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Original article

"A controlled randomized comparative study of effect of two different doses of Dexmedetomidine for attenuation of the hemodynamic response to laryngoscopy and endotracheal intubation."

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ABSTRACT

Aims and Objective: To compare the effectiveness of two doses of intravenous dexmedetomidine, 0.5 µg/kg and 1 µg/kg body weight in attenuating hemodynamic response to laryngoscopy and intubation, Materials and Methods: A comparative study of 90 patients posted for elective surgery under general anaesthesia were randomly divided into 3 groups, group I received inj. Dexmedetomidine 0.5 µg/kg, group II received 1 µg/kg, and group III received 10 ml of normal saline, as infusion over 10 minutes. At the end of the infusion, patients were administered anaesthesia, intubated and maintained by using Sevoflurane inhalation. Cardiovascular parameters were recorded before infusion, at 5 minutes and 1 min. after end of infusion, 1 min. after induction, 1 min., 3 min., 5 min. and 10 min. after laryngoscopy and intubation. Ramsay sedation score and adverse effects were recorded, Statistical Analysis: The groups were compared using ANOVA (Analysis of Variance) in the form of one-way ANOVA test, and repeated measures ANOVA for the parametric interval measures. Intra-group variables were compared using student t test (paired). Quantitative data was compared using Non-parametric Chi-square test. Results of Quantitative data was presented as mean ± 2 SD. Results: statistical evaluation between the groups showed a highly significant fall in HR in groups I and II ($p=0.00001$) compared to the control group III. There was no statistically significant difference in mean HR in group I and II ($p>0.05$). Systolic Blood Pressure, Diastolic Blood pressure and Mean Arterial Pressure statistically showed significant stability in group I ad group II compared to group III. But there is no significant difference in group I and II. There were no adverse effects. Conclusion: Inj. Dexmedetomidine attenuate the hemodynamic response to laryngoscopy and endotracheal intubation and 0.5 µg/kg body weight is safer and equally efficacious compared to 1 µg/kg body weight.

1. Introduction

Laryngoscopy and endotracheal intubation are considered as the most critical events during administration of general anaesthesia leading to various hemodynamic changes. The augmented cardiovascular reflexes in the form of tachycardia, arrhythmias and hypertension brought about by the noxious stimuli of direct laryngoscopy and intubation can prove detrimental to the patients subjected to anaesthesia, especially for those with cardiovascular and cerebrovascular diseases. In these individuals it is very important to blunt this adverse response to prevent serious perioperative complications. The severity of hemodynamic response is greater with increasing force and duration of laryngoscopy and intubation. {5,6}

Several drugs and techniques have been tried by the anaesthesiologists to attenuate the stress response to laryngoscopy and intubation. Dexmedetomidine is an alpha-2 adrenergic agonist having sedative, anxiolytic, sympatholytic and analgesic effect which can be used to control hemodynamic

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response by decreasing catecholamine secretion secondary to laryngoscopy and intubation and maintains adrenergic stability and also decreases requirement of induction doses of anaesthetic agents and intraoperative opioids and volatile anaesthetics to some extent (1,2,3,4,5.6).

The aim of our study is to investigate and compare the effectiveness of two different doses of dexmedetomidine in attenuating cardiovascular responses to direct laryngoscopy and endotracheal intubation

Aims and Objective

1. To study the effect of Dexmedetomidine on hemodynamic response to laryngoscopy and endotracheal intubation.
2. To compare the effectiveness of two doses of intravenous Dexmedetomidine, 0.5 μg/kg body weight and 1 μg/kg body weight, in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.
3. To study any adverse effects associated.

Materials and Methods:

The study was a prospective, randomized, double blind, placebo-controlled study on patients undergoing elective surgeries under general anaesthesia.

The study was conducted after approval from the ethical committee and obtaining informed consent from the patient.
Patients aged between18-60 years, belonging to ASA grade I & II and having Mallampatti Class I & II were included in the study.

Exclusion criteria was patients with history of drug allergy, anticipated difficult intubation, uncontrolled hypertension, cardiac, coronary, renal, hepatic, cerebral diseases and peripheral vascular diseases, pregnancy and lactating females.

Study population: 90 patients undergoing elective surgery under general anaesthesia were randomly divided into three groups with 30 patient each.

