ORIGINAL ARTICLE

EFFICACY OF INTRAVENOUS DEXMEDETOMIDINE IN ATTENUATING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION: A DOUBLE BLIND STUDY

Venugopal S [1], Jitesh M. Rasquinha[2]

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ABSTRACT: BACKGROUND: Laryngoscopy and intubation are associated with cardiovascular changes such as hypertension, tachycardia, dysarrythythmias and even, myocardial ischemia and increased circulating catecholamines. This study highlights that premedication with dexmedetomidine attenuates the pressor response associated with laryngoscopy and tracheal intubation. **METHODS:** This is a double blind randomized controlled clinical study on 62 patients, undertaken to check the efficacy of iv dexmedetomidine 1 µg /kg in attenuating the cardiovascular stress response during laryngoscopy and endotracheal intubation. This study was conducted with a population of patients undergoing elective surgeries. (aged 25-50 yr, ASA-physical class I-II). P value <0.05 was considered statistically significant. **RESULT:** 31 patients, each were categorized into Group A and Group B, Group A patients received 1 µg/kg iv dexmedetomidine in 100 ml of normal saline, 30 minutes before induction. Group B patients received placebo (100 ml normal saline), 30 minutes before induction. **CONCLUSION**: From the study it is concluded that premedication with dexmedetomidine attenuates the pressor response associated with laryngoscopy and tracheal intubation. The attenuation occurs within 5 minutes following laryngoscopy and intubation and becomes maximum by 10 minutes. The haemodynamic parameters reach near base line values after 5-10 minutes of intubation.
KEYWORDS: Dexmedetomidine, Laryngoscopy, Hypertension.

INTRODUCTION: Laryngoscopy and intubation are associated with cardiovascular changes such as hypertension, tachycardia, dysarrythythmias and even, myocardial ischemia and increased circulating catecholamines. Although the reflex responses are of short duration and of little consequences in healthy patients, they may produce profound disturbances in patients with underlying abnormalities, such as coronary artery disease, reactive airway or intracranial neuropathology.

Attempts to reduce these untoward cardiovascular responses during laryngoscopy and intubation have included deep general anesthesia, pretreatment with intravenous lidocaine, narcotics, topical anesthesia, beta-blockers, calcium channel blockers, ACE inhibitors, vasodilators etc. None of these drugs are entirely satisfactory as the reflex is not completely blocked. These agents used to block the response may themselves produce undesirable side effects. Opioids like alfentanil, remifentanil, fentanyl, sufentanil, morphine, pethidine and buprenorphine are used to attenuate pressor response during laryngoscopy and tracheal intubation.[1,2,3,4,5] Intranasal nitroglycerine is also used to attenuate the pressor response to laryngoscopy and intubation.[6] Intravenous lidocaine has been known to reduce anesthetic requirement by 30 percent with a

dose of 1.5mg/kg I.V bolus, which minimally depresses the cardiovascular system and reduces the pressor response. Topical lidocaine spray is not very effective.[7,8] Adrenergic blocking drugs, beta blockers either oral before anaesthesia or I.V at the time of induction is useful in suppressing hypertension, tachycardia and arrhythmia. The effectiveness of intravenous esmolol to suppress the sympatho-adrenal response during laryngoscopy and endotracheal intubation was proved by many authors.[9] Clonidine, a centrally acting Alpha-2 agonist, has a beneficial effect on the hyperdynamic response to endotracheal intubation. Moreover, it attenuates stress-induced sympatho-adrenal responses to painful stimuli, improves the intraoperative hemodynamic stability, reduces the incidence of perioperative myocardial ischemic episodes in patients with suspected or documented coronary artery disease, and decreases anesthetic requirements during surgery. Therefore, oral clonidine seems well suited as premedication for attenuating hemodynamic responses following laryngoscopy and intubation.[10,11,] Present study is aimed to evaluate whether intravenous dexmedetomidine 1 microgram/kg will attenuate the hemodynamic response to laryngoscopy and intubation.

