ORIGINAL RESEARCH PAPER

Anaesthesiology

STUDY THE COMPARATIVE EFFICACY OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE IN ATTENUATION OF HEMODYNAMIC RESPONSE DURING LARYNGOSCOPIC TRACHEAL INTUBATION IN HYPERTENSIVE PATIENTS.

KEY WORDS:

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INTRODUCTION

Endotracheal intubation is a process of trans-laryngeal placement of a tube into the trachea via the nose or mouth. Endotracheal intubation includes laryngoscopy and tracheal intubation. This process of laryngoscopy and tracheal intubation in adults are commonly accompanied by increase in arterial blood pressure and heart rate. [1] The hemodynamic changes are due to release of catecholamines, secondary to intense sympathetic response. [2,3,4] The cardiovascular response is a reflex phenomenon. This is due to nerves that carry the afferent impulse from the epiglottic and infra glottic regions to the vasomotor center to cause peripheral sympathetic response releasing adrenaline and noradrenaline. [5] The magnitude of hemodynamic changes observed may be dependent on various factors such as depth of anaesthesia, whether any measures are taken, prior agent used, the duration of laryngoscopy and intubation.

The increase in the pulse rate and blood pressure are usually transitory and may not be of much clinical significance in normal individuals. However, in patients with limited myocardial reserve, the tachycardia and hypertension may result in myocardial ischemia or infarction (MI); arrhythmias precipitate cardiac failure. [6] The hypertensive response may produce deleterious effects in patients with raised intracranial pressures (ICP) or intra-occular pressures (IOP), pheochromocytomas and vascular lesions such as intracranial arteriovenous malformations or those with aortic aneurysms and dissection. [6,7]

Even when hypertensive patients are pre-operatively made normotensive by anti-hypertensive medication, the pressor response is increased in hypertensive individuals. [8] Individuals with end organ decompensation may experience intra-operative myocardial infarction, abrupt left ventricular failure, dysrhythmias, and cerebral bleed. [6,8,9]

Various pharmacological and non-pharmacological techniques have been used by various authors to reduce the hemodynamic response to laryngoscopy and endotracheal intubation throughout the last half-century.

AIM AND OBJECTIVES:

To study the comparative efficacy of 2 different doses of DEXMEDETOMIDINE in attenuation of hemodynamic response during laryngoscopic tracheal intubation in hypertensive patients

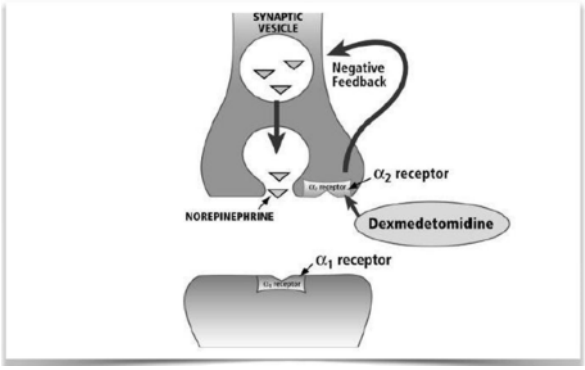
PRIMARY OUTCOMES:

To compare the efficacy of DEXMEDETOMIDINE of different doses on:

- Systolic Blood Pressure
- Diastolic Blood Pressure
- Mean Arterial Pressure
- Heart Rate

SECONDARY OUTCOME:

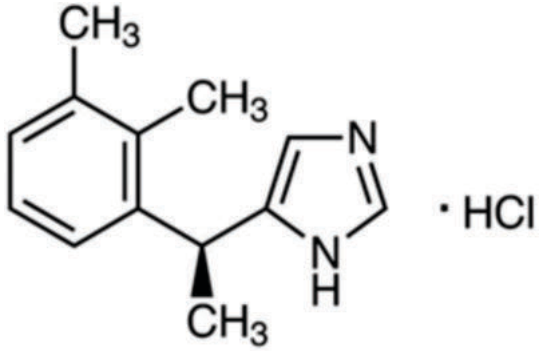
- Effect on ECG
- any side effects



PHARMACOLOGY OF DEXMEDETOMIDINE:

