Original Research Article

A comparative study of dexmedetomidine versus clonidine to attenuate the hemodynamic response to laryngoscopy and endotracheal intubation

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Abstract

Background: General anaesthesia is gold standard and carried out with laryngoscopy and endotracheal intubation. Laryngoscopy and endotracheal intubation are associated with critical events because it accentuates significant sympatho-adrenal response in the form of tachycardia and hypertension. This study was carried out to compare the effect of single dose of clonidine and dexmedetomidine to suppress pressor response to laryngoscopy and endotracheal intubation. **Material and Methods:** Present study was prospective double blind randomized single center clinical study, conducted in patients of age group 18-60 years belonging to ASA status I/II, MPG I/II, who was posted for elective surgery under GA, willing to participate in study. **Results:** The mean age in group I was 36.16 ± 9.86 and in group II was 33.83 ± 10.22. p value is 0.3725. Females predominated in both groups and are comparable in both groups. General Characteristics such as age (years), Sex (M/F), Weight(kg), ASA (I/II) and Surgeries were comparable in both groups, difference was not statistically significant. In group Dexmedetomidine significant reduction in pulse rate compare to Clonidine group. Also pulse rate compared to base line is significantly reduced in dexmedetomidine group. In group Dexmedetomidine significant reduction in systolic blood pressure compare to Clonidine group. Also changes in systolic blood pressure compared to base line was significantly reduced in dexmedetomidine group. Ramsey sedation score after 3 min end of test dose was statistically significant in Dexmedetomidine group as compared to clonidine group. The mean dose of thiopentone sodium (mg) required for loss of eye lash reflex in group I and Group II were 302.5±56.22 and 355.8±82.96 respectively and it was statistically highly significant decrease in dose of thiopentone sodium required for induction in dexmedetomidine group. Intraoperative (bradycardia) and post-operative complication (Post op nausea and vomiting and dryness of mouth) were observed in both groups, which was statistically not significant. **Conclusion:** Dexmedetomidine is better in position when compared to clonidine for attenuation of pressor response to laryngoscopy and endotracheal intubation and also decreases requirement of thiopentone sodium for induction of general anaesthesia

Keywords: Dexmedetomidine, clonidine, attenuation of pressor response, general anaesthesia.

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Received Date: 04/06/2021 Revised Date: 10/07/2021 Accepted Date: 13/08/2021
DOI: https://doi.org/10.26611/10152017

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Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 12 October 2021

INTRODUCTION

General anaesthesia is gold standard and carried out with laryngoscopy and endotracheal intubation. Laryngoscopy and endotracheal intubation are associated with critical events because it accentuates significant sympatho-adrenal response in the form of tachycardia and hypertension. These responses can be detrimental in elderly and hemodynamically compromised patients due to increase in arterial pressure, heart rate and oxygen consumption. Therefore controlling this perioperative stress response is an important goal of modern anaesthesia.[1,2,3] Many pharmacological methods were evaluated either in premedication or during induction to attenuate these

How to site this article: Sachin Madhukar Kumbhar, V V Kulkarni, Shriganesh Kamat. A comparative study of dexmedetomidine versus clonidine to attenuate the hemodynamic response to laryngoscopy and endotracheal intubation. *MedPulse International Journal of Anesthesiology.* October 2021; 20(1):28-32. http://medpulse.in/Anesthsiology/index.php

