COMPARISON OF DEXMEDETOMIDINE WITH FENTANYL IN ATTENUATION OF PRESSOR RESPONSE TO LARYNGOSCOPY AND INTUBATION

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ABSTRACT

BACKGROUND

Direct laryngoscopy and endotracheal intubation elicits a haemodynamic response associated with increased heart rate and blood pressure.

The aim of the study is to compare the efficacy of intravenous dexmedetomidine and fentanyl in attenuation of stress response to laryngoscopy and intubation.

MATERIALS AND METHODS

Study was carried out on 60 patients belonging to ASA grade I & II, aged 15 to 65 years including either gender scheduled for elective surgical procedures under general anaesthesia in Osmania General Hospital. Patients were randomly divided into two groups of 30 each. Group D received 0.6μg/kg dexmedetomidine and Group F received 2 μg/kg fentanyl diluted in 10 mL normal saline 10 minutes before laryngoscopy and intubation. Anaesthesia was standardised in both groups and vital parameters heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded preoperatively, during intubation and up to 10 minutes after intubation.

RESULTS

The groups were well matched for their demographic data. It was observed that increase in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after intubation was highly significant in fentanyl group as compared to dexmedetomidine. There was a statistically significant difference ($P < 0.05$) between dexmedetomidine and fentanyl groups in heart rate, systolic, diastolic blood pressure and mean arterial pressure at all time points after tracheal intubation.

CONCLUSION

Both the drugs attenuated the pressor response. Among the two drugs administered dexmedetomidine 0.6 μg/kg provides reliable and effective attenuation of pressor response to laryngoscopy and tracheal intubation when compared to fentanyl in a dose of 2 μg/kg.

KEYWORDS

Dexmedetomidine, Fentanyl, General Anaesthesia, Pressor Response.

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BACKGROUND

Cardiovascular responses to laryngoscopy and tracheal intubation include hypertension and tachycardia.[1] It is a sympathetic response which may be the result of increasing catecholamine activity.[2,3,4] This sympathetic response is provoked by stimulation of airway leading to transitory, variable and unpredictable increase in heart rate and blood pressure. In healthy patients these responses are well tolerated but they are hazardous to patients with hypertension, myocardial insufficiency and cerebrovascular disease which may lead to intra operative myocardial infarction, dysrhythmias, acute left ventricular failure and cerebrovascular accidents in these predisposed patients.[5,6,7]

Drugs administered for intravenous induction of anaesthesia cannot adequately suppress the circulatory response evoked by endotracheal intubation.[8] Various pharmacological agents have been used to attenuate the stress response to endotracheal intubation. These include increasing the depth of anaesthesia with volatile anaesthetics,[9] topical and IV lidocaine,[10,11] opioids,[12] beta blockers,[13] calcium channel blockers, and vasodilators like sodium nitroprusside,[14] or nitroglycerine.[15]

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Dexmedetomidine is a highly selective α2 adrenergic agonist with sedative, anxiolytic, analgesic, sympatholytic and antihypertensive effects. Generally, presynaptic activation of α2 adrenergic receptors inhibits the release of norepinephrine. Postsynaptic activation of α2 adrenergic receptors in the central nervous system inhibits sympathetic activity and therefore can decrease blood pressure and heart rate. Dexmedetomidine significantly reduces the release of catecholamines, especially norepinephrine release, there by attenuating the increase in systemic vascular resistance.

Fentanyl is a synthetic opioid agonist, chiefly acts on mu receptors. It has various advantages like cardiovascular stability, no histamine release, rapid onset and short duration of action. It is effective in attenuating the increase in pulse rate and blood pressure following tracheal intubation without any adverse effects in low doses.

MATERIALS AND METHODS

After approval from ethical committee, Osmania General Hospital, Hyderabad, the study was carried out on 60 patients belonging to ASA grade I and II, aged 15 to 65 years including either gender, scheduled for elective surgical procedures under general anaesthesia.

