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EVALUATION OF TWO DIFFERENT DOSAGES OF DEXMEDETOMIDINE IN ATTENUATION OF PRESSOR RESPONSE DURING ENDOTRACHEAL INTUBATION AND REDUCING INJ. THIOPENTONE DOSAGES DURING INDUCTION OF ANAESTHESIA

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A B S T R A C T

Tracheal intubation and direct laryngoscopy are considered as the most critical event during administration of general anaesthesia. Dexmedetomidine is an alfa-2 adrenergic agonist use for control of haemodynamic response to laryngoscopy and tracheal intubation. Our study consisted 60 patients of ASA grade I or II, scheduled for surgery, divided into two groups of 30 patients each. Group A received injection dexmedetomidine 0.5 $\mu g.kg^{-1}$ over 10 minutes and Group B received injection dexmedetomidine 0.1 $\mu g.kg^{-1}$ over 10 min. Induction was done with Inj. thiopentone 5mg/kg/wt and Inj. succinylcholine 2 mg/k/wt. Paremeters like arterial blood pressure and requirement of Inj. thiopentone dosage and post- operative sedation score were studied. Data obtained was analaysed using unpaired t-test we have observed statistically highly significant ($P<0.01$). There is increase in mean arterial blood pressure in group A compared to group B. There was a reduction to Inj. thiopentone dosage requirements in group B compared to group A. Post operative sedation score was studied with ramsay sedation score. There was no significant changes in SpO2 in both groups at all intervals ($p>0.05$). We conclude that dexmedetomidine 1$\mu g.kg^{-1}$ is more effective than 0.5 $\mu g.kg^{-1}$ in attenuating haemodynamic responses to laryngoscopy and tracheal intubation, and reducing inj. thiopentone dosages during induction of anaesthesia without any systemic side effects and better post operative sedation score.

INTRODUCTION

Tracheal intubation is placement of a flexible plastic tube into the trachea to maintain an open airway, to facilitate ventilation of the lung and prevention of aspiration in critically ill or anesthetized patients. Direct laryngoscopy and passage of an endotracheal tube are noxious stimuli produces adverse hemodynamic responses, due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. Increases plasma catecholamines concentration [1] leads to hypertension, tachycardia and arrhythmia. The magnitude of hemodynamic response is greater with increasing force and duration of laryngoscopy and endotracheal intubation.[2] The elevation of blood pressure typically starts within 5 sec of laryngoscopy, reached pick in 1-2 min and returns to control level within 5 min.[3] 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. At least in such individuals there is a necessity to blunt this response. Reid and Brace [4] in 1940 were the first to report the circulatory responses to laryngeal and tracheal stimulation in an anesthetized man. Dexmedetomidine, a highly selective alfa-2 adrenergic agonist has sedative, anxiolytic, sympatholytic and analgesic effect. In addition, dexmedetomidine has been shown to decrease perioperative catecholamines concentration and promote hemodynamic and adrenergic stability, as well as

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it decrease induction doses of intravenous anaesthetic and also decrease intra operative opioid and volatile anaesthetic requirements for maintenance of anaesthesia.[5,6] The purpose of our study was to investigate and compare the effects of two different doses of dexmedetomidine on controlling hemodynamic response to tracheal intubation and reducing inj. thiopentone dosages during induction of anaesthesia.

MATERIALS AND METHODS

The study protocol was approved by institutional ethical committee and written informed consent was obtained from all the patients. Sixty normotensive patients (ASA Grade I or II, age between 18-55 years, weight between 35-100 kg, Mallampatti Grade I or II) were randomly allocated in two groups (30 patients each). Group A received inj. dexmedetomidine 0.5µg/kg, IV over 10 min. While Group B received inj. dexmedetomidine 1 µg/kg, IV over 10 min.

In all the patients, IV line was secured and routine monitor like pulse oxymeter (SpO2), non-invasive blood pressure (BP) and electrocardiogram were attached. Vital data like B.P. (SBP, DBP), heart rate (HR) and SpO2 were recorded as pre-induction parameters (basal) and pre-medication inj. Glycopyrrolate 0.2mg IV was given. Anaesthesia was induced with inj. thiopentone 5 mg/kg IVand inj. succinylcholine 2mg/kg. Anaesthesia was maintained using 66% nitrous oxide, 33% oxygen, inj. vecuronium. Measurements of HR, SBP, DBP, and SpO2 were performed. Induction dosages of Inj. thiopentone were recorded and post operative sedation score was measured with ramsay sedation score.

