Original article:

Study of effectiveness of Dexmedetomidine and Fentanyl in attenuating the pressor responses associated with laryngoscopy and endotracheal intubation

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Abstract:

Introduction: Reid and Bruce in 1940 and King Harris in 1951 described response to laryngeal and tracheal stimulation following Laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation.[1,2]which may be the result of increase in catecholamine levels. Dexmedetomidine**,** highly specific and selective α2 adrenoceptor agonist and Fentany l , stereospecific opioid agonist were compared and observed in attenuating pressor responseto laryngoscopy and intubation..

Aims and objectives : To observe and compare the effectiveness of dexmedetomidine and fentanyl in attenuating the pressor responses associated with laryngoscopy and endotracheal intubation .

Material and methods:

In a Prospective, longitudinal, observational study, 110 patients of physical status ASA I and II, aged 18-60 years undergoing elective surgeries under general anaesthesia were included.

Group D – Dexmedetomidine (0.6 mcg/kg diluted in 5ml saline IV)

Group F – Fentanyl (2 mcg/kg diluted in 5ml saline IV)

Results: Maximum decrease in heart rate,10 mins after administration of study solutions, in both groups was found to be highly significant ($p < 0.0001$),but there was greater degree nof decrease in gr.D. There was maximum decrease in mean systolic, diastolic blood pressure 10 mins after premedication in both groups which was significant ($p<0.05$),but there was greater decrease in gr.D. Decrease in MAP from baseline in D group was statistically significant ($p<0.05$)

Conclusion : Thus from the present study it was concluded that Inj. Dexmedetomidine used in a dose of 0.6mcg/kg, administered over a period of 10 mins is superior to fentanyl in a dose of 2mcg/kg , in attenuating pressor response to laryngoscoopy and endotracheal intubation.

Key words: Dexmedetomidine, Fentanyl, Pressor response ,Laryngoscopy,Intubation

Introduction

Endotracheal intubation, an integral part of the anaesthetic management and critical care of the patient, has been in practice following its description by Rawbotham and Magill in 1921. Reid and Bruce in 1940 and King Harris in 1951 described response to laryngeal and tracheal stimulation following Laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation.[1,2]which may be the result of increase in catecholamine levels. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals,but they are

hazardous to the patients with hypertension, myocardial insufficiency or cerebrovascular diseases. [3] This laryngoscopic reaction in such patients will predispose to pulmonary edema, myocardial infarction and cerebrovascular accident.[4, 5]Pressor response may result in intra-operative myocardial infarction, acute Left ventricular failure, dysrhythmias and intracranial bleed in individuals with end organ decompensation.[6] Pressor response is exaggerated in hypertensive patients even though normotensive pre-operatively by the antihypertensive medication.[7]The pressor response is a reflex phenomenon, mediated by Vagus and Glossopharyngeal cranial nerves. They carry the afferent stimulus from Epiglottis and Infraglottic region and activate the Vasomotor centre to cause a peripheral sympathetic adrenal response. Pharmacological methods are aimed at blocking the peripheral sensory receptors , afferent and efferent pathway, by Lidocaine(4% or 2%) infiltration or topical application.[8, 9]Intratracheal lidocaine is used for attenuation of cardiovascular response.[10] Dexmedetomidine**,**α2 agonists is highly specific and selective α2 adrenoceptor agonist having advantages of sedation, analgesia, anxiolysis and improved haemodynamic stability. Fentanyl act as an agonist at stereospecific opioid receptors at presynaptic and postsynaptic sites in the central nervous system, principally the brainstem and spinal cord and in peripheral tissues outside the central nervous system.

Aims and objectives

- To observe and compare the effectiveness of Dexmedetomidine and Fentanyl in attenuating the pressor responses associated with laryngoscopy and endotracheal intubation .

