Original research article

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A COMPARATIVE STUDY OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE ON HAEMODYNAMIC RESPONSES TO INDUCTION OF ANAESTHESIA AND TRACHEAL INTUBATION

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ABSTRACT:
BACKGROUND & AIM: Laryngoscopy & intubation lead to haemodynamic response as tachycardia & hypertension. Dexmedetomidine, α_2 agonist has significance in supressing this haemodynamic response. Aim is to compare two different doses of Dexmedetomidine on haemodynamic response to laryngoscopy and intubation.
MATERIALS AND METHODS: This prospective, randomized, double blind study was conducted in GMERS medical college, Gandhinagar. Total 60 patients of ASA Grade I and II, aged 18– 60 years undergoing elective surgeries under general anaesthesia were chosen for the study. The patients were randomly allocated into two groups. Group D_1 (n=30) received Dexmedetomidine 1 µg/kg & group D_5 (n=30) received Dexmedetomidine 0.5µg/kg in 10ml normal saline over 10min, 10min before induction of anaesthesia. Heart rate, Systolic blood pressure, Diastolic blood pressure, mean arterial pressure & SpO_2 were recorded at different time interval and compared between both groups.
RESULTS: Group D_1 showed a significant fall in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after injecting drug, post intubation & throughout surgeries. Dexmedetomidine 0.5µg/kg attenuates haemodynamic response of laryngoscopy & intubation but not as effective as Dexmedetomidine 1 µg/kg.
CONCLUSION: We conclude that, Dexmedetomidine 1µg/kg is superior to Dexmedetomidine 0.5µg/kg for attenuation of haemodynamic response of laryngoscopy & intubation.

KEYWORDS: DEXMEDETOMIDINE, HAEMODYNAMIC RESPONSE, LARYNGOSCOPY

Introduction

Laryngoscopy and endotracheal intubation are the most important integral part of anaesthetic management and the most critical event during administration of general

anaesthesia. Laryngoscopy and Endotracheal intubation evoke a hemodynamic response by the stimulation of epipharynx and laryngopharynx mediated by the afferent Vagus (X) & Glossopharyngeal (IX) cranial nerves which activate the vasomotor center to cause a peripheral sympathetic adrenal response to release adrenaline & noradrenaline from adrenal medulla which leads to tachycardia and hypertension.[1] The circulatory response to laryngoscopy and tracheal stimulation was first documented by Reid and Brace in 1940 and King et al in 1951.[2],[3] These haemodynamic responses are well tolerated in healthy individuals but in susceptible individuals this transient response can evoke life-threatening conditions like myocardial ischemia, arrhythmias, stroke, left ventricular failure, increase intracranial tension and cerebral haemorrhage.[4] . Various pharmacological and non-pharmacological methods are in vogue to control this haemodynamic response such as Local anaesthetic agents like lignocaine intravenous and topical spray. Beta blockers like labetalol, propranolol and esmolol [5] ,Opioids like fentanyl, alfentanil, sufentanil and remifentanil[6] ,Volatile anaesthetic agents like halothane, Isoflurane, Sevoflurane, Vasodilators like nitro-glycerine, sodium nitroprusside.[7]

Recentlyα2 agonist has gained significance in suppressing laryngosympathetic response. Both clonidine and Dexmedetomidine have actions on α_1 and α_2 receptors but Dexmedetomidine is highly specific and selective α2 adrenoceptor agonist. [8] As a premedicant it induces anxiolysis, analgesia, sedation, haemodynamic stability and anaesthetic sparing effects. [9]

This study aims to attenuate the haemodynamic response of laryngoscopy and intubation in adult patients posted for surgery under general anaesthesia with single intravenous bolus dose of Dexmedetomidine 0.5 µg/kg and Dexmedetomidine 1µg/kg over 10 minutes before induction and to compare effects of both doses.

