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Original Research Article

A Comparison of Two Different Doses of Intravenous Dexmedetomidine to Attenuate Hemodynamic Responses to Direct Laryngoscopy and Intubation in Adult Patients Undergoing Elective Surgeries under General Anaesthesia: A Prospective Observational Study in a Tertiary Care Hospital in Mandya

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ABSTRACT

Background
Laryngoscopic manipulation and the process of endotracheal intubation can trigger harmful responses, such as increased heart rate, irregular heart rhythms, and elevated blood pressure. The aim of the study is to compare the efficacy of two different doses of dexmedetomidine (0.5mcg/kg and 0.75mcg/kg) for attenuation of hemodynamic response to laryngoscopy and endotracheal intubation in adult patients undergoing elective surgeries under general anaesthesia and to determine dose dependent side effects like hypotension, bradycardia and sedation.

Methods
Prospective observational study was conducted on 60 patients aged 18-60 years after obtaining ethical committee clearance. Patients were randomized into two groups. Group D1 (n=30) received Dexmedetomidine 0.5mcg/kg while Group D2 (n=30) received Dexmedetomidine 0.75mcg/kg in 20ml normal saline as infusion over 10min prior to intubation. The primary outcome variables were heart rate and blood pressure at 1, 2, 3, 5, 10 min after intubation. The secondary outcome was on any adverse effects associated with dexmedetomidine.

Results
The hemodynamic responses were attenuated in both groups after laryngoscopy and endotracheal intubation, with statistical significant difference between both groups and better obtundation of hemodynamic response in terms of heart rate, systolic, diastolic and mean arterial pressure at all points of time with dexmedetomidine 0.75mcg/kg compared to 0.5mcg/kg. Sedation scores were more with dexmedetomidine 0.75mcg/kg. No significant side effects were there in both groups.

Conclusion

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Inj. dexmedetomidine 0.75mcg/kg is more effective in attenuating hemodynamic responses to laryngoscopy and endotracheal intubation as compared to inj. dexmedetomidine 0.5mcg/kg without having significant adverse effects.

Keywords: Dexmedetomidine, Intubation, Laryngoscopy, Hemodynamic Response.

INTRODUCTION

Direct laryngoscopy and endotracheal intubation are among the most commonly conducted medical procedures.[1] These interventions can lead to complications such as tachycardia, hypertension, and arrhythmias, which are linked to a notable rise in plasma catecholamines, potentially resulting in myocardial ischemia.[2,3,4,5] To mitigate the stress response associated with laryngoscopy and intubation, various pharmacological regimens and techniques have been employed over time. These include the use of opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, and vasodilators.[5,6]

Alpha-2 agonists, including clonidine and dexmedetomidine, have been utilized by researchers to mitigate the stress response associated with laryngoscopy and intubation.[7] Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that offers several advantages, such as sedation, sympatholysis, analgesia, and maintenance of cardiovascular stability.[1] However, its effects are brief, with an elimination half-life of approximately 2 hours.[7] The hemodynamic responses to dexmedetomidine are both predictable and dependent on dosage.[1,8]

Dexmedetomidine administered at doses of 0.5 µg/kg, 0.75 µg/kg, and 1 µg/kg has been reported by several authors to effectively reduce the stress response associated with laryngoscopy and endotracheal intubation.[7] However, the higher dosage of 1 µg/kg was linked to a greater risk of cardiovascular issues such as hypotension and bradycardia, as well as increased sedation levels. While numerous studies have compared the effects of Dexmedetomidine at 0.5 µg/kg and 1 µg/kg, only two studies conducted in Kolar, Karnataka, and Karachi, Pakistan specifically examined the comparison between 0.5 µg/kg and 0.75 µg/kg doses.[7,9] Additional investigation is necessary to establish the ideal dosage of Dexmedetomidine due to the existing uncertainty regarding optimal dosing for minimizing hemodynamic reactions during laryngoscopy and intubation.[9] Therefore, this study aims to evaluate the effectiveness of two different doses of Dexmedetomidine in reducing hemodynamic responses associated with laryngoscopy and tracheal intubation in adult patients undergoing elective surgeries under general anesthesia.