Parameters Studied

To compare the change in heart rate, systolic, diastolic and mean arterial pressures and SpO_2 readings during laryngoscopy and tracheal intubation with two different dosages of dexmedetomidine. To compare the dose requirements of thiopentone for induction of anaesthesia with both the dosages. To compare the post-operative sedation score with both the dosages of dexmedetomidine.

Modified Ramsay Sedation Score

SCORE	DESCRIPTION
1	Anxious and agitated or restless, or both
2	Cooperative, orientated, and tranquil
3	Drowsy, but responds to commands
4	Asleep, brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep and unarousable

Data were analyzed with unpaired independent sample t-test to measure difference between the groups. P>0.05 was consider as not significant, P<0.05 was considered as significant and p<0.01 was considered as highly significant. The results were presented as means and standard deviation.

RESULTS

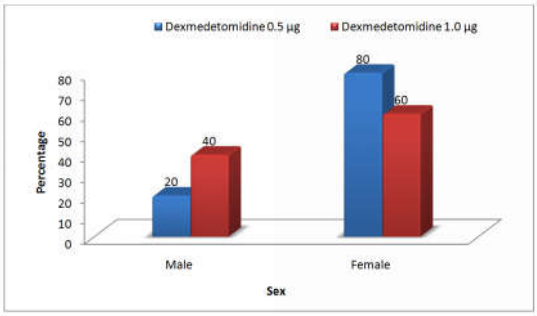
Demographic profile of two groups is given in Table.

Table - 1 Sex difference in both groups

Sex	Drug				Total	
	Dexmedetomidine 0.5 µg		Dexmedetomidine 1.0 µg			
	N	%	N	%	N	%
Male	6	20.0	12	40.0	18	30.0
Female	24	80.0	18	60.0	42	70.0
Total	30	100.0	30	100.0	60	100.0

Chi-Square Tests

	Value	df	Sig.
Pearson Chi-Square	2.857	1	0.091



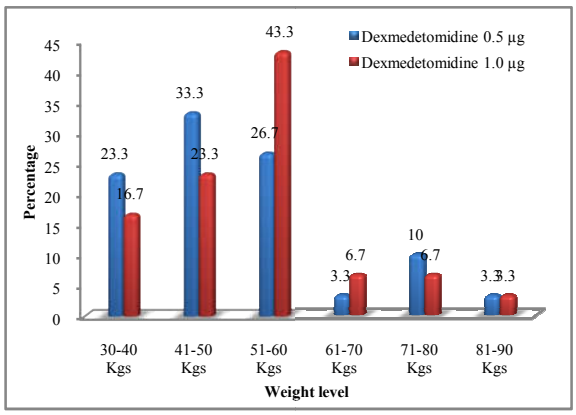
20% (6) of the patients in group (A) were males while in group (B) it was 40% (12). 80% (24) of the patients in the group (A) were females while in contrast it was 60% (18) in group (B).

Table – 2 Weight difference in both groups

Weight level	Drug				Total	
	Dexmedetomidine 0.5 µg		Dexmedetomidine 1.0 µg			
	N	%	N	%	N	%
30-40 Kgs	7	23.3	5	16.7	12	20.0
41-50 Kgs	10	33.3	7	23.3	17	28.3
51-60 Kgs	8	26.7	13	43.3	21	35.0
61-70 Kgs	1	3.3	2	6.7	3	5.0
71-80 Kgs	3	10.0	2	6.7	5	8.3
81-90 Kgs	1	3.3	1	3.3	2	3.3
Total	30	100.0	30	100.0	60	100.0
Mean ± SD	**52.3667±13.44076**		**55.1000±13.05783**		**53.7333 ±13.209**	

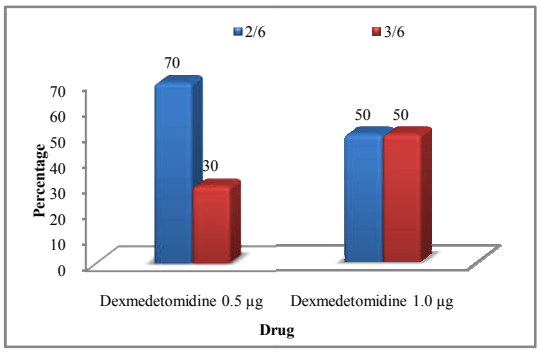
Chi-Square Tests

	Value	df	Sig.
Pearson Chi-Square	2.587	5	.763



The mean weight is 52.36±13.44 kgs in group (A) and 55.100±13.05 kgs in group (B).

