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Original Research Paper

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COMPARISON OF DEXMEDETOMIDINE VERSUS FENTANYL IN ATTENUATING PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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ABSTRACT

Background and objectives: Laryngoscopy and intubation is associated with a sympathetic response that results in a rapid increase in blood pressure and heart rate. The mechanisms underlying these hemodynamic changes are incompletely understood. They may be caused by a reflex sympathetic discharge due to stimulation of the upper respiratory tract. It has been observed that hemodynamic responses to tracheal intubation are associated with an increase in plasma catecholamine concentrations and are attenuated by β-adrenergic blockade. This study was conducted to compare the efficacy of dexmedetomidine and fentanyl for attenuation of pressor response during laryngoscopy and intubation. **Materials and methods** Following approval by ethical committee, 60 ASA grade I and II patients of either sex undergoing general anaesthesia for elective surgery were included in this study. Patients were randomly divided into two groups of 30 patients each. Dexmedetomidine in a dose of 1μg/kg i.v was given to Group A patients and Fentanyl 2 μg/kg i.v was given to Group B patients. Both the drugs were diluted with normal saline solution to make 10ml and were administered slow intravenous 10 min before induction. The hemodynamic parameters were recorded, demographic data was analyzed using unpaired t-test and hemodynamic variables were analyzed by using unpaired and paired t-test. Side effects were analyzed using chi square test. **Result:** The two groups were comparable in their demographic profiles. Dexmedetomidine proved itself to be an excellent drug when given intravenously in dose of 1μg/kg to attenuate hemodynamic response to laryngoscopy and intubation. It blunted the hemodynamic response to laryngoscopy and intubation to a greater magnitude than fentanyl in a dose of 2μg/kg intravenously as a premedication. **Conclusion:** We conclude that fentanyl 2μg/kg i.v. given ten minutes prior to airway instrumentation shows an inconsistent response to laryngoscopy and intubation. Between the two drugs under study, the use of dexmedetomidine 1μg/kg i.v. is satisfactory and produces a more favorable hemodynamic profile while fentanyl 2μg/kg is found to be non- dependable and less effective for the attenuation of the pressor response to laryngoscopy and endotracheal intubation.

KEYWORDS : Dexmedetomidine, Fentanyl, Hemodynamic response, Laryngoscopy, intubation

INTRODUCTION

Th e circulatory response to laryngeal and tracheal stimulation following laryngoscopy and intubation was documented by Reid and Brace [1] in 1940 and by King *et al*. [2] in 1951. The pressor response, which is part of a huge spectrum of stress responses, results from the increase in sympathetic and sympathoadrenal activity, as evidenced by increased plasma catecholamine concentration in patients undergoing surgery under general anesthesia. To blunt this pressor response, various nonpharmacological and pharmacological agents have been tried.

These include among non-pharmacological methods- smooth swift laryngoscopy and deeper planes of anaesthesia at the time of laryngoscopy. The pharmacological methods are aimed at the efferent, the afferent or both the limbs of responses. One of the most studied drugs to attenuate the hemodynamic response to laryngoscopy and tracheal intubation is fentanyl[3-6]. Fentanyl is a short acting synthetic opioids agonist 75-125 times more potent than morphine. Several trials have tried varying doses from 2μg/Kg- 8 μg/Kg given 1 minute to 10 minutes before intubation[7-8]. High dose however are fraught with the risk of respiratory depression and the need for postoperative elective ventilation, we therefore used the lower dose range.

Dexmedetomidine is another drug which is increasingly being used for the same purpose. It is relatively new alpha 2 agonist approved by FDA (Food and drug association) in 1999. Dexmedetomidine is highly selective, short-acting central alpha 2 agonist. It reduces sympathetic responses to airway instrumentation thereby minimizing changes in blood pressure and heart rate during laryngoscopy and intubation. After a bolus of 1μg/kg, a biphasic response is seen. Activation of alpha 2 receptors by dexmedetomidine leads to dose dependant sedation, anxiolysis, analgesia and decrease in plasma catecholamine concentration. It reduces sympathetic responses to airway instrumentation thereby minimizing changes in BP (Blood pressure) and HR (Heart rate) during laryngoscopy and intubation.

The present study is aimed to determine and compare the efficacy of dexmedetomidine and fentanyl in attenuating hemodynamic response to direct laryngoscopy and endotracheal intubation and to detect any complication or side effect as a result of these drugs.