The pharmacologically active s-enantiomer of Dexmedetomidine, a veterinary anaesthetic drug, is Dexmedetomidine hydrochloride, an imidazole molecule. (+)-4-(s)[2 3- (dimethylpheny]) ethyl]-11 H-imidazole monohyrochloride is its chemical name. Ci3H16NHCl is its empirical formula, and its molecular weight is 236.7. [45]

Structural Formula:



PHYSIOCHEMICAL PROPERTIES:

A white or almost white powder having a Pka of 7.1 that is easily soluble in water. Water at pH 7.4 has a partition coefficient of 2.89 in octanol . Dexmedetomidine Hydrochloride for intravenous use (Dexem, Themis Medicare Ltd., 200**µg/kg**) is a preservative-free Dexmedetomidine available in a 2 mL ampoule. It can also be used for epidural and intrathecal anaesthesia.

MECHANISM OF ACTION OF DEXMEDETOMIDINE:

Dexmedetomidine is the dextro enantiomer of medetomedine, a methylated derivative of etomidine. It has an alpha-2:alpha-1 binding affinity ratio of 1620:1, and its effects are dosage dependently reversed by administration of a selective alpha-2 antagonist such as atipamezole. [47]

Dexmedetomedine's pharmacodynamic effects are mediated by certain alpha-2 receptor subtypes. Sedation, hypnosis, analgesia, sympatholytic, neuroprotection, and insulin secretion inhibition appear to be promoted by antagonists of the alpha 2A receptor. [48,49] Shivering is suppressed centrally, analgesia is promoted at spinal cord locations, and peripheral artery vasoconstriction is induced when the alpha -2B receptor is activated. The alpha 2C receptors are involved in the control of epinephrine outflow from the adrenal medulla, as well as cognition, sensory processing, mood, and stimulant-induced locomotor activity. All three alpha-2 receptor subtypes appear to affect the inhibition of nor epinephrine release in the same way. [50]

HYPERTENSION

Definition of Hypertension:

- In accordance with most major guidelines it is recommended that hypertension be diagnosed when a person's systolic blood pressure (SBP) in the office or clinic is ≥140 mm Hg and/or their diastolic blood pressure (DBP) is ≥90 mm Hg following repeated examination (see below, Section 3). Table 1 provides a classification of BP based on office BP measurement, Table 2 provides ambulatory and home BP values used to define hypertension; these definitions apply to all adults (>18 year old). These BP categories are designed to align therapeutic approaches with BP levels.
- High-normal BP is intended to identify individuals who could benefit from lifestyle interventions and who would receive pharmacological treatment if compelling indications are present.
- Isolated systolic hypertension defined as elevated SBP (≥140 mm Hg) and low DBP (<90 mm Hg) is common in young and in elderly people. In young individuals, including children, adolescents and young adults, isolated systolic hypertension is the most common form of essential hypertension. However, it is also particularly common in the elderly, in whom it reflects stiffening of the large arteries with an increase in pulse pressure (difference between SBP and DBP).
- Individuals identified with confirmed hypertension (grade 1 and grade 2) should receive appropriate pharmacological treatment.

Office Blood Pressure Levels (mm Hg)		
<130/85	130–159/85–99	>160/100
Remeasure within 3 years (1 year in those with other risk factors)	If possible confirm with out-of-office blood pressure measurement (high possibility of white coat or masked hypertension). Alternatively confirm with repeated office visits.	Confirm within a few days or weeks

MATERIALS AND METHODS

1) Place of Study:

Department Of Anaesthesiology, Hitech Medical College and Hospital, Bhubaneswar

2) Duration of Study:

September 2019 - August 2021

3)Study Type:

Experimental Study

4) Source of Data:

Patients Admitting to Surgery Ward after taking Informed Consent

5) Data Analysis:

Data was analysed by Statistical Method. P Value < 0.05 was considered to be Significant

6)Sample Size:

The Patients who satisfied the below mentioned criteria were considered for the study.

