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ORIGINAL ARTICLE

DEXMEDETOMIDINE AND FENTANYL FOR ENDOTRACHEAL INTUBATION: A COMPARATIVE STUDY

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ABSTRACT: Severe cardiovascular response in the form of tachycardia and hypertension occur during induction of general anaesthesia and endotracheal intubation. This can cause deleterious effects in hypertensive and other cardiovascular disease patients. Alpha-2 (α-2) agonists are increasingly used as adjuncts in anaesthesia. Nowadays, dexmedetomidine, α-2 adrenoreceptor agonist, is gaining popularity for its sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties without significant respiratory depression. The stable hemodynamic and decreased oxygen consumption due to enhanced sympathoadrenal stability make dexmedetomidine very useful pharmacologic agent. The present study was undertaken to compare the effectiveness of dexmedetomidine and fentanyl in attenuating the response to laryngoscopy and endotracheal intubation during general anaesthesia. We enrolled 100 patients in age range 18-50 years of ASA I-II, and of either sex undergoing elective operation of short duration. Patients were randomly selected and allocated into two Groups. Group D: Received dexmedetomidine 1μg/kg intravenous (IV) bolus and Group F: received fentanyl 1μg/kg IV bolus 10min before induction. All patients were induced with thiopentone sodium and vecuronium. Patients in both the Groups were continuously monitored for heart rate, systolic, diastolic and mean arterial pressure (MAP) and data recorded. After induction and intubation HR, SBP, DBP and MAP were significantly lower in Group D than Group F ($P<0.004$, $P=0.00$, $P<0.04$, $P<0.006$ respectively). The need for thiopentone was decreased by 9% in the dexmedetomidine Group as compared to the fentanyl Group. Post-operative sedation and pain scores were comparably less in Group D than Group F. We conclude, Preoperative infusion of 1μg/kg of both dexmedetomidine and fentanyl are effective in attenuating the sympathetic responses to laryngoscopy and tracheal intubation however, dexmedetomidine blunts this response more effectively than fentanyl. In addition dexmedetomidine has significant anaesthetic sparing effect.

KEYWORDS: α-2 adrenoreceptor, Dexmedetomidine, Fentanyl, Sympathoadrenal response, Intubation.

INTRODUCTION: Severe cardiovascular response in the form of tachycardia and hypertension occur during induction of general anaesthesia and endotracheal intubation. This can cause deleterious effects in hypertensive and other cardiovascular compromised patients. Nowadays, α-2 adrenoreceptor agonists; clonidine and dexmedetomidine are gaining popularity for their sympatholytic, sedative, analgesic, anaesthetic sparing and hemodynamic stabilizing properties.[1,2,3,4,5] Dexmedetomidine, the pharmacologically active d-isomer of medetomidine [1-(2, 3-dimethylphenyl)-ethyl] imidazole is highly specific and selective adrenoreceptor agonist.[6, 7] the α-2: α-1 binding selectivity ratio of dexmedetomidine is 1620:1 as compared to 220:1 of clonidine.

Laryngoscopy and endotracheal intubation results in reflex sympathetic response with the release of catecholeamines. Catecholeamines result in hypertension, tachycardia, arrhythmias, increased intracranial & intraocular pressures.[8,9]

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Various pharmacological agents and techniques have been practiced time to time for attenuating the stress response due to laryngoscopy and intubation, including opioids, benzodiazepins, calcium channel blockers, beta blockers and vasodialators.[10,11,12] Studies have been published regarding the attenuation of haemodynemic response by α-2 adrenoreceptor agonist clonidine.[4] Recently introduced, Dexmedetomidine, α-2 adrenoreceptor agonist, is gaining popularity for its sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties without significant respiratory depression.

It is a highly selective α-2 adrenergic agonist with an affinity of eight times greater than its counterpart clonidine. The stable hemodynamic and decreased oxygen consumption due to enhanced sympathoadrenal stability make dexmedetomidine very useful pharmacologic agent. In this study, we compared the efficacy and safety of dexmeditomidine and fentanyl in attenuating stress response to laryngoscopy and intubation. We evaluated the effect of preoperative dose of dexmedetomidine at a dose of 1μg/kg with fentanyl 1μg/kg on hemodynamic responses to laryngoscopy and endotracheal intubation. In addition, incidence of hypotension and bradycardia was also assessed.