MATERIALS AND METHODS

A prospective comparative observational study was conducted at a tertiary care hospital after receiving approval from the institutional ethical committee and Clinical Trial Registry of India enrolment with registration number (CTRI/2024/03/064847) for a period of six months.

Sample Size: 30 in each group.

Sample size is calculated by using the formula, based on one of the previous studies.

$N = 2(Z\alpha/2 + Z\beta)2\ \sigma2/d2$

$Z\alpha/2=1.96$ (Standard normal variable) $Z\beta=0.84$ (Power of the test 80%) σ= combined standard deviation of mean arterial blood pressure (5.78).[7]

d=10.53(Difference between post intubation mean arterial blood pressure).

$N= 2(1.96 + 0.84)^2\ (5.78)^2/(4.56)^2$

N=25.21 in each group.

So we have considered 30 patients in each group.

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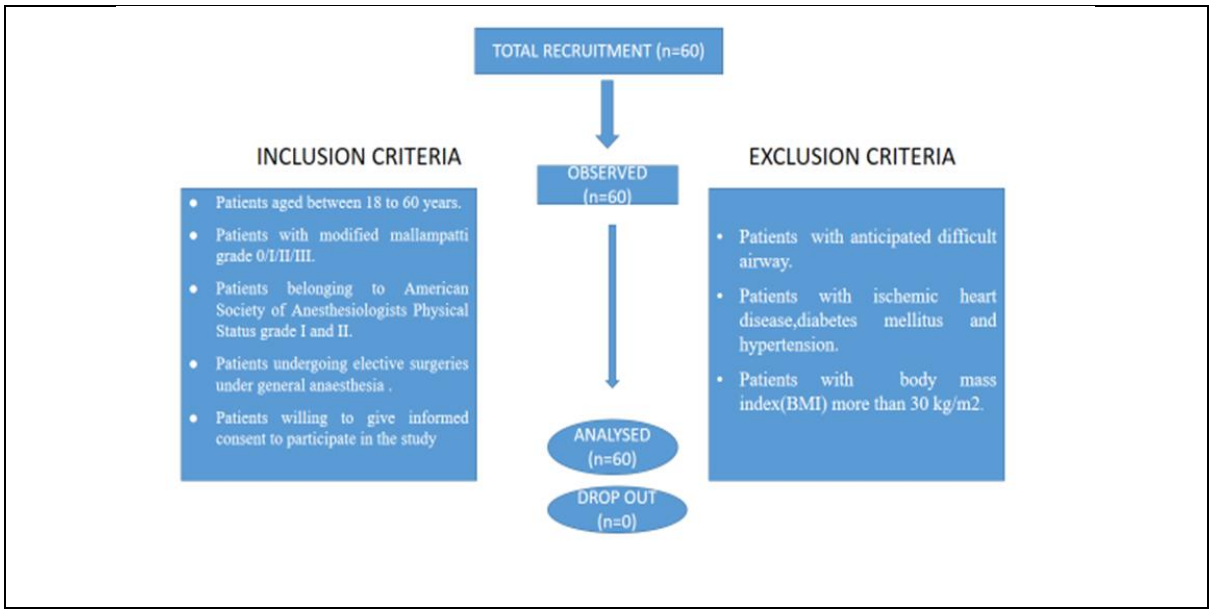

The data was recorded using a semi-structured questionnaire which contained 2 parts. The first part collected the details regarding socio-demographic characteristics like name, age, sex, etc. An informed consent was taken after explaining the procedure to the patient in their own understandable language.