Inclusion Criteria:

1) ASA Grading, I and II.
2) Age Group:35-65 Years of Age
3) Hypertension Grade 1 and Grade 2
4) Newly Detected Hypertensives on Short Duration of Medical Therapy (Less Than 7 Days) Coming for Emergency Surgeries.
5) Mallampatti Grade 1 & 2

Exclusion Criteria:

1) Patient Refusal
2) Pulse Rate <60 Beats/Minutes
3) ECG Showing Heart Block
4) BP>180/100mmhg
5) Other Associated Comorbid Conditions (Diabetes Mellitus, IHD, COPD, History Of Ml In Last 6 Months, Significant Hepatic, Renal And Metabolic Dysfunction)
6) Anticipated Difficult Intubation
7) BMI>30kg/M2
8) History of Reaction To DEXMEDETOMIDINE
9) Psychiatric Illness
10) Pregnant and Nursing Women
11)Patients with Full Stomach and Emergency Surgical Intubation.

METHODOLOGY

Patients satisfying the above said inclusion and exclusion criteria will be subjected to our study.

They will be enrolled in 2 equal groups (A and B) The patients are randomly allocated into 2groups by computer generated random numbers.

GROUP A received injection DEXMEDETOMIDINE 0.75 micrograms/kg diluted in 20 ml normal saline by syringe pump over 10 minutes before induction.

GROUP B will receive injection DEXMEDETOMIDINE 1µg/kg diluted in 20/ml normal saline by syringe pump over 10 minutes before induction.

This was a double blinded study. Drugs were prepared by an anaesthesiologist who was not involved in patient management and recording of data. Anaesthesist involved in patient management and recording of data were provided with both syringes A and B.

After the pre-anaesthetic check up on arrival in operation theatre after taking consent IV line was secured with 18-gauge cannula. RL was administered. A monitor was attached for HR, BP (SBP, DBP, MAP) and oxygen saturation. All patients were premedicated with Inj. GLYCOPYROLATE 0.2mg and Inj. MIDAZOLAM 1mg, 30 minutes before induction. Baseline HR, BP, SPO2 were measured after premedication. Syringe A/B were given over 10 minutes before induction. All patients were pre-oxygenated for 5 minutes and then patients were induced with IV PROPOFOL 2g/kg with IV LIGNOCAINE (preservative free) in concentration of 0.1%, IV SUCCINYLCHOLINE 2mg/kg body weight and IV FENTANYL 1 mcg/kg.

Anaesthesia was maintained with O2 and N2O in a ratio of 50% each of Inj. ISOFLOURANE 0.4% muscle relaxation with IV VECURONIUM 0.1 mg/kg with top ups of 0.04mg/kg. After

surgery reversal was achieved with IV NEOSTIGMINE 0.05mg/kg and IV GLYCOPYROLATE 0.01mg/kg. After adequate recovery patient was shifted to post anesthesia care unit and monitored then shifted to ward.

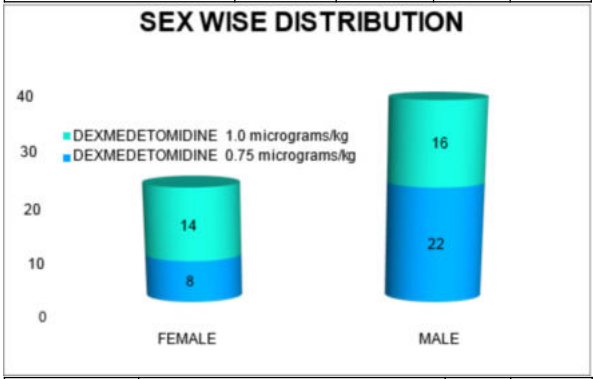
The following parameters were observed:
1) Baseline readings (pre induction) of HR, SBP, DBP, MAP, SPO2
2) Reading of above said parameters at 1,3,5 minutes after induction
3) Continuous ECG monitoring
4)Any adverse effects

