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Original Research Article

Efficacy of intravenous dexmeditomidine versus lidocaine in attenuation of stress response during intubation for laproscopic procedures

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Abstract

Introduction: Haemodynamic instability during intubation is a well documented fact. These responses may produce myocardial ischemia or infarction in susceptible cases. Dexmedetomidine is a newly introduced is a highly selective alpha 2 adrenergic agonist which possesses hypnotic, sedative, anxiolytic, sympatholytic, and opiod sparing, analgesic properties without producing significant respiratory depression. This makes it more favorable drug to be used for attenuating pressor response, as it can be used as an adjunct to anaesthesia. Hence, a randomised controlled trial study is undertaken to compare dexmedetomidine to lidocaine as regards its efficacy on attenuation of intubation response.

Objectives: To study the comparative efficacy of Dexmeditomidine and Lidocaine in attenuation of stress response as measured by changes in haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure & mean arterial pressure.

Methodology: 70 patients belonging to the American Society of Anaesthesiology (ASA) physical status classification class 1 & 2, of either sex between 20-45 years, scheduled for laproscopic surgeries were enrolled for study. The patients were randomly allocated into 2 groups. Group A included 35 patients receiving 1mcg/kg IV Inj. Dexmeditomidine infusion over 10 min before induction. Group B included 35 patients who received plain preservative free Lidocaine 2%, 1.5mg/kg body weight I.V. bolus 1.5 min prior to laryngoscopy.

Results: The study revealed that there is significant difference between(p value <0.05) the two groups during laryngoscopy & intubation with respect to heart rate, systolic blood pressure & diastolic blood pressure. The target group showed significantly less heart rate, systolic & diastolic BP compared to control group. We also found the dose requirement of induction agent; Propofol was also less in study group.

Conclusion: Dexmeditomidine significantly attenuates stress response to tracheal intubation with improved haemodynamic stability.

Keywords: Dexmeditomidine, lidocaine, haemodynamic parameters.

1. Introduction

Haemodynamic instability during intubation is a well documented fact. These responses may produce myocardial ischemia or infarction, left ventricular failure and cerebral haemorrhage in susceptible cases [1,2]. Various drugs like Esmolol, Lidnocaine, Nitroglycerine, Clonidine etc are being used to reduce the pressor responses. But almost all drugs have some contraindications and adverse effects and have to be used with precaution.

Dexmedetomidine a newly introduced highly selective alpha 2 adrenergic agonist (α_2:α_1 receptor activity 1620:1). Dexmeditomidine, s-entanomer of meditomidine, possesses hypnotic, sedative, anxiolytic, sympatholytic, and opiod sparing, analgesic properties without producing significant respiratory depression [3-6]. It has the ability to reduce both the anaesthetic and opioid analgesic requirement during the perioperative period[7,8]. It's sympatholytic effect decreases mean arterial pressure (MAP) and heart rate (HR) by reducing norepinephrine release[9,10]. These properties makes Dexmeditomidine more favorable drug to be used for attenuating pressor response, as it can be used as an adjunct to anaesthesia. Hence, a study is undertaken to compare dexmedetomidine to lidocaine as regards to its efficacy on attenuation of intubation response.

1.1 Aims and Objectives

1) To study the comparative efficacy of Dexmeditomidine and Lidocaine in attenuation of stress response as

measured by changes in haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure & mean arterial pressure.

2) To document any side effects such as hypotension or bradycardia.

1.2 Hypothesis

Intravenous Dexmedetomidine decreases haemodynamic stress response during laryngoscopy and endotracheal intubation as compaired to intravenous Lidocaine.

2. Materials and Method

After getting approval from the institutional ethical committee, this prospective randomized experimental study was carried out at Dr SMCSI Medical College, Karakonam, TVM.

2.1 Study Design: Randomised controlled trial.

2.2 Study Setting: Department of Anaesthesia, Dr SMCSI Medical College Karakonam.

2.3 Study Population: Patients with ASA grade I and II, aged 20-45 years, of both sexes scheduled for laproscopic intervention.

2.4 Exclusion Criteria

1. Patients who did not give consent.
2. Patients with heart block, hypertensive patients on β blockers, morbid obesity, pregnant women & history of psychiatric disorder are excluded from the study.
3. Patients with diabetes and renal disease is not included in the study.