Group I- received IV Inj. Dexmedetomidine in a dose of 0.5 μg/kg body weight diluted in 10 ml of normal saline infused over 10 minutes.

Group II - received IV Inj. Dexmedetomidine in a dose of 1 μg/kg body weight diluted in 10 ml of normal saline infused over 10 minutes.

Group III- received IV Normal saline 10 ml. infused over 10 minutes.

Thorough Preanaesthetic evaluation was done prior to the surgery. All patients were explained about the anaesthesia technique.

All patients included in the study were pre-medicated with Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg orally at bed time the night before surgery and were kept nil orally 10 pm onwards. On arrival of the patient in the operating room, Multipara monitor was attached for recording Heart rate, noninvasive measurements of SBP, DBP, MAP, continuous ECG monitoring and oxygen saturation. The baseline cardiovascular parameters were recorded. After recording these baseline readings, Group I patients received inj. Dexmedetomidine of 0.5 μg/kg body weight and Group II patients received Inj. Dexmedetomidine of 1 μg/kg body weight diluted in 10 ml of normal saline as an infusion over 10 minutes. Patients in group III received normal saline 10 ml. intravenously over 10 minutes using infusion pump.

All the study vital parameters required were recorded at the desired intervals. After finishing the infusion patients were premedicated with Inj. Glycopyrrolate 0.2 mg IV, Inj. Ondansetron 4 mg IV, Inj. Pentazocine 0.25 mg/Kg IV. Then patients were preoxygenated with 100% oxygen for 3 minutes. General anaesthesia was induced with Inj. Propofol 2 -2.5 mg/kg body weight in gradual increments till loss of eye lash reflex which was the criteria for end of induction. For neuromuscular blockade Inj. Vecuronium 0.1 mg/kg body weight IV was given. Patients were ventilated with 60% nitrous oxide and 40% oxygen. with1% sevoflurane with face mask for 3 minutes and then with 100% oxygen with 1% Sevoflurane for 1 minute with rate of 10-12 breaths per minute. Then laryngoscopy was performed by using Macintosh blade and intubation was performed with appropriate sized disposable, low pressure high volume endotracheal tube. Anaesthesia was maintained using 60% nitrous oxide, 40% oxygen and 1% Sevoflurane with positive pressure ventilation with tidal volume of 8-10 ml/kg and rate of 10-12 breath per min. No surgical stimulus was applied during 10 minutes of the study period. At the end of the surgery the residual neuromuscular blockade was reversed with Inj. Glycopyrrolate 0.01 mg/kg IV and Inj. Neostigmine 0.05 mg/kg IV. Patients were extubated when awake and breathing adequately and were shifted to the recovery room.

Monitoring

The following cardiovascular parameters were recorded in all patients.

- Heart rate (HR) in beats per minute
- Systolic blood pressure (SBP) in mm of Hg
- Diastolic blood pressure (DBP) in mm of Hg
- Mean arterial pressure (MAP) in mm of Hg
- SPO2

The above cardiovascular parameters were monitored in the following time interval,

T0: Baseline: 5 min of settling patient in OT

T1: at 5 minutes of infusion of study drug

T2: 1 minute after end of study drug infusion

T3: 1 minute after induction with Inj. Propofol

T4: 1 minute after laryngoscopy & intubation

T5: 3 minutes after laryngoscopy & intubation

T6: 5 minutes after laryngoscopy & intubation

T7: 10 minutes after laryngoscopy & intubation

Adverse effects like bradycardia, hypotension, excessive sedation etc. noted before premedication in all groups. Sedation scoring was done as per Ramsay sedation scale at the end of infusion of study drug.

RAMSAY SEDATION SCALE:

Score	Description	Response
1	Awake	Anxious or restless or both
2	Awake	Cooperative, oriented and tranquil
3	Awake	Responding to commands only
4	Asleep	Brisk response to stimulus
5	Asleep	Sluggish response to stimulus
6	Asleep	No response to stimulus

Statistical Tests

The groups were compared using ANOVA (ANALYSIS OF VARIANCE) in the form of one-way ANOVA test, and repeated measures ANOVA for the parametric interval measures.

Intra –group variables were compared using student t test (paired).