MATERIALS AND METHODS: After approval from the institutional ethical committee, 100 patients in the age Group 18-50 years of either sex belonging to ASA physical status I/II, scheduled for elective surgery of short duration lasting up to 1hour under general anaesthesia were included in this prospective randomized controlled trial. Informed written consent was obtained from each patient.

Patients having compromised hepatic, renal and cardio respiratory disorder, hypertension, and diabetes were excluded from the study. Pregnant and nursing woman and morbidly obese patients were not included in the study. The patients were randomly assigned to one of the two Groups of 50 each using computer generated random numbers into Group D and Group F. Patients were premedicated with tab alprazolam 0.25mg and tab ranitidine 150mg the night before and 1hour before on the morning of surgery with sips of water. In the pre-operative hold up area, peripheral intravenous cannulation was secured. Essential standard monitoring devices connected and baseline parameters were observed and recorded, which included heart rate (HR), mean arterial pressure (MAP), electrocardiogram, respiratory rate and pulse oximetry (SpO2).

All patients were hydrated with 500 ml of ringer's lactate fluid. Thereafter Group F received 1μg/kg of fentanyl whereas, Group D received 1μg/kg of dexmedetomidine over a period of 10min through infusion pump. After 5 minutes of the study drugs infusion hemodynamic variables were recorded again. Induction of anaesthesia was carried out with thiopentone sodium sufficient to abolish eyelash reflex. Vecuronium bromide 0.1mg/kg was administered to facilitate laryngoscopy and tracheal intubation. The trachea was intubated after 3 minutes of mask ventilation. All the intubations were performed by the same anaesthesiologist. Hemodynamic variables were recorded again, immediately before intubation, after intubation and thereafter were observed continuously but recorded at 5min intervals till completion of surgery. During surgery, anaesthesia was maintained with isoflurane and N_2O in O_2 (50:50). The inhalation agent was used in lowest possible concentration so as to maintain blood pressure and heart rate within 20% limits of pre op baseline values.

At the end of the surgery, neuromuscular blockade was antagonised with inj. neostigmine 0.05mg/kg and inj. Glycopyrrolate 0.02mg/kg intravenously. Extubation was carried out as routine procedure. Post-operative sedation score was assessed with Ramsay Sedation Score (1. Anxious, Agitated, 2. Cooperative, Oriented, Tranquil, 3. Responds only to verbal commands,

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4. Asleep with brisk response to light stimulation, 5. Asleep with sluggish response to stimulation, 6. Asleep without response to stimulation).

STATISTICAL ANALYSIS: All recorded values were expressed as mean±standard deviation (SD). Statistical comparisons were performed by analysis of variance (ANOVA), followed by the Student's t test. A probability value <0.05 was regarded as statistically significant, P<0.001 was taken as highly significant, and P>0.05 was regarded as non-significant.

RESULTS: Both the Groups were well matched in patient characteristics with respect to age, gender, mean weight (Table 1) and distribution of surgical procedures (Fig 1 & 2). The mean sleep dose of inj. thiopentone required was 4.5mg/kg in Group D as compared to 4.9mg/kg in Group F. the decrease in dose requirement of thiopentone was approximately 9% (Fig 3) in Group D as compared to Group F (P=0.00) which was significant. The base line heart rate and blood pressure did not differ significantly between the two Groups. There was an increase in heart rate in both the Groups immediately after intubation. This increase was noticed to be more in the Group F than in Group D (Table 2, Fig 4). There was 32% increase in heart rate in Group F as compared to only 25% increase in Group D which was significant (P=0.004). There was an increase in systolic, diastolic and mean blood pressures in both the Groups following intubation (Table 3, 4 & 5). This increase was found to be more in the Group F as compared to Group D (Fig 5, 6 & 7).

There was 21% increase in MAP in Group F as compared to only 13% in Group D which was significant (P=0.006). Post-operative sedation scores were assessed using Ramsay sedation score. 50% of the patients had a sedation score of 2 in Group D (Co-operative, oriented and tranquil) as compared to 20% in Group F (Table 6 & Fig 8).