Patients were instructed to be nil per oral 6-8hrs prior to surgery. They were premedicated with Cap. Omeprazole 20mg and Tab. Alprazolam 0.5mg orally on the night before the surgery. Patients were shifted to pre-operative area after a complete preoperative check up one day prior to the surgery with all the routine investigations. Patient were shifted to operation theatre and standard monitors such as ECG, Pulse oximeter, NIBP were connected and basal values of heart rate, blood pressure, SPO_2, and respiratory rate were recorded. 18G intravenous line was secured in the upper limb and IV fluid (ringer-lactate) started. The anesthesiologist administered the decided dose of dexmedetomidine. Group D1 patients received inj.Dexmedetomidine 0.5ug/kg diluted to 20ml normal saline IV infusion over 10 min. Group D2 patients received inj.Dexmedetomidine 0.75mcg/kg diluted to 20ml normal saline IV infusion over 10min. Patients were preoxygenated with 100% oxygen for 3 minutes. Patients were then induced with Inj.Propofol(2mg/kg). Thereafter they were administered with Inj.succinylcholine (2mg/kg) followed by laryngoscopy and endotracheal intubation under direct vision using Macintosh blade size 3 or 4 by the same experienced anaesthesiologist. Positioning of tube was confirmed by bilateral equal air entry and capnography. Based on the dexmedetomidine dose given by anesthesiologist, the intubation response in patients receiving 0.5mcg/kg and 0.75mcg/kg of dexmedetomidine was observed. Heart rate, systolic and diastolic blood pressures, mean arterial pressure and Spo2 were documented by an investigator.

Intubation response was graded and recorded.
T0- Baseline readings.
T1- Just before injection of study drug.
T2- Just before induction.
T3- Just before intubation.
T4- 1 minute after intubation.
T5- 2 minutes after intubation.

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T6- 3 minutes after intubation.
T7- 5 minutes after intubation.
T8-10 Minutes after intubation.
Surgical stimulus was allowed only after 5 minutes following intubation. Any episode of bradycardia (heart rate less than 60) and hypotension were recorded. Ramsay sedation score was assessed at the end of 1, 2, 3, 5, 10 minutes.
The following parameters were observed and recorded:
Heart Rate:
Systolic Blood Pressure
Diastolic Blood Pressure
Mean Arterial Blood Pressure:
Sedation scores.
Any side effects.

Statistical Analysis
The data was entered in to a Microsoft excel spread-sheet. The data was analysed using SPSS software. Continuous data was represented as mean + / - standard deviation and categorical data was represented as absolute numbers and percentages. Intergroup comparison of HR, SBP, DBP and MAP values was carried out by student's t test. Pearson's correlation coefficient was used to find the correlation between the variables. P value < 0.05 was considered statistically significant.

RESULTS
60 patients were studied in the two groups, 30 in each group.

Parameter	**Group**		**p value- Student t test**
	D1	**D2**	
Age	47.30 (±11.155)	46.37 (±5.592)	0.695
Table 1: Mean age distribution of study groups			

Gender	**Group**		**p value- chi sq test**
	D1	**D2**	
Male	17 (56.7%)	16 (53.3%)	0.795
Female	13 (43.3%)	14 (46.7%)	
Total	30 (100.0%)	30 (100.0%)	
Table 2: Distribution of cases according to gender			

ASA grading	**Group**		**p value- chisq test**
	D1	**D2**	
I	13 (43.3%)	8 (26.7%)	0.176
II	17(56.7%)	22 (73.3%)	
Total	30 (100.0%)	30 (100.0%)	
Table 3: Distribution of cases according to ASA grading			

