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COMPARISON OF DEXMEDETOMIDINE AND FENTANYL FOR ATTENUATION OF THE HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION

Anaesthesiology

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ABSTRACT

INTRODUCTION: 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 anaesthesia. To blunt this pressor response, various non pharmacological and pharmacological agents have been tried. **MATERIALS AND METHODS:** Sixty patients of ASA I and II were randomly divided into two groups. Group D patients received an injection of dexmedetomidine at a dose of 0.5 µg/kg, whereas group F patients received an injection of fentanyl at a dose of 2 µg/kg preoperatively over 10 min before induction of anaesthesia with thiopentone. Intravenous vecuronium bromide was given after inducing the patient to facilitate endotracheal intubation. After laryngoscopy, anaesthesia was maintained with sevoflurane (2%v/v) + N_2O (50%) + O_2 (50%). Intra operatively, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO_2, and ECG were recorded at the following intervals: at baseline, 5 minutes after the study drug administration, immediately after induction, and after laryngoscopy at (1, 3, 5, 10, 15 minutes). **RESULTS:** Dexmedetomidine significantly attenuated the sympathetic response to laryngoscopy and intubation in terms of heart rate, systolic blood pressure, and diastolic blood pressure compared with fentanyl. The total dose of thiopentone for induction of general anesthesia was significantly less in the dexmedetomidine group as compared with the fentanyl group. Incidence of bradycardia and hypotension was higher in patients of the dexmedetomidine group when compared with the fentanyl group. **CONCLUSION:** An intravenous infusion of dexmedetomidine at 0.5 µg/kg is better than fentanyl at 2 µg/kg when administered 10 min before direct laryngoscopy and endotracheal intubation in attenuation of haemodynamic response to intubation.

KEYWORDS

Dexmedetomidine, Fentanyl, hemodynamic response, laryngoscopy, tracheal intubation

INTRODUCTION

Endotracheal intubation for the purpose of providing anaesthesia was first described by William MacEwan[1] in 1878 when he passed a tube from the mouth into the trachea, using fingers as a guide in the conscious patient. Edgar Rowbotham and Ivan Magill[1] gained wide experience of endotracheal intubation during the first world war and popularized it subsequently. It is the translaryngeal placement of endotracheal tube into the trachea, via the mouth.This technique of direct laryngoscopy and endotracheal intubation is essential in critical care medicine for airway protection and mechanical ventilation and in anaesthesia it provides a definitive airway for delivering anaesthesia and also in avoiding aspiration of gastric contents in anaesthetised patients.

Direct laryngoscopy and endotracheal intubation are always associated with haemodynamic responses like increase in blood pressure and heart rate due to reflex sympathetic discharge caused by stimulation of pharynx, epipharynx, larynx and trachea. The catecholamine release via increase in sympathico-adrenal activity leads to hypertension, tachycardia and arrhythmias. The circulatory response to laryngeal and tracheal stimulation following direct laryngoscopy and endotracheal intubation was documented by Reid and Brace[2] for the first time in 1940 and by King et al[3] in 1951. A study done by Tomori and Widdicombe[4] in 1969 showed that mechanical stimulation of the respiratory tract caused increase in nervous system activity in cervical sympathetic efferent fibers.

Though these changes are well tolerated by healthy individuals, they may be fatal in patients with illness like untreated hypertension, coronary artery disease, intracranial aneurysm, poor myocardial function, open eye injury etc[5]. The laryngoscopic response in such patients may predispose to the development of pulmonary oedema, myocardial insufficiency, left ventricular failure and cerebrovascular accidents[6]. Till recently dexmedetomidine was not available in India though it is being used in other countries since many years. Since it has been currently introduced in India and not many studies have been done in India regarding its usefulness in suppressing intubation response, there is a need to study its effectiveness.

With emphasis on the multidimensional features of α_2 agonist like dexmedetomidine and a very reputed opioid like fentanyl the present study was designed as a cross-sectional, prospective, observational study to compare the efficacy of dexmedetomidine and fentanyl in attenuating the hemodynamic response to direct laryngoscopy and endotracheal intubation and also on the dose sparing effects of induction drugs.

OBJECTIVES:

1. In attenuating the haemodynamic response to direct laryngoscopy and endotracheal intubation.
2. The dose sparing effects on induction drugs.
3. The incidence of side effects with the use of study drugs.

MATERIALS AND METHODS

Study was done in 60 patients of ASA physical status I and II, aged between 20-60 years, posted for surgeries under general anaesthesia. All the patients were randomized and divided into groups such that each group consists of 30 patients (n=30) using 'slips of paper in a box' technique:

Group D received intravenous dexmedetomidine 0.5 µg/kg body weight.

Group F received intravenous fentanyl 2 µg/kg body weight.

INCLUSION CRITERIA:

ASA I and ASA II patients.