	Group D	Group F
Age(Years)	30.64±10.25	32.84±10.79
Weight(Kg)	50.12±5.77	53.28±5.93
Sex(M/F)	23/27	26/24

Table 1: Demographic and other data (mean±SD)

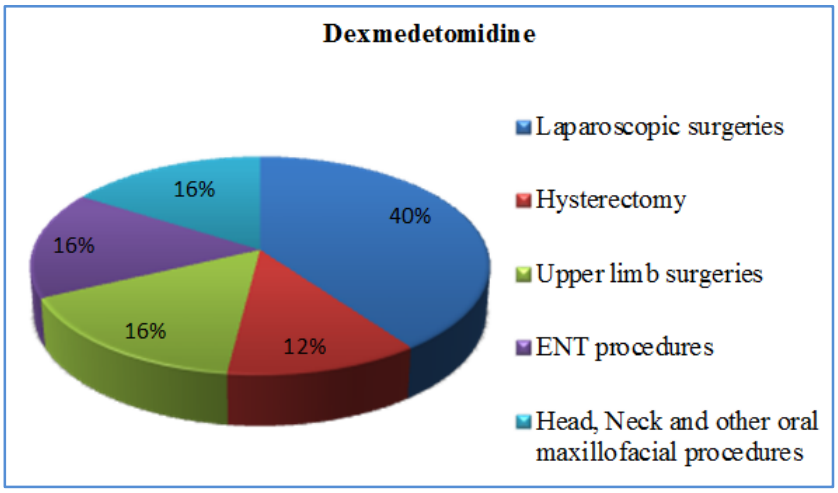

Fig. 1: Distribution of surgical procedures

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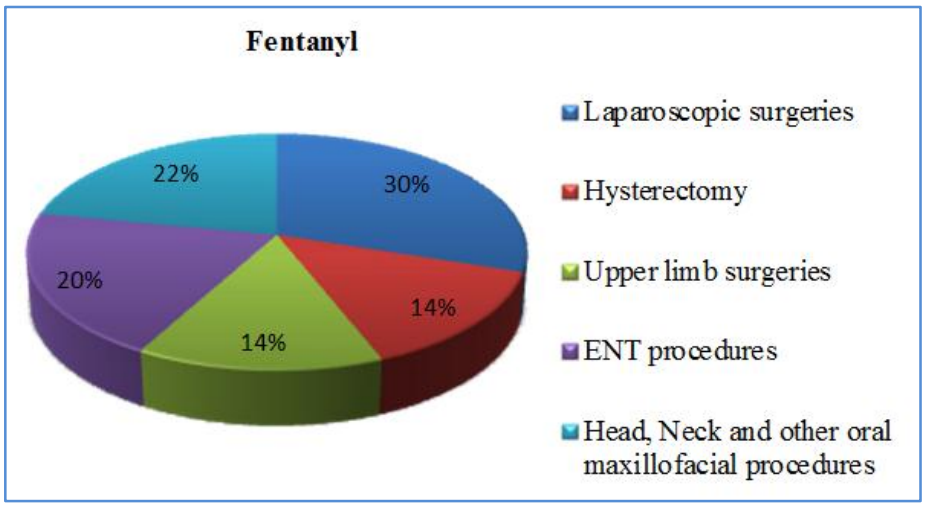

Fig. 2: Distribution of surgical procedures

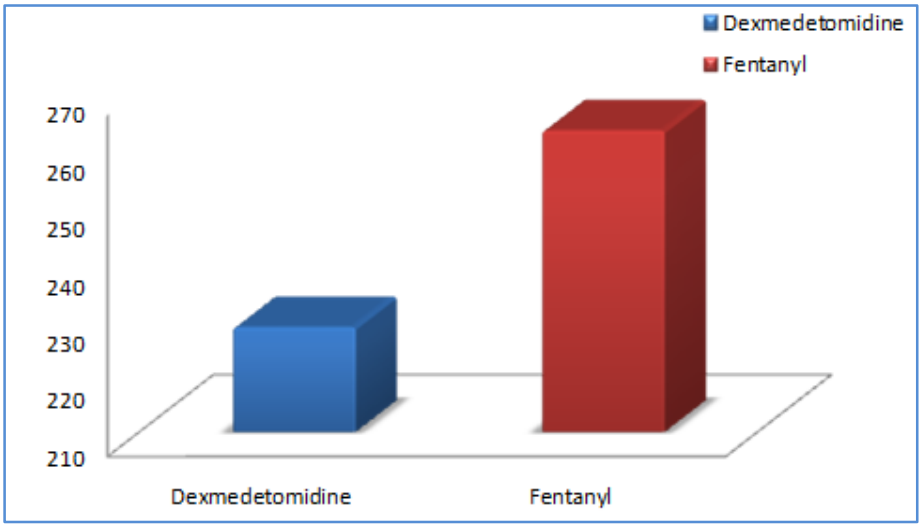

Fig. 3: Comparison of Thiopentone doses between two Groups

The mean dose of inj. thiopentone for induction was 228.4000±33.85805 mg in Group D as compared to 263.0000±24.34866 mg in Group F. The mean sleep dose of inj. thiopentone required was 4.5mg/kg in Group D as compared to 4.9mg/kg in Group F. The decrease in dose requirement was approximately 9% in the dexmedetomidine Group as compared to the fentanyl Group (P=0.00) which was significant.