Patients who were physically dependent on narcotics, those with a history of bronchial asthma, drug or alcohol abuse, known drug allergy to either clonidine or dexmedetomidine, cerebrovascular, neurologic, respiratory or ischemic heart disease (history of angina, previous myocardial infarction) and renal and hepatic dysfunction were excluded from the study. Patients with hypertension, diabetes mellitus, pheochromocytoma, patients on β-blockers, antidepressants, anxiolytics, anticonvulsant or antipsychotics and with any predicted difficult airway were also excluded from the study. Patients in whom laryngoscopy time exceeded 15 seconds were excluded from analysis. All patients were thoroughly examined and routine investigations were carried out.

The patients were kept fasting overnight after 10:00 p.m. and received Tablet Ranitidine 150 μg orally and Tablet Alprazolam 0.5 μg orally as premedication at night before surgery.

Patients were randomly divided into two groups of 30 each. Group D received 0.6 μg/ kg Dexmedetomidine and Group F received 2 μg/ kg Fentanyl diluted in 10 ml normal saline 10 minutes before laryngoscopy and intubation. The procedure was explained to the patient and written informed consent was taken. IV access was obtained with number 18G IV cannula and all patients were preloaded with crystalloid fluid, 8-10 mL/kg. Routine standard monitors such as pulse oximetry, ECG and noninvasive blood pressure were applied and monitoring started. All patients were premedicated with Inj. Glycopyrrolate 0.004 μg/ kg IV and Inj. Ondansetron 0.08 μg/ kg IV. Heart rate, systolic and diastolic blood pressure and mean arterial pressure was recorded before pre-medication and 10 minutes after pre-medication in all patients. Then group D patients received dexmedetomidine 0.6 μg/ kg diluted in 10 ml saline and group F patients received fentanyl 2 μg/ kg diluted in 10 ml saline intravenously, 10 mins. before laryngoscopy and intubation. Patients were preoxygenated with 100% oxygen for 10 minutes and induced with intravenous thiopentone sodium 5 μg/ kg and muscle relaxation was facilitated with suxamethonium 2 μg/ kg. The patient's lungs were ventilated manually with 100% oxygen. Laryngoscopy was attempted 90 secs after administration of succinylcholine and trachea was intubated with appropriate size cuffed disposable endotracheal tube. The parameters heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were recorded during laryngoscopy and intubation, 1, 4, 7 and 10 minutes after intubation. After intubation, patients were maintained with sevoflurane (0.8% v/v), O_2 (33%), N_2O (66%) and non-depolarising muscle relaxant (vecuronium) with bolus IV dose of 0.08 μg/ kg followed by intermittent dose of 0.02 μg/ kg was used for muscle relaxation. At the end of surgery, patients were adequately reversed with IV glycopyrrolate 0.008 μg/ kg and IV neostigmine 0.05 μg/ kg.

Statistical analysis was done using tables, charts and bar diagrams. Analysis was done using unpaired t-test for comparing changes in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure keeping $p < 0.05$ as statistically significant.

OBSERVATION AND RESULTS

The demographic data were comparable in both the groups and are given in Table 1.

Baseline heart rate of all patients are comparable to each other and there is no significant difference between them. Increase in heart rate after intubation is highly significant in fentanyl group as compared to dexmedetomidine group at 1 min. (p-value = 0.02), 4 mins. (p-value = 0.018), 7 mins. (p-value = 0.0145), and 10 mins. (p-value = 0.0003) of intubation which is statistically significant (Table 2, graph 1). The baseline systolic blood pressure in two groups was comparable without statistical significance (p = 0.2744). In both fentanyl and dexmedetomidine groups systolic blood pressure increased during intubation and laryngoscopy however the increase in systolic blood pressure is highly significant in fentanyl group when compared to dexmedetomidine group during laryngoscopy and intubation (p-value = 0.006), 1 min. (p-value = 0.05), 4 mins. (0.05), 7 mins. (p-value = 0.01) and 10 mins (p-value=0.0002) after intubation, which is statistically significant (Table 3, Graph 2). In present study, the diastolic blood pressure is increased in fentanyl group when compared to dexmedetomidine group during laryngoscopy and intubation (p–value= 0.002), 1 min (p–value=0.0000001), 4 mins. (p-value=0.04), 7 mins. (p-value=0.04) and 10 minutes (p-value= 0.04198) after intubation which is statistically significant (Table 4, Graph 3). In both fentanyl and dexmedetomidine groups mean