METHODS: After Institutional Ethics Committee approval and written informed consent of the participants, 62 patients admitted in KMC Medical College, Mangalore, Hospital during the period from May 2012 to March 2014. Patients undergoing surgery under general anesthesia were considered for the study.

INCLUSION CRIATERIA:

- Patient undergoing surgery under general anesthesia.
- ASA grade 1, grade 2.
- Patients of either gender between ages 25-50 yr.
- Weighing 40-80 kilograms.
- Patients with normal renal, hepatic and cardiac functions.

EXCLUSION CRITERIA:

- Hypertensive and IHD patients.
- Patients with 1st 2nd and 3rd degree heart blocks.
- Patients with H/o psychiatric illnesses.
- Patients with renal diseases hepatic disease.
- Patients with H/o Allergy.
- And inpatients on medication for chronic illness.

Before administration of dexmedetomidine in the patients, pre anesthetic evaluation will be done. Following insertion of IV line ringers lactate was started, base line values were noted and patients were premedicated with Fentanyl (2µg/kg body wt) IV half an hour before surgery. The patient was pre oxygenated for 3 minutes and anesthesia was induced with titrating dose of propofol 2mg/kg and Succinyl choline 1.5 mg/kg was given for a period of 1 minute. After induction one minute later, laryngoscopy using appropriate size endotracheal tube intubation was done by qualified anaesthesiologist.

Patients were monitored by non-invasive blood pressure, electrocardiogram (ECG) and pulse oxymetry on arrival to the pre operating room. A randomization list will be used to assign patients to one of two study groups.

The first group (A) received an intravenous dose of 1µg/kg dexmedetomidine in 0.9% of 48 ml NaCl over a period of 10 minutes and

The second group (B) received 50 ml NaCl over a period of 10 minutes, 30 minutes before laryngoscopy and intubation.

After conformation of endotracheal tube position, anesthesia was maintained using 0.4-0.6% Halothane/Isoflurane and nitrous oxide in oxygen in a 2:1 ratio using bains circuit and vecuronium 0.1 mg/kg was used as a muscle relaxant. Interventions with other drugs will be done if one of the following adverse events would be observed: apnea lasting longer than 20 seconds, oxygen saturation lower than 90%, decrease of heart rate (HR) below 50 beats per min, mean arterial pressure (MAP) below 30% of the initial value. The following parameters would be measured continuously: Heart rate (HR); Systolic blood pressure (SBP); Diastolic blood pressure (DBP); and Mean arterial pressure (MAP).

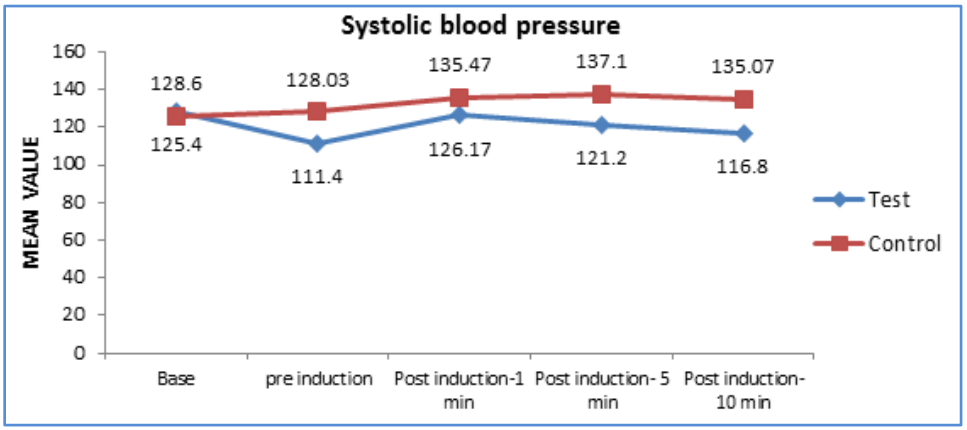
STATISTICAL ANALYSIS: The results were analyzed using SPSS Software. Patient characteristics between two groups were compared with STUDENTS T- TEST for unpaired observations. Time wise comparisons were done with ANOVA (F test), intergroup comparisons were done with BONFERRONNIS T –TEST. P value <0.05 was considered significant.