Material and methods

This prospective longitudinal, observational study was carried out in a tertiary care teaching hospital, over 2 years time after approval from the institutional ethical committee. The Study was conducted on 110 adult patients of American Society of Anaesthesiologists (ASA) grade I or II in the age group of 18-60 years undergoing elective surgeries under General anaesthesia .

Inclusion criteria

- Patients with American Society of Anaesthesiologists (ASA) grade I or II
- Undergoing elective surgeries under general anaesthesia.
- Patients consenting to participate in study.
- Patients in the age group of 18 to 60 years.

Exclusion criteria

- American Society of Anaesthesiologists (ASA) grade III or IV
- uncontrolled diabetes mellitus or hypertension, peripheral neuropathy, hepatic or renal disease, pregnant patients.
- abnormal Bleeding time, clotting time or on anticoagulation therapy, severe anaemia, hypovolemia, shock, septicaemia and history of seizure.
- unstable hemodynamic status.
- Patient not willing to participate in the study.
- difficult airway.

Patients were evaluated by detailed history and examination. The

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written informed valid consent was taken from all the patients participating in the study after explaining the procedure in the local language.

Selected patients were allocated into 2 groups, each containing 55 patients depending upon the drug administered by senior anaesthesiologist:-

Group D – Dexmedetomidine (0.6 mcg/kg diluted in 5ml saline IV)

Group F – Fentanyl (2 mcg/kg diluted in 5ml saline IV)

1. Patients were fasted 6 hrs prior to surgery
2. After securing IV line, all patients were preloaded with crystalloid fluid, 8-10 ml/kg.
3. All patients were pre-medicated with inj. Glycopyrrolate 0.04mg/kg iv and inj.Ondansetron 0.15 mg/kg i.v.
4. On arrival in the operation theatre, multichannel monitors with the facility to measure pulse-oximeter, non-invasive blood pressure (NIBP), ECG, temperature and respiratory gas monitor (RGM) were attached and baseline vital parameters of the patients were recorded.
5. Heart rate, systolic and diastolic blood pressure, mean arterial blood pressure were recorded before pre-medication and 10 minutes after pre-medication in patients.

- Following solutions were prepared by managing anaesthesiologist:

  Group D – Dexmedetomidine (0.6 mcg/kg diluted in 5ml saline IV)

  Group F – Fentanyl (2 mcg/kg diluted in 5ml saline IV)

  - With patient in supine position, the respective study solutions were administered intravenously 10 minutes before laryngoscopy and intubation.
  - After 10 mins of premedication with Dexmedetomidine non invasive blood pressures and heart rate were recorded.
  - After pre-oxygenation for 3 min, patients were induced with inj.thiopentone (4-7 mg/kg) i.v. and inj. Suxamethonium (2mg/kg) i.v. followed by Laryngoscopy and intubation.
  - Variables monitored were heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, SPO2 and ECG.

- All parameters were recorded at following time points:

  T_1: Before premedication

  T_2: 10 minutes after premedication

  T_3: 30 seconds after endotracheal intubation

  T_4: 1 minute after intubation

  T_5: 2 minutes after intubation

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$T_{6:}$ 3 minutes after intubation

T_7: 4 minutes after intubation

T_8: 5 minutes after intubation.

T_9: 6 minutes after intubation.

T_{10}: 7 minutes after intubation.

T_{11}: 8 minutes after intubation.

T_{12}: 9 minutes after intubation.

T_{13}: 10 minutes after intubation.

- All intubations were accomplished within 15 seconds by an expert anaesthesiologist.
- Only one attempt of intubation was accepted in the study.
- Patient who had coughed or bucked during procedure were excluded from study.
- After intubation, patients were maintained with Isoflurane(0.4 % v/v), O2 (50%) ,N2o (50%) and non-depolarizing muscle relaxant Vecuronium 0.1 mg/kg.
- The lung was ventilated to maintain the End Tidal Carbon Dioxide partial pressure within the normal limits.
- Decrease in systolic blood pressure (more than 30% below baseline) was recorded as hypotension and treated with Crystalloids and Phenylephrine , Such cases were excluded from the study.
- Bradycardia [heart rate (HR) <50 beats/min] was treated by I.V. Atropine. Such cases were excluded from the study.
- At the end of surgery, neuromuscular blockade reversed with inj. Glycopyrrolate and Neostigmine.
- Patients were watched for any complication like tachycardia, hypotension, arrhythmias, bronchospasm during intraoperative and post operative period.

