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Dexmeditomidine as an adjunct to anaesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing CABG

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KEYWORDS

Dexmeditomedine, Pressor response

A B S T R A C T

To assess the efficacy of Dexmedetomidine in blunting hemodynamic stress response during endotracheal intubation and to assess the hemodynamic compromise occurred during the induction of Dexmedetomidine. After obtaining Ethics Committee approval, 60 patients undergoing CABG* were chosen for the study. The study was designed in a placebo controlled, double blinded, randomized, prospective fashion. The patients will be randomly separated into two groups i.e. Placebo (PLA, n1=30) and Dexmedetomidine (DEX, n2=30). Pre medication with Injection Midazolam 0.04mg/kg, Injection Butarphanol 0.02mg /kg is done. Monitoring with 12 lead ECG, Invasive BP (Radial artery catheter), Pulmonary artery pressure (Pulmonary artery catheter), Urine output, Pulse oximeter and Temperature monitoring is done. Dexmedetomidine group received total dose of 1 microgram/kg Dexmedetomidine diluted in 100ml NaCl solution in 15 min. Placebo group will receive 100 ml of NaCl solution in 15 min. Hemodynamic measurements will be repeated after administration of Dexmedetomidine and placebo 1(t3), 3(t4) and 5(t5) minutes after intubation. CABG is performed off pump with normothermia. Dexmedetomidine at dose of 1ugm/kg body weight diluted in 100 ml of 0.9% N.S. over 15 minutes before induction preoperatively significantly obtunded the haemodynamic stress responses to laryngoscopy and tracheal intubation without significant side effects (like hypotension and bradycardia). Use of Dexmedetomidine preoperatively significantly obtunded the haemodynamic stress responses to laryngoscopy and tracheal intubation and this drug can be used regularly in ICU setting as alternative to other drugs because of its lower side effects.

Introduction

Laryngoscopy and tracheal intubation in adults are commonly accompanied by increase in arterial blood pressure and heart rate (Reid, 1940). Hypertension,

arrhythmias and myocardial infarction induced by endotracheal intubation are results of reflex increase in sympathetic and sympathoadrenal activity. The principle mechanism in hypertension and tachycardia is the sympathetic response (Kayhan *et al.*, 2005; Morin *et al.*, 2004) which may be the result of increase in catecholamine activity (Kovac, 1996).

So prior to initiating laryngoscopy, additional pharmacological measures like use of volatile anaesthetics (King *et al.*, 1951), topical and intravenous lidocaine (Donlinger *et al.*, 1974), opioids (Dahlgreen and Messeter, 1981), vasodilators – Sodium nitroprusside (Stoelting, 1979), Nitroglycerine (Fossoulaki and Kaniasis, 1983), Calcium channel blockers (Puri and Batra, 1988) and β-blockers (Prys-Roberts *et al.*, 1973) have been tried. High dose opoid is preferred to attenuate this response in cardiac surgery patients. α-2 adrenergic agonists like clonidine decreases sympathetic tone & blunts the haemodynamic responses to noxious stimuli & prevents the overall haemodynamic variability. It also reduces the need for adjuvant anesthetics. Dexmedetomidine, a more specific & selective α-2 adrenergic agonist than clonidine has a shorter duration of action & because of its sedative and analgesic properties, it also can be used as an adjunct to General Anesthesia. Since it has been recently introduced in India and not many studies have been done in India regarding its usefulness in suppressing intubation response, there is a need to study its effectiveness.

The present study is aimed to investigate the haemodynamic effects of intra venous Dexmedetomidine used as an anesthetic adjunct during induction of anesthesia in our local population with fentanyl 1mcg/kg in adult patients for CABG. The advantages of intravenous dexmedetomidine as premedicant in anaesthesia setting include sedation, analgesia, anxiolysis and improved haemodynamic stability. Because of these beneficial properties it has been found that the minimum alveolar concentration (MAC) of volatile anaesthetics also decreases significantly up to 90% and hence decreases the requirement of anaesthetics (Aho *et al.*, 1991).

In our study, we plan to investigate the haemodynamic effects of intravenous dexmedetomidine used as an anaesthetic adjunct during induction of anaesthesia in our local population with fentanyl 1microgram/kg in adult patients for CABG.

Materials and Method

After obtaining ethics committee approval and informed consent from all the 60 patients undergoing CABG were chosen for the study. The study was conducted in Anandrishiji Hospital & Medical Research Centre, Ahmednagar, Maharashtra.

Those patients who were aged 50–70 years, Ischeamic heart disease patients with normal Left Ventricular function, Patients on tablet. Metoprolol 25mg twice day for at least 1 week before surgery and ASA Grade 1&2 of both sexes included in the study. Patients who had Ejection fraction less than 50%, Age more than 70 years & less than 50 years, BMI more than 30kg/$m^{2,}$ Left main coronary artery occlusion more than 50%, Valvular dysfunction, Pre-operative medication with Clonidine and Alfa methyl dopa, History of sensitivity to drugs used during the study, Pre-operative Left Bundle Branch Block, Right bundle branch block, Sick sinus syndrome, Severe systemic disorders like Insulin dependent Diabetes mallites, kidney or liver insufficiency, severe respiratory disorders, patients with

anticipated and unanticipated difficult intubation were excluded from the study.

The study designed in a placebo controlled, Double blinded, Randomised, prospective fashion. The patients were randomly separated into two groups by computer generated randomisation as Placebo (Group C, N_1=30) and Dexmedetomidine (Group D, N_2=30).

Pre anaesthetic evaluation was done on the evening before surgery. A routine pre anaesthetic examination was conducted assessing general condition of the patients, airway assessment by mallampatti grading, nutritional status and body weight of the patient, a detailed examination of cardio vascular system and respiratory system was done.