METHODOLOGY

The study design was prospective, randomised, double blind. Purposive sampling method, which is a non-probability sampling technique, was used considering the patient inflow rate in the institute during the study duration and the time duration was fixed.A total of 60 patients who were admitted in GMERS civil hospital, Gandhinagar for elective surgical procedure under spinal anaesthesia, qualifying other inclusion criteria were asked for the consent and included in this study for 9 months (June 2017 to April 2018) and study was conducted at GMERS Medical College and Civil Hospital, Gandhinagar.

1. **Sample size:**

Sample size of Group D1	30
Sample size of Group D5	30
Total sample size	60

Inclusion criteria were patients posted for elective surgery under General Anaesthesia,
under ASA grade: I and II, aged between 18 to 60 years of either sex. Exclusion criteria were patients with anticipated difficult airway and if Laryngoscopy time >30 seconds, known allergy to any drug, taking antihypertensive drugs, known case of cardiovascular, respiratory, hepatic and renal diseases. A through Preanaesthetic evaluation was done. Patients were counselled and written informed consent was taken. Patients were kept fasting for 8 hrs prior to surgery. Routine investigations were done.

Patient was reviewed before surgery and Written informed consent were taken. In operation theatre, all baseline vital parameters i.e., Heart rate (HR), systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) and SPO2 were recorded by multipara monitor. Inj Ranitidine 1mg/kg IV, Inj Ondansetron 0.08mg/kg IV,Inj Glycopyrrolate 4 μg/kg IV,Inj Midazolam 0.02mg/kg IV were given to the patients. Study drug was injected 10 minutes before induction. Group D1: Dexmedetomidine 1μg/kg and Group D5: Dexmedetomidine at 0.5μg/kg body weight diluted to 10ml of normal saline injected over 10 minutes. After Pre oxygenation, induction was done with Inj. Thiopentone 2.5%: 5mg/kg IV and Inj. Suxamethonium2mg/kg IV. Direct Laryngoscopy and Intubation was done with proper size endotracheal tube. Patient was maintained on O2: N2O (50:50), Sevoflurane, Inj Vecuronium bromide. Volume controlled positive pressure mechanical ventilation was maintained through tidal volume of 7-10 ml/kg, respiratory rate of 14-16 /min and fresh gas flow at the rate of 4L/min. IV fluids were to be given as per requirement. Incision was allowed 5 minutes after intubation. At the end of surgery, reversal was done with Inj. Neostigmine 50 μg/kg + Inj Glycopyrrolate 8 μg/kg and patient was extubated. Vitals were recorded at Baseline, after study drug (at 10 minute), Induction, after intubation (at 1,2,3,5,10,15,30,45 ,60 minutes)

All patients were kept in Post anaesthesia care unit (PACU) for two hours and vitals were monitored. Side Effects were defined as Bradycardia: HR < 50 beats/min, Tachycardia: HR > 100 beats/min. Hypertension: SBP > 30% of baseline value Hypotension: defined as SBP < 30% of baseline value. Intraoperative and postoperative complications for 24 hours after completion of surgery were monitored.

The results obtained in the study were presented in tabulated manner and analysed using Microsoft Excel and Epi info software (version 6.1) for windows. Statistical analysis was carried out using Student's t test. Haemodynamic variables were expressed as Mean ± SD. P value <0.05 was regarded as statistically significant, P value <0.001 was taken as highly significant and P value >0.05 was regarded as no significant

RESULT:

Table 1: Demographic distribution:

	Group D1	**Group D5**	**P value**
No. of patient	30	30	
Age (years) (mean ± SD)	32.167±11.154	33.333±11.174	0.687
Weight (in kg) (mean ± SD)	51.6±8.97	54.3±10.93	0.30
Sex (M:F)	9:21	11:19	0.30

Table 2: Comparison of Heart rate (in bpm) in both the groups

Time (in minutes)	**Group D1 (n=30)**		**Group D5 (n=30)**		**P value**	**Remark**
	Mean	**SD**	**Mean**	**SD**		
Baseline	91.9	11.1	87.5	8.07	0.08	NS