adverse hemodynamic responses but the drugs which were used where either partially effective or they produced other undesirable effects. Dexmedetomidine is more potent α-2 receptor agonist when compared to clonidine. So, Dexmedetomidine is better drug of choice among α-2 receptor agonist to suppress deleterious hemodynamic response to laryngoscopy and endotracheal intubation.[4] Though Dexmedetomidine is costly compared to clonidine, it significantly reduces drug requirement of anaesthetic agent with better haemodynamic blunting response to laryngoscopy and intubation.[5] Various Studies are done with different doses of Dexmedetomidine and Clonidine.[4,6] Sagiroglu *et al.*,[6] conducted study with different doses of dexmedetomidine to control hemodynamic responses to intubation and he found that dexmedetomidine 1 µg /kg is more effective than 0.5 µg/kg without any side effects. The effects of clonidine on the hemodynamic variables are dose related but this dose of Clonidine (1 µg /kg) was consider appropriate to provide adequate clinical effects.[7] This study was carried out to compare the effect of single dose of clonidine and dexmedetomidine to suppress pressor response to laryngoscopy and endotracheal intubation.

MATERIAL AND METHODS

Present study was prospective double blind randomized single centre clinical study, conducted in Department of Anaesthesiology, Dr V M Government Medical College, Solapur, India. Study duration was of 2 years (July 2018 to June 2019). Study was approved by institutional ethical committee.

Inclusion criteria: patients of age group 18-60 years belonging to ASA status I/II, MPG I/II, who was posted for elective surgery under GA, willing to participate in study.

Exclusion criteria: ASA grade III, IV and V. Age More than 60 years. Patient on anti-hypertensive. Patient with difficult airway.

Written informed consent of the patient has been taken after explaining the anaesthesia technique. Patient under the study was undergone through preanesthetic evaluation including detailed history, clinical examination and necessary investigation depending on ages, sex, disease of patient. Pre-operative, Xylocaine sensitivity test (XST) was done and patients were kept nil per oral for 6 hrs. before surgery

In present study, 60 patients were selected and were randomly divided into two groups.

- Group-1 Dexmedetomidine 1 Mcg /Kg diluted up to 10 cc over 10 min.
- Group-2 Clonidine 1 Mcg/Kg. diluted up to 10 cc over 10 min.

On arrival in the anaesthetic room, heart rate, oxygen saturation and non-invasive blood pressure monitoring will be instituted. Premedication: All patients of both Groups were premedicated with Inj. Ranitidine 1 mg/kg and Inj. Metoclopramide 0.2mg/kg body weight intravenously. Inj. Glycopyrrolate 0.004mg/kg body weight were given intravenously 20 minutes before IV premedication. All patients were preoxygenated with 100% oxygen for 5 minutes. prior to induction.

Anaesthesia were induced with Inj. Thiopentone till loss of eyelash reflex. Succinylcholine 2mg/kg body weight were given for relaxation. Patient were intubated with appropriate size cuffed endotracheal tube. Anaesthesia were maintained on 0_2(50%), N_{20}(50%) and Isoflurane (0.5-1%). Any intraoperative complications such as hypotension, bradycardia, Airway obstruction, Regurgitation and Laryngospasm or postoperative complications such as delayed recovery, Hoarseness of voice and sore throat, hypotension, bradycardia if occurred were noted. After surgery, neuromuscular block was antagonized with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). and extubated after deflating the cuff when the patient regained consciousness and protective airway reflexes. All the above recorded observations were compared statistically and the results were analysed and concluded. Quantitative data was analyzed by student 't' test and qualitative data was

RESULTS

The mean age in group I was 36.16 $\pm$ 9.86 and in group II was 33.83 $\pm$ 10.22. p value is 0.3725. Females predominated in both groups and are comparable in both groups. General Characteristics such as age (years), Sex (M/F), Weight(kg), ASA (I/II) and Surgeries were comparable in both groups, difference was not statistically significant.