RESULTS

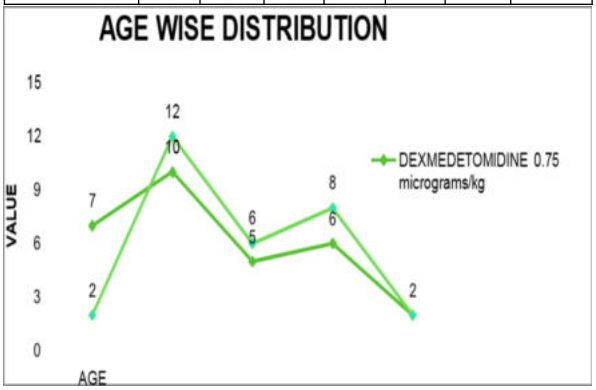
60 patients under this study were categorized into 2 groups (DEXMEDETOMIDINE 0.75 micrograms/kg & DEXMEDETOMIDINE 1.0 micrograms/kg). They comprised both sexes with age ranging from 40-62 years.

Demographic profile, baseline parameters between two groups were comparable and were not statistically significant (P>0.05).

INJECTION	SEX		Total	P VALUE
	FEMALE	MALE		
DEXMEDETOMIDINE (0.75 micrograms/kg)	8	22	30	0.108
DEXMEDETOMIDINE (1.0 micrograms/kg)	14	16	30	
Total	22	38	60	

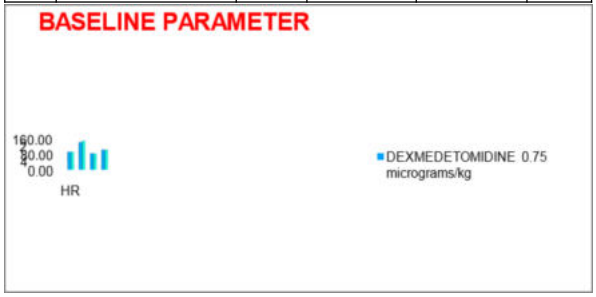


INJECTION	AGE					Total	P VALUE
	40-45	46-50	51-55	56-60	61-65		
DEXMEDETOMIDINE 0.75 micrograms/kg	7	10	5	6	2	30	0.503
DEXMEDETOMIDINE 1.0 micrograms/kg	2	12	6	8	2	30	
Total	9	22	11	14	4	60	



The mean & S.D. age of the patients is 51.56 ± 6.24 in Group D & E. There is no significant difference in the age composition of the cases in the two groups(P 0.503).

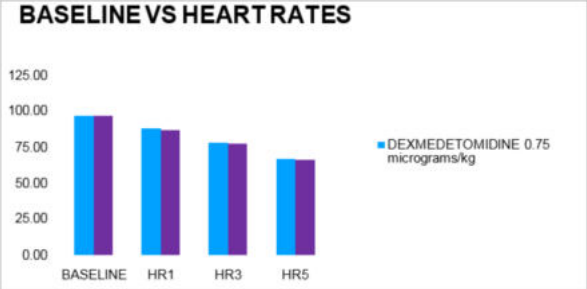
BASELINE PARAMETER					
Group		Mean	Std. Deviation	t Statsistics	P Value
HR	DEXMEDETOMIDINE 0.75 micrograms/kg	96.97	11.59	0.035	0.972
	DEXMEDETOMIDINE 1.0 micrograms/kg	96.87	10.72		
SBP	DEXMEDETOMIDINE 0.75 micrograms/kg	148.80	15.57	1.275	0.207
	DEXMEDETOMIDINE 1.0 micrograms/kg	156.20	27.70		
DBP	DEXMEDETOMIDINE 0.75 micrograms/kg	88.73	7.07	0.893	0.376
	DEXMEDETOMIDINE 1.0 micrograms/kg	86.93	8.49		
MAP	DEXMEDETOMIDINE 0.75 micrograms/kg	108.23	8.96	0.336	0.738
	DEXMEDETOMIDINE 1.0 micrograms/kg	107.43	9.49		



The mean and SD of HR, SBP, DBP, MAP of the patients were given in the above table respectively. There is no statistical difference in baseline parameters between two groups.