RESULTS: Group A patients received 1 mcg/kg iv dexmedetomidine in 100 ml of normal saline, 30 minutes before induction. Group B patients received placebo (100ml normal saline), 30 minutes before induction.

Systolic blood pressure before intubation and immediately after intubation were comparable in both groups. The reduction in the systolic blood pressure at pre-induction and at 1, 5 and 10 minutes after intubation were significantly lower in the dexmedetomedine group in a statistically highly significant manner. The subsequent mean blood pressure in the test group pre-induction was 111.4 compared to 128.3 and at 1 minute was 126.17 compared to 135.47 and 121.2 compared to 137.1 at 5 minutes, and 116.8 compared to 135.07, 10 minutes post intubation. The mean blood pressure never touched the baseline following laryngoscopy and endotracheal intubation.

	GROUP	N	Mean	Std. Deviation	t
Base	Test	31	128.6000	12.60432	.92100
	Control	31	125.4000	14.25047	p=0.361ns
Pre induction	Test	31	111.1000	10.58415	5.41600
	Control	31	128.0333	13.46383	<0.001vhs
Post induction-1 min	Test	31	126.1667	9.66359	2.78000
	Control	31	135.4667	14.88979	=0.006 hs
Post induction-5 min	Test	31	121.2000	11.51431	4.57200
	Control	31	137.1000	15.17564	<0.001 vhs
Post induction-10 min	Test	31	116.8000	12.02698	5.43200
	Control	31	135.0667	13.94802	<0.001 vhs

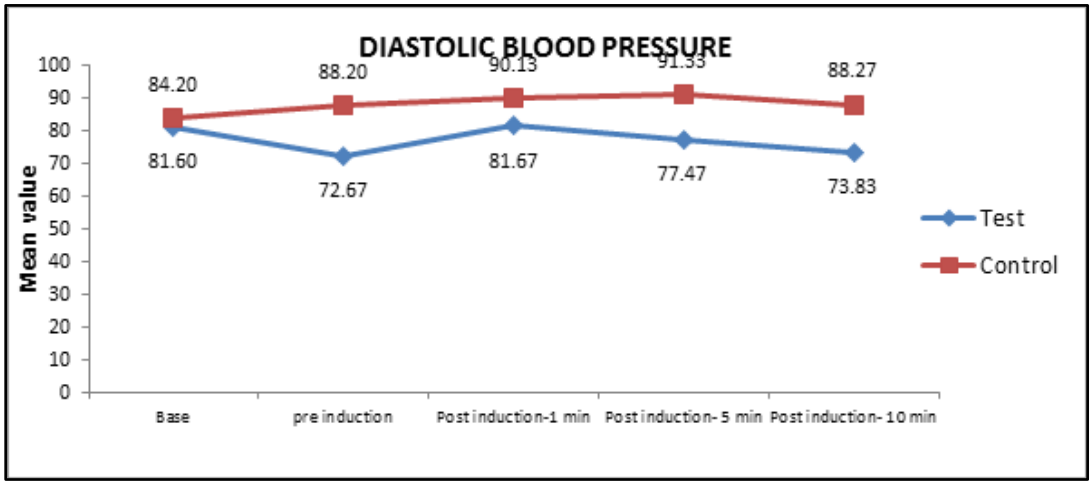
Table 1: Systolic blood pressure



The reduction in the diastolic blood pressure, pre-induction and at 1, 5 and 10 minutes after intubation were significantly lower in the dexmedetomedine group in a statistically highly significant manner than the non dexmedetomidine group. The mean baseline blood pressure in the test and control group was 84.2 and 81.6 respectively, lower in the test group.