Table 1: General Characteristics

Characteristics	Group I	Group II	P-value
Age (years)	36.16 ± 9.86	33.83 ± 10.22	0.0786
Sex (M/F)	8/22	13/17	0.1770
Weight(kg)	53.2 ± 6.82	54.5 ± 6.63	0.3308
ASA (I/II)	24/6	26/4	
Surgeries			
Fibroadenoma Excision	3 (10 %)	4 (13.33%)	
Lipoma Excision	2 (6.66%)	2 (6.66%)	

cholecystectomy	6 (20 %)	4 (13.33%)
laminectomy	4 (13.33%)	3 (10 %)
FESS	4 (13.33%)	4 (13.33%)
mastoidectomy	4 (13.33%)	4 (13.33%)
LAVH	2 (6.66%)	2 (6.66%)
thyroidectomy	2 (6.66%)	4 (13.33%)
Parotid excision	1 (3.33%)	1 (3.33%)
MRM	2 (6.66%)	2 (6.66%)

Mean pulse rates in both groups at baseline before test dose, after 3 min test dose, after induction, during intubation, after intubation 1min,3min,5min,10min wear recorded. In group Dexmedetomidine significant reduction in pulse rate compare to Clonidine group. Also pulse rate compared to base line is significantly reduced in dexmedetomidine group.

Table 2: comparison of Changes in PR at Various Term Periods

	Group I		Group II		P-Value
Time	Mean ±SD	% Change from baseline	Mean ± SD	% Change from baseline	
Basal	79.93+8.09	-	81.86±9.91	-	0.409
After study drug	76.1+7.29	↓4.79	81.96+8.50	↑0.12	0.001
At induction	73.2+6.95	↓8.41	87.1+8.51	↑6.01	0.001
At intubation	74.53+6.16	↓6.75	90.2+8.89	↑9.24	0.001
1 min after intubation	72.33+6.81	↓9.5	86.36+8.75	↑5.2	0.001
3 min. after intubation	71.63+6.69	↓10.38	87.26+8.78	↑6.2	0.001
5min after intubation	70.93+6.48	↓11.25	87.13+841	↑6.04	0.001
10 min after intubation	73.44+4.79	↓8.11	87.81+9.31	↑6.7	0.003

In group Dexmedetomidine significant reduction in systolic blood pressure compare to Clonidine group. Also changes in systolic blood pressure compared to base line was significantly reduced in dexmedetomidine group.

Table 3: Comparison of changes in systolic blood pressure (SBP)

	Group I		Group II		P-Value
Time	Mean ±SD	% Change from baseline	Mean ± SD	%Change from baseline	
Basal	122.73+11.11	-	121.06+8.56	-	0.516
After test dose 3 min	114.13+10.30	↓7.0	129.4+8.94	↑5.1	0.0001
At induction	112.26+9.37	↓8.5	130.2+8.12	↑5.7	0.0001
At intubation	133.1 ±0.9132	↑7.79	140.3 ±1.283	↑13.52.	<0.001
1 min after intubation	111.06+9.19	↓9.50	130.2+8.12	↑7.01	0.0001
3 min. after intubation	109.72+8.25	↓10.60	130.53+6.94	↑7.25	0.0001
5min after intubation	108.66+8.36	↓12.94	130.5+7.98	↑7.2	0.0001
10 min after intubation	109+1.41	↓11.18	128.6+8.08	↓5.8	0.0001

In group Dexmedetomidine significant reduction in diastolic blood pressure compare to Clonidine group. Diastolic blood pressure compared to base line was significantly reduced in dexmedetomidine group.

Table 4: Comparison of changes in mean diastolic blood pressure (DBP)

	Group I		Group II		P-Value
Time	Mean ±SD	% Change from baseline	Mean ± SD	% Change from baseline	
Basal	78.06±6.65	-	75.26±5.23	-	0.075
After 3 min test dose	73.8±6.75	↓5.4	80.66±6.11	6.6	0.0001
At induction	71.2±6.86	↓8.78	82.8±6.48	9.10	0.001
At intubation	73.33±4.61	↓6.05	86.033±5.48	↑12.51	0.0001
1 min after Intubation	69.2±5.47	↓11.3	83.33±1.306	↑9.68	0.0001
3 min. after intubation	69.06±6.57	↓11.5	83.33±5.31	↑9.68	<0.0001
5min after intubation	68.96±5.77	↓11.65	84.13±4.03	↑10.54	<0.0001
10 min after intubation	70.22±4.52	↓9.97	84.37±3.36	↑10.7	<0.0001

In group Dexmedetomidine group significant reduction in mean arterial pressure compare to Clonidine group. Also percent changes in mean arterial pressure compared to base line was significantly reduced in dexmedetomidine group.