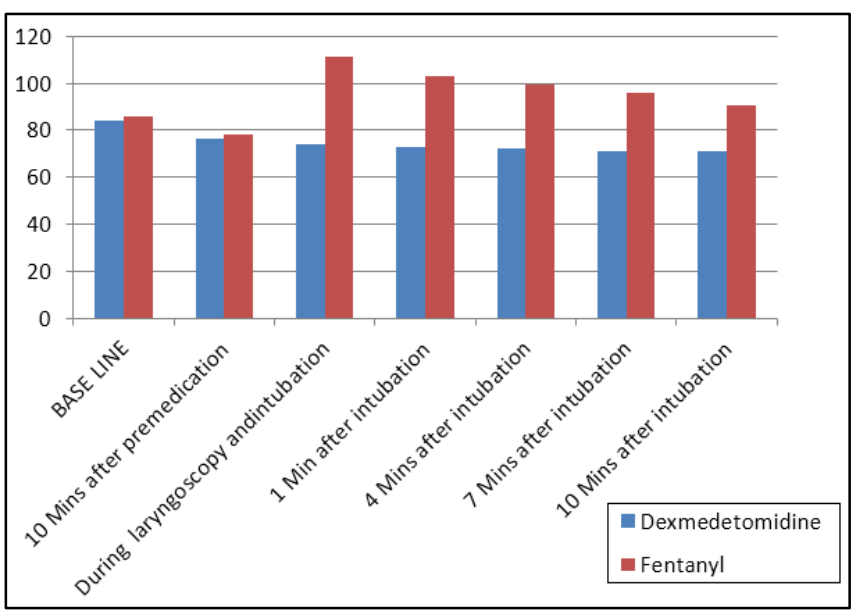
arterial pressure was increased after intubation, however increase in mean arterial pressure was highly significant in fentanyl group when compared to dexmedetomidine group during laryngoscopy and intubation (p-value=0.01), 1 min (p-value=0.02), 4 min (p-value=0.02), 7 (p-value= 0.00008553) and 10 minutes (p-value=0.00008553) of intubation (Table 5, Graph 4).

Demographic Characteristics	Group D	Group F	p-value
Age	37.66 ± 10.68	36.53 ± 10.44	0.75 (>0.05, not significant)
Gender (M/F)	11:19	14:16	0.43 (>0.05)
Weight	56.70 ± 9.86	60.40 ± 12.95	0.10 (>0.05)

Table 1. Demographic Data

Heart Rate in Beats Per Min.					
	Group Dexmedetomidine		Group Fentanyl		
	Mean	± SD	Mean	± SD	P value
Baseline	83.93#	10.04#	85.93#	7.98#	0.22
10 mins. after premedication	76.13*	10.53*	77.9*	5.58*	0.001
During laryngoscopy and intubation	73.73#	9.92#	111.13#	11.25#	0.5
1 min. after intubation	72.63*	9.43*	102.8*	14.66*	0.02
4 mins. after intubation	72.4*	9.33*	99.6*	14.6*	0.018
7 mins. after intubation	71.27*	8.35*	96*	13.3*	0.0145
10 mins. after intubation	70.8*	8.65*	90.8*	17.27*	0.0003