Investigations done in all patients were haemoglobin, urine routine, microscopy, standard 12-lead ECG, X-ray chest [postero anterior view], random blood sugar, blood urea and serum creatinine, LFT, serum electrolytes (sodium and potassium), bleeding time and clotting time

Pre-operative preparation including keeping the patient Nil by Mouth for 8- 10hrs, written Informed consent was taken for all patients, shaving and preparation of body parts, T.Ranitidine 150mg stat, T.Metaclopramide 8mg stat and T.Lorazepam 2mg stat All these were given one day prior to surgery at night (10pm). T.Ranitidine 150mg stat And T. Metaclopramide 8mg stat these were given on the day of surgery at 6am with sips of water. Anti hypertensive drugs were continued till the day of surgery except angiotensinogen converting enzyme inhibitor and angiotensin receptor antagonist. Before arriving to operating room, 18 gauge peripheral venous cannula was inserted and according to study protocol all patients were pre hydrated with 500ml of Ringer Lactate solution.

Premedication with Inj. Midazolam 0.04mg/kg intra venous and Inj.Butarphanol 0.02mg/kg intra venous given 30 minutes before the surgery.

Monitoring was done with 12-lead ECG, Invasive Blood Pressure (through Radial Artery Catheter), Pulmonary artery pressure (through pulmonary artery catheter), Et CO_2, Pulseoxy meter, Temperature, Urine output. All cannulations were done under local anaesthesia in all patients.

Baseline Heart rate, Systolic arterial pressure (SAP t0), Diastolic arterial pressure (DAP t0), Mean arterial pressure (MAP t0), Mean pulmonary arterial pressure (PAP t0) were recorded after 3 minutes of the resting period following insertion of radial artery and pulmonary artery catheter.

Group D received total dose of 1µg/kg Dexmetamidone diluted in 100ml of 0.9% sodium chloride solution over 15 minutes. Group C received 100ml of 0.9% sodium chloride solution over 15 minutes. After stabilation period of 5 minutes HR (t1), SAP (t1), DBP (t1), MAP (t1) &M PAP (t1) were recorded.

Induction of anaesthesia was planned three minutes after t1 haemodynamic recordings with Inj. Fentanyl 1µg/kg, inj. Propofol 1.5-2.5 mg/kg, and inj. Midaz 0.1 mg/kg, after loss of eyelid reflex inj. Vecuronium 0.08 – 0.1 mg/kg given intra venous to facilitate endotracheal intubation. Two minutes after administering the induction agents HR (t2), SAP (t2), DAP (t2), MAP (t2), &MPAP (t2) recordings were done, and the trachea was intubated. Each intubation was performed by an anaesthesiologist and accomplished

within 20 seconds. Haemodynamic measurements were repeated after 1 (t3), 3 (t4), & 5 (t5) minutes after intubations. Maintenance of General Anaesthesia was done with O_2 50% + N_2O 50%+ Sevoflurane. MAC -1.80+inj.Fentanyl. Urinary catheterisation was done 5 minutes after intubation. CABG was performed off pump with normothermia.

Side effct monitored were Hypotension defined as systolic blood pressure ≤ 20% of base line value or SBP<90mmhg (Jakola *et al.,* 1992), Tachycardia - defined as HR > 25% of base line value (Kallio *et al.,* 1989), Bradycardia - defined as HR < 45 Beats/min. (Jones and Maze, 2001), Any dysarrthmia defined as any ventricular or supra ventricular beats or any rhythm other than sinus (Kallio *et al.,* 1989), Hypertension - >140/90 mmhg (systolic/diastolic) respectively (Millers anaesthesia, 7th edition).

Normal mean pulmonary artery pressure is-9-19mmhg (Millers anaesthesia, 7th edition).

Incidences of hypotension and bradycardia were recorded in the both the groups. Hypotension can be treated with infusion of crystalloid solutions or inj. Mephentermine in 6mg increments, inj. noradrenaline (0.03–0.05microgm/kg) infusion. Bradycardia can be treated with inj. glycopyrrolate 0.2mg or inj. atropine 0.6mg.

Result and Discussion

The sample size was determined by power analysis performed by a pilot study. A sample size of 22 patients per group was required to detect a 20% change in heart rate, blood pressure & pulmonary artery pressure between baseline & intubation time with power of 80% at the 5% significance level. Data are expressed as mean ± standard deviation. The data was analysed with unpaired t test to compare the study &control group and paired student 't' test used to compare the variables before & after intervention and 'p' value calculated for statistical significance. $p < 0.05$ was considered significant. Chi-squire test was used to analyse the adverse effects in the study drug. The package SPSS version 15, open epi version 2.3.1& Microsoft excel 2007 was used for statistical analysis. T0-basal, t1-after dexmedetomidine administration, t2-after induction, t3-1minute after intubation, t4-3minutes after intubation, t5-5minutes after intubation.

The mean age in Group C and Group D are 61.90 ± 6.255 and 60.80± 6.359 respectively. There is no significant difference in the age of patient between Group C and Group D. both groups are similar with respect to age distribution (p – 0.5

In Group C the basal mean HR is 63.03 ± 3.917. The mean HR 5 minutes after drug administration is 62.83 ± 4.086 which is statistically not significant compared to basal value (P – 0.463) done by paired t test. After induction there is a decrease in HR of 2.5bpm compared to basal value. The HR at 01 minute after intubation increased by 14bpm compared to basal value, which is statistically highly significant (p – 0.00). Maximum heart rate increased at 1min after intubation. By 3 & 5 minutes after intubation increase in HR were by 12 and 8bpm respectively compared to basal. The increase in HR at all times after intubation is statistically significant (p – 0.00) compared to basal value.

In Group D, basal mean HR is 63.77 ± 3.928 minutes. 5min after drug administration the HR decreases by 3.5bpm compared to basal, it shows there is statistically significant

decrease in HR (p = 0.00) done by paired t test. The HR after induction decreases by 7bpm, it shows there is statistically significant decrease in HR (p = 0.00). The HR after intubation at 1 minute is 63 bpm which is same as basal value, so statistically not significant (p = 0.293). By 3 & 5 minutes after intubation the HR decreases by 2&3bpm compared to basal value (p = 0.00), this is statistically highly significant. Highest HR was at basal & lowest HR achieved at 5 min after intubation.

The basal HR are comparable in both Groups (p = 0.472). Statistical evaluation between the groups showed a significant fall in HR in group D 05 minutes after drug administration & after induction. The mean HR increases at 1,3& 5 minutes after intubation in group C is statistically highly significant compared to mean HR in group D (p=0.00).