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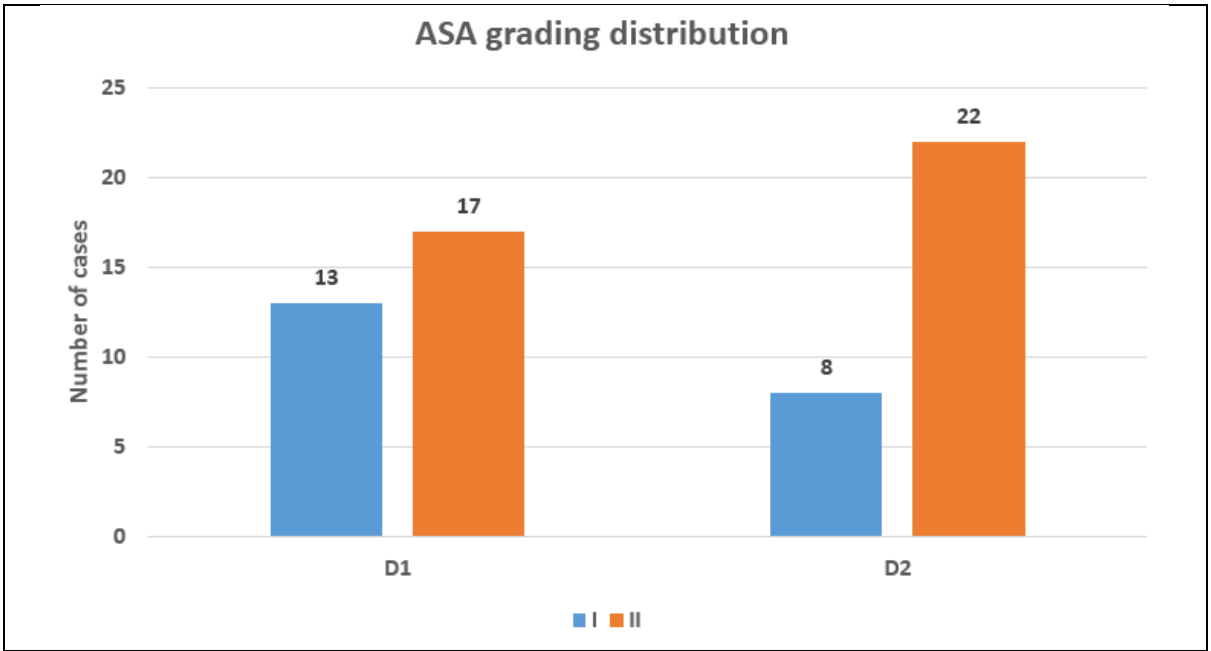

Graph 1

The proportion of study subjects with regard to age, gender and ASA were comparable between the study groups. (p>0.05).

Mean SBP	D1		D2		p value- Student t test
	Mean	SD	Mean	SD	
Baseline	131.67	15.041	127.5	13.602	0.265
Before injection of test drug	132.4	14.068	127.43	13.793	0.173
Before induction	130.27	13.997	125.93	13.352	0.225
Before intubation	128.2	14.126	124.9	13.089	0.352
1 min AI	135.07	13.326	125.37	13.459	0.007
2 min AI	133	13.3	123.17	12.9	0.005
3 min AI	130.5	13.127	121.1	12.807	0.007
5 min AI	127.6	13.454	118.6	12.361	0.009
10 min AI	130.03	13.244	126.83	13.527	0.353

Table 4: Comparison of mean systolic blood pressure between the study groups

Mean SBP showed significant difference (p<0.05) between the two groups at post intubation 1min, 2 min, 3min & 5 min and it was not significant at rest of the time intervals with p value >0.05 (baseline, before injecting test drug, before induction, before intubation and after intubation 10 min).