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Results

Table 1: Comparison of Mean and Standard Deviation of Heart Rate in Group D and Group F at all time points

TIME POINTS	HEART RATE		MEAN DIFFERENCE	STUDENT'S UNPAIRED 'T' TEST VALUE	P VALUE	SIGNIFICANCE
	GROUP D	GROUP F				
	MEAN + SD	MEAN + SD				
T_1	81.84 ± 9.21	83.53 ± 10.30	1.691	0.908	0.366	NOT SIGNIFICANT
T_2	69.67 ± 8.24	81.58 ± 10.32	11.909	6.69	<0.0001	SIGNIFICANT
T_3	75.80 ± 8.41	94.47 ± 9.87	18.673	10.684	<0.0001	SIGNIFICANT
T_4	77.89 ± 8.96	96.45 ± 10.96	18.564	9.725	<0.0001	SIGNIFICANT
T_5	80.82 ± 8.42	101.44 ± 10.88	20.618	11.114	<0.0001	SIGNIFICANT
T_6	81.98 ± 9.18	100.15 ± 10.79	18.164	9.509	<0.0001	SIGNIFICANT
T_7	77.47 ± 9.32	97.75 ± 10.26	20.273	10.848	<0.0001	SIGNIFICANT
T_8	75.91 ± 9.59	95.80 ± 10.62	19.891	10.306	<0.0001	SIGNIFICANT
T_9	74.96 ± 9.56	94.75 ± 10.97	19.782	10.081	<0.0001	SIGNIFICANT
T_{10}	73.05 ± 9.34	93.67 ± 10.40	20.618	10.942	<0.0001	SIGNIFICANT
T_{11}	72.82 ± 9.60	92.78 ± 10.61	19.964	10.346	<0.0001	SIGNIFICANT
T_{12}	71.67 ± 9.63	91.76 ± 10.40	20.091	10.515	<0.0001	SIGNIFICANT
T_{13}	70.98 ± 9.52	90.80 ± 10.54	19.818	10.349	<0.0001	SIGNIFICANT

Graph 1

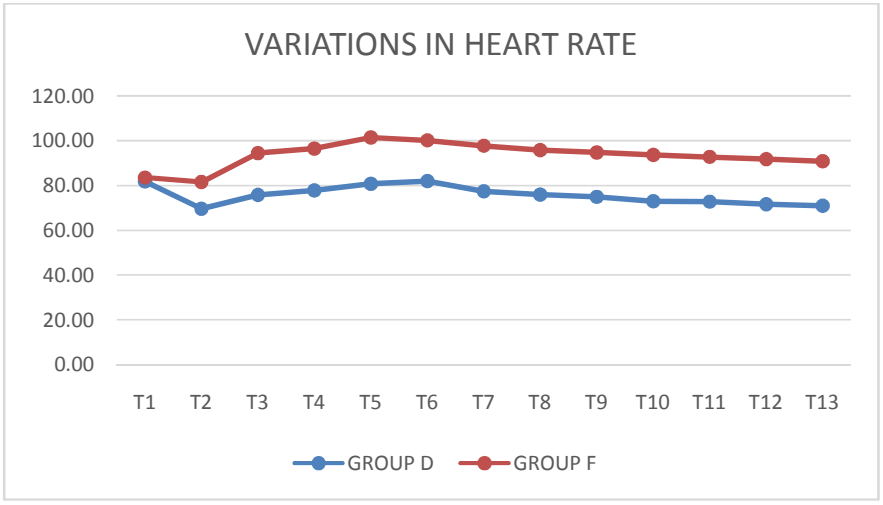

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Table 2: Comparison of Mean and Standard Deviation of Systolic Blood Pressure in Group D and Group F at all time points.