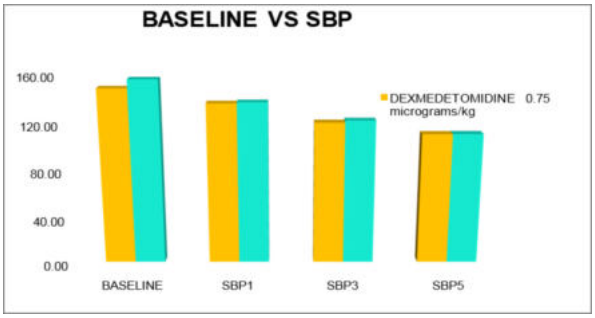
INJECTION		Mean	Std. Deviation	t Statistics	P Value
HR	DEXMEDETOMIDINE 0.75 micrograms/kg	96.97	11.59	.035	.972
	DEXMEDETOMIDINE 1.0 micrograms/kg	96.87	10.72		
HR1	DEXMEDETOMIDINE 0.75 micrograms/kg	87.90	9.33	.338	.737
	DEXMEDETOMIDINE 1.0 micrograms/kg	87.07	9.78		
HR2	DEXMEDETOMIDINE 0.75 micrograms/kg	78.47	7.53	.499	.620

	DEXMEDETOMIDINE 1.0 micrograms/kg	77.47	8.00		
HR3	DEXMEDETOMIDINE 0.75 micrograms/kg	67.10	5.38	.377	.708
	DEXMEDETOMIDINE 1.0 micrograms/kg	66.57	5.58		



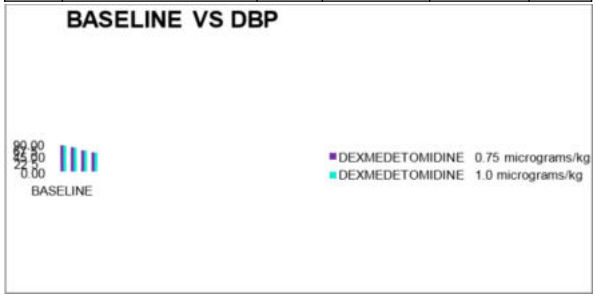
The mean and SD of HR, with different time interval of the patients were given in the above table respectively. There is no statistical difference in baseline parameters between two groups.

INJECTION		Mean	Std. Deviation	t Statistics	P Value
SBP	DEXMEDETOMIDINE 0.75 micrograms/kg	148.80	15.57	-1.275	.207
	DEXMEDETOMIDINE 1.0 micrograms/kg	156.20	27.70		
SBP1	DEXMEDETOMIDINE 0.75 micrograms/kg	136.50	11.77	-.291	.772
	DEXMEDETOMIDINE 1.0 micrograms/kg	137.37	11.32		
SBP2	DEXMEDETOMIDINE 0.75 micrograms/kg	120.60	12.39	-.572	.570
	DEXMEDETOMIDINE 1.0 micrograms/kg	122.33	11.04		
SBP3	DEXMEDETOMIDINE 0.75 micrograms/kg	111.00	9.62	-.054	.957
	DEXMEDETOMIDINE 1.0 micrograms/kg	111.13	9.52		



The mean and SD of SBP, with different time interval of the patients were given in the above table respectively. There is no statistical difference in baseline parameters between two groups.

