

# Study of intravenous clonidine Vs intravenous dexmedetomidine to attenuate the response to laryngoscopy and intubation

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## Abstract

**Introduction:** Laryngoscopy and intubation is associated with sympathoadrenal stimuli and heightened cardio respiratory and neurological reflexes such as tachycardia, hypertension, bronchospasm and increased intracranial pressure. These reflexes are potentially harmful for the patients more so in patients with hypertension, ischemic heart disease or associated neurological problem. Clonidine and dexmedetomidine are alpha 2 agonists acting in the central nervous system to reduce the sympathetic outflow. **Aim:** To compare clonidine and dexmedetomidine in attenuating the hemodynamic response to laryngoscopy and intubation when given as a infusion before induction. **Material and Methods:** A prospective double blinded randomized study involving patients coming to the operation theater for surgery under general anesthesia. Patients were divided into two groups, group C n=30 received clonidine 1µgm/kg intravenously 10 minutes as infusion before intubation and group D n=30 received dexmedetomidine 1µgm/kg intravenously 10 minutes as infusion before intubation. The hemodynamic variables were noted at 1, 3 and 5 minutes after intubation. **Statistical Analysis:** The obtained data were analyzed using the independent sample t-test. **Results:** There was no statistically significant difference between the two groups with respect to the heart rate, systolic and diastolic blood pressure, mean arterial pressure or the rate pressure product. **Conclusion:** Clonidine and dexmedetomidine are equally effective in reducing the stress response to Laryngoscopy and intubation. **Keywords:** Clonidine, Dexmedetomidine, Laryngoscopy, Intubation.

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## INTRODUCTION

General anesthetic procedures with muscle relaxant require the securing of airway with endotracheal tube. Laryngoscopy and intubation with an endotracheal tube involves sympathetic response due to stimulation of the afferent somatic and visceral receptors in the airway mainly epiglottis and vocal cords.<sup>1</sup> Although this stimuli

is transient it is very unpredictable and usually manifest as undesirable cardio respiratory effects like increase in heart rate and blood pressure and neurological effects like increased intracranial pressure.<sup>2,3</sup> These responses are due to increased levels of plasma catecholamine concentration,<sup>4</sup> and cause for increased morbidity and mortality in hypertensive and cardiac patients.<sup>5,6</sup> Many pharmacological agents have been tried to nullify this effect including local anesthetics like lignocaine both topically and intravenous, antihypertensives like labetalol and esmolol, venodilators like nitroglycerine and magnesium to blunt these harmful effects with varying results.<sup>7-11</sup> Centrally acting Alpha 2 adrenoceptor agonist reduces nor adrenaline release in the central nervous system leading to reduced sympathetic outflow.<sup>12</sup> The commonly used alpha2 agonist is clonidine which is being used as a premedicant because of its sedative effects.<sup>13</sup> Dexmedetomidine is a recent addition to this class which is more specific for alpha 2 receptor than

clonidine.<sup>14</sup> It is approved by the FDA for sedation in mechanically ventilated patients in the critical care unit. It is also indicated for procedural sedation of patients during the Intraoperative period. Lot of studies are available using clonidine or dexmedetomidine for perioperative sympathoadrenal response attenuation.<sup>15-18</sup>

**AIMS AND OBJECTIVES**

To study and compare the hemodynamic response of clonidine and dexmedetomidine given intravenously before induction and intubation

The hemodynamic response will be studied with respect to

- Systolic pressure
- Diastolic pressure
- Mean arterial pressure
- Heart rate
- Rate pressure product

**MATERIALS AND METHODS**

Designed to be a prospective and double blinded study involving patients admitted to chettinad hospital and research institute posted for elective surgery under general anesthesia. After obtaining the institutional ethical committee approval, patients are divided into group-C and group-D using computer generated randomization code. Group-C n= 30 patients receiving injection clonidine 1µgm/kg intravenously over 10 minutes before induction.

Group-D n=30 patients receiving injection dexmedetomidine 1µgm/kg over 10 minutes before induction.

**INCLUSION CRITERIA**

1. Age 18- 60 years of both sex
2. Patient posted for elective surgery under general anesthesia
3. Patient under ASA I and II
4. Weight 50-90kgs

**EXCLUSION CRITERIA**

1. Anticipated difficult airway.
2. Known allergy to the study drugs.
3. BMI >35kg/m<sup>2</sup>
4. Sinus bradycardia.
5. Heart blocks.
6. Patient on beta blockers.
7. Pregnant women.