2.6 Sample Size:

70 patients belonging to the American Society of Anaesthesiology (ASA) physical status classification class 1 & 2 of either sex between 20-45 years, scheduled for laproscopic surgeries in Dr SMCSI Medical College is divided into two groups each consisting of 35 patients.

Sample size calculated using the formula

$n=2\sigma^2 (z\alpha+z\beta)^2/\delta^2$

When $\alpha=0.01$, $z\alpha=2.58$

When $\beta=0.1$, $z\beta=1.2$

σ=standard deviation, is found out as 32, δ=effect size, is found to be 30

n=2×〖32〗^2 〖(2.58+1.28)〗^2/〖30〗^2=33.9.

So the final sample size (n) of each group is taken as 35.

2.6 Study Period: One year.

2.7 Study Tool: Predesigned & pretested proforma used.

2.8 Procedure

70 patients belonging to the American Society of Anaesthesiology (ASA) physical status classification class 1& 2, of either sex between 20-45 years, scheduled for laproscopic surgeries in Dr SMCSI Medical College.

2.8.1 Pre operative checkup

A thorough pre-anaesthetic check-up was carried out. Detailed history was taken and systems were examined. Pulse, blood pressure and respiratory rate were noted. Height and weight were recorded. Routine investigations like haemogram, bleeding time, clotting time, chest X-ray, ECG were obtained before taking up for surgery. After applying the exclusion criteria, 70 patients about to undergo laproscopic surgeries with endotracheal intubations were selected.

2.8.2 Pre-operative Preparation

All the selected patients were visited on the day prior to surgery, explained in detail about the anaesthetic procedure and informed written consent was obtained. All patients were kept NPO 8 hours prior to surgery. They received Tablet Ranitidine 150mg and Tablet metoclopramide 10mg on the previous night and on the morning of surgery. Patients were premedicated with Inj Glycopyrrolate 0.2 mg intramuscularly 1 hour before surgery.

Intra-operative monitoring included- Pulse oximetry, non-invasive blood pressure, ECG & Capnography.

The patients were randomly assigned to one of the two groups, each containing 35 patients, using a "slips of paper in a box" technique.

The grouping is as follows

Interventional Group: Dexmeditomidine Group

Control Group: Lidocaine Group

All the patients in Interventional group received inj. dexmedetomidine in a dose of 1 µg/kg over a period of 10 min prior to induction of anaesthesia through an infusion pump. All the patients in Control group received plain preservative free Lidocaine 2%, 1.5mg/kg body weight I.V. bolus 1.5 min prior to laryngoscopy which is the routine standard practice.

In operation theatre all monitors were attached and baseline values recorded. Patients were pre-oxygenated with 100% oxygen for 3 minutes followed by inj. Fentanyl 1.5mcg/kg IV. Anaesthesia was induced with inj. Propofol 2mg/kg IV. This was followed by succinyl choline 2mg/kg and endotracheal intubation was done with appropriate size endotracheal tube. Patients requiring more than 20 seconds achieving successful tracheal intubation were excluded from the study. Maintenance of anaesthesia was done with Nitrous oxide: Oxygen 2:1 and Vecuronium for muscle relaxation after intubation. Heart rate, systolic and diastolic blood pressures were recorded preinduction, induction, during intubation, 1 min & 3 minutes after intubation .Any further need for analgesia was supplemented by IV fentanyl. At the end of surgery neuro-muscular blockade was reversed using inj. neostigmine 0.05mg/kg and inj. glycopyrrolate 0.008mg/kg and the patients were extubated and observed in the post anaesthesia care room for 2 hours. Side effects if any were noted.

2.8.3 Observations

Pulse rate and blood pressure were recorded as per the proforma.

Mean arterial Pressure was calculated by the formula

MAP = DBP + 1/3 (SBP-DBP)

Where DBP – diastolic blood pressure, SBP – systolic blood pressure.

