significant
MAP	81.40 ± 5.36	81.80 ± 4.33	0.683	Not Significant
SPO_2	100.00	100.00	0	Not Significant

HR was significantly lower in Group D as compared to Group C. When we compared the HR at after 10 minutes after intubation between two groups, the difference was statistically significant ($p<0.05$).

Table 8: Comparison of parameters after 10 minutes after intubation

after 10 minute after intubation	Group C	Group D	p value	Inference
SBP	113.16 ± 6.10	111.72 ± 6.55	0.258	Not significant
DBP	65.60 ± 5.86	67.16 ± 5.64	0.178	Not significant
HR	75.80 ± 12.83	71.40 ± 6.22	0.031	Significant
MAP	81.45 ± 5.02	82.15 ± 4.84	0.484	Not significant
SPO_2	100.00	100.00	0	Not Significant

SBP, DBP, MAP and HR was significantly lower in Group D as compared to Group C. When we compared the mean SBP, DBP, MAP and HR at after 15 minutes after intubation between two groups, the difference was statistically significant ($p<0.05$).

Table 9: Comparison of parameters after 15 minutes after intubation

after 15 minute after intubation	Group C	Group D	p value	Inference
SBP	116.28 ± 5.17	109.48 ± 7.63	0.0001	Highly significant
DBP	71.72 ± 5.30	68.40 ± 6.82	0.008	Significant
HR	74.38 ± 12.71	66.94 ± 5.89	0.0001	Highly significant
MAP	86.57 ± 4.46	82.16 ± 6.14	0.0001	Highly significant
SPO_2	100.00	100.00	0	Not Significant

DISCUSSION

Studies have been done to evaluate the effects of clonidine and dexmedetomidine on the hemodynamic response during laryngoscopy and tracheal intubation. α2-adrenergic agonist has been shown to be beneficial in preventing cardiac complications, however, a recent meta-analysis did not show mortality benefit in cardiac patients.[8] It is evident that clonidine brings about bradycardia, hypotension, reduction in systemic vascular resistance (SVR) and cardiac output.[9] It is considered to be a potent antihypertensive drug. Clonidine also prohibits vasopressin and catecholamines secretion and modulates the hemodynamic changes induced by laryngoscopy and in pneumoperitoneum. While Dexmedetomidine has additional advantage of having anxiolytic and sedative property making it popular among Anaesthesiologists.[10] K. Selvarju *et al.*,[11] reported mean age as 38.4+9.32 in Group D and 37.8+10.1 Group C. Mean weight from Group D was 57.1+9.9 kg and from Group C was 58.3+10.56 kg which is similar to our findings. Mean SBP, DBP, MAP and HR was significantly lower in Group D as compared to Group C after induction, immediately after intubation, after 1 minute, 3 minutes, 5 minutes, 10 minutes and 15 minutes. So Dexmedetomidine is superior than Clonidine in reducing SBP, DBP, MAP and HR. Sarkar *et al.*,[12] reported that mean systolic blood pressure in Group D and Group C were significantly lower (<0.01) than group P. However, at all the subsequent intervals, Group D was significantly lower as compared to Group C which is similar to our findings. Singh S *et al.*,[2] observed that the mean SBP (mm Hg) in group II (Dexmed) was 122.6, and in group III (Clonidine) was 127.4, DBP (mm Hg) was 76.2 in group I, 78.4 in group II and 78.2 in group III. MAP (mm Hg) was 93.2 in group II and 92.5 in group III. HR (bpm) was 78.4 in group II and 77.3 in group III. % oxygen saturation was 98.5 in group II and 97.9 in group III. The difference was non- significant (P> 0.05). These findings are against findings of our study. Sebastian *et al.*,[13] in their study reported that statistically significant difference was found between dexmedetomidine and normal saline in heart rate, systolic, diastolic and mean arterial pressures at all time points after tracheal intubation with dexmedetomidine 0.75 µg/kg dose was most effective which is consistent with our study findings. Saoyroolu AE, *et al.*,[14] compared the clinical effects of two different doses of Dexmedetomidine (1 µg/kg and 0.5µg/kg) on hemodynamic responses of tracheal intubation and concluded that Dexmedetomidine in dose of 1 µg/kg was more effective than dexmedetomidine 0.5µg/kg. Scheinin, *et al.*,[15] reported that the use of α2-agonist leads to bradycardia. Belleville, *et al.*87 found that the dexmedetomidine given in 2 min in the doses of 1–2 µg/kg causes irregular ventilation and apnea episodes. Ebert, *et al.*88 did not observe any episode of apnea, airway

obstruction and hypoxemia with bolus doses of dexmedetomidine in their study, and they reported that the depression of respiration may be seen due to deep sedation, for the reason that the α2 adrenergic agonists don't have an active role on the respiration center. They noted that dexmedetomidine causes significant reduction in circulating catecholamine with a decrease in blood pressure and heart rate. Yildiz M, *et al.*,[16] and Varshali M K, *et al.*,[17] studied the effect of dexmedetomidine on hemodynamic response to laryngoscopy and intubation and intraoperative anaesthetic requirement. They concluded that increase in blood pressure and heart rate were significantly less in dexmedetomidine group. When dexmedetomidine premedication was compared to clonidine, a significant control of blood pressure and heart rate within a normal range was observed in the present study. Various other studies have also concluded that dexmedetomidine is effective in keeping the patient hemodynamically stable during laryngoscopy and intubation as well as throughout the intraoperative period.[16,17]

CONCLUSION

On basis of our study we can conclude that IV Dexmedetomidine 1 µg/kg in 100 ml normal saline is superior and better drug compared to IV Clonidine 1 µg/kg in 100 ml normal saline to reduce hemodynamic response i.e. attenuation of pressure response to laryngoscopy and tracheal intubation with single premedication dose.

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