TIME POINTS	SYSTOLIC BLOOD PRESSURE		MEAN DIFFERENCE	STUDENT'S UNPAIRED 't' TEST VALUE	P VALUE	SIGNIFICANCE
	GROUP D	GROUP F				
	MEAN + SD	MEAN + SD				
T1	131.95 ± 8.96	129.60 ± 10.50	2.345	1.260	.210	NOT SIGNIFICANT
T2	110.27 ± 9.60	121.65 ± 10.77	11.382	5.849	<0.0001	SIGNIFICANT
T3	119.35 ± 9.96	128.58 ± 10.86	9.236	4.649	<0.0001	SIGNIFICANT
T4	120.40 ± 9.75	131.60 ± 11.32	11.200	5.558	<0.0001	SIGNIFICANT
T5	124.44 ± 9.49	146.58 ± 11.50	22.145	11.016	<0.0001	SIGNIFICANT
T6	120.09 ±10.05	144.40 ± 12.11	24.309	11.457	<0.0001	SIGNIFICANT
T7	117.27 ± 9.80	141.96 ± 12.20	24.691	11.702	<0.0001	SIGNIFICANT
T8	115.53 ± 9.73	136.82 ± 10.74	21.291	10.899	<0.0001	SIGNIFICANT
T9	114.13 ± 9.66	132.07 ± 10.82	17.945	9.177	<0.0001	SIGNIFICANT
T10	112.24 ± 9.42	126.84 ± 11.04	14.600	7.461	<0.0001	SIGNIFICANT
T11	113.47 ± 9.79	123.84 ± 10.91	10.364	5.243	<0.0001	SIGNIFICANT
T12	108.47 ± 9.45	120.75 ± 10.56	12.273	6.423	<0.0001	SIGNIFICANT
T13	105.02 ± 9.60	117.67 ± 10.83	12.655	6.485	<0.0001	SIGNIFICANT