Change in pulse rate 20% of base line value was considered bradycardia or tachycardia. Patients who developed bradycardia were given inj. atropine 0.6mg IV

2.9 Statistical Analysis

Data was entered in Microsoft Excel & statistical analysis was done by SPSS (16.0) version. Statistical analysis of demograhic data, heart rate changes, blood pressure changes were done by Independent t –test. Student's t test were used for comparing means of two groups

P values less than 0.05 ($p<0.05$) are considered significant at 95% confidence interval

A p value >0.05 is not significant

<0.05 is significant

<0.001 is highly significant

3. Observation & Results

A sample size of 35 was obtained in each group. The data were collected with the help of a prestructural proforma

3.1 Comparison of demographic data

Table 1: Distribution of Sample according to Age

Age	Study		Control	
	Count	Percent	Count	Percent
20-30	10	28.6%	11	31.4%
30-40	14	40%	18	51.4%
>40	11	31.4%	6	17.2%

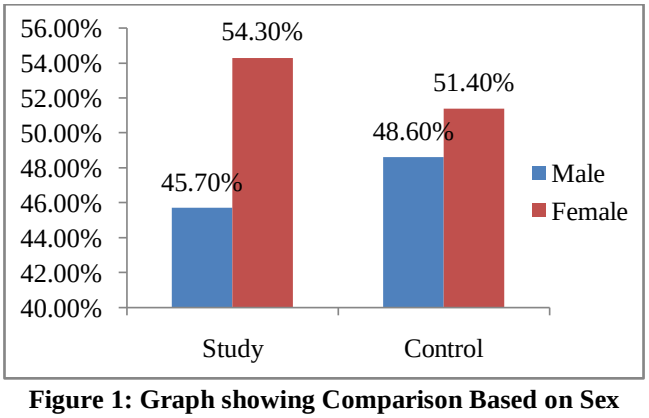

Figure 1: Graph showing Comparison Based on Sex

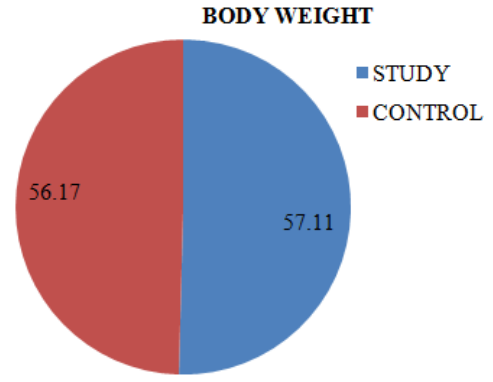

Figure 2: Graph showing Comparison of mean body weight between controls and study group

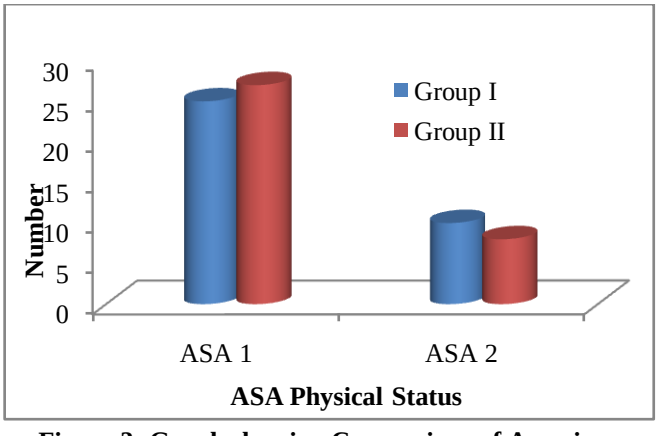

Figure 3: Graph showing Comparison of American Society of Anaesthesiologists score between control and study group

3.2 Heart rate changes

Table 2: Comparison of heart rate changes between groups at various time intervals

Group		N	Mean	STD Deviation	P Value	95% Confidence Interval of the Difference	
						Lower	Upper
Baseline	1	35	82.86	1.789	0.428	-3.219	7.505
	2	35	80.71	2.004			
Preinduction	1	35	69.26	1.384	<0.001	-19.838	-10.391
	2	35	84.37	1.915			
Induction	1	35	66.51	1.766	<0.001	-27.653	-17.261
	2	35	88.97	1.913			
Intubation	1	35	76.97	1.303	<0.001	-30.410	-20.333
	2	35	102.34	2.151			
Intubation I min	1	35	76.51	1.437	<0.001	-27.549	-17.537
	2	35	99.06	2.050			
Intubation 3 min	1	35	70.80	1.365	<0.001	-23.367	-14.519
	2	35	89.74	1.744			