All patients will be explained about the study and a written informed consent obtained. A detailed history, complete physical examination and basic blood investigation done and the patient is kept nil per oral for 8 hours prior to surgery. In the operation room all patients are connected to the standard basic monitors and secured with a 18G venflon. Basal heart rate blood pressure mean arterial pressure and saturation is noted. Injection fentanyl is given at a dose of 1µgm/kg and followed by one of the infusion of either clonidine 1µgm/kg or dexmedetomidine 1µgm/kg over 10 minutes in 100 ml normal saline. The patients vitals are again noted after completion of infusion. Patient is induced with propofol 2mg/kg and intubated with rocuronium 1mg/kg and the patients vitals are noted one minute after, followed by 3 and 5 minutes .The heart rate, systolic, diastolic and mean arterial pressure are noted and the rate pressure product is calculated from these values. Any fall in heart rate to less than 50 beats per minute will be treated with a bolus of glycopyrrolate injection 0.2µgm/kg. If the anesthetist takes more than 10 seconds or more than one attempt for intubation or finds the need for bougie or a stylet to intubate, the patient will be excluded from the study.

**STATISTICS:** The obtained data was subjected to statistical analysis using the independent sample t test.

**RESULT**

The groups were comparable with respect to age, sex and weight.

**Table 1:** Age group statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Age	C	30	41.03	8.798	1.606
	D	30	41.67	8.572	1.565

**Table 2:** Age Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	Df
Age	Equal variances assumed	.001	.978	-.282	58
	Equal variances not assumed			-.282	57.960

The sig p value for age for the two groups is 0.978 which is above 0.05 and hence not significant

**Table 3:** Weight group statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Wt in kg	C	30	67.87	9.587	1.750
	D	30	69.63	6.950	1.269

**Table 4:** Weight Independent Samples Test

		Levene's Test for Equality of Variances	t-test for Equality of Means		
		F	Sig.	t	df
Wt in kg	Equal variances assumed	4.663	.035	-.817	58
	Equal variances not assumed			-.817	52.886

**Table 5:** Weight Independent Samples Test

		t-test for Equality of Means		
		Sig. (2-tailed)	Mean Difference	Std. Error Difference
Wt in kg	Equal variances assumed	.417	-1.767	2.162
	Equal variances not assumed	.418	-1.767	2.162

Although the sig p value for weight between the two groups is 0.035 which is significant the sig (2 tailed) value is 0.147 which interprets that the difference was due to chance.

**Table 5:** Basal values Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Basal heart Rate	C	30	81.83	6.471	1.181
	D	30	80.23	5.469	.998
Basal systolic Blood pressure	C	30	130.83	5.754	1.051
	D	30	130.30	6.535	1.193
Basal diastolic Blood pressure	C	30	84.03	5.957	1.088
	D	30	82.57	5.697	1.040
Basal mean arterial pressure	C	30	99.633333	5.2026739	.9498740
	D	30	98.477778	5.1175330	.9343294

**Table 6:** Basal values Independent Samples Test

		Levene's Test for Equality of Variances	t-test for Equality of Means		
		F	Sig.	t	df
Basal heart Rate	Equal variances assumed	1.117	.295	1.034	58
	Equal variances not assumed			1.034	56.434
Basal systolic Blood pressure	Equal variances assumed	.020	.887	.336	58
	Equal variances not assumed			.336	57.086
Basal diastolic Blood Pressure	Equal variances assumed	.046	.831	.975	58
	Equal variances not assumed			.975	57.886
Basal mean arterial pressure	Equal variances assumed	.001	.974	.867	58
	Equal variances not assumed			.867	57.984

There is no statistical difference between the two groups with respect to the heart rate, systolic and diastolic blood pressure and mean arterial pressure. The p value for the basal heart rate is 0.295. The p value for the basal systolic

blood pressure between the two groups is 0.887, for the basal diastolic blood pressure is 0.831 and for the basal mean arterial pressure is 0.974.