INJECTION		Mean	Std. Deviation	t Statistics	P Value
DBP	DEXMEDETOMIDINE 0.75 micrograms/kg	88.73	7.07	.893	.376
	DEXMEDETOMIDINE 1.0 micrograms/kg	86.93	8.49		
DBP1	DEXMEDETOMIDINE 0.75 micrograms/kg	81.93	7.08	.819	.416
	DEXMEDETOMIDINE 1.0 micrograms/kg	80.27	8.60		
DBP2	DEXMEDETOMIDINE 0.75 micrograms/kg	71.20	5.22	.406	.686
	DEXMEDETOMIDINE 1.0 micrograms/kg	70.57	6.76		
DBP3	DEXMEDETOMIDINE 0.75 micrograms/kg	64.80	6.04	.785	.436
	DEXMEDETOMIDINE 1.0 micrograms/kg	63.57	6.12		



The mean and SD of DBP, with different time interval of the patients were given in the above table respectively. There is no statistical difference in baseline parameters between two groups.

INJECTION		Mean	Std. Deviation	t Statistics	P Value
MAP	DEXMEDETOMIDINE 0.75 micrograms/kg	108.23	8.96	.336	.738
	DEXMEDETOMIDINE 1.0 micrograms/kg	107.43	9.49		
MAP1	DEXMEDETOMIDINE 0.75 micrograms/kg	99.53	7.64	.391	.697
	DEXMEDETOMIDINE 1.0 micrograms/kg	98.73	8.18		
MAP2	DEXMEDETOMIDINE 0.75 micrograms/kg	87.63	6.35	.493	.624

	DEXMEDETOMIDINE 1.0 micrograms/kg	86.80	6.73		
MAP 3	DEXMEDETOMIDINE 0.75 micrograms/kg	79.30	6.49	.158	.875
	DEXMEDETOMIDINE 1.0 micrograms/kg	79.03	6.54		

DISCUSSION

Laryngoscopy and endotracheal intubation are known to be associated with perioperative hemodynamic instabilities, such as, hypertension, cardiac arrhythmia, and tachycardia, occurring secondary to the stimulation of the sympathetic nervous system [3,4,5]. In addition, sudden hemodynamic changes may lead to serious complications, especially in patients with a comorbid disease like hypertension [113]. Accordingly, anesthesiologists have devised means of attenuating the sympathetic stimulation in order to decrease the incidences of perioperative complications by using drugs, including opioids, adrenergic blockers, vasodilators, calcium channel blockers, lidocaine, and inhaled anesthetics . Although many reports claim various drugs effectively attenuate hemodynamic responses, they also mention unexpected side effects like hypoventilation, hypotension, bradycardia, and muscle rigidity.

Dexmedetomidine is a selective alpha-2 agonist with a sympatholytic effect as well as sedative, hypnotic, anxiolytic, analgesic, and anesthetic sparing effects [27], which are mediated through alpha-2 adrenoreceptors in the central and peripheral nervous systems. Because of these effects, anesthesiologists use Dexmedetomidine as a spinal anaesthesia adjunct as well as for general anaesthesia. In addition, Dexmedetomidine can be administered for intensive care unit sedation, procedural sedation, and monitored anaesthesia care.

In previous studies, researchers have used doses of Dexmedetomidine ranging from 0.25 to 2 μg/kg. The effects of Dexmedetomidine are known to be dose-dependent, but the probabilities of side effects like bradycardia or hypotension also increase with dosage. Therefore, optimal dose adjustment according to the characteristics of the patient group is important. Lawrence et al. [116] reported that a single dose of Dexmedetomidine before anaesthesia induction attenuated the hemodynamic response to intubation and extubation; however, they used 2 μg/kg Dexmedetomidine, and hypotension and bradycardia were foundto occur more frequently in their Dexmedetomidine group than in the control group. Keniya et al. [117] reported that patients administered 1 μg/kg Dexmedetomidine required more treatment for bradycardia than the controls did. In contrast, Scheinin et al. [118] reported that 0.6 μg/kg Dexmedetomidine attenuated cardiovascular responses to laryngoscopy and tracheal intubation in healthy individuals without serious side effects, and Basar et al. [119] reported that 0.5 μg/kg Dexmedetomidine decreased thiopental requirements without causing serious hemodynamic effects or affecting recovery time. However, the abovementioned studies were conducted in young and normotensive individuals. Dose reduction is required in the elderly because of age-associated pharmacodynamic changes, and some studies have reported more pronounced hemodynamic responses to drugs in patients with hypertension[23,24].