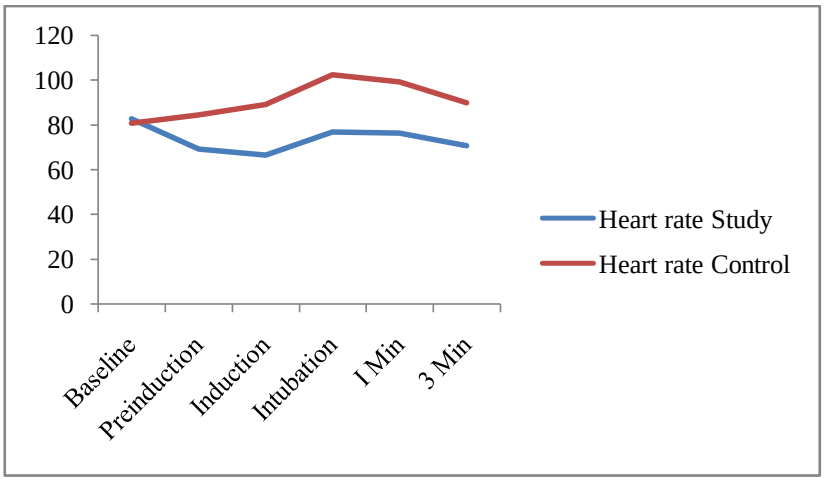

Figure 4: Graph showing Mean Heart Rate Variation

There was no difference in the baseline heart rate values. Statistically significant reduction in heart rate occurred in Dexmeditomidine group patients during preinduction, induction, intubation and 1min & 3min after intubation(p value <0.001)

3.3 Systolic Blood Pressure Changes

Table 3: Comparison of mean systolic blood pressure changes between groups at various time intervals

Group		N	Mean	STD Error	P Value	95% Confidence Interval of the Difference	
						Lower	Upper
Baseline	1	35	128.91	1.721	0.431	-2.603	6.032
	2	35	127.20	1.307			
Preinduction	1	35	112.51	1.295	<0.001	-14.370	-7.116
	2	35	123.26	1.276			
Induction	1	35	112.57	1.542	<0.001	-15.318	-6.853
	2	35	123.66	1.456			
Intubation	1	35	123.03	1.584	<0.001	-28.703	-19.525
	2	35	147.14	1.667			
Intubation I min	1	35	121.2	1.599	<0.001	-26.712	-16.373
	2	35	142.74	2.035			
Intubation 3 min	1	35	117.29	1.743	<0.001	-21.441	-12.199
	2	35	134.11	1.523			

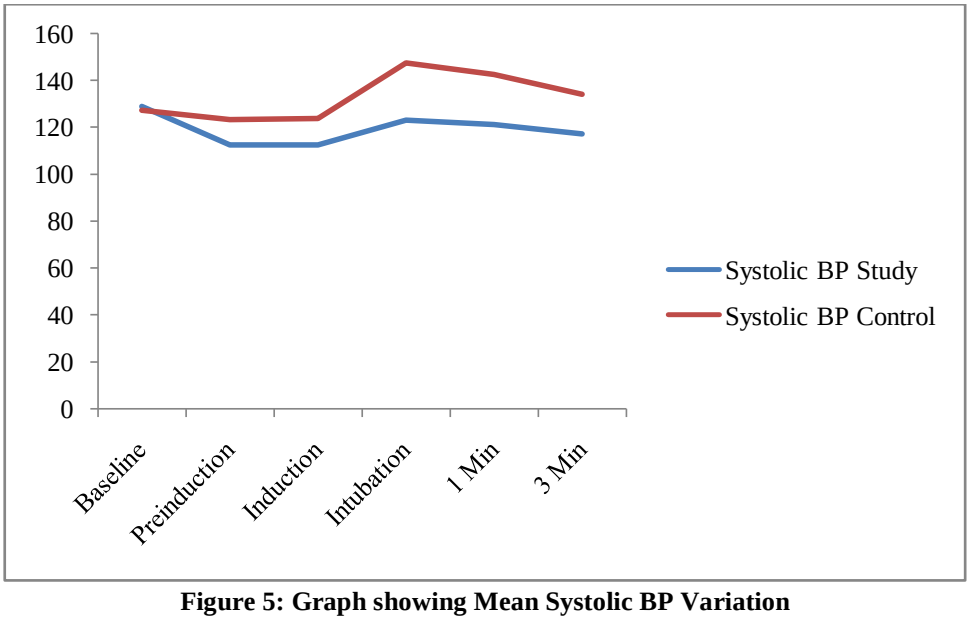

Figure 5: Graph showing Mean Systolic BP Variation

There was no difference in the baseline systolic blood pressure. Statistically significant reduction in systolic blood pressure occurred in Dexmeditomidine group patients during preinduction, induction, intubation and 1min & 3min after intubation(p value <0.001)