Patients with age between 20-60 yrs of either sex.

Patients posted for surgery under general anaesthesia.

EXCLUSION CRITERIA:

Patients with anticipated difficult intubation.

Patients with history of Hypertension, Cerebrovascular disease, Ischemic heart disease,Arrhythmias, Shock, Chronic obstructive pulmonary disease.

Patients requiring laryngoscopy for duration longer than 15 seconds and with multiple attempts.

All patients were assessed as per the routine preanaesthetic check protocol. After taking informed written consent, all patients included were kept nil per oral since midnight.

After the patient was taken inside the operation theatre preoperative baseline vital parameters were recorded. Subsequently, an intravenous

access was established and ringer lactate @ 10 ml/kg was started. All patients were premedicated with injections of glycopyrolate 5 µg/kg body weight and midazolam 0.02 mg/kg body weight intravenously 3 min before induction, and with the study drugs as follows:
Group D received dexmedetomidine at 0.5 µg/kg body weight diluted in 50 ml normal saline.
Group F received fentanyl at 2 µg/kg body weight diluted in 50 ml normal saline.

The study drugs were administered intravenously over 10 min using an infusion pump before induction of anaesthesia. After denitrogenation with 100% O_2, general anaesthesia was induced with intravenous thiopentone sodium 2.5% until loss of eyelash reflex and with intravenous vecuronium bromide 0.1mg/kg body weight was administered to facilitate endotracheal intubation.

All patients were ventilated for 5 min with o_2 & 1%sevoflurane.Thereafter, direct laryngoscopy and endotracheal intubation was performed by an expert anaesthesiologist. Only a single attempt at intubation that could be accomplished within 15 seconds was accepted in the study. After intubation, patients were maintained with sevoflurane (2%) + N_2O (50%) + O_2 (50%) and non depolarizing muscle relaxant injection of vecuronium bromide 0.02mg/kg body weight given intermittently.

Incision was allowed after 15 min of endotracheal intubation. At the end of the surgical procedure, the residual neuromuscular blockade was antagonized and extubation was performed after fulfilling the criteria for 'extubation'.

Intraoperatively following parameters were considered:
Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial blood pressure, SpO_2, Rate pressure product, ECG were recorded at the intervals: At baseline, 5 min after the study drug administration, Immediately after induction of anaesthesia, After direct laryngoscopy (at 1, 3, 5, 10, and 15 min), Patients were observed postoperatively for 24 hours for any complications.

STATISTICALANALYSIS:
Data were entered in MS-Excel and analyzed in SPSS V21. Descriptive statistics were represented with percentages, Mean with SD. Chi-square test, Independent t-test were calculated. P<0.05 was considered as statistically significant.

RESULTS
The mean age of the patients in group-D and group-F was 33.33±10.02 years and 38.57±14.08 years respectively. In a total number of 30 patients the number of males and females in group-D were 10 (33%) and 20 (67%) respectively with male to female ratio of 0.5:1. There were 9 (30%) males and 21 (70%) females in Group-F with male to female ratio of 0.43:1. The mean body weight of the patients in Group-D and Group-F was 61.07±12.08 and 60.27±9.33 respectively. Of all the 30 patients in group-D patients belonging to ASA physical status grade I were 16 and where as in group-F were 15 and patients belonging to grade II were 14 in group-D and 15 in group-F. Out of 30 patients in group-D patients with Mallampatti (MP) grade I and II are 17 and 13 respectively where as in group-F patients with mallampatti grade I and II were 12 and 18 respectively. Both groups were comparable and there was no statistically significant difference with regard to mean age, weight, sex distribution, Mallampatti grading and ASA physical status. The mean dosage of thiopentone required for induction of anaesthesia in group-D and group-F was 141.27 ± 30.67mg (2.31 mg/kg body weight) and 281.73 ± 42.56mg (4.67 mg/kg body weight) respectively. The mean duration of surgery in group-D and group-F was 162±25.33 min and 151±26.14 min respectively. There was a reduction of 2.36 mg/kg body weight in the dose of thiopentone requirement in group-D when compared to group-F which is statistically significant with a *p* value of <0.0001. The duration of surgery compared between group-D and group-F is not statistically significant and the *p* value is 0.101.

Table-1: Comparison of Heart Rate between two groups at various time periods.