Haemodynamic changes: There was increase in mean SBP, DBP and MAP in Group A as compare to Group B, which was statistically highly significant (P<0.01). SBP, DBP, MAP, These haemodynamic changes after tracheal intubation were significantly lesser with the use of dexmedetomidine group B than with group A. The induction dose of thiopentone was significantly, lesser in dexmedetomidine group B than with dexmedetomidine group A. The post – operative sedation was comparably good in dexmedetomidine group B .we demonstrated that administration of a single dose of dexmedetomidine (1µg/kg/wt) before induction is an effective method for attenuation the haemodynamic responses to laryngoscopy and tracheal intubation in patients undergoing general anaesthesia along with a decreased dose of thiopentone. None of patients in either group had any cardiovascular or respiratory side effects due to dexmedetomidine.



Inj. Thiopentone Dose (mg)

This table compares the dosages of Thiopentone sodium for induction of anaesthesia in both the groups.

Table – 3 Variation in mean arterial pressure in both groups

Drug	N	Mean induction (mmhg)		Std. Deviation		t	Sig.
		Pre	Post	Pre	Post		
Dexmedetomidine 0.5 µg	30	89.66	99.80	9.976	10.317	6.350	0.000
Dexmedetomidine 1.0 µg	30	88.00	83.16	11.444	9.969		

The mean (MAP) post intubation was 99.80±10.31 in group (A) as compared to 83.16±9.96 in group (B).

The mean arterial pressure was increased about 11% in group (A) as compared to 6% decrease in group (B) which was highly significant (P=0.00).

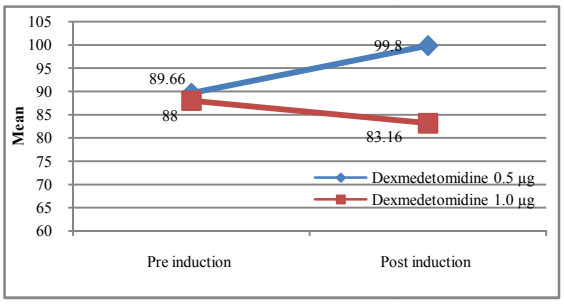


Table – 4 Post-Operative Sedation Score

Post- op Sedation Score	Drug				Total	
	Dexmedetomidine 0.5 µg		Dexmedetomidine 1.0 µg			
	N	%	N	%	N	%
2/6	21	70.0	15	50.0	36	60.0
3/6	9	30.0	15	50.0	24	40.0
Total	30	100.0	30	100.0	60	100.0

Chi-Square Tests

	Value	df	Sig.
Pearson Chi-Square	2.500	1	0.114

70% of patients had a sedation score of 2 in group (a) (co-operative, oriented and tranquil) as compared to 50% in group (B). Only 30% of them had a sedation score of 3 in group (A) in contrast to group (B) were 50% of them had a sedation score of (3).

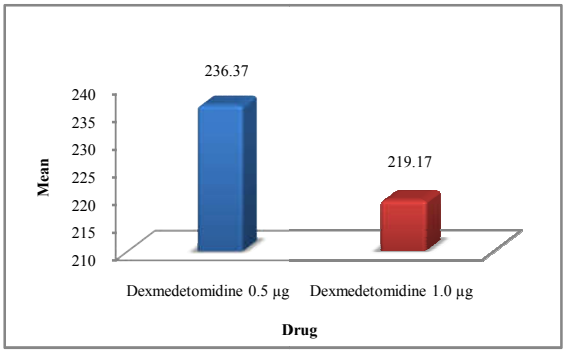
Table – 5 Comparison of Thiopentone dosages between two groups

Drug	N	Mean	Std. Deviation	t	Sig.
Inj. Thiopentone sodium	30	236.67	32.65106	2.216	0.031
Inj. Thiopentone sodium	30	219.17	28.37809		

The mean dosages of inj. Thiopentone for induction was 236.67±32.65 mg in group (A) as compared to 219.17±28.37 in group (B).