In Group C the basal mean SBP is 128.00 ± 7.377, after drug administration at 05 minutes the mean SBP is 127.10 ± 5.868 which is comparable to basal value. There is significant fall in SBP of 8mmhg after induction (p =0.00) compared to basal value. The SBP at 1 minute after intubation increases by 30mmhg compared to basal, which is statistically highly significant (p = 0.00). By 3 & 5 minutes after intubation the SBP increases by 20 & 10mmhg respectively compared to basal. The increase in mean SBP at 1, 3 & 5 minutes after intubation are statistically highly significant (p =0.00) compared to basal value. Highest SBP obtained at 1 min after intubation.

In group D the basal value of mean SBP is 127.17 ± 11.341, after drug administration at 5 minutes the SBP decreases by 12mmhg compared to basal, representing a significant fall in SBP (p = 0.00). After induction the SBP decreases by 25mmhg compared to basal value. After 1, 3 & 5 min after intubation SBP decreases by 16,22,25 compared to basal, which is statistically highly significant. The SBP continued to be at lower levels compared to basal values even 5min post intubation. Highest SBP was at basal & lowest reached at 5 min after intubation.

The mean SBP are comparable in both groups (p = 0.737) after 5v minutes of drug administration the mean SBP is significantly low (p = 0.00) compared to group C. The increase in SBP in group C at 1, 3 & 5 minutes after intubation is statistically highly significant (p = 0.00) compared to group D.

In group C the basal mean DBP is 76.83 ± 5.902 after drug administration at 5 minutes and after induction the mean DBP are statistically not significant compared to basal value (p > .791). By 1 minute after intubation the DBP is increased by 22mmhg compared to basal value. By 3 & 5 minutes after intubation DBP values increased by 17 & 10mmhg respectively compared to basal value. The increase in mean DBP at 1, 3, 5 minutes is statistically highly significant (p = 0.00) compared to basal value. Highest DBP reached at 1 min after intubation.

In group D the basal mean DBP is 76.50 ± 5.906. The DBP at 5 minutes of drug administration and after induction were decreased by 10 & 6mmhg respectively compared to basal value, representing a significant fall in DBP (p = 0.00). After intubation the mean DBP at 1min was equal to basal value, at3 & 5 minutes DBP decreases by 5 & 7 mmhg respectively compared to basal which is statistically significant. The DBP continue to be lower than basal value even after 5 min. Hghest DBP was at basal & lowest was after induction.

The mean basal DBP are comparable in both groups (p = 0.828). The mean DBP values at 5 minutes after drug administration and after induction are significantly low (p = 0.00) in group D compared to group C. The increase in DBP in group C at 1, 3 & 5 minutes after intubation is statistically highly significant (p = 0.00) compared to group D.

In group C the basal MAP is 92.23 ± 3.997. The MAP at 5 minutes after drug administration is 91.77 ± 3.607 which is statistically not significant (p = 0.65). After induction MAP decreases by 7mmhg compared to basal, which represents a significant fall in MAP (p = 0.00). The MAP at 1, 3 &5 min after intubation increases by 26,18,10 mmhg compared to basal values, which was statistically significant. Highest MAP reached at 1 minute after intubation.

In group D the basal MAP is 93.17 ± 4.488. The mean MAP at 5 minutes after drug administration and after induction decreases by 7 & 13 mmhg respectively compared to basal value, representing a significant fall in MAP (P = 0.00). After intubation the MAP values at 1, 3 & 5 minutes were decreased by 6, 13 &14mmhg compared to basal value, which is statistically significant (p=0.00). Highest MAP was at basal & lowest MAP reached at 5 min after intubation.

The mean basal MAP are comparable in both groups (p >0.39). There is significant difference in MAP values at 5 minutes after drug administration and after induction which is highly significant. The increase in MAP in group C is statistically highly significant at 1, 3 & 5 minutes after intubation (p = 0.00) compared to group D.

In group C the basal mean PAP is 13.90 ± 1.269. After drug administration at 5 minutes and after induction the PAP values were equal to basal which is statistically not significant compared to basal value (p>0.05). By 1, 3 &5 min after intubation the PAP was increased by 2.5, 2 & 2mmhg compared to basal value which is statistically significant compared to basal values. Highest MPAP reached at 1 min after intubation.

In group D the basal mean PAP is 13.90 ± 1.269. The mean PAP after drug administration at 5 minutes and after induction 13.53 ± 1.279 and 14.23 ± 0.817 which are statistically not significant compared to basal values. By 1, 3 and 5 minutes after intubation the PAP increased by 3, 3&2mmhg respectively. Which shows statistical significant increase in mean PAP (p = 0.00) compared to basal value. Highest MPAP reached at 1min after intubation & lowest was at basal.

The mean basal PAP are comparable in both groups (p = 1.0). The mean PAP values at 5 minutes after drug administration and after induction are statistically not significant. The increase in mean PAP in group C at 1, 3, & 5 after intubation are statistically not significant compared to group D.

Chi-square test is applied

In group C, none of the patients had side effects like bradycardia and hypotension.

In group D, 1 patient had bradycardia that was 8 min after dexmedetomidine administration, 5 had hypotension 5 min after intubation and one patient had both bradycardia and hypotension in this bradycardia occurred 8 min after drug administration & hypotension 5 min after intubation.

One patient required inj.atropine 0.6mg for bradycardia & no patient required

vasopressors for correction of B.P, hypotension was managed by decreasing volatile anaesthetic concentration & infusing I.V fluids.

Most of the general anaesthetic procedures in the modern anaesthetic practice are carried out with endotracheal intubation. Laryngoscopy and tracheal intubation are considered as the most critical events during administration of general anaesthesia as they provoke transient but marked sympathoadrenal response manifesting as hypertension and tachycardia (Prys-Roberts *et al.,* 1971).