Time	N	Group D		Group F		*P*- value
		Mean	SD	Mean	SD	
Base Line	30	98.50	10.16	92.73	13.10	0.062
5 min after drug	30	85.97	14.83	79.93	10.85	0.077
After Induction	30	89.67	18.27	98.17	13.03	**0.042**
After Intubation 1 min	30	89.23	14.71	100.73	12.54	**0.002**
3 min	30	79.17	10.05	91.23	12.78	**<0.0001**
5 min	30	77.57	9.92	86.00	12.48	**0.005**
10 min	30	68.70	9.74	77.97	11.36	**0.001**
15 min	30	65.63	8.15	70.13	10.47	0.068

From table-1: The mean heart rate at baseline & at 5 min after the study drug administration compared between group-D and group-F is not statistically significant. The mean heart rate compared between group-D and group-F immediately after induction and after intubation at 1, 3, 5, 10 min is statistically significant. At 15 min after endotracheal intubation the change in mean heart rate is not statistically significant between group-D and group-F.

Table-2: Comparison of systolic blood pressure between two groups at various time periods.

Time	N	Group D		Group F		*P*- value
		Mean	SD	Mean	SD	
Base line	30	120.90	6.20	120.83	5.83	0.965
5 min after Drug	30	114.77	12.23	118.97	6.02	0.097
After induction	30	112.2	6.84	116.87	6.56	**0.010**
after intubation 1 min	30	120.57	9.84	123.13	5.67	0.221
3 min	30	111.97	10.03	117.23	8.03	**0.028**
5 min	30	104.17	9.43	111.33	8.45	**0.003**
10 min	30	98.10	9.10	105.93	8.46	**0.001**
15 min	30	97.00	8.42	100.00	6.56	0.129

From Table-2: The mean systolic blood pressure at baseline & at 5 min after the study drug administration compared between group-D and group-F is not statistically significant. The mean systolic blood pressure compared between group-D and group-F immediately after induction is statistically significant. The mean systolic blood pressure at 1 min after intubation compared between group-D and group- F is statistically not significant. The mean systolic blood pressure after intubation at 3, 5, 10 min compared between group-D and group- F is statistically significant. At 15 min after endotracheal intubation the change in mean systoilic blood pressure is not statistically significant between group-D and group-F.

Table-3: Comparison of diastolic blood pressure between two groups at various time periods

Time	N	Group D		Group F		*P*- value
		Mean	SD	Mean	SD	
Base line	30	73.43	9.51	70.53	8.59	0.230
5 min after drug	30	63.70	12.27	66.93	8.26	0.236
After induction	30	73.27	8.39	73.53	8.61	0.904
After intubation 1 min	30	82.23	10.38	88.23	7.84	**0.014**
3 min	30	73.63	10.13	79.00	8.10	**0.027**
5 min	30	67.40	9.01	74.43	8.37	**0.002**
10 min	30	60.33	7.27	65.23	9.10	**0.024**
15 min	30	59.87	8.33	65.47	7.94	**0.009**

From table-3: The mean diastolic blood pressure at baseline, at 5 min after the study drug administration & immediately after induction compared between group-D and group- F is not statistically significant. The mean diastolic blood pressure after intubation at 1, 3, 5, 10 and 15 min compared between group-D and group- F is statistically significant.

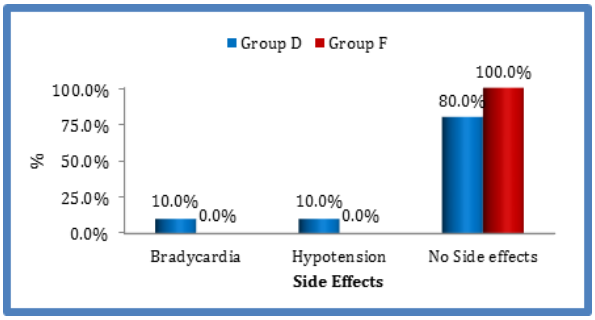
Table-4: Comparison of arterial blood pressure between two groups at various time periods

Time	N	Group D		Group F		*P*- value
		Mean	SD	Mean	SD	
Base line	30	89.26	6.94	87.30	6.48	0.264
5 min after Drug	30	80.72	11.23	84.28	6.10	0.133
After induction	30	86.24	6.65	87.96	6.76	0.327
After intubation 1 min	30	95.01	9.30	99.87	5.89	**0.019**
3 min	30	86.41	9.20	91.74	6.60	**0.012**
5 min	30	79.66	8.31	86.73	6.80	**0.001**
10 min	30	72.92	6.88	78.80	6.73	**0.001**
15 min	30	72.24	7.23	76.98	5.75	**0.007**

From table-4: The mean arterial blood pressure at baseline, at 5 min after the study drug administration & immediately after induction compared between group-D and group- F is not statistically

significant. The mean arterial blood pressure after intubation at 1, 3, 5, 10 and 15 min compared between group-D and group- F is statistically significant.