MATERIALS AND METHODS

Following approval by the Institutional Ethical Clearance Committee and informed consent, this study was conducted on 60 adult patients of either sex. The inclusion criteria consisted of patients of ASA (American Society of Anaesthesiologists) grade I & II of either sex, patients aged between 18 -60 years and patients posted for elective surgery. Exclusion criteria consisted of patient with cardiovascular diseases, asthma, COPD (chronic obstructive pulmonary disease) and Cor pulmonale, patients with history of intake of drugs like alpha – 2 agonist or beta-2 agonist, patients with anticipated difficult intubation, laryngoscopy and intubation time more than 30 seconds and multiple attempts at laryngoscopy and intubation.

Patients were randomly divided into two groups (Group D and Group F) of thirty patients each based on computer generated random number tables. Baseline parameters like – PR (Pulse rate), SBP (Systolic blood pressure), DBP (Diastolic blood pressure) and MAP (mean arterial pressure) were recorded. Anaesthetic technique comprised of a uniform premedication with midazolam 0.03 mg/kg, ondansetron 4.0mg i.v. and tramadol 2.0mg/kg. All other premedicants which had any effect whatsoever on the heart rate, blood pressure or on autonomic nervous systems were strictly excluded from the pre-operative medication schedule. Then patients of Group A received dexmedetomidine 1μg/kg i.v. and patients of Group B

received fentanyl 2 g/kg i.v. ten minutes before induction of anaesthesia. Both drugs were diluted with NSS (Normal saline solution) to make 10ml volume. All drugs were administered 5min prior to transfer of the patient to the operation theatre.

Patients were pre-oxygenated with 100% oxygen for 3 minutes and then induced with thiopentone sodium 4 to 6 mg/kg till the loss of eye lash reflex. This was followed by relaxation which was achieved with inj. vecuronium 0.1mg/kg and 4 minutes after vecuronium administration, laryngoscopy was attempted using standard technique. The laryngoscopy was kept smooth, swift and gentle without multiple attempts. Similarly, intubation was done using an appropriate sized cuffed tube. Patients were subsequently maintained with 60% N_2O (Nitrous oxide) in oxygen. No other pharmacological agents, intravenous or inhalational were administered to the patient during the following 10 minutes. In the same, surgery was allowed to commence only after the collection of the last hemodynamic data at 10 minutes post intubation.

Patients demographic data were analyzed using unpaired t-test and hemodynamic variables were analyzed using unpaired and paired t-test. Side effects were analyzed using chi square test. The difference was considered statistically significant at a p value of <0.05 with 95% confidence interval

RESULTS

It was seen that the age, body weight, and duration of the surgery was comparable in between the two groups.

Table 1: Demographic profile

	Group D	Group B	P value
Age (years)	55.40±9.10	58.40±56	0.53 (NS)
Weight (kg)	71.72±6.17	67.59±7.63	0.57(NS)
Duration of surgery (min)	61.42±7.36	60.55±8.43	0.61(NS)

NS- Non-significant, Group D- Dexmedetomidine group, Group F-Fentanyl group.

The mean age of patients receiving dexmedetomidine was 55.40 years which was comparable to the mean age of patients in fentanyl (58.40 years) group. The weight of patients in dexmedetomidine group was 71.72 kgs which was similar to those of patients who received fentanyl (67.59 kgs). The duration of surgery between the two groups was also comparable, 61.42 minutes in dexmedetomidine group and 60.55 minutes in fentanyl group.

The baseline heart rate between the two groups was similar (Table 2). In group D (dexmedetomidine), the mean baseline HR was 74.75±7.06 beats per minute (bpm) while in the group F (fentanyl) it was 77.21±6.21 bpm.

After administration of the study drug dexmedetomidine or fentanyl it was observed that the mean HR at 5 and 8 minutes after administration of the study drug , decreased in both groups. However, on comparing the two groups there was no significant difference in heart rates in patients receiving dexmedetomidine or fentanyl. However, it was observed that Heart rate, after induction, and after laryngoscopy at 2, 5, 10 and 15 min was lower in the dexmedetomidine group when compared with the fentanyl group.