Graph 2

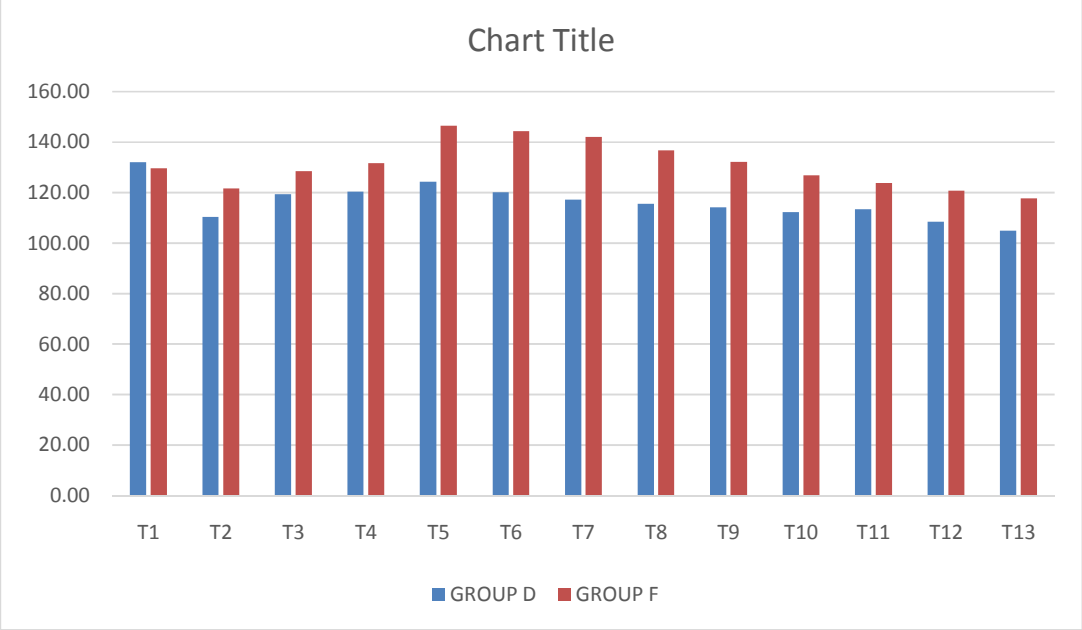

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Table 3: Comparison of Mean and Standard Deviation of Diastolic Blood Pressure in Group D and Group F at all time points.

TIME POINTS	DIASTOLIC BLOOD PRESSURE		MEAN DIFFERENCE	STUDENT'S UNPAIRED 'T' TEST VALUE	P VALUE	SIGNIFICANCE
	GROUP D	GROUP F				
	MEAN + SD	MEAN + SD				
T1	77.82 ± 5.31	76.56 ± 2.73	1.255	1.558	.122	NOT SIGNIFICANT
T2	68.85 ± 5.42	72.55 ± 2.85	3.691	4.470	<0.0001	SIGNIFICANT
T3	72.67 ± 5.69	75.45 ± 3.13	2.782	3.179	.002	SIGNIFICANT
T4	74.75 ± 5.43	78.16 ± 3.07	3.418	4.067	<0.0001	SIGNIFICANT
T5	78.71 ± 5.56	83.55 ± 4.94	4.836	4.823	<0.0001	SIGNIFICANT
T6	75.71 ± 5.69	81.15 ± 3.98	5.436	5.806	<0.0001	SIGNIFICANT
T7	72.89 ± 5.46	81.09 ± 4.74	8.200	8.406	<0.0001	SIGNIFICANT
T8	70.84 ± 5.53	79.16 ± 3.48	8.327	9.456	<0.0001	SIGNIFICANT
T9	69.87 ± 5.55	78.55 ± 3.24	8.673	10.005	<0.0001	SIGNIFICANT
T10	67.73 ± 5.51	77.42 ± 3.19	9.691	11.295	<0.0001	SIGNIFICANT
T11	66.95 ± 5.84	77.62 ± 2.70	10.673	12.301	<0.0001	SIGNIFICANT
T12	65.82 ± 5.62	76.53 ± 2.95	10.709	12.506	<0.0001	SIGNIFICANT
T13	63.64 ± 5.44	76.78 ± 3.07	13.145	15.618	<0.0001	SIGNIFICANT