After injecting drug	89.7	11.7	84.2	11.8	0.08	NS
10 min of injection	74.7	10.1	81.1	10.6	0.02	S
At Induction	87.9	15.6	89.9	11.2	0.7	NS
After 1 min	96.9	11.6	99.7	14.8	0.41	NS
5 min	84.4	8.52	90.8	11.9	0.02	S
10 min	80.1	9.16	87.1	13.9	0.03	S
15 min	87.2	9.28	86.7	12.7	0.84	NS
30 min	83.9	11.2	84.2	14.1	0.93	NS
45 min	78.4	9.23	81	13.7	0.42	NS

Significant; NS-Non significant)

Figure 1: Comparison of Heart rate (H.R) in both the groups

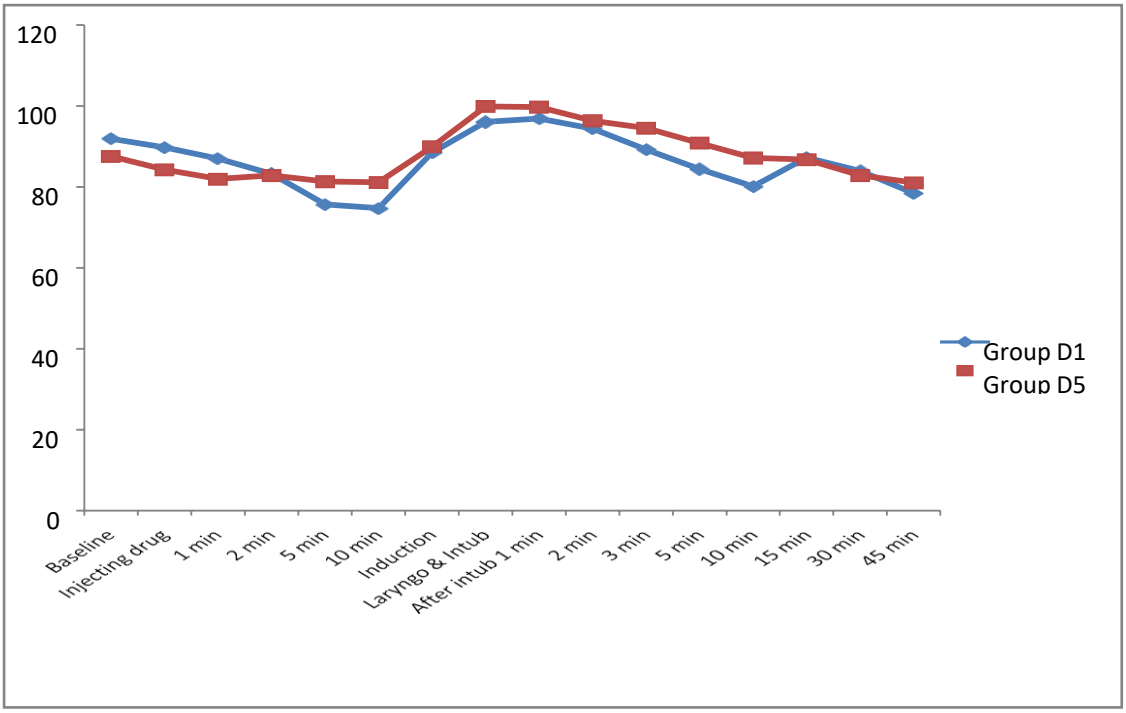

Table 3: Comparison of Systolic blood pressure (mm of Hg) in both the groups

FIGURE 2:COMPARISON OF SYSTOLIC BP IN BOTH GROUP

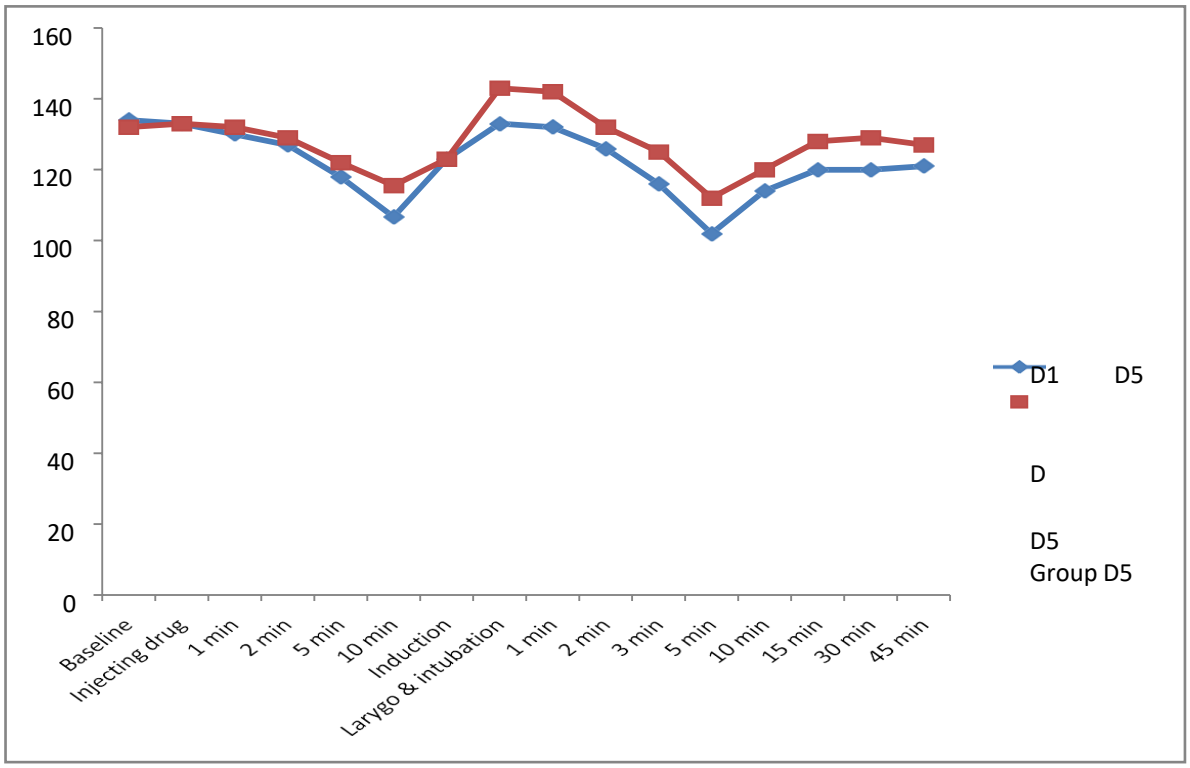

Table 4: Comparison of Diastolic blood pressure (mm of Hg) in both thegroup

Duration (in minutes)	Group D1 (n=30)		Group D5 (n=30)		P value	Remark
	Mean	SD	Mean	SD		
Baseline	81.9	6.34	81.4	10.6	0.83	NS
Injecting drug	82.5	8.34	83.8	9.29	0.57	NS
10 min	71.2	6.5	76.4	8.68	0.01	S
Induction	79.6	11.8	80.4	12.7	0.81	NS
1 min	84.7	9.61	96.3	21.4	0.01	S
5 min	69.5	8	77.5	12.5	0.01	S
10 min	72.1	12.6	75.8	15.1	0.31	NS
15 min	79.3	15.4	82.3	13.1	0.41	NS
30 min	79	13.8	84.4	12.1	0.11	NS
45 min	77.4	13	81.9	10.6	0.17	NS

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15 min	120	16.8	128	16.8	0.08	NS
30 min	120	14.9	129	14.7	0.03	S
45 min	121	17.1	127	14.1	0.13	NS