Analysis of Qualitative data was compared using Non –parametric chi-square test.

Results for quantitative data was presented as mean ± 2SD and actual numbers (Percentage).

Results

All the three groups were comparable with respect to age, sex and baseline values of HR, SBP, DBP, MAP.

In control group HR, SBP, DBP and MAP were significantly higher when compared to group I and group II at various time intervals after laryngoscopy and endotracheal intubation.

In group receiving 0.5µg/kg body weight of dexmedetomedine (Group I) there was highly significant attenuation of rise of HR, SBP, DBP and MAP as compared to control group.

In group receiving 1µg/kg body weight of dexmedetomedine (Group II) there was highly significant attenuation of rise of HR, SBP, DBP and MAP as compared to control group. But there was no statistically significant difference between Group I and II with respect to attenuation of rise in HR, SBP, DBP and MAP at 1, 3, 5 and 10 minutes after laryngoscopy and intubation.

Comparing the heart rate at 1 minute after end of study drug infusion there is significant decrease in heart rate in group II compared to group I indicating 1µg/kg body weight having more tendency for bradycardia compared to 0.5µg/kg body weight of Dexmedetomidine.

There were no significant SPO2 changes in groups at studied intervals.

Sedation was more in group II when compared to group I which was statistically significant.

No patient had bradycardia, hypotension or any other side effect.

Table 1: Showing the age distribution

Age in Years	Group I	Group II	Group III
	No. of patients (%)	**No. of patients (%)**	**No. of patients (%)**
18-30	7 (23.33)	8 (26.67)	9 (30)
31-45	11 (36.67)	12 (40)	8 (26.67)
46-60	12 (40)	10 (33.33)	13 (43.33)
Total	30 (100)	30 (100)	30 (100)
Mean age in years ± SD	40.87±11	40.9±12.01	39.83±12.88
p-value	**0.95 (NS)**		

NS – Not significant

Table 2: Showing the sex distribution between three groups

Sex	Group I	Group II	Group III
	No. of patients (%)	No. of patients (%)	No. of patients (%)
Male	15 (50)	15 (50)	17 (56.66)
Female	15 (50)	15 (50)	13 (43.33)
Total	30 (100)	30 (100)	30 (100)
p-value	0.83 (NS)		

NS – Not significant

Table 3: Showing the intergroup comparison of mean heart rate (HR/min) changes between all three groups

	Group I	Group II	Group III	p-value
T_0	79.93±8.2	80.07±5.64	79.8±9.66	0.99 (NS)
T_1	69.8±6.92	68.9±3.99	79.87±8.72	0.00001(HS)
T_2	67.73±6.55	64.23±3.1	79.13±10.22	0.00001(HS)
T_3	75.47±9.26	74.53±7.51	89.57±10.05	0.00001(HS)
T_4	85.07±10.06	84.47±8.63	115.43±13.51	0.00001(HS)
T_5	82±9.21	81.63±8.84	108.3±13.35	0.00001(HS)
T_6	80.2±9.07	77.7±7.81	100.3±11.37	0.00001(HS)
T_7	77.53±7.78	75.97±11.63	91.13±11.19	0.00001(HS)

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

Table 4: Showing the intergroup comparison of Systolic Blood Pressure (mm Hg) changes between all three groups

	Group I	Group II	Group III	p-value
T_0	126.17±8.04	126.03±8.24	126.33±7.62	0.99(NS)
T_1	118±8.14	116.87±8.32	126.43±7.39	0.0001(HS)
T_2	113.17±8.26	112.3±6.7	127.37±7.06	0.00001(HS)
T_3	105.67±10.11	104.77±6.84	120.17±7.31	0.00001(HS)
T_4	131.87±9.87	129.73±10.03	157.87±6.74	0.00001(HS)
T_5	121.07±9.8	120.4±8.57	147.33±7.7	0.00001(HS)
T_6	114.3±8.72	113.93±8.63	138.6±7.45	0.00001(HS)
T_7	111.23±7.33	110.23±7.76	128.23±7.5	0.00001(HS)

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

Table 5: Showing the intergroup comparison of Diastolic Blood Pressure (mm Hg) changes between all three groups