Graph 3

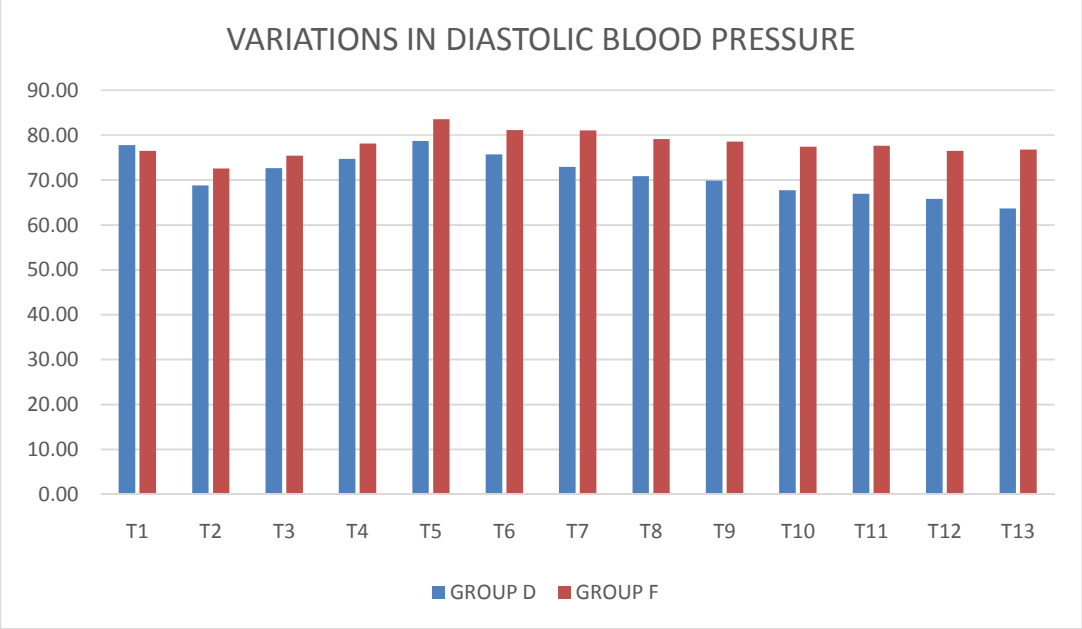

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Table 4: Comparison of Mean and Standard Deviation of Mean Arterial Pressure in Group D and Group F at all time points.

TIME POINTS	MEAN ARTERIAL PRESSURE		MEAN DIFFERENCE	STUDENT'S UNPAIRED 'T' TEST VALUE	P VALUE	SIGNIFICANCE
	GROUP D	GROUP F				
	MEAN + SD	MEAN + SD				
T1	95.87 ± 4.69	94.18 ± 3.82	1.691	2.075	.040	NOT SIGNIFICANT
T2	82.69 ± 4.71	88.91 ± 3.95	6.218	7.510	<0.0001	SIGNIFICANT
T3	88.24 ± 5.02	93.16 ± 4.00	4.927	5.690	<0.0001	SIGNIFICANT
T4	89.96 ± 4.73	96.05 ± 4.02	6.091	7.277	<0.0001	SIGNIFICANT
T5	93.96 ± 5.06	104.58 ±4.85	10.618	11.230	<0.0001	SIGNIFICANT
T6	90.58 ± 4.88	102.27 ±4.96	11.691	12.466	<0.0001	SIGNIFICANT
T7	87.67 ± 4.77	101.36 ±5.45	13.691	14.023	<0.0001	SIGNIFICANT
T8	85.71 ± 4.88	98.42 ± 4.07	12.709	14.832	<0.0001	SIGNIFICANT
T9	84.64 ± 4.94	96.35 ± 4.01	11.709	13.638	<0.0001	SIGNIFICANT
T10	82.56 ± 4.79	93.87 ± 4.05	11.309	13.362	<0.0001	SIGNIFICANT
T11	82.42 ± 5.08	93.00 ± 3.87	10.582	12.291	<0.0001	SIGNIFICANT
T12	80.05 ± 4.58	91.29 ± 4.03	11.236	13.665	<0.0001	SIGNIFICANT
T13	77.44 ± 4.76	90.49 ± 4.11	13.055	15.382	<0.0001	SIGNIFICANT

Discussion:

Laryngoscopy and tracheal intubation are associated with stressful, exaggerated cardiovascular response. Although transient hypertension and tachycardia are usually of little consequence, they may be hazardous, especially in patients with persistent hypertension, limited coronary and myocardial reserve,[5] or cerebrovascular diseases [1,2]. These are by far the most important indications for attenuation of hemodynamic response to laryngoscopy and tracheal intubation [2]. Many methods like the use of inhalational anesthetic agents, lidocaine [5,6], opioids, direct-acting vasodilators [12 13] , calcium-channel blockers [14 15] , and β-blockers [15], have been tried by various authors for blunting hemodynamic responses to laryngoscopy and intubation. However, all such maneuvers were associated with limitations. Blunting of sympathetic response is dose dependent. Fentanyl at 2mcg/kg significantly attenuates, arterial blood pressure and heart rate increase during laryngoscopy and intubation [16]. In the present study dexmedetomidine was given as intravenous infusion 0.6 mcg/kg in 10 ml normal saline over 10 min. Rapid administration of a bolus dose of dexmedetomidine results in an initial transient increase in blood pressure and reflex decrease in heart rate because of peripheral a-2 adrenoceptor stimulation of vascular smooth muscle. Hence in the present study dexmedetomidine was administered over 10 min [17].