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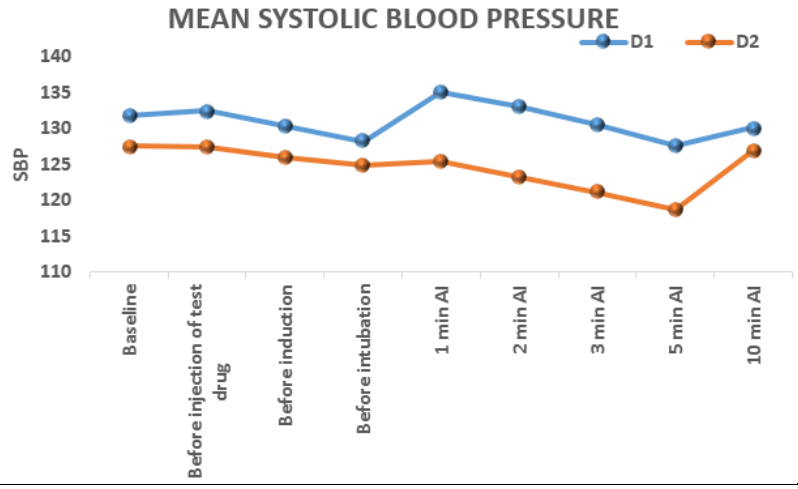
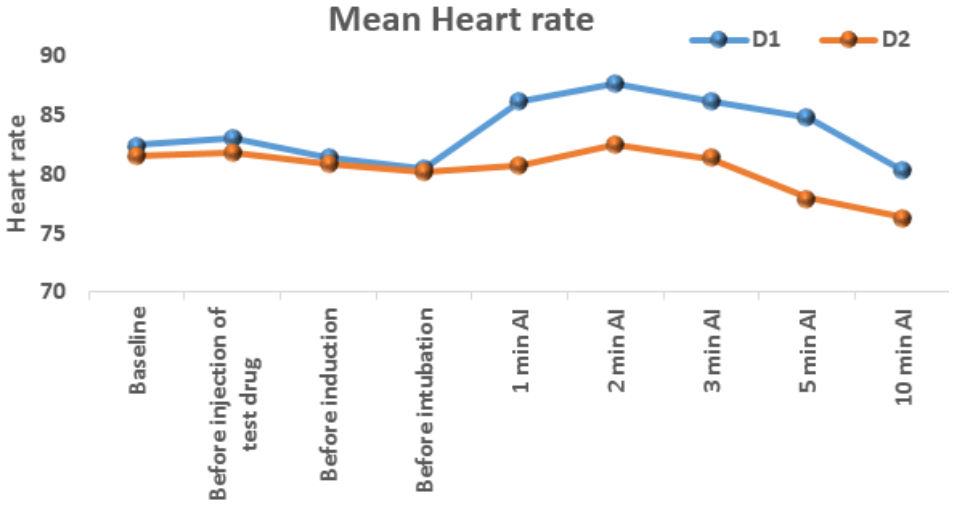


Graph 2

Mean Heart rate	D1		D2		p value- Student t test
	Mean	SD	Mean	SD	
Baseline	82.43	9.077	81.53	9.867	0.714
Before injection of test drug	83	9.184	81.8	10.128	0.633
Before induction	81.43	9.153	80.9	9.845	0.829
Before intubation	80.5	9.104	80.17	10	0.893
1 min AI	86.2	9.180	80.7	9.128	0.023
2 min AI	87.63	9.434	82.5	9.776	0.043
3 min AI	86.17	9.071	81.27	9.566	0.046
5 min AI	84.73	9.552	77.93	8.614	0.005
10 min AI	80.3	9.61	76.3	8.417	0.096

Table 5: Comparison of mean heart rate (bpm) between the study groups

Mean heart rate showed significant difference ($p<0.05$) between the two groups at post intubation 1min, 2 min, 3min & 5 min and it was not significant at rest of the time intervals with p value >0.05 (baseline, before injecting test drug, before induction, before intubation and after intubation 10 min).