Groups	No. of Pts.	Mean induction (beats/min)		Std. Deviation		t	Sig.
		Pre	Post	Pre	Post		
Group D	50	75.76	94.44	12.74	11.00	2.956	0.004
Group F	50	76.36	100.96	12.83	11.05		

Table 2: Change in Heart Rate between the two Groups

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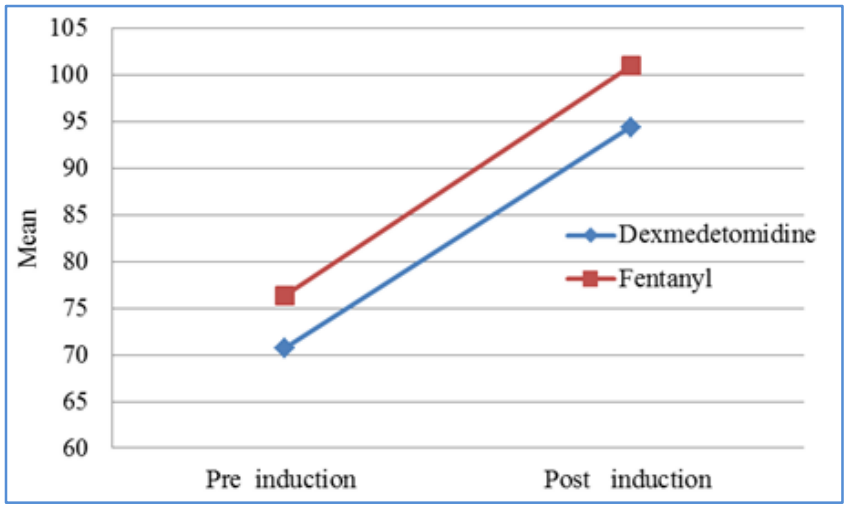

Fig. 4: Change in Heart Rate between the Two Groups

This increase was noticed to be more in the Group F than in Group D. The mean heart rate post intubation was 100.96±11.057 beats/min in Group F as compared to Group D 94.44±11.00 beats/min in Group D. There was 32% increase in heart rate in Group F as compared to only 25% increase in Group D which was significant (P=0.004).

Groups	No. of Pts.	Mean induction (mm hg)		Std. Deviation		t	Sig.
		Pre	Post	Pre	Post		
Group D	50	117.12	132.64	15.03	14.66	3.913	0.000
Group F	50	116.40	144.00	8.51	14.37		

Table 3: Change in Systolic Blood Pressure between the two Groups

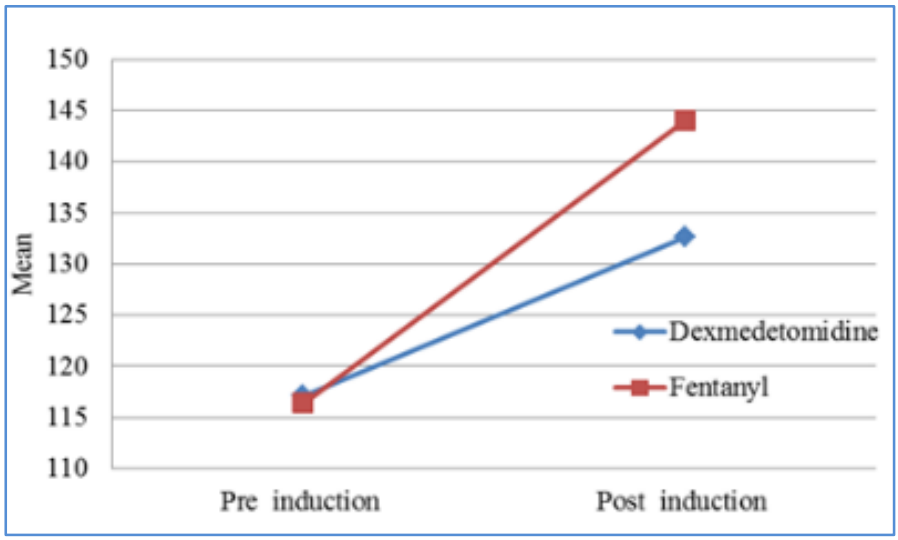

Fig. 5: Change in Systolic Blood Pressure Between the Two Groups

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Groups	No. of Pts.	Mean induction (mmhg)		Std. Deviation		t	Sig.
		Pre	Post	Pre	Post		
Group D	50	75.48	85.40	9.20	9.02	2.195	0.040
Group F	50	74.12	88.56	7.18	7.86		