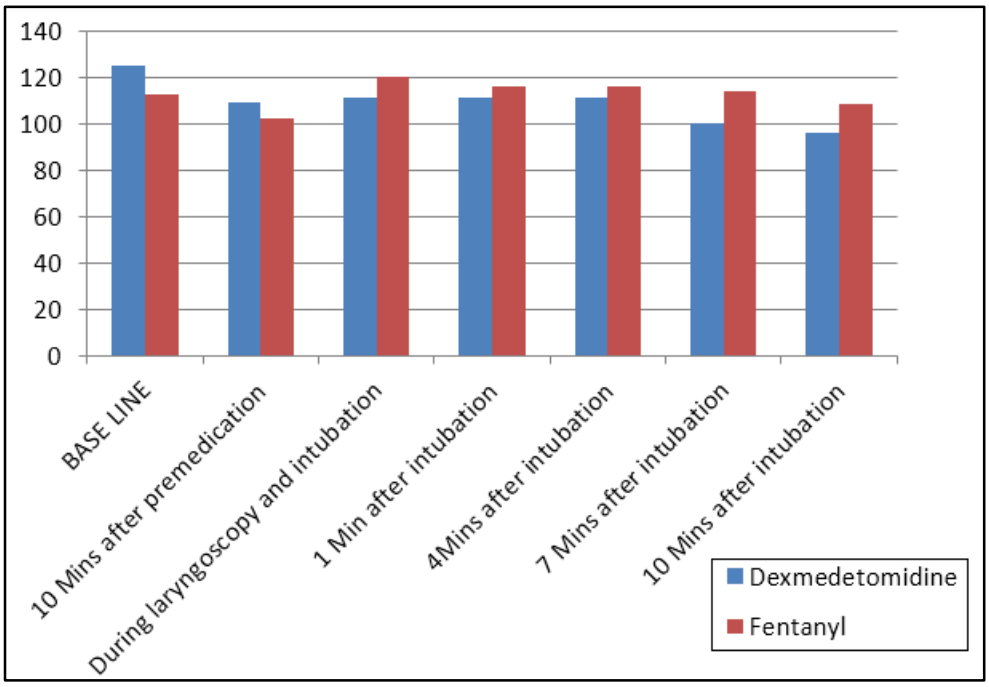
Table 2. Changes in Heart Rate at Various Time Intervals in Both the Study Groups



Graph 1. Comparison of Changes in Heart Rate at Various Time Intervals in Dexmedetomidine and Fentanyl Groups

Systolic Blood Pressure in mmHg					
	Group Dexmedetomidine		Group Fentanyl		
	Mean	± SD	Mean	± SD	P value
Baseline	125#	8.2#	112.45#	10.07#	0.27
10 mins. after premedication	108.8*	8.89*	102.33*	13.58*	0.003189
During laryngoscopy and intubation	111.33*	9.3*	120*	15.72*	0.006
1 min. after intubation	111.33*	9.3*	115.87*	13.48*	0.05
4 mins. after intubation	111.33*	9.3*	115.87*	13.48*	0.05
7 mins. after intubation	99.93*	7.07*	113.8*	11.19*	0.01
10 mins. after intubation	95.8*	5.34*	108.73*	10.88*	0.0002