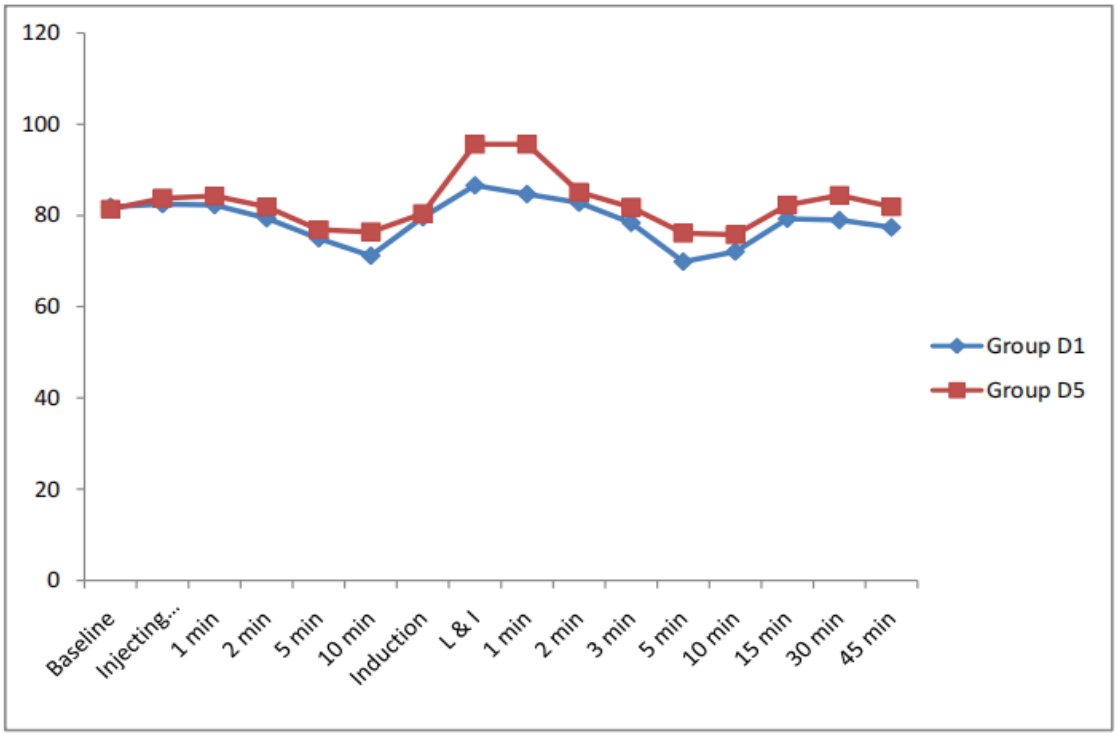

Figure 3: Comparison of Diastolic blood pressure (mm of Hg) in both group

Table 5: Comparison of Mean arterial pressure (mm of Hg) in both group

Duration (in minutes)	**Group D1 (n=30)**		**GroupD5 (n=30)**		**P value**	**Remark**
	Mean	**SD**	**Mean**	**SD**		
Baseline	99.4	10	98.6	12.6	0.78	NS
Injecting drug	99.2	9.22	99.3	9.43	0.94	NS
1 min	99.9	10.5	98.9	13	0.74	NS
10 min	87.3	10	93.2	10.7	0.03	S
Induction	96.6	10.2	94.3	14	0.47	NS
1 min	103	10.5	112	20.6	0.04	S
5 min	85.6	8.56	92.6	12.1	0.01	S
10 min	88.3	13	92	16	0.33	NS
15 min	95.5	15.3	99.5	12.9	0.28	NS
30 min	92.1	12.6	98.9	12.2	0.04	S
45 min	93.1	13.6	98.3	10.3	0.11	NS

Table 6: Comparison of SPO_2 (%) in both the groups

Duration (in minutes)	Group D1 (n=30)		Group D5 (n=30)		P value	Remark
	Mean	SD	Mean	SD		
Baseline	99.2	0.81	99.2	0.77	0.87	NS
10 min after inj	99.6	0.67	96.4	16.3	0.3	NS
Induction	99.8	0.48	99.8	0.5	0.79	NS
15 min	99.8	0.48	99.8	0.5	0.79	NS
30 min	99.7	0.52	99.6	1.48	0.56	NS
45 min	99.9	0.47	100.0	0.62	0.17	NS

Table 7: Complications in both the groups

Sr no.	Complication	Group D1 (n=30)	Group D5 (n=30)	P value	Remarks
1.	Bradycardia	2	1	0.6412	NS
2.	Hypotension	2	2		
3.	Hypertension	1	0		