Table 4: Change in Diastolic Blood Pressure between the two Groups

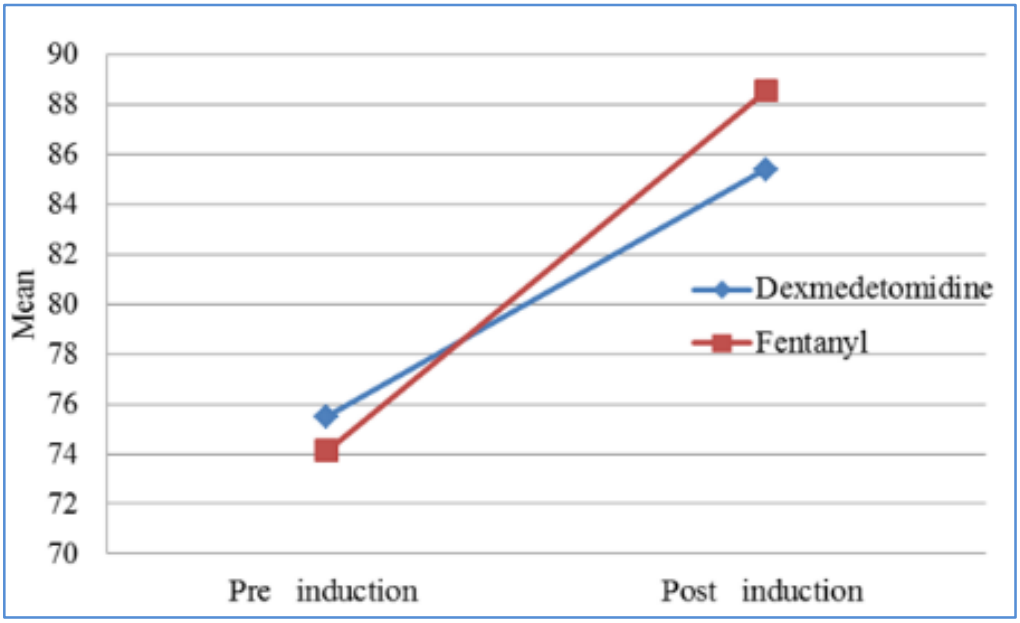

Fig. 6: Change in Diastolic Blood Pressure between the two Groups

Groups	No.of Pts.	Mean induction (mmhg)		Std. Deviation		t	Sig.
		Pre	Post	Pre	Post		
Group D	50	89.38	101.18	10.21	9.62	2.828	0.006
Group F	50	87.88	106.40	7.04	8.81		

Table 5: Change in Mean Arterial Pressure between the two Groups

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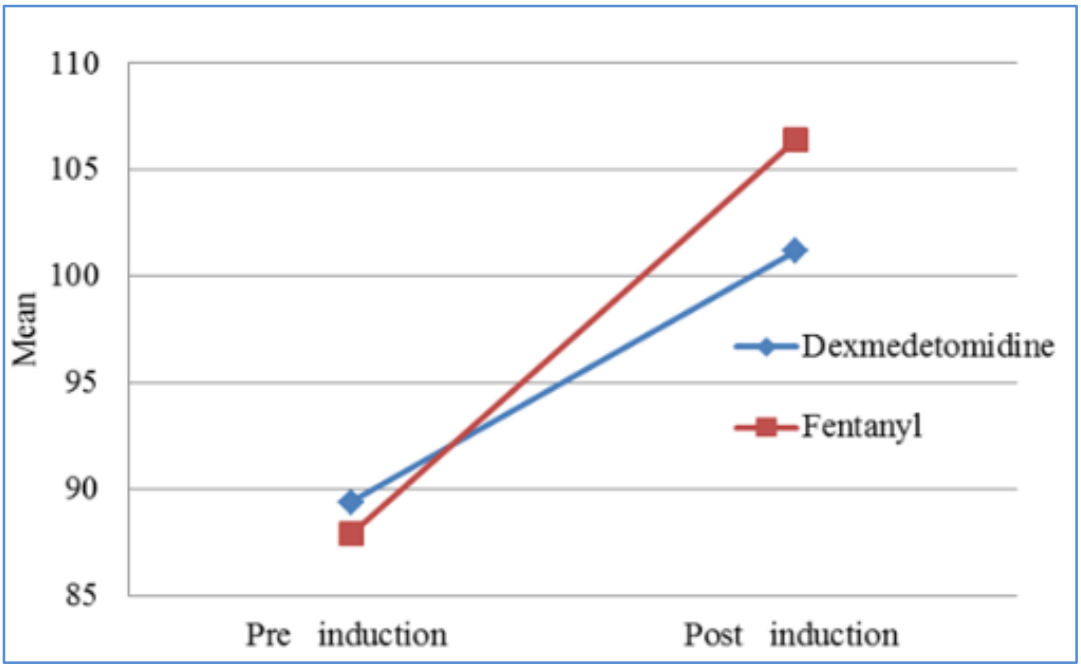