The decrease in dosages requirement was approximately 17% in the group (B) dexmedetomidine (1µg/kg/wt) as compared to the group (A) (0.5µg/kg/wt) (P=0.031) which was significant.

Comparison of Thiopentone dosages between two groups



DISCUSSION

Most of general anaesthetic procedures in modern anaesthetic practice are carried out with endotracheal intubation. Tracheal intubation and direct laryngoscopy are considered as the most critical event during administration of general anesthesia as they provoke transient but marked sympathoadrenal response as hypertension and tachycardia. [7] These responses are

transitory variable and may not be significant in otherwise normal individuals. But in patient with cardiovascular compromise like hypertension, IHD, Cerebrovascular disease and in patient with intracranial aneurysms, even these transient changes in haemodynamics can result in potentially harmful effects like left ventricular failure, pulmonary oedema, myocardial ischemia [3], ventricular dysrrhythmias and cerebral haemorrhage. [8] This is by far the most important indication for attenuation of haemodynamic response to laryngoscopy and tracheal intubation during general anaesthesia.

Many methods like use of inhalational anaesthetic agents, lidocaine [9], opioids [10,11], direct acting vasodilator [12,13], calcium channel blockers [14,15], and β-blockers [16] have been tried by various authors for blunting haemodynamic response to laryngoscopy and tracheal intubation. But all such manoeuvres had their own limitations. For example, with opioids respiratory depression [17] and chest wall rigidity [18] were potential problems, use of halothane was associated with dysrhythmias [19], calcium channel blocker produced reflex tachycardia [20], direct acting vasodilator needed invasive haemodynamic monitoring and lidocaine did not give consistent result in blunting the haemodynamic responses to laryngoscopy and intubation. Beta blockers are also one group of pharmacological agents employed for blunting haemodynamic response to laryngoscopy and intubation but they blunt HR response better than BP response. [16]

The α -2 adrenoreceptor are involved in regulating the autonomic and cardiovascular systems, which are located on blood vessels, where they mediate vasoconstriction and on sympathetic terminals they inhibit norepinephrine release. The α -2 receptors are also located within the central nervous system (CNS) and their activation leads to sedation, a reduction of tonic levels of sympathetic outflow and an augmentation of cardiac-vagal activity. This can result in a decrease in HR and cardiac output. The use of α-2 agonists in the perioperative period has been associated with reduced anaesthetic requirements and attenuated HR and BP responses to stressful events. In addition α-2 receptors within the spinal cord modulate pain pathways, providing some degree of analgesia.[21,22] The analgesic, sedative, anxiolytic, sympatholytic and blunting of exaggerated haemodynamic responses by administration of dexmedetomidine are being extensively studied and are mainly mediated by the activation of alpha- 2 receptors located in the post-synaptic terminals in the CNS, which causes decreased neuronal activity and augmentation of the vagal activity.[23] Another α -2 agonist Clonidine, is also used by various authors to blunt the haemodynamic response for laryngoscopy and intubation.[24] Recently, the use of dexmedetomidine has been dramatically increased. This highly selective α-2 agonist has a set of unique effects that include titratable sedation, sympatholysis and analgesia without significant respiratory depression.[25]

The present study was undertaken to know two different doses of dexmedetomidine (0.5μg/kg and 1μg/kg), in attenuation of haemodynamic response to laryngoscopy and tracheal intubation during general anaesthesia and reducing in thiopentone dosages during induction of anaesthesia and calculating post operative sedation score.

In our study after giving dexmedetomidine the mean HR, SBP, DBP and MAP were decreased in both groups. In Group A, we have observed increases in mean SBP, DBP and MAP as compare to Group B (during laryngoscopy and intubation) which was statistically highly significant. ($p<0.01$) There were increases in mean HR in Group A as compare to Group B (during laryngoscopy and intubation was statistically highly between groups ($p>0.05$).There was no significant change in Spo2 in both groups. The decrease in dosages requirement of Inj. thiopentone was approximately 17% in the group (B) dexmedetomidine (1μg/kg/wt) as compared to the group (A) (0.5μg/kg/wt) ($P=0.031$) which was significant. 70% of patients had a sedation score of 2 in group (a) (co-operative, oriented and tranquil) as compared to 50% in group (B). Only 30% of them had a sedation score of 3 in group (A) in contrast to group (B) were 50% of them had a sedation score of (3).