These responses are transitory, variable and may not be significant in otherwise normal individuals. But in patients with cardiovascular compromise like hypertension, ischemic heart disease, cerebrovascular disease and in patients with intracranial aneurysms, even these transient changes in haemodynamics can result in potentially harmful effects like left ventricular failure (Fox *et al.,* 1977), pulmonary edema, myocardial ischemia (Fox *et al.,* 1977), ventricular dysrrhythmias (Ronald D Miller, 2010) and cerebral haemorrhage (Fox *et al.,* 1977). This is by far the most important indication for attenuation of haemodynamic response to laryngoscopy and tracheal intubation (King *et al.,* 1951). Many methods like use of inhalational anaesthetic agents, lidocaine (Stoelting, 1978), opioids (Martin *et al.,* 1982), direct acting vasodilators (Fossoulaki and Kaniasis, 1983), calcium channel blockers (Nishikawa and Naiki, 1989) and β-blockers (Mc Cammon *et al.,* 1981) have been tried by various authors for blunting haemodynamic responses to laryngoscopy and intubation. But all such manoeuvres had their own limitations. For example, with opioids respiratory depression and chest wall rigidity were potential problems, use of halothane was associated with dysrrhythmias, calcium channel blockers produced reflex tachycardia, direct acting vasodilators needed invasive haemodynamic monitoring and lidocaine did not give consistent results in blunting the haemodynamic responses to laryngoscopy and intubation.

Recently α-2 agonists like clonidine (Kulka *et al.,* 1995) and dexmedetomidine (Ralph Getler *et al.,* 2001) have been tried for suppressing the response to intubation and have been found to have better effects compared to all the drugs mentioned above, without any of the side effects like respiratory depression or increased incidence of PONV. Clonidine being less potent (α-1:α-2=1:220) compared to dexmedetomidine (α-1:α-2=1:1620) in its agonism to α-2 receptors (Ralph Getler *et al.,* 2001). Hence dexmedetomidine may be a better drug among α-2 agonists for suppressing the haemodynamic responses to laryngoscopy and intubation.

Dexmedetomidine has been found by various authors (Millers anaesthesia,7 th edn; Scheinin *et al.,* 1992) to blunt the haemodynamic response for laryngoscopy and intubation. Dexmedetomidine is recently introduced in India (only in 2009) and available as 200 µg/2ml ampoule (Dexem, Themis Medicare Limited) and not many studies have been done using dexmedetomidine for suppression of intubation response. Hence the effects of dexmedetomidine for suppression of haemodynamic response to laryngoscopy and intubation were taken up as our study topic.

The present study was undertaken to study the efficacy of dexmedetomidine in blunting the haemodynamic response to laryngoscopy and intubation.

In the present study dexmedetomidine is diluted in 100 ml of normal saline and given IV over 15 minutes. Rapid administration of bolus dose of dexmedetomidine initially results in transient increase in blood pressure and reflex decrease in heart rate. The initial response is due to peripheral alpha2 adrenoreceptors stimulation of vascular smooth muscle contraction and can be attenuated by a slow infusion over 10 minutes. Hence in our study we administered the bolus dose over 15 minutes (Ralph Getler *et al.,* 2001).

From the pharmacokinetic profile, it is seen that the distribution of half life of IV dexmedetomidine is approximately six minutes (Ralph Getler *et al.,* 2001). In view of above, in the presence study dexmedetomidine is employed 8 minutes before induction to blunt haemodynamic response to laryngoscopy and intubation.

After dexmedetomidine and saline administration, It has been found by various authors (Aho *et al.,* 1991; Jakola *et al.,* 1992; Basar *et al.,* 2008; Kunisawa *et al.,* 2009; Menda *et al.,* 2010) that dexmedetomidine has decreased heart rate at various intervals of 2,5,8 &10minutes. Our study also found similar changes in heart rate (studied at 5min after drug infusion) which is statistically significant.

In control group initially there is not much variation in heart rate after administration of the saline in first five minute. Where as in dexmedetomidine group there was decrease in a heart rate which is statistically highly significant.

Compared to pre induction values, it was found that there was a decrease of 1bpm in control compared to decrease of 3bpm in dexmedetomidine group which is statistically highly significant.
Compared to basal values in control group, there was an decrease of 3bpm compared to dexmedetomidine group where there is decrease of 7bpm which is statistically significant.

In present study following laryngoscopy and intubation at 1 minute, the mean heart rate increased by 14.43bpm in control group whereas in dexmedetomidine group mean heart rate decreases by 0.54bpm which is statistically highly significant[p=0.00]. The increase in mean heart rate at 3 minutes in control group was 12.5bpm where as in dexmedetomidine group H.R decreases by 2.2bpm which is statistically highly significant. The increase in mean H.R in control group was sustained even at 5 min &it was about 8.4bpm whereas in dexmedetomidine group there was further decrease in H.R by 3.77bpm which is statistically significant. In control group statistically highly significant increase in H.R occurred at various intervals after intubation at 1,3 & 5 min with maximum rise of 14.4bpm (1 min after intubation), similar findings were also noted by Aho *et al.* (1991) & Basar *et al.* (2008). In dexmedetomidine group there was decrease in H.R at 1 min after intubation & maximum decrease in H.R was sustained till 5 min after intubation was less by 3.77bpm which is statistically highly significant [p=0.00].

At 5th minute there was decrease in SBP of about 11.57mmhg compared to basal value which is statistically significant. There was reduction of 0.9mmhg in SBP in control group which was statistically not significant. There was reduction in SBP of 8mmhg in control group compared to 25mmhg in dexmedetomidine group compared to basal value, which is statistically highly significant.

In the control group the increase in SBP was maximum at 1 min about 30mmhg compared to basal value& even at 5 min the

SBP did not reach the basal value &it was 10mmhg higher than basal value.

At 5th minutes there is decrease in DBP of about 9mmhg compared to basal which statistically significant. In control group there is no significant change in DBP. There was no change in DBP in control group & 6mmhg reduction in dexmedetomidine group compared to basal value which is statistically significant.

In our study after laryngoscopy and intubation there is increase of DBP by 22 mmhg in control group which at 5 min still remained about 10mmhg higher than basal value. In dexmedetomidine group there was no change in DBP at 1 min& about 7mmhg decrease compared to basal values which is statistically significant. However there was increase of 21mmhg in control group compared with 6mmhg increase in dexmedetomidine group in comparison with the values of DBP immediately after induction which is statistically significant.

After dexmedetomidine administration at 5min there was reduction in MAP by 7mmhg compared to basal value which is statistically significant. In control group not much variation observed compared to basal value. After induction there was reduction in MAP by 13mmhg in dexmedetomidine group & 7mmhg in control group which is statistically significant.