	Group I	Group II	Group III	p-value
T_0	74.93±5.9	75.13±6.1	74.73±5.07	0.99(NS)
T_1	70.73±6.96	69.83±6.24	74.5±4.53	0.01(S)
T_2	68.63±7.1	68.47±6.11	75.03±4.57	0.0007(HS)
T_3	67.93±6.97	66.73±6.02	72.07±5.91	0.00001(HS)
T_4	82.93±7.23	82.17±5.98	97.43±7.37	0.00001(HS)
T_5	77.03±6.48	76.93±7.18	91.1±7.24	0.00001(HS)
T_6	71.33±7.07	71.2±6.4	85.03±8.19	0.00001(HS)
T_7	68.1±5.03	67.83±5.45	79.33±5.82	0.00001(HS)

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

Table 6: Showing the intergroup comparison of Mean Arterial Pressure (mmHg) changes between all three groups

	Group I	Group II	Group III	p-value
T_0	92±6.03	91.47±6.83	91.9±5.28	0.99 (NS)
T_1	86.57±5.85	85.5±5.65	91.87±4.74	0.001(HS)
T_2	83.47±6.25	83.07±5.61	92.47±4.82	0.0001(HS)
T_3	80.43±6.51	79.37±5.25	88.2±5.32	0.00001(HS)
T_4	99.3±6.76	98.03±5.69	117.57±6.06	0.00001(HS)
T_5	91.7±5.97	91.43±5.81	109.87±6.4	0.00001(HS)
T_6	85.7±5.49	85.43±5.72	102.9±7.36	0.00001(HS)
T_7	82.47±3.82	81.9±4.64	95.63±5.36	0.00001 (HS)

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

Table 7: Showing the intergroup comparison of SP02

	Group I	Group II	Group III	p-value
T_0	99.87±0.35	99.9±0.31	99.8±0.41	0.67(NS)
T_1	99.87±0.35	99.87±0.35	99.83±0.38	0.68 (NS)
T_2	99.9±0.31	99.97±0.18	99.83±0.38	0.65(NS)
T_3	100±0	100±0	100±0	
T_4	100±0	100±0	100±0	
T_5	100±0	100±0	100±0	
T_6	100±0	100±0	100±0	
T_7	100±0	100±0	100±0	

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

Table 8: Showing the sedation score between three groups

	Sedation score
Group I	2.23±0.43
Group II	2.47±0.51
Group III	2.03±0.18
p-value	0.0003 (HS)

(p<0.01) – Highly significant (HS)

Table 9: Showing the adverse effects between three groups

	Nil	Bradycardia	Hypotension	Others
Group I	30	0	0	0
Group II	30	0	0	0
Group III	30	0	0	0

Discussion:

Laryngoscopy and endotracheal intubation are considered as the most critical event during administration of general anaesthesia leading to various hemodynamic changes due to mechanical stimulation of larynx and trachea. The augmented cardiovascular reflexes in the form of tachycardia, arrhythmias and hypertension brought about by the noxious stimuli of direct laryngoscopy and intubation can prove detrimental to the patients subjected to anaesthesia, especially for those with cardiovascular and cerebrovascular diseases. Hence, it is very important to blunt this adverse response to prevent serious perioperative complications and safe outcome of the surgery. The severity of hemodynamic response is greater with increasing force and duration of laryngoscopy and intubation (5,6).

Several drugs and techniques have been tried by the anaesthesiologists to attenuate the stress response to laryngoscopy and intubation (8,9). Dexmedetomidine is an alpha-2 adrenergic agonist having sedative, anxiolytic, sympatholytic and analgesic effect which can be used to control hemodynamic response by decreasing catecholamine secretion secondary to laryngoscopy and intubation and maintains adrenergic stability and decreases requirement of anaesthetic agents (3,6,7).

Various studies have used Dexmedetomidine in the dose of 0.3µg/kg to 0.5µg/kg body weight dose but found not very effective in attenuating the hemodynamic response (8,11). Both 0.6µg/kg and 1µg/kg (12) have been found to be effective but 1µg/kg was associated with higher adverse effect such as bradycardia. Hence, in our study these two doses, 0.5µg/kg & 1µg/kg of Dexmedetomidine have been compared to know the effective dose for the purpose with least adverse effects.