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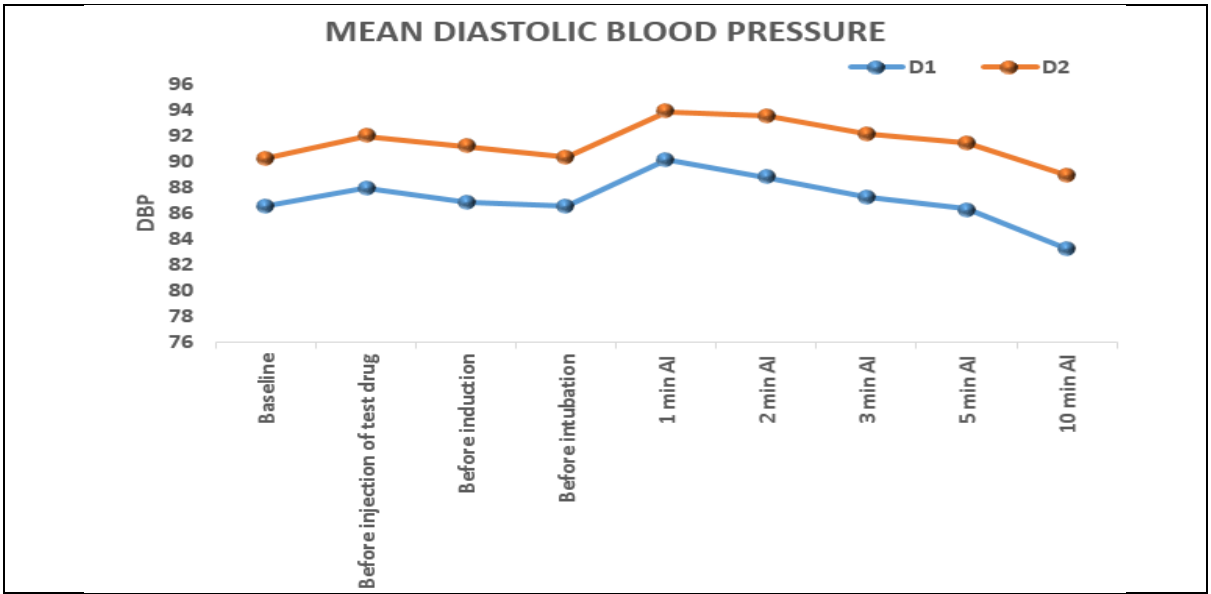
Graph 3

Mean DBP	D1		D2		p value- Student t test
	Mean	SD	Mean	SD	
Baseline	86.5	7.630	90.3	6.70	0.057
Before injection of test drug	87.9	7.911	92.0	8.701	0.061
Before induction	86.8	8.900	91.2	8.710	0.063
Before intubation	86.5	8.730	90.4	7.761	0.072
1 min AI	90.2	7.391	93.9	7.108	0.041
2 min AI	88.8	8.936	93.6	8.568	0.038
3 min AI	86.9	7.963	91.2	7.89	0.049
5 min AI	86.3	7.17	90.3	7.178	0.030
10 min AI	83.2	8.630	89.0	8.501	0.011

Table 6: Comparison of mean diastolic blood pressure between the study groups

Mean DBP showed significant difference ($p<0.05$) between the two groups at post intubation 1 min, 2 min, 3 min, 5 min & 10 min and it was not significant at rest of the time intervals with p value >0.05 (baseline, before injecting test drug, before induction and before intubation).



Graph 4

MAP	D1		D2		p value- Student t test
	Mean	SD	Mean	SD	
Baseline	94.23	12.255	89.37	7.351	0.102
Before injection of test drug	94.8	11.684	89.5	7.191	0.070
Before induction	95.7	11.624	88.73	7.211	0.065
Before intubation	95.07	11.438	89.93	7.172	0.051
1 min AI	98.77	11.236	90.2	7.363	0.001
2 min AI	98.7	11.363	89.6	7.625	0.006
3 min AI	97.33	11.678	89.2	7.13	0.003