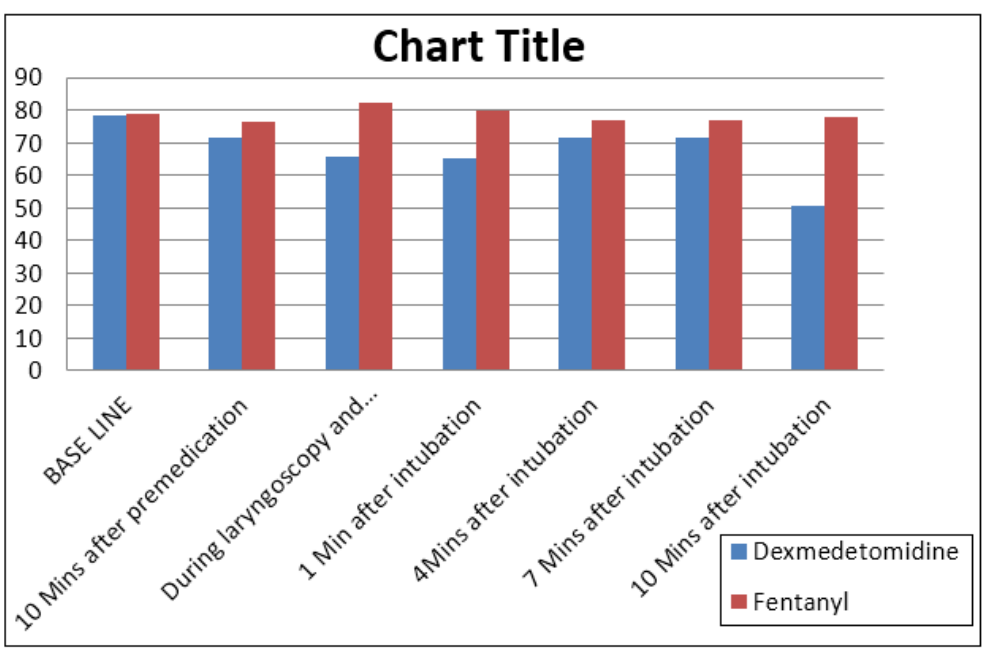
Table 3. Changes in Systolic Blood Pressure At Various Time Intervals in Both the Study Groups



Graph 2. Comparison of Changes in Systolic Blood Pressure at Various Time Intervals in Dexmedetomidine and Fentanyl Groups

Diastolic Blood Pressure in mmHg					
	Group Dexmedetomidine		**Group Fentanyl**		
	Mean	**± SD**	**Mean**	**± SD**	**P value**
Baseline	78.33#	3.79#	78.87#	4.22#	0.565
10 mins. after premedication	71.7*	4.3*	76.20*	6.34*	0.04
During laryngoscopy and intubation	65.7*	4.68*	82.2*	10.79*	0.002
1 min. after intubation	65.3*	3.5*	79.60*	10.48*	0.0000001
4 mins. after intubation	71.7*	4.3*	76.67*	6.34*	0.04
7 mins. after intubation	71.7*	4.3*	76.67*	6.34*	0.04
10 mins. after intubation	50.4*	2.31*	78.0*	4*	0.004198

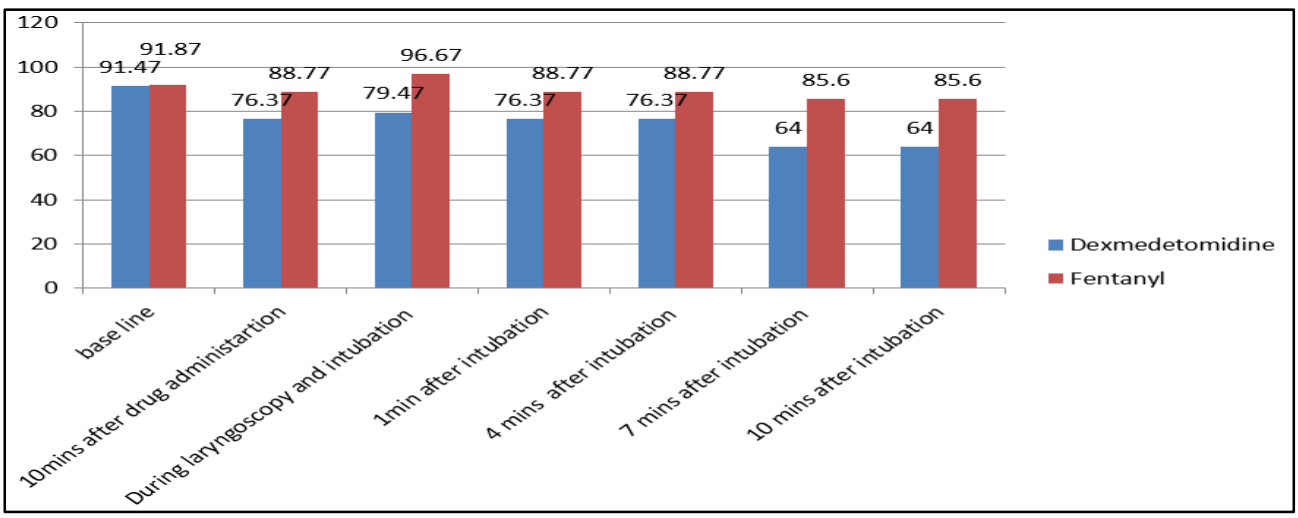
Table 4. Changes in Diastolic Blood Pressure at Various Time Intervals in Both the Study Groups