Note:There was no significance between both the groups regarding side effects. ($p>0.05$)

DISCUSSION

Dexmedetomidine is highly specific and selective α_2 adrenoceptor agonist. As a premedicant it induces anxiolysis, analgesia, sedation, haemodynamic stability and anaesthetic sparing effect. Hence dexmedetomidine may be a better choice among α_2 agonists for studying theattenuation of haemodynamic response to laryngoscopy and intubation. [10,11]

Sagiroglu et al conducted as a study in 2010 with different doses of Dexmedetomidine (0.5µg/kg and 1 µg/kg) for controlling haemodynamicresponse to tracheal intubation. [12] RachitB et al in 2016 conducted a study to evaluate the dose of Dexmedetomidine0.5µg/kg and dexmedetomidine 1µg/kg in blunting the response to laryngoscopy and intubation. [14]

In our study we used two different doses of Dexmedetomidine0.5µg/kg and 1µg/kg was given as IV infusion in 10 ml normal saline over 10 min. Rapid administration ofa bolus dose of Dexmedetomidine results in a biphasic response. Hence in the present study Dexmedetomidine was administered over 10 min.Dose and method of administration was similar to Gulabani M.[13], Rachit B et al[14], ,Sebastian Bon [15]and Raval DL [16]

Demographic data:

In the our study, there was no significant difference in demographic data in both the groups($p>0.05$) like age,sex,height,weight.which is comparable with the study by Smitha K[17], Raval D L,[16]Gulabani M,[13] Sebastian Bon[15]and Rachit B et al.[14]

Hemodynamic parameter:

Heart Rate

The basal HR in group D1 was 91.9±11.1 bpm and group D5 was 87.5±8.07 bpm which was comparable in both groups. ($p>0.05$). After injecting the drug, both groups showed fall in HR.from 1st min onwards.At 10th min the mean HR in group D1 was 74.7±10.1bpm and group D5 was 81.1±10.6 bpm which was significant. ($p<0.05$). Even at the time of induction the mean HR in group D1 was lower than base line (87.9±15.6bpm). Post intubation there was increase HR in both the group however it was more in group D5 than group D1. Increased HR started decreasing after 2nd min onwards. At 5th min, the mean HR in group D1 was 84.4±8.52 bpm and group D5 was 90.8±11.9bpm which was significant. ($p<0.05$) At 10th min, the mean HR in group D1 was 80.1±9.16bpm and group D5 was 87.1±13.9bpm which was significant. ($p<0.05$)

Results of mean HR in our study were comparable with the study done by Smitha K et al [17], Rachit B et al [14] & Raval DL et al. [16]

Systolic Blood Pressure

The basal mean SBP in group D1 134±13.5 mm of Hg and group D5132±12.4 mm of Hg which was comparable in both groups. ($p>0.05$) After injecting drug Group D1 showed fall in SBP from 1st min onwards.) Even at the time of induction the SBP was lower than baseline in both groups.Post intubation there was increase in SBP in both the groups; however groupD1 showed faster decrease in SBP starting from 2nd min post intubation. At 5th min, the mean SBP in group D1 was 102±12.6 mm of Hg and group D5 was 112±14.6 mm of Hg which was significant. ($p<0.05$). Intraoperative even at 30th min, the mean SBP in group D1 was 120±14.9 mm of Hg and group D5 was 129±14.7 mm of Hg which was significant. ($p<0.05$)

The result of mean SBP in our study are comparable with study done by Smitha K et al[17],Rachit B et al[14] and Raval DL et al.[16]

Diastolic Blood Pressure

The basal mean DBP in group D1 was 81.9±6.34 mm of Hg andgroup D5 was 81.4±10.6
mm of Hg which was comparable in both groups. ($p>0.05$). Even at the time of induction the DBP was lower than baseline in bothgroups.Post intubation, there was increase in DBP in both the groups, group D1 showed faster decrease in DBP. At 1St min after intubation, the mean DBP in group D1 was 84.7±9.61 mm of Hg and group D5 was 96.3±21.4 mm of Hg which was significant. ($p<0.05$. ($p<0.05$) At 5th min after intubation, the mean DBP in group D1 was 69.5±8 mm of Hg and group D5 was 77.5±12.5 mm of Hg which was significant. ($p<0.05$)