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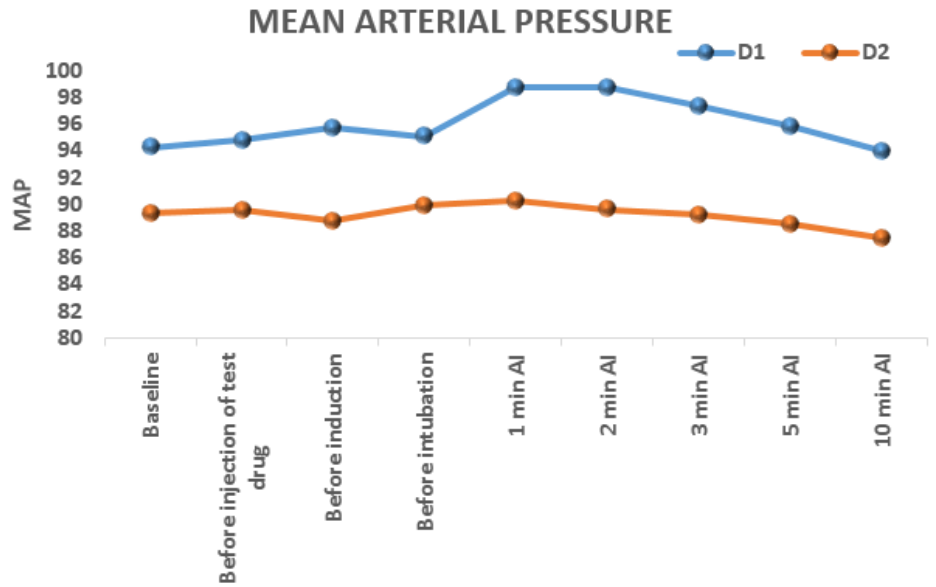
5 min AI	95.83	11.552	88.5	7.113	0.004
10 min AI	93.93	11.765	87.5	6.611	0.011

Table 7: Mean arterial pressure of both the groups

Mean arterial pressure showed significant difference ($p<0.05$) between the two groups at post intubation 1min, 2 min, 3min, 5 min & 10 min and it was not significant at rest of the time intervals with p value >0.05 (baseline, before injecting test drug, before induction and before intubation).



Graph 5

Sedation scoring in min	Score	Group		Total	P value – Chisq test
		D1	D2		
2MIN	1	0	0	0	<0.0001
		0.0%	0.0%	0.0%	
	2	24	0	24	
		100.0%	0.0%	100.0%	
	3	6	18	24	
		25.0%	75.0%	100.0%	
	4	0	12	12	
		0.0%	100.0%	100.0%	
	5	0	0	0	
		0.0%	0.0%	0.0%	
	6	0	0	0	
		0.0%	0.0%	0.0%	
5MIN	1	0	0	0	<0.0001
		0.0%	0.0%	0.0%	
	2	11	0	11	
		100.0%	0.0%	100.0%	
	3	19	5	24	
		79.2%	20.8%	100.0%	
	4	0	25	25	

		0.0%	100.0%	100.0%	
	5	0	0	0	
		0.0%	0.0%	0.0%	
	6	0	0	0	
		0.0%	0.0%	0.0%	
10MIN	1	0	0	0	<0.0001
		0.0%	0.0%	0.0%	
	2	4	0	4	
		100.0%	0.0%	100.0%	
	3	26	0	26	
		100.0%	0.0%	100.0%	
	4	0	18	18	
		0.0%	100.0%	100.0%	
	5	0	12	12	
		0.0%	100.0%	100.0%	
	6	0	0	0	
		0.0%	0.0%	0.0%	
Table 8: Distribution of subjects based on sedation scoring between the two groups					
Sedation scores were more for D2 > D1 with p value<0.05					

DISCUSSION

Dexmedetomidine is a highly selective agonist for α2-adrenoreceptors.[3] It leads to decreased blood pressure, a reduction in heart rate, sedation, and pain relief.[4] The drop in blood pressure primarily results from the suppression of central sympathetic activity and the activation of presynaptic α2 adrenoceptors, which reduces the release of norepinephrine.[10,11]

Dexmedetomidine has been examined by several researchers at doses of 0.5 and 1 µg/kg. However, only two studies have specifically investigated the effectiveness of dexmedetomidine at a dose of 0.75 µg/kg in reducing the physiological response to laryngoscopy and intubation. Therefore, in our study, we decided to incorporate dexmedetomidine at doses of 0.5 and 0.75 µg/kg to compare its effects on hemodynamic responses during laryngoscopy and intubation.