It was observed from this study that the baseline systolic, diastolic and mean blood pressures between the two groups were similar. After administration of the study drug dexmedetomidine or fentanyl it was observed that the systolic, diastolic and mean blood pressure at 5 and 8 minutes after administration of the study drug decreased in both groups.

However, on comparing the two groups there was no significant difference in systolic, diastolic or mean blood pressures in patients receiving dexmedetomidine or fentanyl. However, it was observed that systolic, diastolic and mean blood pressures after induction, and after laryngoscopy at 2, 5, 10, and 15 min was lower in the dexmedetomidine group when compared with the fentanyl group. (Tables 3, 4 and 5) None of the patients in dexmedetomidine group or fentanyl group developed hypotension or bradycardia during duration of the study.

Table 2: Comparison of mean heart rate at different time intervals in the dexmedetomidine and fentanyl groups

Time	Heart rate (mean+SD) Group D	Heart rate (mean+SD) Group F	P value	Significance
Baseline	74.75±7.06	77.21±6.21	>0.05	NS
After drug				
5 minutes	71.23±6.17	73.35±5.59	>0.05	NS
8 minutes	71.22±6.21	72.31±6.01	>0.05	NS
Before induction	72.75±5.11	70.33 ±7.02	>0.05	NS
After induction	73.81± 6.96	82.81±6.96	<0.05	S
After intubation				
2 minutes	76.15±6.01	84.87±8.10	<0.05	S
5 minutes	77.32±6.32	85.88±7.14	<0.05	S
10 minutes	75.39±6.31	83.12±7.12	<0.05	S
15 minutes	74.17±6.96	82.75±6.96	<0.05	S

NS-Non significant, S- Significant, bpm-beats /minute, Group D- Dexmedetomidine group, Group F-Fentanyl group

Table 3: Comparison of systolic blood pressure at different time intervals in the dexmedetomidine and fentanyl groups

Time	Systolic blood pressure(mean+SD) Group D	Systolic blood pressure(mean+SD) Group F	P value	Significance
Baseline	126.15±6.76	124.63±5.98	>0.05	NS
After drug				
5 minutes	123.65±5.47	125.13±5.48	>0.05	NS
8 minutes	123.59±6.21	124.53±5.78	>0.05	NS
Before induction	121.66±6.27	123.41 ±6.12	>0.05	NS
After induction	119.76± 6.36	120.66±5.88	<0.05	S
After intubation				
2 minutes	123.18±6.93	128.43±7.19	<0.05	S
5 minutes	122.55±6.36	128.54±6.95	<0.05	S
10 minutes	120.45±6.91	126.66±6.86	<0.05	S
15 minutes	121.35±6.17	126.05±6.16	<0.05	S

NS-Non significant, S- Significant, Group D Dexmedetomidine group, Group F-Fentanyl group

Table 4: Comparison of diastolic blood pressure at different time intervals in the dexmedetomidine and fentanyl groups.

Time	diastolic blood pressure (mean+SD) Group D	diastolic blood pressure (mean+SD) Group F	P value	Significance
Baseline	79.21±7.17	79.16±6.88	>0.05	NS
After drug				
5 minutes	76.15±5.07	77.25±6.39	>0.05	NS
8 minutes	75.76±7.19	75.71±6.88	>0.05	NS

Before induction	75.98±7.19	76.65 ±6.76	>0.05	NS
After induction	73.69± 7.29	77.39±6.58	<0.05	S
After intubation				
2 minutes	76.31±5.19	82.13±6.21	<0.05	S
5 minutes	76.35±5.45	81.15±5.89	<0.05	S
10 minutes	74.14±6.09	80.66±6.86	<0.05	S
15 minutes	74.35±6.17	79.05±6.16	<0.05	S

NS-Non significant, S- Significant, Group D-Dexmedetomidine group, Group F-Fentanyl group

Table 5: Comparison of mean blood pressure at different time intervals in the dexmedetomidine and fentanyl groups

Time	diastolic blood pressure (mean+SD) Group D	diastolic blood pressure (mean+SD) Group F	P value	Signifi cance
Baseline	71.11±6.97	71.16±6.98	>0.05	NS
After drug				
5 minutes	70.17±5.18	72.44±6.44	>0.05	NS
8 minutes	69.72±6.91	72.71±6.98	>0.05	NS
Before induction	69.18±6.11	71.15 ±6.26	>0.05	NS
After induction	68.20± 6.12	73.19±5.35	<0.05	S
After intubation				
2 minutes	68.13±5.17	73.21±6.19	<0.05	S
5 minutes	68.47±6.14	73.25±6.19	<0.05	S
10 minutes	67.34±6.19	72.97±8.91	<0.05	S
15 minutes	67.45±5.77	72.15±5.76	<0.05	S