	GROUP	N	Mean	Std. Deviation	t
Base	Test	31	81.6000	9.14858	.96200
	Control	31	84.2000	11.63645	p=0.34 ns
Pre induction	Test	31	72.6667	8.79394	6.39500
	Control	31	88.2000	9.98413	<0.001vhs
Post induction-1 min	Test	31	81.6667	9.00702	3.76200
	Control	31	90.1333	8.41482	=0.006 hs
Post induction-5 min	Test	31	77.4667	6.84676	7.16600
	Control	31	91.3333	8.09143	<0.001vhs
Post induction-10 min	Test	31	73.8333	6.09173	7.95200
	Control	31	88.2667	7.85618	<0.001vhs

Table 2: Diastolic blood pressure

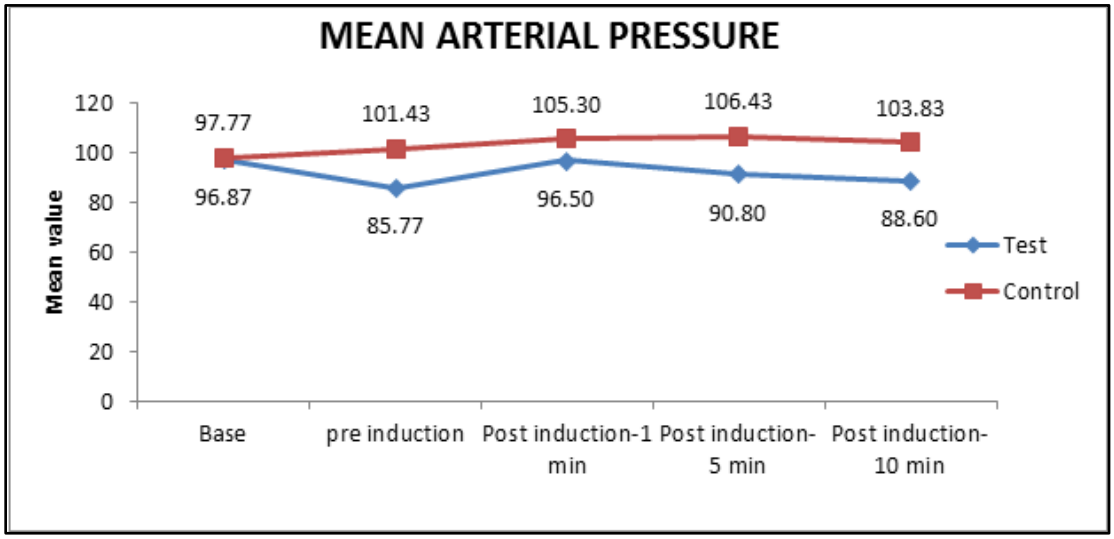


The subsequent mean diastolic blood pressure in the test group base line was 81.6 compared to 84.2 for the control group. Pre-induction values were 72.67 compared to 88.20 and at 1 minute were 81.67 compared to 90.13 and to 77.47 compared to 91.33 at 5 minutes, and 73.83 compared to 88.27, 10 minutes post intubation. The test group here showed better suppression of diastolic blood pressure in response to the control group.

The reduction in the mean arterial blood pressure pre-induction and at 1, 5 and 10 minutes after intubation were significantly lower in the dexmedetomedine group in a statistically highly significant manner. The subsequent mean, mean arterial pre-induction values were 85.77 compared to 101.43 and at 1 minute were 96.50 compared to 105.30 and 90.80 compared to 106.43 at 5 minutes, and 88.60 compared to 103.83, 10 minutes post intubation.