After laryngoscopy and intubation at 1 min in dexmedetomidine group there is increase in MAP by 7mmhg compared to values immediately after induction but compared to basal values there is reduction in MAP by 6mmhg, even at 5 min the MAP was lower by 13mmhg, compared to basal value in dexmedetomidine group which is statistically significant. However in control group there is increase in MAP by 33mmhg compared with 7mmhg of increase in dexmedetomidine group comparison with the values of MAP immediately after induction which is statistically significant. At 1 min after intubation the increase in MAP in control group 26mmhg whereas in dexmedetomidine group there is fall in MAP by 6mmhg which is statistically significant. The MAP value did not reach to basal values even after 5 min in control group.

After dexmedetomidine administration at 5 min there was not much change of MPAP in both dexmedetomidine & control group compared to basal values. And also there was no significant difference between control & dexmedetomidine group. After induction there is no statistically significant difference in both dexmedetomidine group and control group.

After laryngoscopy and intubation in dexmedetomidine group there was about 2.47mmhg increase in MPAP at 1 min compared to basal value which is statistically significant & even at 5 min there was increase in MPAP by 1.67mmhg compared to basal value. Similar changes observed in control group, so by comparing control & dexmedetomidine group the values are almost similar so statistically not significant.

In dexmedetomidine group 2 patients developed bradycardia 8 min after drug administration & 6 developed hypotension 5 min after intubation. One patient required inj. atropine 0.6mg for bradycardia & no patient required vasopressors for correction of B.P., hypotension was managed by decreasing volatile anaesthetic concentration & infusing I.V fluids.

As limitation of study we did not measure the plasma nor epinephrine level & extubation response, post operative sedation and haemodynamic variations were not studied.

Table.1 Showing the intergroup comparison of mean heart rate (bpm) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

	Group C	Group D	p-value
Basal (t0)	63.03 ± 3.917	63.77 ± 3.928	0.472 (NS)
20th min (t1)	62.83 ± 4.086 p-value0.463 (NS)	60.03 ± 4.453 p-value0.000 (HS)	0.014 (S)
25th min (t2)	61.33 ± 3.346 p-value0.000 (HS)	56.97 ± 5.391 p-value0.000 (HS)	0.000 (HS)
26th min (t3)	77.43 ± 5.412 p-value0.000 (HS)	63.23 ± 5.237 p-value0.293 (NS)	0.000 (HS)
28th min (t4)	75.50 ± 5.412 p-value0.000 (HS)	61.57 ± 5.110 p-value0.001 (HS)	0.000 (HS)
30th min (t5)	71.40 ± 4.938 p-value0.000 (HS)	60.00 ± 3.930 p-value0.000 (HS)	0.000 (HS)

(Unpaired't' test)
P < 0.01 – Highly Significant (HS); P < 0.05 – Significant (S); P > 0.05 – Not Significant (NS)

Table.2 Showing the intergroup comparison of mean systolic blood pressure (SBP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

	Group C	Group D	p-value
Basal (t0)	128.00 ± 7.377	127.17 ± 11.341	0.737 (NS)
20th min (t1)	127.10 ± 5.868 p-value0.119 (NS)	115.60 ± 10.721 p-value0.000 (HS)	0.000 (HS)
25th min (t2)	120.40 ± 6.463 p-value0.000 (HS)	102.60 ± 11.174 p-value0.000 (HS)	0.000 (HS)
26th min (t3)	158.03 ± 4.657 p-value0.000 (HS)	111.13 ± 9.493 p-value0.000 (HS)	0.000 (HS)
28th min (t4)	148.93 ± 7.688 p-value0.000 (HS)	105.93 ± 9.896 p-value0.000 (HS)	0.000 (HS)
30th min (t5)	138.83 ± 8.437 p-value0.000 (HS)	102.07 ± 11.219 p-value0.000 (HS)	0.000 (HS)

(Unpaired't' test)
P < 0.01 – Highly Significant (HS); P < 0.05 – Significant (S); P > 0.05 – Not Significant (NS)

Table.3 Showing the intergroup comparison of mean diastolic blood pressure (DBP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

	Group C	Group D	p-value
Basal (t0)	76.83 ± 5.902	76.50 ± 5.906	0.828 (NS)
20th min (t1)	76.43 ± 8.460 p-value0.791 (NS)	67.07 ± 6.362 p-value0.000 (HS)	0.000 (HS)
25th min (t2)	77.07 ± 6.823 p-value0.891 (NS)	70.43 ± 9.235 p-value0.004 (HS)	0.002 (HS)
26th min (t3)	98.10 ± 7.963 p-value0.000 (HS)	76.13 ± 9.906 p-value0.860 (NS)	0.000 (HS)
28th min (t4)	93.03 ± 8.036 p-value0.000 (HS)	71.87 ± 9.066 p-value0.032 (S)	0.000 (HS)
30th min (t5)	86.40 ± 7.582 p-value0.000 (HS)	69.47 ± 7.749 p-value0.000 (HS)	0.000 (HS)

(Unpaired't' test); P < 0.01 – Highly Significant (HS); P < 0.05 – Significant (S); P > 0.05 – Not Significant (NS)

Table.4 Showing the intergroup comparison of mean arterial pressure (MAP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

	Group C	Group D	p-value
Basal (t0)	92.23 ± 3.997	93.17 ± 4.488	0.399 (NS)
20th min (t1)	91.77 ± 3.607 p-value 0.656 (NS)	86.50 ± 4.524 p-value0.000 (HS)	0.000 (HS)
25th min (t2)	65.37 ± 4.774 p-value0.000 (HS)	80.80 ± 8.376 p-value0.000 (HS)	0.012 (S)
26th min (t3)	118.13 ± 4.524 p-value0.000 (HS)	87.23 ± 7.537 p-value0.001 (HS)	0.000 (HS)
28th min (t4)	110.97 ± 6.764 p-value0.000 (HS)	80.97 ± 7.299 p-value0.000 (HS)	0.000 (HS)
30th min (t5)	102.73 ± 6.828 p-value0.000(HS)	79.47 ± 6.532 p-value0.000 (HS)	0.000 (HS)