**Table 7:** After drug infusion Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
After infusion Heart rate	C	30	69.70	5.370	.980
	D	30	65.53	3.785	.691
After infusion systolic blood pressure	C	30	113.40	8.165	1.491
	D	30	111.20	8.339	1.523
After infusion diastolic blood pressure	C	30	70.97	5.666	1.034
	D	30	69.10	4.759	.869
After infusion mean arterial pressure	C	30	85.111111	5.8324849	1.0648612
	D	30	83.133333	4.6143205	.8424558

**Table 8:** After drug infusion Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
After infusion heart rate	Equal variances assumed	1.570	.215	3.474	58
	Equal variances not assumed			3.474	52.110
After infusion systolic blood pressure	Equal variances assumed	.021	.885	1.032	58
	Equal variances not assumed			1.032	57.974
After infusion diastolic blood pressure	Equal variances assumed	2.028	.160	1.382	58
	Equal variances not assumed			1.382	56.319
After infusion mean arterial pressure	Equal variances assumed	1.666	.202	1.457	58
	Equal variances not assumed			1.457	55.084

After infusion of clonidine and dexmedetomidine there is no statistical difference between the two groups with respect to the heart rate, systolic blood pressure, diastolic blood pressure and the mean arterial pressure. The lowest

heart rate in the C group is 58 per minute and in the D group is 56 per minute. The lowest mean arterial pressure in the C group is 73 mmHg and in the D group is 75 mmHg.

**Table 9:** 1 min after intubation Group Statistics

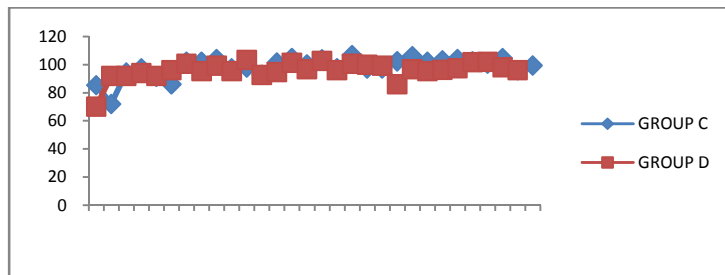
	Group	N	Mean	Std. Deviation	Std. Error Mean
1 min heart rate	C	30	81.53	4.833	.882
	D	30	78.50	3.998	.730
1 min systolic blood pressure	C	30	128.63	9.988	1.824
	D	30	128.13	7.606	1.389
1 min diastolic blood pressure	C	30	83.23	7.065	1.290
	D	30	80.00	6.192	1.131
1 min mean arterial pressure	C	30	98.366667	7.2768725	1.3285691
	D	30	96.044444	6.2408451	1.1394172
1min rate pressure product	C	30	10501.73	1147.346	209.476
	D	30	10077.13	957.225	174.765

**Table 10:** 1 min after intubation Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
1 min heart rate	Equal variances assumed	1.847	.179	2.649	58
	Equal variances not assumed			2.649	56.030
1 min systolic blood pressure	Equal variances assumed	1.426	.237	.218	58
	Equal variances not assumed			.218	54.169
1 min diastolic blood pressure	Equal variances assumed	2.017	.161	1.885	58
	Equal variances not assumed			1.885	57.021
1 min mean arterial pressure	Equal variances assumed	.978	.327	1.327	58
	Equal variances not assumed			1.327	56.684
1min rate pressure product.	Equal variances assumed	1.776	.188	1.556	58
	Equal variances not assumed			1.556	56.195

There is no statistical difference with respect to the heart rate, blood pressure both systolic and diastolic, mean

arterial pressure and the rate pressure product 1 minute after intubation between group C and D.