The administration of the test drugs over 10 minutes in our study, to prevent bradycardia, is like the studies conducted by Mowafi et al (13), Basar et al (15) and Kunisawa et al (16).

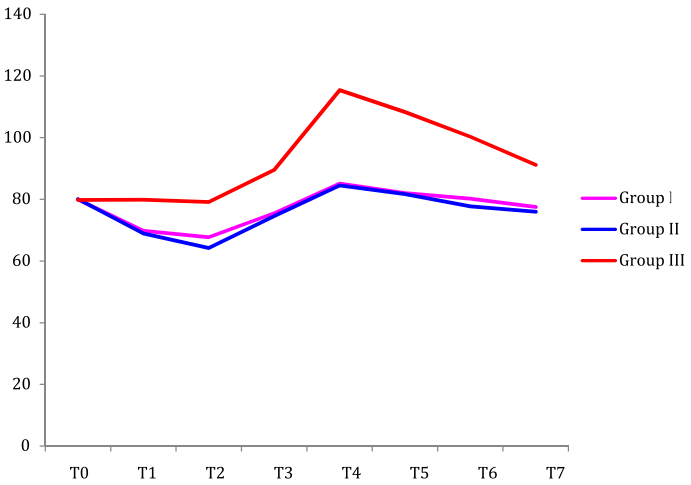
In our study, all the three groups were comparable with respect to age, sex and baseline values of HR, SBP, DBP, MAP and SPO2.

I. Changes in heart rate (HR): (Fig. 1)

At 5 min of infusion of study drug, in group I and II heart rate decreased compared to baseline values significantly. whereas there are no significant changes in group III. At various intervals there is statistically significant rise in HR in group III compared to group I & II.

At 1 minute after end of study drug infusion there is significant decrease in heart rate in group II compared to group I indicating 1µg/kg body weight having more tendency for bradycardia compared to 0.5µg/kg body weight of Dexmedetomidine. Comparing the heart rate at 1 min, 3 min, 5 min and 10 min after laryngoscopy and intubation between group I and group II, there was no statistically significant difference indicating that there was no significant difference between the effectiveness of two doses of Dexmedetomidine, 0.5µg/kg and 1µg/kg body weight intravenous, in attenuating heart rate response to laryngoscopy and endotracheal intubation. Our results are similar to the results obtained by Scheinin et al (10), Jaakola et al (11) and Martina Aho et al (12).

Figure 1: Showing the intergroup comparison of mean heart rate (HR/min) changes in response to laryngoscopy and intubation between three groups



II. Changes in systolic blood pressure (SBP): (Fig. 2)

After administration of Dexmedetomidine, there is statistically significant decrease in systolic blood pressure at 5 min & at 1 minute after end of study drug infusion in group I and in group II, compared to control group III, similar to the results obtained by Aho et al (12) and Ralph Getler et al (9).

In our study, at 1 minute, 3 minutes and 5 minutes after laryngoscopy and intubation, in control group III SBP is increased significantly over the baseline whereas it remained almost similar to baseline at 1 minute and even decreased at 3 and 5 minutes in group I & II. Thus, showing highly significant attenuation of rise in SBP in group I & group II compared to group III but statistically no significant difference between group I and II.

At 10 min after laryngoscopy & intubation in control group III SBP returned to near baseline values where as it is decreased in group I & II showing highly significant difference in group I & II compared to group III which resembles the results from studies done by Scheinin et al (10) and Jaakola et al (11).

Comparing the SBP at 1 min, 3 min, 5 min and 10 min after laryngoscopy and intubation between group I and group II, there was no statistically significant difference indicating that there was no significant difference between the effectiveness of two doses of intravenous Dexmedetomidine in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

Figure 2: Showing the intergroup comparison of Systolic Blood Pressure (mm Hg) changes in response to laryngoscopy and intubation between all three groups