	GROUP	N	Mean	Std. Deviation	t
Base	Test	31	96.8667	8.73255	.34000
	Control	31	97.7667	11.55104	p=0.736ns
Pre induction	Test	31	85.7667	8.64504	6.50600
	Control	31	101.4333	9.96090	<0.001vhs
Post induction-1 min	Test	31	96.5000	8.06760	3.84400
	Control	31	105.3000	9.59939	=0.006 hs
Post induction-5 min	Test	31	90.8000	7.81863	6.95600
	Control	31	106.4333	9.50747	<0.001vhs
Post induction-10 min	Test	31	88.6000	6.90127	7.34600
	Control	31	103.8333	9.02137	<0.001vhs

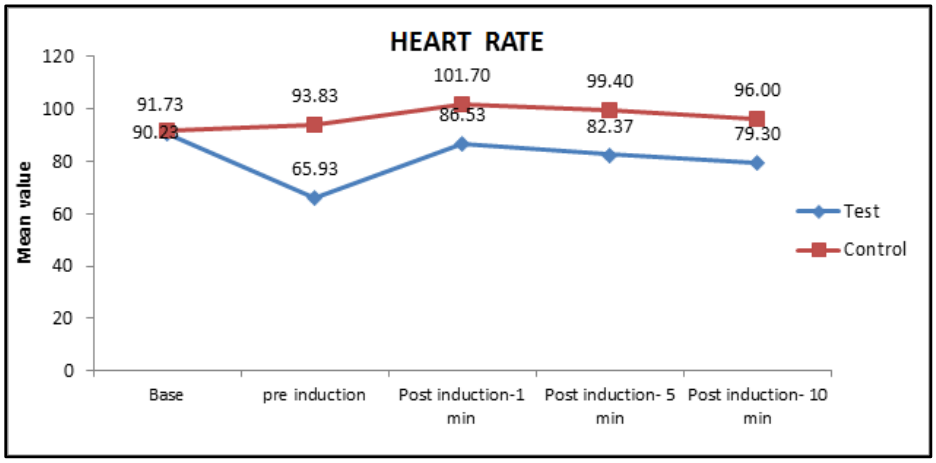
Table 3: Mean arterial pressure



There were significant heart rate variations in both groups, the mean heart rate never touched the baseline following laryngoscopy and endotracheal intubation. The fall in mean, mean arterial blood pressure pre-induction was 28 beats/min to 15 beats after 1 minute post intubation and 17 beats/min at 5 minute and 17 beats/minute after 10 minutes as compared to the control group. The mean heart rate following 10 minutes was 79.30 and even at the end of 10 minutes did not touch the base line of 90.23. The test group here showed better suppression of mean heart rate in response to the control group.

	GROUP	N	Mean	Std. Deviation	t
Base	Test	31	90.2333	13.11141	.41900
	Control	31	91.7333	14.57663	p=0.677ns
Pre induction	Test	31	65.9333	14.70851	7.29900
	Control	31	93.8333	14.89754	<0.001vhs
Post induction-1 min	Test	31	86.5333	13.09576	4.68400
	Control	31	101.7000	11.95725	=0.001vhs
Post induction-5 min	Test	31	82.3667	11.12773	5.89400
	Control	31	99.4000	11.25749	<0.001vhs
Post induction-10 min	Test	31	79.3000	9.09395	6.63100
	Control	31	96.0000	10.37238	<0.001vhs

Table 4: Heart rate



DISCUSSION: Dexmedetomidine is a new alpha2-agonist that received FDA approval in 1999 for use as a short-term (less than 24 h) sedative analgesic in the intensive care unit. The use of alpha2-agonists as anesthetics is not new since many alpha2-agonists are used in veterinary medicine to induce anesthesia. Clonidine, the prototype of alpha2- agonists, it is widely used as an adjunct to anesthesia and pain medicine; however, it has been little used as sedative. With dexmedetomidine, there are a number of reasons for the growing and renewed interest in the use of alpha2-adrenoceptors agonists as sedatives.