**Figure 1:** Mean arterial pressure 1 minute after intubation

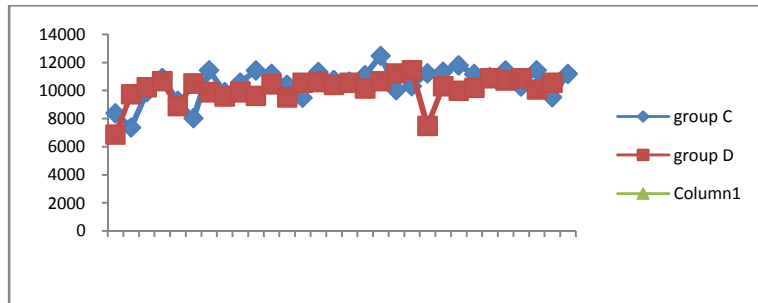


Figure 2: Rate pressure product 1 minute after intubation

Table 11: 3 minutes after intubation group statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
3 min Heart rate	C	30	73.03	4.335	.791
	D	30	70.60	3.147	.575
3min systolic blood pressure	C	30	117.07	10.346	1.889
	D	30	116.00	7.334	1.339
3min diastolic blood pressure	C	30	73.00	4.934	.901
	D	30	72.77	3.748	.684
3min mean arterial pressure	C	30	87.688889	6.1848494	1.1291939
	D	30	87.177778	4.4487144	.8122204
3 min rate pressure product	C	30	8561.57	992.723	181.246
	D	30	8198.13	748.795	136.711

Table 12: 3 Minutes after intubation Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
3 min heart rate	Equal variances assumed	3.335	.073	2.488	58
	Equal variances not assumed			2.488	52.922
3min systolic blood pressure	Equal variances assumed	1.228	.272	.461	58
	Equal variances not assumed			.461	52.272
3min diastolic blood pressure	Equal variances assumed	.108	.743	.206	58
	Equal variances not assumed			.206	54.107
3min mean arterial pressure	Equal variances assumed	.084	.773	.367	58
	Equal variances not assumed			.367	52.672
3 min rate pressure product	Equal variances assumed	.814	.371	1.601	58
	Equal variances not assumed			1.601	53.929

Three minutes after intubation there was no statistically significant difference between the two groups with respect to the blood pressure, heart rate and rate pressure product.

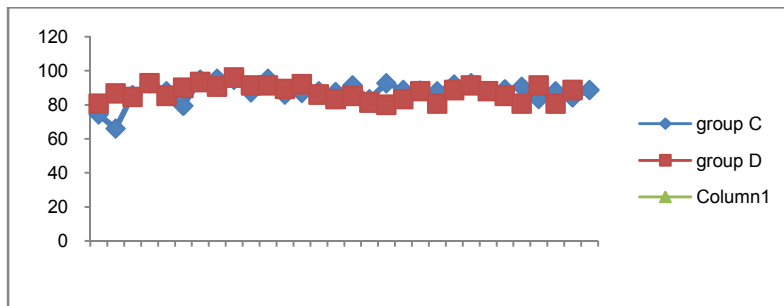


Figure 3: Mean arterial pressure 3 minutes after intubation

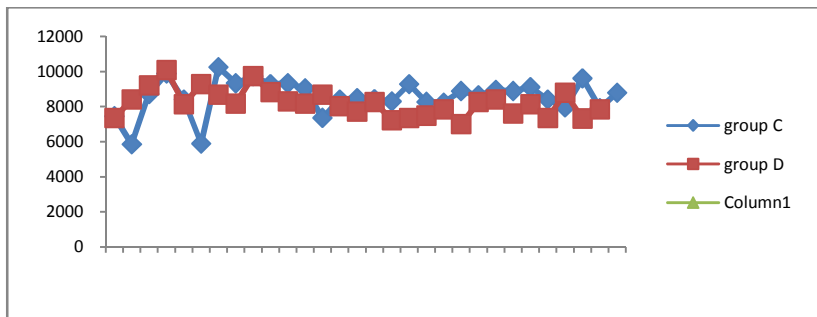


Figure 4: Rate pressure product 3 min after intubation

Table 13: 5 min after intubation Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
5min heart rate	C	30	70.70	4.632	.846
	D	30	69.00	3.140	.573
5min systolic blood pressure	C	30	110.50	11.491	2.098
	D	30	113.03	9.072	1.656
5min diastolic blood pressure	C	30	69.13	6.004	1.096
	D	30	69.97	4.255	.777
5min mean arterial pressure	C	30	82.922222	7.3048996	1.3336861
	D	30	84.322222	4.9406309	.9020317
5min rate pressure product	C	30	7820.70	995.719	181.793
	D	30	7810.70	834.305	152.323

Table 15: 5 min after intubation Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	df
5min heart rate	Equal variances assumed	1.561	.217	1.664	58
	Equal variances not assumed			1.664	51.008
5min systolic blood pressure	Equal variances assumed	.835	.365	-.948	58
	Equal variances not assumed			-.948	55.036
5min diastolic blood pressure	Equal variances assumed	.702	.406	-.620	58
	Equal variances not assumed			-.620	52.259
5min mean arterial pressure	Equal variances assumed	1.464	.231	-.870	58
	Equal variances not assumed			-.870	50.941
5min rate pressure product	Equal variances assumed	.527	.471	.042	58
	Equal variances not assumed			.042	56.276

after 5 minutes after intubation there was no significant difference statistically between the group C and D with

respect to the heart rate , systolic diastolic and mean arterial pressure and rate pressure products.