Graph-1: Side Effects between two groups



From Graph-1: In the dexmedetomidine group, three patients developed hypotension at 5 min after endotracheal intubation and three patients had bradycardia at 5 min after drug administration. Three patients required an injection of atropine 0.6 mg bolus for bradycardia, bolus of intravenous fluid & vasopressor for correction of blood pressure. No side effects were noted in group F

DISCUSSION

According to Madhu Sudhan et al[7] and Shirshendu Mondu et al[8] dexmedetomedine in the dose of 1 µg/kg body weight is effective in attenuating the heart rate and blood pressure response during direct laryngoscopy and endotracheal intubation, but the dose of 1 µg/kg has been found to be associated with increased incidence of adverse effects such as bradycardia and hypotension.

Fentany is a potent analgesic opioid acting on mu receptors can also be used as a sole anaesthetic agent for induction of anaesthesia. Attenuation of sympathetic response by intravenous fentanyl is dose dependent[9]. According to Judd LK et al[10] intravenous fenntanyl at a dose 6 µg/kg completely abolishes laryngoscopic response, but it causes tissue accumulation and thus patients may require mechanical support.

Because of less number of the studies were done comparing the two drugs dexmedetomedine and fentanyl at a dose of 0.5 µg/kg and 2 µg/kg respectively for attenuation of direct laryngoscopy and endotracheal intuabation response, the present study was embarked to compare dexmdetomidine and fentanyl with respect to change in haemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and rate pressure product) from postinduction/prelaryngoscopic values in response to direct laryngoscopy and endotracheal intubation values.

This study Comparing the mean heart rate values of patients between the two groups i.e., group D and group F has no statistically significant difference until the induction of anesthesia (p>0.05). The increase in mean heart rate after the induction of anaesthesia with intravenous thiopentone was lower in group D as compared with group F. Analysis of mean heart rate variation from the baseline to 10 min after induction showed a statistically high significant difference between the two groups (p<0.05). However, the mean heart rate values at 15 min after intubation were comparable to each other, demonstrating no statistically significant difference (p>0.05).

Analysis of preinduction and postinduction values of the mean variations as compared with the baseline values in the two groups showed a statistically significant difference (p<0.05). At 1 min after intubation, mean systolic blood pressure showed no statistically significant difference between the two groups (p >0.05). The mean systolic blood pressure comparison at 2, 5, and 10 min after intubation demonstrated significant differences between the two groups (p<0.05). At 15 min after intubation, the mean systolic blood pressure values were comparable in the two groups (p>0.05). Gandhi et al[11] observed that dexmedetomidine in a dose of 0.6 µg/kg body weight produces more significant attenuation of increase in systolic blood pressure during laryngoscopy and intubation as compared with fentanyl in a dose of 2 µg/kg body weight, which is in concordance with the present study.

This study showed no statistically significant difference of mean diastolic blood pressure between group D and group F in terms of baseline values, after the study drug administration ie., preinduction values and postinduction/prelaryngoscopic values (p>0.05). Postlaryngoscopic comparison of the mean diastolic blood pressure values showed a statistically significant variation in mean diastolic blood pressure values at 1, 2, 5, 10, and 15 min, demonstrating better suppression of the pressor response to intubation. The present study is in concordance with that of Gandhi et al[11] who observed a significant increase in diastoloic blood pressure during laryngoscopy and endotracheal intubation in the fentanyl group compared with the dexmetomedine group (p<0.05).

The present study demonstrated no statistically significant difference of mean arterial blood pressure between group D and group F in terms of baseline values and after the study drug administration ie., preinduction values and postinduction/prelaryngoscopic values (p>0.05). The postlaryngoscopic mean mean arterial blood pressure values showed a statistically significant difference between the two groups, with intravenous dexmedetomidine group at 1, 2, 5, 10, and 15 min demonstrating better suppression of the pressor response to intubation.

The present study is in concordance with that of Kharwar et al[12] and Jain et al[13] who observed hypotension and bradycardia in patients in the dexmedetomidine group, whereas no side effects were observed in the fentanyl group. However, postoperatively patients in both groups had nausea and vomiting, in the study done by kharwar et al[12] which is in contrast with the presrent study also the study done by Jain et al[13].

Limitations of the present study:

Invasive blood pressure monitoring would have provided a better comprehension in recording haemodynamic parameters. This was not performed due to cost constraints.

Including the effect of both the drugs dexmedetomidine and fentanyl on plasma catecholamines response in addition to haemodynamic respone would have provided better information on the pressor response to direct laryngoscopy and endotracheal intubation which was not in the present study.

CONCLUSION

- Dexmedetomidine significantly attenuated the sympathetic response to laryngoscopy and intubation in terms of heart rate, systolic blood pressure, and diastolic blood pressure, compared with fentanyl.
- The mean rate pressure product was below 13,000 in both groups, being significantly lower in group D.
- The total dose of thiopentone for induction of general anesthesia was significantly lower in the dexmedetomidine group compared with the fentanyl group.
- Incidence of bradycardia and hypotension was higher in patients of the dexmedetomidine group compared with the fentanyl group, which was managed easily.

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