Table 5: Changes in MAP at Various Term Periods

Time	Group I		Group II		P-Value
	Mean ±SD	% Change from baseline	Mean ± SD	% Change from baseline	
Basal	92.95 ± 7.87	-	90.53 ± 5.96	-	0.075
After 3 min test dose	88.55 ± 7.482	↓4.7	95.99 ± 6.994	5.68	0.0001
At induction	88.55± 7.48	↓4.7	96±6.99	5.69	0.001
At intubation	89.54 ± 5.070	↓3.6	101.60 ±6.032	↑10.89	0.0001
1 min after intubation	85.73±7.54	↓7.76	98.33 ± 7.002	↑7.93	0.0001
3 min. after intubation	85.73±7.54	↓7.76	98.95 ± 5.88	↑8.5	<0.0001
5min after intubation	83.06±7.11	↓10.64	98.95 ± 5.88	↑8.5	<0.0001
10 min after intubation	82.55±6.26	↓11.18	99.6 ± 4.63	↑9.1	<0.0001

Ramsey sedation score after 3 min end of test dose was statistically significant in Dexmedetomidine group as compared to clonidine group. The mean dose of thiopentone sodium (mg) required for loss of eye lash reflex in group I and Group II were 302.5±56.22 and 355.8±82.96 respectively and it was statistically highly significant decrease in dose of thiopentone sodium required for induction in dexmedetomidine group. Intraoperative (bradycardia) and post-operative complication (Post op nausea and vomiting and dryness of mouth) were observed in both groups, which was statistically not significant.

Table 5: other characteristics

	Group I	Group II	P value
Ramsey sedation score after 3 min end of test dose	2.866+0.7302	2.366+0.85028	0.0176
Total Dose of Inj. Thiopentone (2.5%)	302.5±56.22	355.83±82.96	.0051
intra operative Complications - Bradycardia	1	0	-
Post-operative Complications			
PONV	3	4	-
Dryness of mouth	1	1	-

DISCUSSION

Two predictors of perioperative cardiac morbidity are increase in heart rate and blood pressure. Increase in heart rate and acute hypertension deleteriously affect myocardial oxygen supply and demand. Different techniques are being tried to prevent or attenuate the hemodynamic effects following laryngoscopy and tracheal intubation, like deepening of anaesthesia, avoiding anticholinergic drugs prior to surgery, pre-treatment with lignocaine, vasodilators like nitroglycerin, beta blockers, calcium channel blockers and opioids. Baseline pulse rate in both groups were comparable and there was no statistically difference. Baseline pulse rate as group I and group II were 79.93+8.09 and 81.85+9.91 respectively. Similar to our study Bijoy Kumar *et al.*,[4] and Shirsendu *et al.*,[8] who have done comparison of clonidine and Dexmedetomidine and have also found fall in HR after its infusion. Scheinin *et al.*,[9] reported that use of α2 agonist leads to bradycardia, not significant with present study. During intubation there was rise in pulse rate in both the groups which was more in Group II compare to Group I and this rise in PR in group II was statistically significant Similar to our result Shrisendu *et al.*,[8] has also found statistically significant rise in PR during intubation in clonidine group compare to dexmedetomidine. In his study this statistically significant higher PR in clonidine group last upto 3 min after intubation.