Hence, we decided to preoperatively administer 0.75 μg/kg Dexmedetomidine rather than 1.0 μg/kg to our elderly patients undergoing treatment for hypertension, and we found at this dose effectively suppressed the hemodynamic responses caused by endotracheal intubation without serious side effects.

In 0.75 μg/kg group all hemodynamic parameters were significantly lower at 5 min after intubation than at baseline and showed a decreasing trend from 1 min to 5 min after intubation. However, at 5 min after intubation, the hemodynamic values were still in the normal range (changes within 20%), and the commencement of surgical procedures halted this decreasing trend.

Basar et al. [119] reported that 0.5 μg/kg Dexmedetomidine decreased thiopental requirements, with an administered dose of 4.9 mg/kg for anesthesia induction. Keniya et al. [117] reported that 1 μg/kg Dexmedetomidine decreased thiopental requirements, with an administered dose of 4.4 mg/kg for anaesthesia induction. Therefore, in the present study, we decided to administer 5 mg/kg of thiopental for anaesthesia induction.Propofol is another favourable induction agent with a cardiovascular depressive property, and is more effective at suppressing stress hormone release than is thiopental .Studies have shown severe hypotensive episodes requiring vasoconstrictor treatment after general anaesthesia induction in patients chronically using angiotensin II antagonists .Although none of our patients experienced a hypotensive episode, additional study of the hemodynamic responses to different antihypertensive drugs and alpha-2 agonists, and the use of propofol rather than thiopental for anaesthesia induction, may be needed.

In conclusion, our study shows that the preoperative administration of 0.75 μg/kg Dexmedetomidine before anaesthesia induction effectively suppresses the hemodynamic changes caused by endotracheal intubation in hypertensive patients without causing any side effects.

CONCLUSION

From the present study it can be concluded that, 1μg/kg is effective for hemodynamic response but using a lower dose ie 0.75μg/kg is equally effective in hypertensive patients for hemodynamic response after tracheal intubation.

REFERENCES

1. Reid, Brace: Irritationof respiratory tractand its reflex effecton heart-SurgeryGynecology Obstetrics. 1940:70:157.
2. Kovac AL. Controlling the haemodynamic response to laryngoscopy andendotracheal intubation. Journal of Clinical Anaesthesia 1996;8:63-79.
3. Kayhan Z, Aldemir D, Metler H, Ogus E. Which is responsible for thehaemodynamic responseduetothelaryngoscopyande n d o t r a c h e a l intubation Catecholamines, vasopressin Orangiotensin? European Journal of Anesthesiology 2005;22:780-5.
4. Morin AM, Gelbner G, Schwarz U, Kahl M, Adams HA, Hulf H, et al.Factorsinfluencing pre-operative stress responses in coronary artery bypass graft patients. BMC Anaesthesiology 2004;4(7).
5. Derbyshire DR, Chmielewski A, Fell D, Vaters M, Achola K, Smith G. Plasmacatecho lamine response to tracheal intubation. Br J Anaesth 1983;55:855-9.
6. Fox EJ, Sklar GS, Hill CH, Villanue Var, King BD. Complications related tothe pressor response to endotracheal intubation. Anaesthesiology. 1977;47:524-5.
7. King BD: Harris L, Greifenstein F, Elder J, Dripps RD. Reflex circulatory responses to direct laryngoscopy and intubation under general anaesthesia. Anaesthesiology.1951;12:556-66.
8. Cedric Preys Roberts. Anaesthesia and hypertension. Br J Anaesth 1984;56:711-24.
9. Ronald D Miller. Miller's Anesthesia volume 2 Seventh edition 2010.
10. Karl et al- Insertion of LMA in place of endotracheal intubation to attenuate thecardiovascular response. IJA, 1999:43:30-35.