The results of mean DBP in our study are comparable with the results of Smitha K et al [17], Rachit B et al[14] and Raval DL et al.[16)

Mean Arterial Pressure

The basal mean MAP in group D1 was 99.4±10 mm of Hg and group D5 was 98.6±12.6 mm of Hg which was comparable in both groups. ($p>0.05$) After injecting drug both group showed decrease in MAP from 1st min onwards.At the time of induction the MAP was lower than base line in both groups. D1 showed decrease in mean MAP starting from 2nd min post Intubation. At 5th min post Intubation, the meanMAP in group D1 was 85.6±8.56 mm of Hg and group D5 was 92.6±12.1 mm of Hg which was significant. ($p<0.05$) At 30th min intra operative, the mean MAP in group D1 was 92.1±12.6 mm of Hg and group D5 was 98.9±12.2 mm of Hg which was significant. ($p<0.05$).

The results of mean MAP in our study are comparable with the results of Smitha K et al [17], Rachit B et al [14]and Raval DL et al. [16]

The highest density of α_2 receptors is present in the pontine locus caruleus. Dexmedetomidine stimulatesα_2 adrenergic inhibitory neurons inthe medullary vasomotor center resulting in a decrease sympathetic nervous system outflow from the central nervous system to peripheral tissues. It is manifested as peripheral vasodilatation, decrease systemic blood pressure, heart rate and cardiac output. Postsynaptic α_2 receptors produce vasoconstriction, whereas presynaptic α_2 inhibit the release of norepinephrine potentially attenuating the vasoconstriction. [20,21]

Spo2:

In our study there was no difference in Spo2 before and after injecting the drug, intra operative and post-operative period between group D1 and D5.

Results of SPO2 in our study are comparable with study done by Smitha K et al [17], Rachit B et al [14] and Raval DL et al. [16]

Side Effects

In our study 2 patients of group D1 developed bradycardia, 1 patients developed bradycardia intra operatively but did not need any treatment. Postoperatively there was bradycardia in 1 patients treated with inj atropine 0.6mg IV successfully. In group D5, 1 patient developed bradycardia postoperatively which was treated successfully.

Hypotension was there in 1 patients of group D1 and 1 patients of group D5 intra operatively treated successfully with IV fluids only. Hypertension was noted in 1 patient in group D1 after the injecting the drug which came to normal within 5min. There was no significance between both the groups regarding side effects. ($p>0.05$)

Our study is comparable with study done by Rachit B et al[58]

Sagiroglu A et al (15) in 2009 compared the effect of dexmedetomidine at two different doses i.e 0.5µg/kg vs 1µg/kg on attenuation of haemodynamic responses to laryngoscopy & intubation. They concluded that 1µg/kg is better in obtunding hemodynamic response to laryngoscopy. Thus comparable with our study.

Our study results were also in accordance with the results of Yildizet al. (17) and Bijoy kumar panda et al (18). They too observed that dexmedetomidine when

administered at a dose of 1µg/kg was able to suppress the heart rate response to laryngoscopy. SBP, DBP and MAP were better managed in the group receiving dexmedetomidine 1µg/kg.

Sunil et al (16) in 2012 compared the effect of dexmedetomidine at two different doses i.e 0.5µg/kg vs 1µg/kg on attenuation of haemodynamic responses to laryngoscopy & intubation. They concluded that 1µg/kg is better in obtunding hemodynamic response to laryngoscopy. Thus comparable with our study

CONCLUSION:

From the present study it is concluded that Dexmedetomidine1µg/kg is superior to Dexmedetomidine 0.5µg/kg for attenuation of the pressor response to laryngoscopy and intubation. It is safe and effective method to attenuate the haemodynamic response to laryngoscopy and intubation.

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