(Unpaired't' test); P < 0.01 – Highly Significant (HS); P < 0.05 – Significant (S); P > 0.05 – Not Significant (NS)

Table.5 Showing the intergroup comparison of mean pulmonary arterial pressure (MPAP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

	Group C	Group D	p-value
Basal (t0)	13.90 ± 1.269	13.90 ± 1.269	1.000 (NS)
20th min (t1)	13.53 ± 1.224 p-value0.086 (NS)	13.53 ± 1.279 p-value0.054 (NS)	1.000 (NS)
25th min (t2)	13.43 ± 1.305 p-value0.070 (NS)	14.23 ± 0.817 p-value0.125 (NS)	0.480 (NS)
26th min (t3)	16.50 ± 1.280 p-value0.000 (HS)	16.37 ± 0.964 p-value0.000 (HS)	0.650 (NS)
28th min (t4)	16.10 ± 0.995 p-value0.000 (HS)	16.27 ± 0.868 p-value0.000 (HS)	0.492 (NS)
30th min (t5)	15.50 ± 1.137 p-value0.000 (HS)	15.57 ± 0.971 p-value0.000 (HS)	0.808 (NS)

(Unpaired‘t’ test); P < 0.01 – Highly Significant (HS); P < 0.05 – Significant (S);
P > 0.05 – Not Significant (NS)

Table.6 Showing the side effects between control and dexmedetomidine group

	Nil	**Bradycardia**	**Hypotension**	**Bradycardia and hypotension**	**Treatment required**
Group C	30	0	0	0	
Group D	23	1	5	1	1
p-value	0.047[s]				

p<0.01) – Highly significant (HS); (p<0.05) – Significant (S);
(p>0.05) – Not significant (NS)

Figure.1 Showing the intergroup comparison of mean heart rate (bpm) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

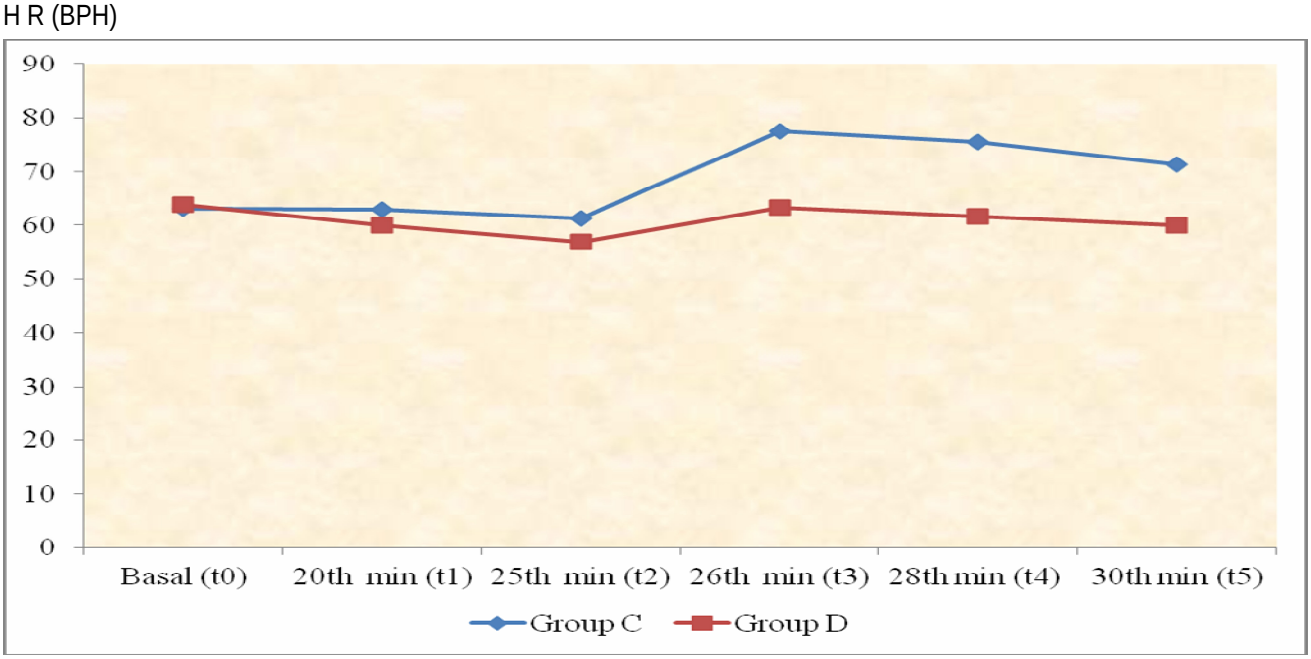


Figure.2 Showing the intergroup comparison of mean systolic blood pressure (SBP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