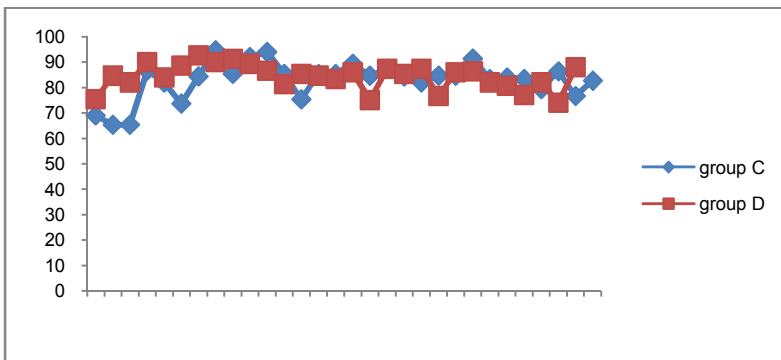


Figure 5: Mean arterial pressure 5 minutes after intubation

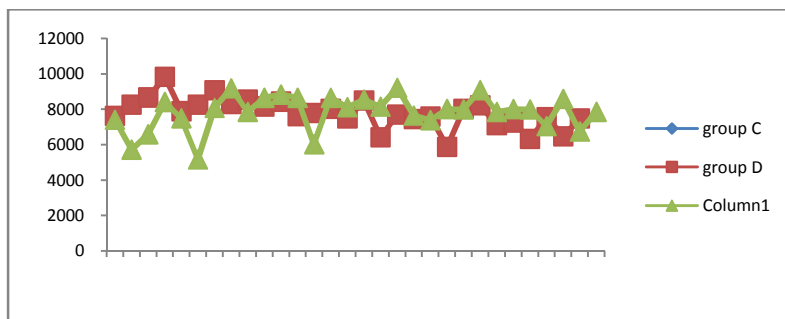


Figure 6: Rate pressure product 5 minutes after intubation

In neither of the groups we had to use glycopyrrolate. However in the D group one patient had a increase in the systolic blood pressure to 210 mmHg after infusion of dexmedetomidine and had to be given labetalol injection to bring down the blood pressure.

## DISCUSSION

$\alpha_2$  receptor agonist reduce sympathetic outflow from the central nervous system by acting on the imidazoline receptor mainly in the locus coeruleus.<sup>19</sup> Clonidine is an  $\alpha_2$  receptor agonist which had been used for treating hypertensive patients and now is being used for preoperative and Intraoperative sedation. Dexmedetomidine is a highly selective  $\alpha_2$  receptor agonist.<sup>20</sup> in our study we found both the drugs to be equally effective in reducing the stress response to intubation at 1,3 and 5 minutes. We also found no difference with respect to the basal pressures and heart rates after infusion of the drugs. rate pressure product is an indirect measure of the myocardial workload. It is a measure of the stress put on the cardiac muscle. A value of 10000 to 14999 is considered low hemodynamic response. in our study the rate pressure product 1 minute after intubation was below 12000 for both the groups. Sarkar A *et al* in his study of 75 adult patients compared clonidine 3 $\mu$ g per kg or dexmedetomidine 0.5 $\mu$ g per kg and concluded that both drugs were effective in reducing the sympathetic response to intubation.<sup>21</sup> Mondal S *et al* in his study on patients who were pretreated with either dexmedetomidine 1  $\mu$ g/kg or clonidine 2  $\mu$ g/kg concluded that clonidine was less effective than dexmedetomidine in attenuating the stress response to intubation.<sup>22</sup>

## CONCLUSION

clonidine and dexmedetomidine when given as a infusion preoperatively are equally effective in reducing the rate pressure product as well as the stress response to laryngoscopy and intubation .

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