3.4 Diastolic blood pressure changes

Table 4: Comparison of mean diastolic blood pressure changes between groups at various time intervals

Group		N	Mean	STD Error	P Value	95% Confidence Interval of the Difference	
						Lower	Upper
Baseline	1	35	82.86	0.932	0.372	-1.394	3.680
	2	35	81.71	0.864			
Preinduction	1	35	78.51	0.838	0.591	-2.952	1.695
	2	35	79.14	0.809			
Induction	1	35	76.06	0.918	0.049	-4.900	-0.014
	2	35	78.51	0.809			
Intubation	1	35	82.51	0.849	<0.001	-9.246	-4.469
	2	35	89.37	0.843			
Intubation I min	1	35	81.14	0.753	<0.001	-6.362	-1.981
	2	35	85.31	0.799			
Intubation 3 min	1	35	79.83	0.857	0.063	-4.226	0.112
	2	35	81.89	0.666			

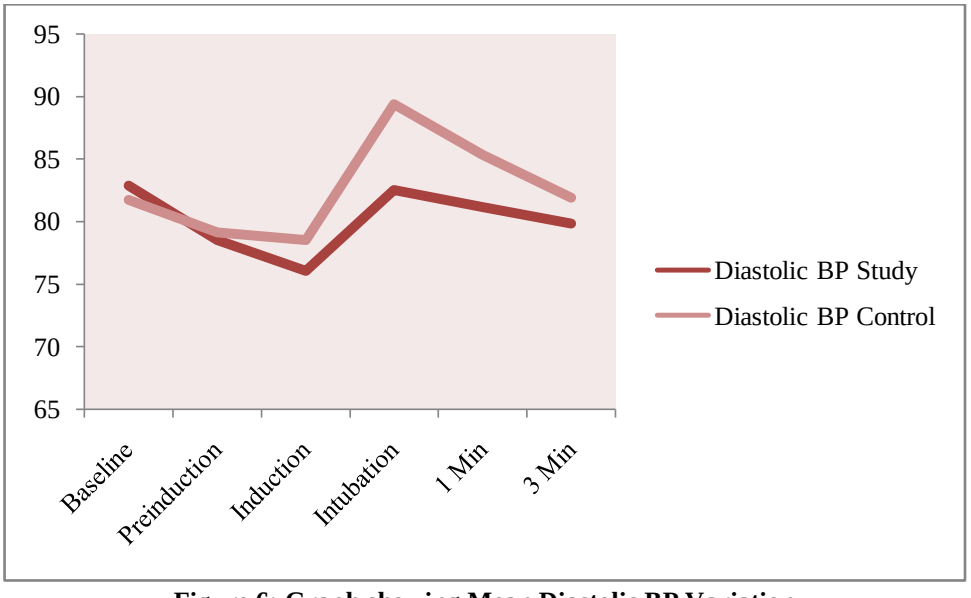

Figure 6: Graph showing Mean Diastolic BP Variation

There was no difference in the baseline diastolic blood pressure and preinduction diastolic BP. Statistically significant reduction in diastolic blood pressure occurred in Dexmeditomidine group patients during induction, intubation and 1min after intubation(p value <0.05) and no difference in diastolic BP 3 min after intubation.