III. Changes in diastolic blood pressure (DBP): (Fig. 3)

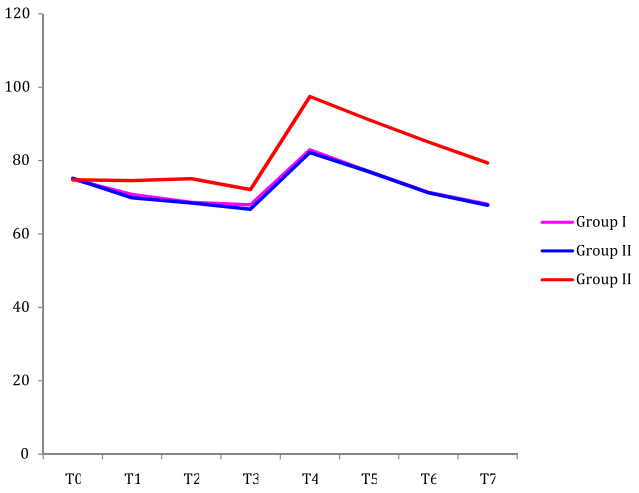
After administration of Dexmedetomidine, there is decrease in diastolic blood pressure at 5 min of infusion & at 1 minute after end of study drug infusion in group I and in group II, which was highly significant and unlike in control group. Similar observations were also found by Aho et al (12) and Kunisawa et al (16).

In our study, at 1 minute & 3 minutes after laryngoscopy and intubation, in control group III DBP was increased significantly compared to baseline value whereas it increased minimally in group I and group II, showing statistically highly significant attenuation of rise in DBP in group I & group II compared to control group. Intergroup comparison between group I & II showed no significant difference.

At 5 & 10 minutes after laryngoscopy and intubation, there is a significant increase in DBP in control group compared to baseline value. On the other hand, in group I and group II, there is significant decrease in DBP compared to group III. Intergroup comparison between group I & II showed no significant difference, like results obtained by Jaakola et al (11) and Kunisawa et al (16).

DBP values were higher at all observed intervals in control group compared to those in Dexmedetomidine treated group II and group III. Comparing the DBP at 1 min, 3 min, 5 min and 10 min after laryngoscopy and intubation between group I and group II, there was no statistically significant difference indicating that there was no significant difference between the effectiveness of two doses of Dexmedetomidine in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

Figure 3: Showing the intergroup comparison of Diastolic Blood Pressure (mm Hg) changes in response to laryngoscopy and intubation between all three groups



IV. Changes in mean arterial pressure (MAP): (Fig. 4)

At 5 minutes of infusion and 1 minute after end of study drug infusion, there is highly significant fall in MAP, in group I and in group II. There was no significant change in MAP in control group. Basar et al (10) and Mowafi et al (13) found results resembling our study.

In our study, at 1 & 3 minute after laryngoscopy and intubation, in control group III, MAP was increased significantly compared to baseline value where as it increased negligibly in group I and group II showing statistically highly significant attenuation of rise in MAP in group I & group II compared to group III. Intergroup comparison between group I & II showed no significant difference.

At 5 & 10 minutes after laryngoscopy and intubation, there is a significant increase in MAP in control group compared to baseline values. But group I and group II, show statistically significant decrease in MAP. Intergroup comparison between group I & II showed no significant difference. These results are comparable with those of Mowafi et al (13) and Basar et al (15).

In control group MAP increase was maximum at 1 minute after laryngoscopy & intubation which gradually declined but persisted even by 10 min. MAP values were higher at all observed intervals in control group compared to those in Dexmedetomidine treated groups. Comparing the MAP at 1 min, 3 min, 5 min and 10 min after laryngoscopy and intubation between group I and group II, there was no statistically significant difference between the effectiveness of two doses of intravenous Dexmedetomidine in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

There were no statistically significant SPO2 changes in group I, II and III at studied intervals.

The sedation score in group I & group II was statistically highly significant when compared to group III. Group II patients were more sedated, when compared to group I which was statistically significant. This is like observations obtained by Aho et al (12) and Yildiz et al (14)

No patient had bradycardia, hypotension, dry mouth or any other side effect

Figure 4: Showing the intergroup comparison of Mean Arterial Pressure (mm Hg) changes in response to laryngoscopy and intubation between all three groups

Conclusion

Intravenous Dexmedetomidine attenuates the haemodynamic response to laryngoscopy and endotracheal intubation and the dose of 0.5µg/kg body weight is safer, cost effective and equally efficacious compared to 1µg/kg body weight. However, the incidence of sedation and tendency for bradycardia is more with 1µg/kg body weight of Dexmedetomidine.

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