Graph 3. Comparison of Changes in Diastolic Blood Pressure at Various Time Intervals in Dexmedetomidine and Fentanyl Groups

Mean Arterial Blood Pressure in mmHg					
	Group Dexmedetomidine		Group Fentanyl		
	Mean	± SD	Mean	± SD	P value
Baseline	91.47#	6.93#	91.87#	6.64#	0.8
10 mins. after premedication	76.37*	7.15*	88.77*	10.89*	0.02
During laryngoscopy and intubation	79.47*	7.59*	96.67*	4.8*	0.01
1 min. after intubation	76.37*	7.15*	88.77*	10.89*	0.02
4 mins. after intubation	76.37*	7.15*	88.77*	10.89*	0.02
7 mins. after intubation	64.0*	3.36*	85.60*	7.25*	0.00008553
10 mins. after intubation	64.0*	3.36*	85.60*	7.25*	0.00008553

Table 5. Changes in Mean Arterial Blood Pressure at Various Time Intervals in Both the Study Groups



Graph 4. Comparison of Changes in Mean Arterial Blood Pressure at Various Time Intervals in Dexmedetomidine and Fentanyl Groups

DISCUSSION

Stress response under anaesthesia has been universally recognized phenomenon, which maybe in the form of endocrine or autonomic disturbance. The pressor response to laryngoscopy and endotracheal intubation in form of tachycardia, hypertension and arrhythmias may be potentially dangerous. Complications of pressor responses that follow laryngoscopy include myocardial ischaemia, cardiac failure, intracranial haemorrhage and increase in ICP. This haemodynamic change is due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. These changes are the maximum at 1 minute after intubation and lasts for 5-10 minutes. A wide variety of pharmacological agents were used to attenuate the haemodynamic response. The search for ideal technique or agents for attenuation of haemodynamic changes still continues.

Both dexmedetomidine and fentanyl have ability to control haemodynamic responses, suppress the gag, laryngeal and cough reflexes during laryngoscopy and endotracheal intubation by virtue of their central mechanism of action. Hence, considering all above factors a decision was taken by us to compare IV dexmedetomidine and IV fentanyl.

Dr Ramesh Kumar Kharwar et al[16] (2014) carried out a study to evaluate the effect of dexmedetomidine and fentanyl for attenuation of haemodynamic responses during laryngoscopy and tracheal intubation. It was observed in this study that after laryngoscopy and intubation, increase in pulse rate and mean arterial blood pressure was more in fentanyl group than in dexmedetomidine group.

Dr. Sagar Gandhi et al[17] (2014) compared the effectiveness of dexmedetomidine with fentanyl in attenuating the pressor response associated with laryngoscopy and endotracheal intubation in groups belonging to normotensive. ASA Grade I and II risk surgical patients. The study was carried out on 100 patients belonging to ASA Grade I and II, aged 15 to 65 years; including either gender, scheduled for elective surgical procedures under general anaesthesia. This study proved that dexmedetomidine when used as IV premedicant in dose of 0.6 mcg/kg provides beneficial effect in attenuation of pressor response to laryngoscopy and endotracheal intubation as compared to fentanyl in dose of 2 mcg/kg.