3.5 Mean arterial pressure changes

Table 5: Comparison of mean arterial pressure changes between groups at various time intervals

Group		N	Mean	STD Error	P Value	95% Confidence Interval of the Difference	
						Lower	Upper
Baseline	1	35	97.83	1.091	0.368	-1.507	4.021
	2	35	96.57	0.853			
Preinduction	1	35	89.46	0.791	<0.001	-6.246	-1.869
	2	35	93.51	0.760			
Induction	1	35	85.54	1.655	<0.001	-12.008	-4.792
	2	35	93.94	0.728			
Intubation	1	35	95.74	0.987	<0.001	-15.206	-9.822
	2	35	108.26	0.920			
Intubation I min	1	35	94.11	0.922	<0.001	-12.769	-7.346
	2	35	104.17	0.998			
Intubation 3min	1	35	65.63	0.770	<0.001	-10.368	-6.204
	2	35	73.91	0.703			

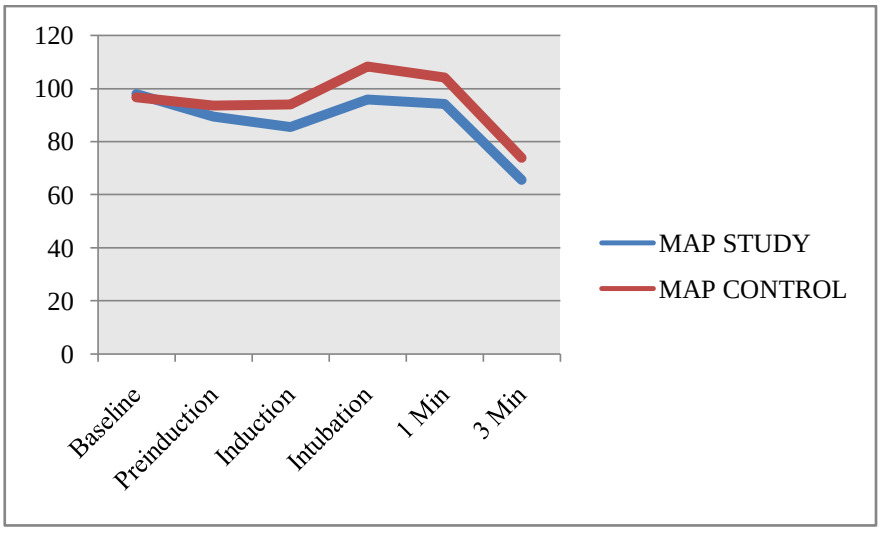

Figure 7: Graph showing MAP Variation

There was no difference in the baseline Mean arterial pressure between two groups. Statistically significant reduction in mean arterial pressure occurred in Dexmeditomidine group patients during preinduction, induction, intubation and 1min & 3min after intubation(p value <0.001)

3.6 Supplemental opioid requirement in the intraoperative period

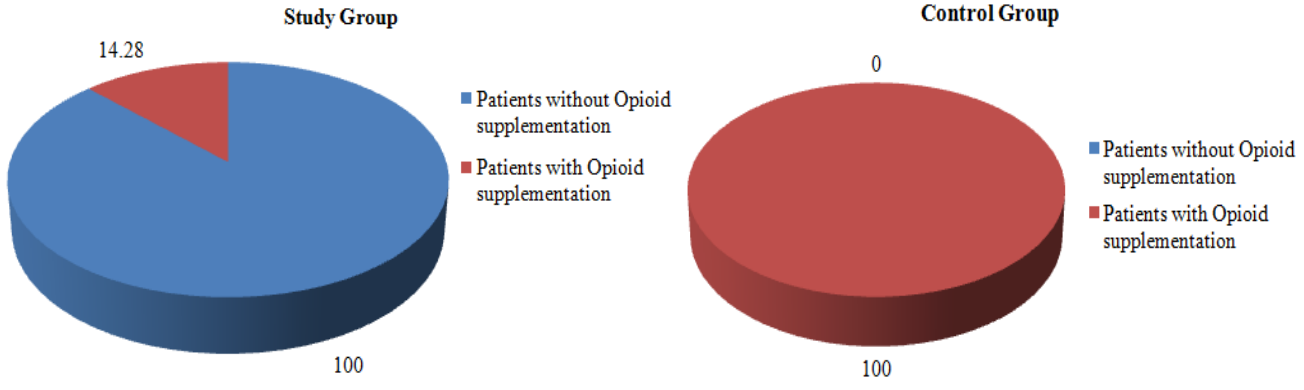

Figure 8: Graph showing number of patients receiving supplemental Opioid in intraoperative period

3.7 Side Effects

Two patients developed bradycardia in the study group, out of which one needed intervention and other settled without intervention. None of the patients developed hypotension, hypertension or respiratory depression.