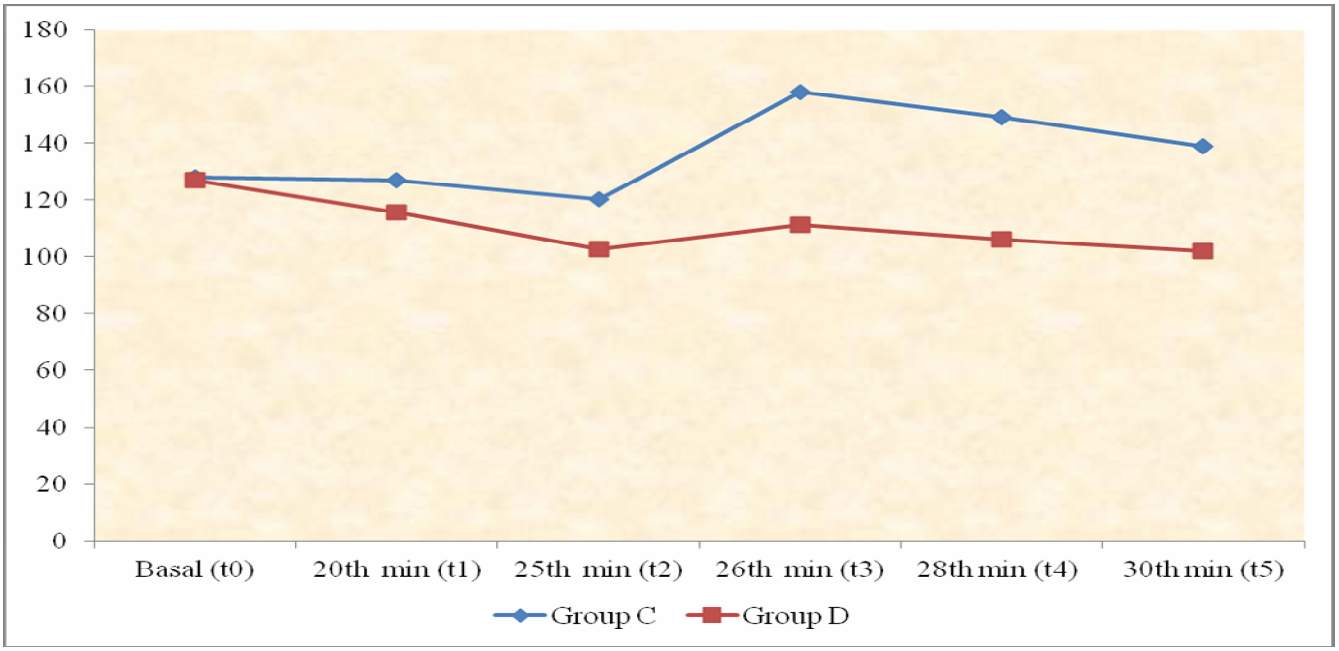


Figure.3 Showing the intergroup comparison of mean diastolic blood pressure (DBP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

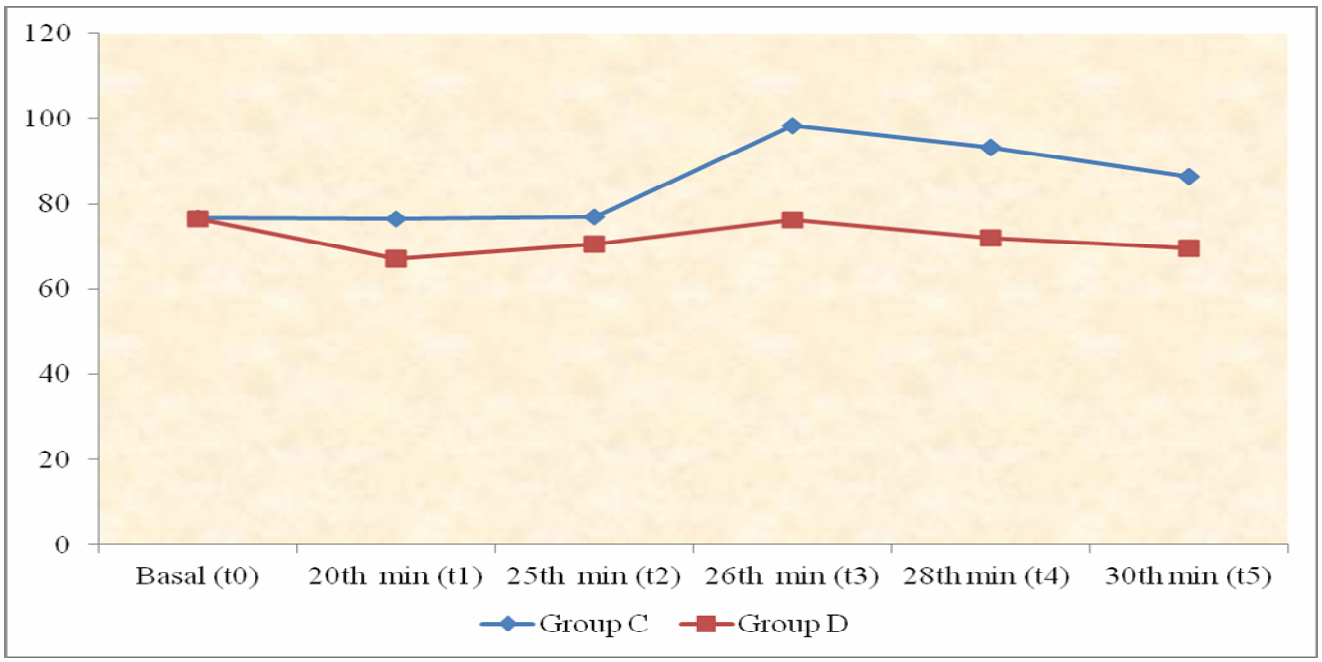


Figure.4 Showing the intergroup comparison of mean arterial pressure (MAP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