NS- Non-significant, S- Significant, Group D-Dexmedetomidine group, Group F-Fentanyl group

DISCUSSION

The sympathomimetic stress response to laryngoscopy and intubation results in an increase in the myocardial oxygen demand and may lead to ischemia and acute heart failure in susceptible individuals. Hypertension and tachycardia during laryngoscopy can occur even in normotensive individuals and is rather surprising that complications have not been met very often probably because of its transient nature. Though numerous drugs have been tried to obtund haemodynamic response, none of them are totally satisfactory.[11,15]

An advantage with dexmedetomidine is its ability to provide a dose dependent sedation allowing it to be useful for cooperative sedation in remote locations. Because of its pharmacological profile, dexmedetomidine can be used as an anaesthetic adjuvant and also for intensive care unit sedation[9]

Various studies have concluded that dexmedetomidine attenuates the stress-induced sympathoadrenal responses to tracheal intubation. These studies used various dosage of dexmedetomidine infusion for this purpose.[12-14]

Fentanyl acts on the opioid receptors, mainly receptors, for its analgesic action. Because of its ability to reduce sympathetic outflow, it brings about haemodynamic stability. Fentanyl is used routinely as part of general anaesthesia in a dose of 2 mcg/kg and this dose is effective for stress attenuation when given five minutes before laryngoscopy [10]. The main aim of this study was to compare the effectiveness of fentanyl and dexmedetomidine for attenuation of the pressor response to laryngoscopy and endotracheal intubation. It was observed that there was no statistically significant difference in heart rate between the two groups until induction of anesthesia (P >0.05). However, after induction and intubation at 2 minutes, 5 minutes, 10 minutes and 15 minutes the decrease in heart rate in the dexmedetomidine group was more (P >0.05) when compared with the fentanyl group. Our results were similar to a study conducted by Patel et al, who also observed that dexmedetomidine significantly attenuates stress response at intubation with lower increase in HR in the dexmedetomidine group when compared to fentanyl group. Similarly, Kharwar et al, observed that there was a marked decrease in pulse rate from baseline in the dexmedetomidine group as compared with the fentanyl group. [16,17] Similarly, dexmedetomidine caused a marked blunting of sympathetic responses post intubation when compared to the fentanyl group. This was similar to the results obtained in our study.

In this study, there was no statistically significant difference in systolic, diastolic and mean blood pressure between the two groups until induction of anesthesia (P >0.05). However, after induction and intubation at 2 minutes, 5 minutes, 10 minutes and 15 minutes the decrease in systolic, diastolic and mean blood pressure in the dexmedetomidine group was more when compared with the fentanyl group (P >0.05). Our results were similar to a study conducted by Patel et al who also observed that dexmedetomidine significantly attenuates stress response at intubation with lower increase in systolic, diastolic and mean blood pressures in the dexmedetomidine group when compared to fentanyl group.[16]

Laha et al., studied the effects of preinduction loading dose of dexmedetomidine 1 mcg/kg on attenuation of sympathoadrenal responses and requirements of anaesthetic agents [18]. They concluded that administration of dexmedetomidine not only attenuates the rise in mean heart rate, systolic blood pressure after intubation at 1, 2, 3 and 5 min but also significantly reduces the requirement of anaesthetic drugs. The dose of dexmedetomidine used and the results were similar to our study.

Gupta et al, observed similar findings to this study [19] . They found that Intravenous fentanyl (2 μg/kg) failed, addition of clonidine to fentanyl was able to partially blunt it, but the addition of dexmedetomidine to fentanyl completely abolished the hemodynamic response to laryngoscopy and intubation.

CONCLUSION

Present study demonstrates that dexmedetomidine is superior to fentanyl for attenuation of hemodynamic response during laryngoscopy and intubation. An intravenous infusion of dexmedetomidine at 1microgram/kg administered before laryngoscopy and endotracheal intubation is effective in blunting the noxious hemodynamic sympathetic response to laryngoscopy and intubation

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