4. Discussion

Laryngoscopy and tracheal intubation are considered as the most critical events during general anaesthesia, as they provoke a transient but significant, sympathetic and sympathoadrenal response. Various antihypertensive drugs are available for treating perioperative hypertension. Beta blockers like esmolol and metoprolol is commonly used to treat hypertensive episode, its use is complicated by bradycardia and conduction delays. Calcium channel blockers cause dose dependent cerebral vasodilatation, inhibition of auto regulation and higher incidence of hypotension. The final common pathway which leads to perioperative hypertension appears to be sympathetic nervous system activation. α_2-adrenergic drugs like clonidine or dexmedetomidine reduce these potentially harmful cardiovascular responses during anaesthesia induction**.**

This prospective, randomized, double blind placebo controlled study was conducted to know whether dexmedetomidine, a newer α 2 -agonist, with additional properties such as sedation, anxiolysis and sympatholysis is effective for attenuating the hemodynamic response to laryngoscopy and endotracheal intubation with the conventionally used agent Lignocaine. The study demonstrated that a loading dose of 1 mcg/kg of intravenous dexmedetomidine caused significant attenuation of heart rate and blood pressure response to laryngoscopy and intubation and also reduced intraoperative opioid requirement as compared to control group receiving Lignocaine.

Dexmedetomidine exhibits a unique pharmacological profile with sedation, sympatholysis, analgesia and haemodynamic stability along with the great advantage of avoiding respiratory depression.

Dexmedetomidine offers a dose-dependent cooperative sedation which allows interaction with the patient. These above-said aspects of the pharmacological profile of dexmedetomidine render it suitable as an anaesthetic adjuvant and also for intensive care unit sedation.

In our study the two groups were comparable in terms of age, gender and weight. The pre-operative heart rate and blood pressure of the two groups were having no significant difference ($p > 0.05$). After infusion of dexmedetomidine, there was a fall in heart rate and blood pressure in the study group. Patients were sedated but arousable.

Lawrence *et al* [11]found that a single dose of 2 mcg/kg of dexmedetomidine before induction of anaesthesia reduced the hemodynamic response to intubation as well as that to extubation. Bradycardia was seen at the 1st and 5th min after administration. This might have been due to relatively higher dose given as bolus administration. A former study evaluated different bolus doses of dexmedetomidine for premedication [12] and as recommended in literature we selected 1 ug/kg bolus dose. Given the property of the drug to cause hypotension or bradycardia when administered to patients, it is important to find out an infusion rate that would maximize the anaesthetic effect and analgesic sparing effect while minimizing the incidence of adverse cardiovascular effects which require therapeutic intervention.

During our study two patients developed bradycardia, out of which one was self-limiting and other one required intervention.

Dexmedetomidine increases the cardiovascular stability by altering the stress-induced sympathoadrenal responses to endotracheal intubation, during surgery and during emergence from anaesthesia [13]. Jaakola *et al* [14] in a study concluded that dexmedetomidine attenuates the increase in heart rate and blood pressure during endotracheal intubation.

Scheinin *et al* [15] studied the effect of dexmedetomidine on endotracheal intubation, required dose of induction agent and perioperative analgesic requirements. They concluded that the required dose of thiopentone was considerably lower in the dexmedetomidine group and the drug reduced the hemodynamic effects to endotracheal intubation. The concentration of noradrenaline in mixed venous plasma was lesser in the dexmedetomidine group. Varshali *et al* [15] showed that dexmedetomidine reduces sympathoadrenal response to endotracheal intubation and decreases perioperative anaesthetic requirements hence the need for thiopentone and isoflurane reduced by 30% and 32% respectively in the dexmedetomidine group compared to control group.

Villela NR *et al* [16] observed that anaesthetic consumption is reduced in the group given dexmedetomidine. Yildiz M *et al* [17] found out that preoperative administration of a single dose of dexmedetomidine reduced opioid and anaesthetic requirements. Hassan S [18] also observed in his study that the intra-operative infusion of dexmedetomidine reduced the total dose of propofol and fentanyl required to maintain anaesthesia, offered a better control of intra-operative and postoperative hemodynamic, reduced postoperative pain level, reduced the total dose of morphine used and showed a better recovery profile compared to placebo.