Dexmedetomidine compared to clonidine is a much more selective alpha2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha1-receptors. In addition, dexmedetomidine is shorter-acting drug than clonidine and has a reversal drug for its sedative effect, atipamezole. These properties render dexmedetomidine suitable for sedation and analgesia during the whole perioperative period: as premedication, as an anesthetic adjunct for general and regional anesthesia, and as postoperative sedative and analgesic.

Our study was aimed to evaluate weather intravenous dexmedetomidine will attenuate the haemodynamic response to laryngoscopy and intubation. Ours was a study where neither the subjects of the experiment nor the persons administering the experiment knew the critical aspects of the experiment; ”a double-blind procedure is used to guard against both experimenter bias and placebo effects".

Before administration of dexmedetomidine to the patient’s pre anesthetic evaluation was done to rule out any cardiac, renal, respiratory systems involvement. Consent was taken before administration of the drug. Patients were premedicated with fentanyl (2µg/kg body wt) IV half an hour before surgery. Patients were monitored by non-invasive blood pressure, electrocardiogram (ECG) and pulse oxymetry on arrival to the pre operating room. A randomization list was used to assign patients to one of two study groups. The first group (A) received a intravenous dose of 1 µg./kg dexmedetomidine in 0.9% of 48 ml NaCl over a period of 10 minutes and the second group (B) received 50 ml NaCl over a period of 10 minutes, 30 minutes before laryngoscopy and intubation. The following parameters were measured continuously: Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial pressure (MAP).

We found that group A, that is, the dexmedetomidine group attenuated pressor response to tracheal intubation as evidenced by only a minimal rise in systolic blood pressure and heart rate. Dexmedetomidine had shown better suppression of tachycardia throughout the observation period. Laryngoscopy and intubation are associated with cardiovascular changes such as hypertension, tachycardia, dysrhythmias and even, myocardial ischemia and increased circulating catecholamines. Although the reflex responses are of short duration and of little consequences in healthy patients, they may produce profound disturbances in patients with underlying abnormalities, such as coronary artery disease, reactive airway or intracranial neuropathology. To prevent the above untoward complications pressor response to laryngoscopy and intubation needs to be controlled. Here are a few studies which have been beneficial for us to attenuate stress responses. Farber NE, Samso E, Staunton M, Schwabe D, Schmeling WT showed that dexmedetomidine modulates cardiovascular responses to stimulation of CNS pressor sites,[12] which was comparable to our study. Seybold JL, Rammurthy and Hammer reported the use of dexmedetomidine for laryngoscopy, rigid bronchoscopy, and tracheal extubation in the operating room in two children who had undergone tracheal reconstruction 1 week previously. Dexmedetomidine in combination with propofol provided appropriate deep anesthesia during these brief but stimulating procedures without cardiovascular or respiratory depression[13] which was comparable to our study. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S showed that the effect of a single pre-induction intravenous dose of dexmedetomidine 1 mcg/kg on cardiovascular response resulting from laryngoscopy and endotracheal intubation, decreased blood pressure and heart rate as well as the recovery time after the operation[14] was comparable to our study.

CONCLUSION: From the study it is concluded that premedication with dexmedetomidine attenuates the pressor response associated with laryngoscopy and tracheal intubation. The attenuation occurs within 5 minutes following laryngoscopy and intubation and becomes maximum by 10 minutes. The haemodynamic parameters reach near base line values after 5-10 minutes of intubation.

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AUTHORS:

1. Venugopal S.
2. Jitesh M. Rasquinha

PARTICULARS OF CONTRIBUTORS:

1. Post Graduate, Department of Anaesthesiology, KMC, Mangalore.
2. Associate Professor, Department of Anaesthesiology, KMC, Mangalore.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Venugopal S,
Kasturba Medical College Mangalore,
Manipal University, Mangalore.
E-mail: venug17@yahoo.in

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