In a similar study done by A Esra Sağıroğlu *et al*[26], they found that after giving dexmedetomidine 1 $\mu g.kg^{-1}$ (Group A) and 0.5 $\mu g.kg^{-1}$ (Group B), SAP, DAP, MAP and HR levels were significantly lower after induction and 5 min after intubation than baseline levels. But in Group B, these levels were significantly higher after tracheal intubation while in Group A, SAP, DAP, MAP were significantly lower ($p<0.01$). They conclude that dexmedetomidine 1 $\mu g.kg^{-1}$ is effective to suppress haemodynamic responses to tracheal intubation but dexmedetomidine 0.5 $\mu g.kg^{-1}$ hasn't the same effect. In this study any hypotension or bradycardia were not observed and any medical intervention was not required. Significant respiratory depression, apnea, muscle rigidity or decrease in SpO2 were also not seen in any patient.

In study done by Ferdi Menda *et al* [27], they demonstrated that in dexmedetomidine 1μg/kg group, SAP, DAP and MAP were lower at all times in comparison to baseline values. While in the placebo group, SAP, DAP and MAP decreased after the induction of general anesthesia and five min after the intubation compared to baseline values. They also demonstrated that after induction of general anaesthesia, the drop in HR was higher in dexmedetomidine 1μg/kg group than placebo group. Whereas, 1 min after intubation HR increased significantly in placebo group, while it decreased in dexmedetomidine group.

Tanyoung Pipanmekaporn *et al* [28] demonstrated that during intubation and 10 min afterward (T1- T10), the mean HR, SBP, DBP and MAP in the control Group were significantly higher than those in the dexmedetomidine 0.7μg/kg Gr throughout the study period.

In similar study by Varshali M. Keniya *et al*.[29], the increase in SBP after intubation was 40% in control Group as compared to 8% in dexmedetomidine 1μg/kg Gr ($P=0.00$). While the increase in DBP after intubation was 25% in control Group as compared to 11% in dexmedetomidine 1μg/kg Group ($P=0.001$). They also found that 1 μg/kg of dexmedetomidine Group received more treatments for bradycardia than patients in the

control Group. Arpita Laha *et al*. [30] demonstrated that pretreatment with dexmedetomidine 1µg/kg attenuated but did not totally abolish cardiovascular and catecholamine responses to tracheal intubation after induction of anaesthesia. They found increase in HR, SBP and DBP after intubation and at 1, 2, 3 and 5 min in both dexmedetomidine and control Gr, but this rise was significantly less with dexmedetomidine. Bajawa SS *et al* [31] found that the dose of 1 µg/kg of dexmedetomidine attenuate but did not completely obtund the haemodynamic responses to laryngoscopy and tracheal intubation. In a similar study done by Jeong Han Lee *et al* [32], they observed that in dexmedetomidine 1 µg/kg Group, the increase in SBP and DBP due to tracheal intubation were significantly lower than that of control Group.

Scheinin *et al* [33] reported that the use of α-2 agonist leads to bradycardia. Basar *et al* [34] had also reported that the incidence of bradycardia after single dose of 0.5µg/kg of dexmedetomidine was about 5%.

In our study, there was no significant changes in Spo2 in both groups at all intervals. Similar to our study, Ebert *et al* [11] didn't observe any apnea, airway obstruction or hypoxemia with bolus doses of dexmedetomidine. They reported that depression of respiration may be seen due to deep sedation, for the reason that α-2 adrenergic agonists don't have active role on the respiration centres. In contrary to our study, Belleville *et al* [21] found that dexmedetomidine, given as bolus dose of 1-2 µgkg-1, intravenously within two minutes, causes irregular ventilation and apnea episodes.

Limitation: There were three important limitations regarding this study.

1. Not assessed the quality of intubation.
2. We had not measured the plasma catecholamines levels.
3. We have not studied extubation response,

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