In our study the intraoperative requirement of opioids was also significantly reduced in the study group. Only 5 out of 35 patients in the study group required supplemental opioid while all patients in control group required supplemental opioid.

In a prospective, randomized study by Menda F *et al* [19] dexmedetomidine was used for attenuation of hemodynamic response to tracheal intubation with low dose fentanyl and etomidate in patients undergoing myocardial revascularization receiving beta blocker treatment. In the dexmedetomidine group systolic, diastolic and mean arterial pressures were lower at all times compared to baseline values. After induction of anaesthesia, the decrease in heart rate was higher in dexmedetomidine group compared to placebo group. One minute after intubation, heart rate considerably increased in placebo group while, it reduced in the dexmedetomidine group. The incidence of hypertension requiring treatment was considerably higher in the placebo group. It is concluded that dexmedetomidine can be safely used to reduce the hemodynamic response to intubation in patients undergoing myocardial revascularization receiving beta blockers.

Sulaiman *et al* [20] conducted a similar study regarding the efficacy of intravenous dexmedetomidine for attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation in patients having coronary artery disease. Dexmedetomidine at a dose of 0.5 mcg/kg as 10 minutes infusion administered before induction of general anaesthesia reduces the sympathetic response to laryngoscopy and endotracheal intubation in patients undergoing myocardial revascularization. The authors suggest that it can be administered even in patients receiving beta blockers. This confirms the observations in our study though we chose ASA I & II patients.

Similarly, Bajwa *et al* [21] demonstrated that the pressor response to laryngoscopy, intubation, surgery and extubation were effectively reduced by dexmedetomidine. The mean dose of fentanyl and isoflurane were also decreased significantly (>50%). The mean recovery time was also shorter in the dexmedetomidine group.

In our study the baseline values of heart rate and blood pressure were comparable in both groups. The maximal rise in heart rate and blood pressure occurred at the time of tracheal intubation when compared to the values before intubation in both groups. The dexmedetomidine group had a significantly lower mean heart rate 76.97± 1.30 after

intubation compared to control group with mean heart rate of 102.34±2.15 ($p<0.001$). The study group also had lower heart rates at 1 min & 3 minutes after intubation compared to control group.

In comparison with the control group, the study group had a smaller rise in systolic blood pressure after intubation with mean 123.03±1.58mm Hg in study group and mean of 147.14±1.66 mm Hg in the control group. The values of systolic blood pressure returned to the values before intubation earlier in the study group.

Likewise the diastolic blood pressure and mean arterial pressure of both groups were having comparable baseline values. The values for both these parameters were near the value before intubation at all-time intervals for patients given dexmedetomidine. For the control group there was a significant rise in diastolic blood pressure and mean arterial pressure soon after intubation. Thus in our study pretreatment with dexmedetomidine 1mcg/kg over 10 minutes attenuated but not totally obtunded the cardiovascular response to tracheal intubation after induction of anaesthesia.

The limitation regarding this study is we would have measure the plasma catecholamine levels, which is more objective means of hemodynamic response.

The present study findings corroborate with those of previous studies. No major adverse effects from the drug were seen in our study.

5. Summary and Conclusion

This study was done to evaluate the effectiveness of intravenous dexmedetomidine in attenuating the haemodynamic stress response during laryngoscopy and intubation in comparison with intravenous lignocaine. 70 patients belonging to American Society of Anesthesiology physical status classification 1 and 2 of either sex, between 20-45 years scheduled for elective surgeries were divided into two groups each consisting of 35 patients. After premedication, group I patients were given dexmedetomidine 1mcg/kg 10 minutes prior to induction followed. All patients were induced with propofol, intubated using succinyl choline and were maintained with vecuronium and isoflurane. Analgesic used was fentanyl. Group II patients received intravenous lignocaine 1.5 mg/kg, 90 sec before intubation.

Based on the results obtained in the study, it can be concluded that dexmedetomidine causes statistically significant attenuation of the haemodynamic stress response to laryngoscopy and intubation. All patients in the study group were better sedated and cardiostable. The study group also had lesser requirement of intraoperative opioids.

In conclusion, Dexmedetomidine, as a pre anaesthetic medication, significantly attenuates sympathoadrenal response to laryngoscopy and endotracheal intubation and also cause reduction in intra operative anaesthetic requirement, without affecting intraoperative cardiovascular stability.

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