Viabhav Jan et al[18] in 2015 their study compared the efficacy of dexmedetomidine and fentanyl for attenuation of laryngoscopic pressor response. Group-D patients received an injection of dexmedetomidine at a dose of 1

mcg/kg, whereas Group-F received fentanyl at a dose of 2 mcg/kg preoperatively over 10 minutes. before induction of anaesthesia. Intraoperatively heart rate; systolic blood pressure; diastolic blood pressure, mean arterial pressure. SpO_2 and ECG were monitored. According to this study, dexmedetomidine significantly reduced the sympathetic response to laryngoscopy and intubation when compared to fentanyl.

Nidhi D Patel et al[19] (2015) did a prospective randomised double-blinded study to determine whether the fentanyl or dexmedetomidine would decrease the attenuation of haemodynamic response during laryngoscopy and tracheal intubation during general anaesthesia. It was observed that in this study that the increase in systolic blood pressure was highly significant in group-F who received fentanyl 2 mcg/kg as compared to group-D who received dexmedetomidine during laryngoscopy and intubation at 1, 3, 5 and 10 mins. period after intubation (P <0.0001). Similar results were noticed in our study.

Jaakola et al[20] in their study found that a decreased BP and HR response occurs during intubation following the administration of 0.6 mcg/kg bolus of dexmedetomidine preoperatively.

In our study, we found a significant fall in HR after 1 min after intubation with a mean of (73.7) in Group D. (dexmedetomidine) compared to Group F (fentanyl) with a mean of (111.3) and significant fall in MAP after intubation with a mean of (79.47) in Group D (dexmedetomidine) compared to Group F (fentanyl) with a mean of (96.67).

In a study by Lawrence et al[21] found that a single dose of dexmedetomidine before induction of anaesthesia attenuated the haemodynamic response to intubation and extubation.

They used a large dose (2 mcg/kg) of dexmedetomidine; bradycardia was observed on the 1st and 5th minutes after administration. In our study, single of dose 0.6 mcg/ kg preoperative dexmedetomidine given 10 minutes before intubation, maintained haemodynamic stability after intubation, extubation and in the intraoperative period, with incidence of bradycardia only in one subject among 30 patients who received dexmedetomidine.

The study of Kallio et al[22] found that the hypotensive effect of dexmedetomidine reached its maximum (18%) between 60 and 120 minutes after a 75 µg bolus administration. Temporary bradycardia, especially between 0 and 15 minutes after administration of 50 and 75 µg has been noted.

In our study, we observed bradycardia response in one subject in Group D after 1 minute of administration of IV dexmedetomidine. After administration of dexmedetomidine, HR response to intubation was almost completely depressed. Hence, depression of sympathetic response against intubation is an important advantage, especially in high-risk patients.

In a study conducted by Patel et al,[23] it was observed that dexmedetomidine significantly attenuates stress response at intubation with lower increase in heart rate (10%) as compared with fentanyl (17%), this is in contrast with our study in which heart rate decreased in the dexmedetomidine group. Dexmedetomidine significantly attenuates stress response at intubation with lower increase in systolic blood pressure (6%) when compared to fentanyl (23%), which is similar to this study.

R. Saraf et al[24] also found that the dexmedetomidine (0.6 µg/ kg) given 10 mins. before induction effectively attenuates the pressure response to laryngoscopy and intubation without any side effects.

Studies suggest that perioperative use of dexmedetomidine may result in a decreased risk of adverse cardiac events, including myocardial ischaemia.[25] α-adrenoreceptors stimulation can beneficially modulate coronary blood flow during myocardial ischaemia by preventing transmural redistribution of blood flow away from the ischaemic endocardium by specific epicardial vasoconstrictive effects leading to improvement in endocardial perfusion (the reverse steal effect) and by decreasing heart rate. This property along with haemodynamic stability and attenuation of intubation response makes dexmedetomidine an ideal anaesthetic adjuvant, particularly for patients undergoing coronary bypass grafting.

CONCLUSION

Thus it was concluded that both the drugs attenuated the pressor response. Among the two drugs administered, dexmedetomidine 0.6 µg/kg provides reliable and effective attenuation of pressor response to laryngoscopy and intubation when compared to fentanyl in a dose of 2 µg/kg.

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