An important benefit of dexmedetomidine is its minimal impact on respiratory depression while providing strong sedative and analgesic effects, especially when compared to opioids and other sedatives.[12] Research indicates that a dose of 1 µg/kg can enhance sedation levels and may increase the need for supplemental oxygen, as noted by several authors. However, doses of 1.0 and 2.0 µg/kg have been associated with irregular breathing patterns, including apnoea episodes. Consequently, in our study, dexmedetomidine was administered gradually as an infusion over a period of 10 minutes before the induction phase.

In the current study, both groups exhibited a gradual decline in heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) following the infusion of dexmedetomidine. After laryngoscopy and intubation, there was an increase in the mean heart rate, SBP, DBP, and MAP in both groups, which subsequently began to decrease when assessed at various time intervals post-intubation. In group D1, heart rate returned to baseline levels five minutes after intubation, whereas in group D2, it returned to baseline or below within three minutes post-intubation. Bon Sebastian et al.[7] also noted that following laryngoscopy and intubation, there was a rise in heart rate from baseline in both dexmedetomidine groups. Specifically, in the dexmedetomidine 0.5 µg/kg group, heart rate

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approached baseline at five minutes, while in the 0.75 µg/kg group, it returned to baseline at three minutes or earlier.

The study of systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) in both groups revealed that following drug infusion, there was a reduction in these parameters. After laryngoscopy and intubation, the mean SBP, DBP, and MAP increased at one minute in group D1, while in group D2, these values returned nearly to baseline within three minutes before beginning to decline again. Significant differences were noted at all time points, specifically at five and ten minutes. Similar findings were reported by G. L. Dhanachandra et al.[13] who concluded that SBP, DBP, and MAP tend to rise after laryngoscopy and intubation. Both doses of dexmedetomidine (0.5 µg/kg and 0.75 µg/kg) were effective in mitigating the hemodynamic responses associated with these procedures; however, the higher dose of 0.75 µg/kg demonstrated superior and more prolonged effects, lasting up to ten minutes compared to the 0.5 µg/kg dose.

In our study, the patients who received dexmedetomidine 0.75µg/kg had significantly more Sedation score as compared to dexmedetomidine 0.5µg/kg. Jyoti Kabara et al[14] and Bon Sebastian et al.[7] found almost similar observation being sedation score were higher in dexmedetomidine 0.75µg/kg group.

None of the patients required treatment for bradycardia, hypotension, or hypertension. Additionally, no patient experienced a drop in SpO2 levels below 97%. Respiratory depression was not observed in any patients from either group. The study by Singh et al.[13] also did not reveal any side effects such as bradycardia or sinus pause, which would have necessitated the administration of atropine.

In our study, we found that dexmedetomidine at a dose of 0.75 µg/kg successfully reduced the stress response associated with laryngoscopy and intubation, while not causing any negative effects on hemodynamics or the respiratory system.

LIMITATIONS

Small Sample Size: If sample size is relatively small, statistical power might be compromised when analyzing differences between the two dosages. Larger samples sizes generally provide more robust findings.

Patient selection bias: Some degree of selection bias might still occur if certain demographic factors influence participation rates differently across the two treatment arms.

Measurement Errors: Accuracy in recording hemodynamic parameters like mean arterial pressure (MAP) and heart rate (HR) is essential. Any measurement errors could skew the results and impact the validity of comparisons between dosage groups.

Potential Confounding Variables: Other interventions or medications used concurrently with dexmedetomidine could confound the results. For example, variations in anesthesia protocols or the use of other vasoactive agents might influence hemodynamic responses independently of the dexmedetomidine dosage.

CONCLUSION

The study findings indicate that the hemodynamic responses to laryngoscopy and endotracheal intubation can be effectively managed with the administration of dexmedetomidine, particularly at a dosage of 0.75 mcg/kg. This higher dosage resulted in significantly better attenuation of heart rate, systolic, diastolic, and mean arterial pressure compared to the lower dosage of 0.5 mcg/kg. Additionally, sedation scores were notably higher in the group receiving

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0.75 mcg/kg, suggesting enhanced sedative effects without significant adverse reactions in either group.

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Conflicts of interest
There are no conflicts of interest

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