The demographic profile of the two groups D and F was comparable and statistically insignificant (p>0.05).

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Hemodynamic changes

Heart rate: There was maximum decrease in heart rate at time point T2, i.e.,10 mins after administration of study solutions, in both groups which was found to be highly significant ($p < 0.0001$), but there was greater degree of decrease in Group D. This decrease reached the base line (time point T1) 3 mins after endotracheal intubation(ETI) in Group D and thereafter the mean heart rate decreased below the baseline till 10 mins after ETI. Whereas in Group F, after the decrease in mean heart rate at time point T2, it increased significantly above the base line till 2 mins after ETI which again approached the base line after 10 mins of ETI.The variation in mean heart rate from baseline at all time intervals was greater in group F as compared to group D.

Although a fall in heart rate was documented in both the groups after administration of study solutions, the percentage of fall from baseline in Group D was 14.86%, which was more significant than that of Group F in which the fall was 2.33 % from baseline. There was an increase in heart rate from the pre-laryngoscopy values in both the groups, immediately after laryngoscopy and intubation, but the increase in Group F was 13.10% which was much higher than the increase of 7.38% in Group D, which was below the baseline value. This difference was statistically highly significant ($p<0.001$). Our observations were also in concordance with those of Sagar Gandhi *et al.* [18] who observed that the heart rate increased after laryngoscopy and intubation in both groups and it started to return to baseline values at the end of 10 min after endotracheal intubation.

*Systolic blood pressure:*There was maximum decrease in mean systolic blood pressure 10 mins after premedication in both groups which was found to be significant ($p<0.05$), but there was a greater degree of decrease in group D .There was increase in SBP immediately after ETI in both the groups but, it did not rise above the baseline in Group D, whereas, in Group F there was a significant rise in mean SBP above baseline after 30 secs of ETI. The percentage increase in SBP from baseline in Group D after ETI was 5.69%, whereas it was 13.10% in Group F, which was statistically highly significant ($p<0.001$). Our observations are comparable with those in study by Sagar Gandhi *et al.*[18] where they concluded that dexmedetomidine produces more significant attenuation of increase in SBP during laryngoscopy and intubation as compared with fentanyl. Vaibhav Jain *et al.* [19] observed that after intubation, dexmedetomidine caused lower increase in SBP as compared to fentanyl, which is in concordance with our study.

*Diastolic blood pressure:*There was decrease in mean values of DBP in both the groups 10 mins after premedication, but the degree of decrease was more in Group D. The percentage decrease from baseline was 11.52% in Group D, whereas it was lesser in Group F with 5.25% decrease from baseline. Immediately after intubation, there was increase in DBP in both the groups, which was statistically highly significant ($p<0.001$) in Group F with an increase of 9.12% from baseline, compared to 1.14% increase in Group D.

Mean Arterial Pressure: There was decrease in MAP from baseline in both groups which was statistically significant ($p<0.05$), but it was more profound in Group D with a decrease of 13.75% from baseline when compared to a decrease of 5.6% in Group F. After intubation, there was a significant rise in MAP in Group F with an increase of 11.04% from baseline, whereas the increase of 1.99% in Group D did not cross the baseline throughout. Our observations were comparable with those of Sagar Gandhi *et al* and Vaibhav Jain *et al.*

Conclusion:

Thus from the present study it was concluded that Inj. Dexmedetomidine used in a dose of 0.6mcg/kg, administered over a period of 10 mins is superior to fentanyl in a dose of 2mcg/kg , in attenuating pressor response to laryngoscoopy and endotracheal intubation.

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