In our study, after intubation there was statistically significant difference in PR between two groups. Bijoy Kumar *et al.*,[4] in his study found rise in PR after intubation with only clonidine but not with Dexmedetomidine. A biphasic cardiovascular response has been described after the administration of Dexmedetomidine.[10] A bolus of 1μg/kg results in a transient increase in arterial blood pressure and reflex increase in heart rate is due to α2 receptor stimulation of vascular smooth muscle. This can be markedly decreased by slow infusion over 10 min. In our study this effect was not noticed due to the slow infusion of the drug over 10 min.[11] Similarly to our study Nermin *et al.*,[12] found fall in BP after infusion of Dexmedetomidine and Gupta *et al.*,[7] found fall in BP with Clonidine Shirsendu *et al.*,[8] has also noticed significant rise in SBP in clonidine group almost 14.67% than in Dexmedetomidine where rise in SBP was only 7%. Bijoy Kumar *et al.*,[4] has found comparatively more increase in SBP with Clonidine than Dexmedetomidine. Similar findings were noted in present study. Similar to SBP, DBP had significant rise in Group II in response to intubation compare to Group I. During laryngoscopy and intubation and immediately after it, rise in the HR and Blood pressure was maximum, these findings are in agreement with the studies done by Derbyshire *et al.*,[12] and Shribman *et al.*,[1] who concluded that the plasma catecholamine concentration increased to the maximum within 1 min after intubation. In both groups SBP and DBP started falling immediately after intubation but rate of fall in BP was more gradual in Group II, so Dexmedetomidine was more efficient in the attenuation of rise in MAP compared to Clonidine in response to

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intubation. Similarly, Scheinin*et al. et al.*,[9] has proved that Dexmedetomidine attenuate the cardiovascular response to laryngoscopy and intubation by measuring catecholamine concentration and found that the concentration of noradrenaline in mixed venous plasma was smaller in the Dexmedetomidine group during all phases of induction. In the study done by Bajwa S *et al.*,[14] studied the attenuation of pressor response and dose sparing of opioid and anaesthetic requirement with preoperative administration of dexmedetomidine 1µcg/kg compared with fentanyl 2µcg/kg. They found that mean MAP was significantly lower in group D, 20 minutes after infusion of study drug compared with similar parameter in group F. Ramsay sedation score in Group I was higher than Group II. Shirsendu *et al.*,[8] has also showed statistically higher Ramsay sedation score with Dexmedetomidine than with Clonidine. The major sedative and antinociceptive effects of Dexmedetomidine are attributable to its stimulation of α2 A subtype located in locus ceruleus. It is the 8 times more specificity of Dexmedetomidine for α2 receptor that makes it a more effective sedative and analgesic agent than Clonidine. Even though higher sedation score seen with Dexmedetomidine was not associated with fall in SpO2. Similarly Shirsendu *et al.*,[8] also found no respiratory depression or decrease in SpO2 with similar doses of Dexmedetomidine, so we can conclude that Dexmedetomidine doesn't cause significant respiratory depression. In clonidine group, no side effects were observed. One patient in group Dexmeditomine had developed bradycardia at 3rd minute after intubation; which was managed by inj. Atropine 0.6 mg. Bajwa S *et al.*,[14] suggested that cardiac side effects of Dexmedetomidine like bradycardia and sinus pause could have warranted the use of atropine. Bijoy Kumar *et al.*,[4] cleared that clonidine and dexmedetomidine does not cause any serious side effect. Use of intraoperative Bi - spectral Index monitoring might have been more precise for the depth of anaesthesia and anaesthetic dose requirement and this might be limitation of our present study.

CONCLUSION

Dexmedetomidine is better in position when compared to clonidine for attenuation of pressor response to laryngoscopy and endotracheal intubation and also decreases requirement of thiopentone sodium for induction of general anaesthesia. There were no any significant adverse effects found with intravenous Dexmedetomidine. This technique will definitely add to the safety of anaesthetic management of patients who are at increased risk of harmful effects of stress response during intubation.

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Source of Support: None Declared
Conflict of Interest: None Declared