MAP in mmHG

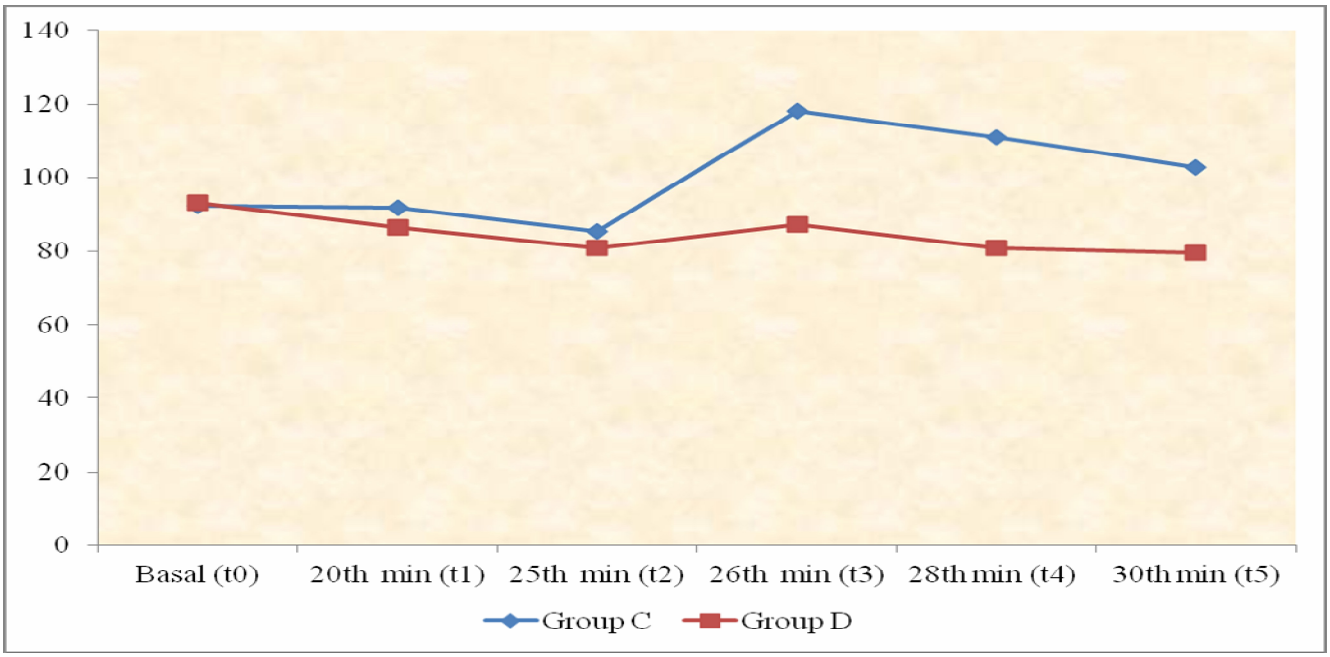


Figure.5 Showing the intergroup comparison of mean pulmonary arterial pressure (MPAP in mmHg) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

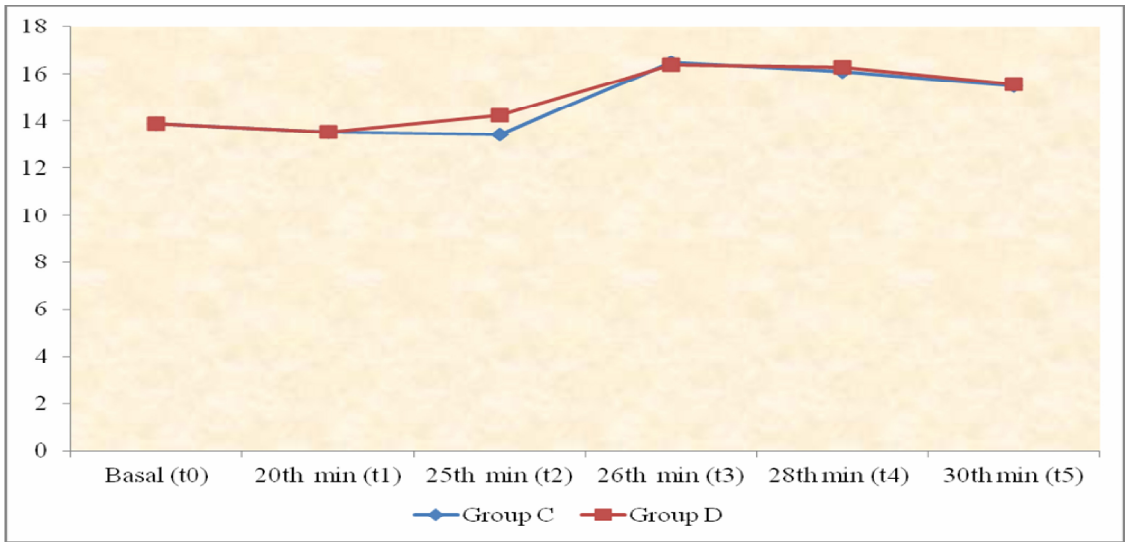
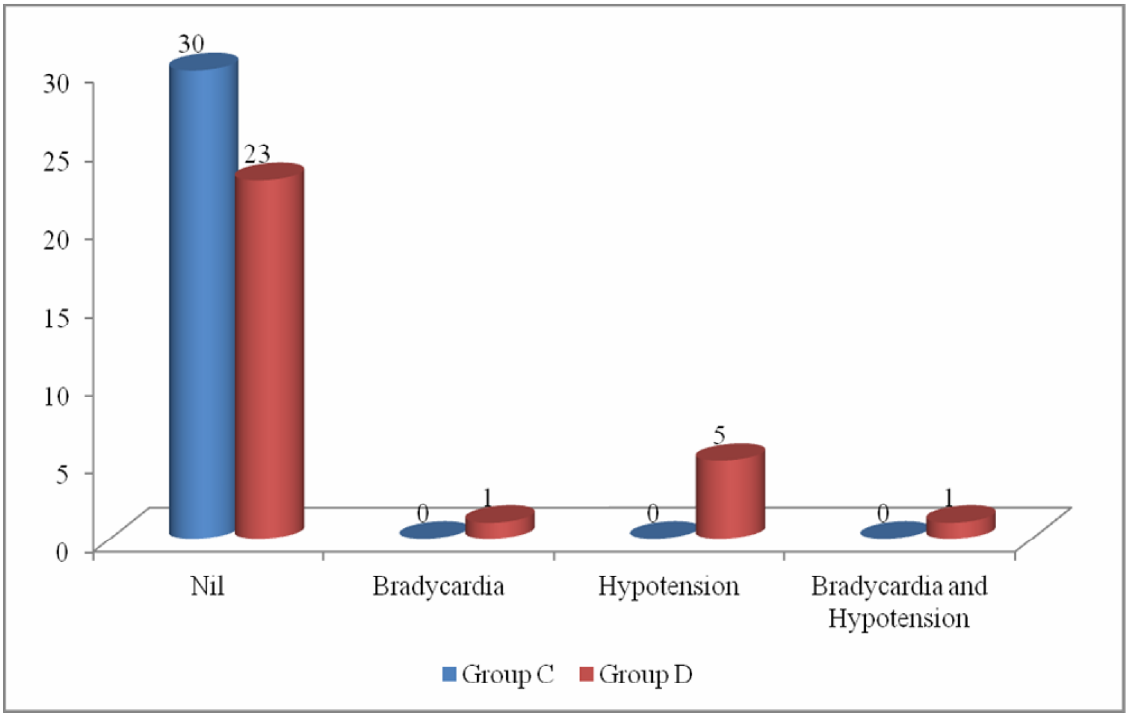


Fig.6 Effects between control and dexmedetomidine group



Conclusion

Dexmedetomidine at dose of 1ugm/kg body weight diluted in 100 ml of 0.9% N.S. over 15 minutes before induction significantly obtunded the haemodynamic stress responses to laryngoscopy and tracheal intubation without significant side effects [like hypotension and bradycardia]

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