Fig. 7: Change in Mean Arterial Pressure between the two Groups

There was an increase in mean arterial pressure in both the Groups post intubation which was found to be more in the fentanyl Group. The mean MAP post intubation was 106.40±8.81mmhg in Group F as compared to 101.18±9.62mmhg in Group D. There was 21% increase in MAP in Group F as compared to only 13% in Group D which was significant (P=0.006).

The duration of recovery was similar in both the Groups. Post-operative sedation scores were assessed using Modified Ramsay scale and results are given in table 6.

Sedation score	Groups	
	Group D	Group F
1	1(2.0%)	0(0%)
2	25(50.0%)	10(20.0%)
3	24(41.4%)	34(58.6%)
4	0(0%)	6(12.0%)
Total	**50**	**50**

Table 6: Comparison of Sedation Score between the two Groups

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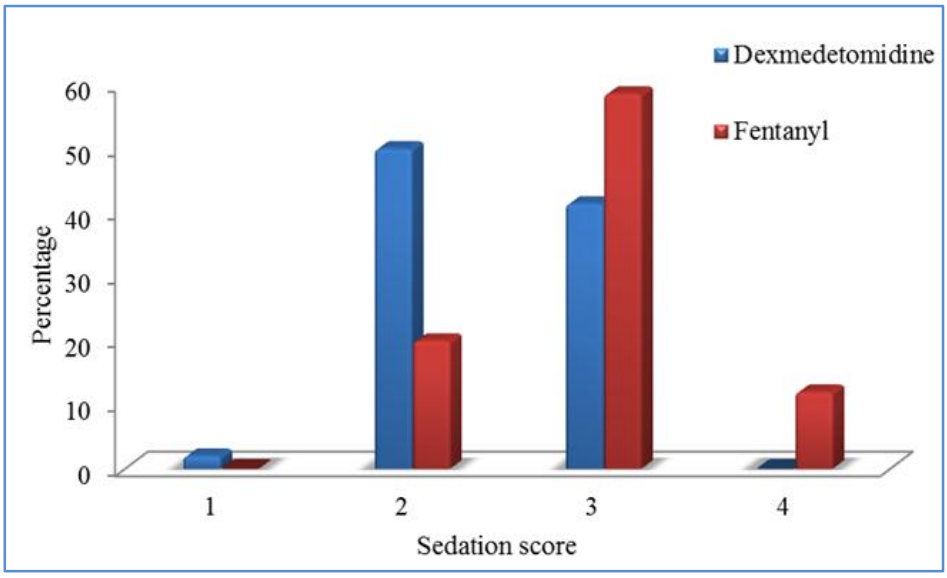

Fig. 8: Comparison of Sedation Score between the two Groups

50% of the patients had a sedation score of 2 in Group D (Co-operative, oriented and tranquil) as compared to 20% in Group F. Only 2% of them were anxious and restless in Group D. 41% of them were drowsy and obeying commands (Score 3) in Group D as compared to 58% in Group F.

DISCUSSION: Laryngoscopy and endotracheal intubation are considered to be the most critical events during general anaesthesia. They trigger a transient, but marked sympathetic response. The resulting hemodynamic pressure response has been a constant problem for anaesthesiologists hence, multiple pharmacological agents have been used to counter act this. Alpha-2 adrenergic drugs, such as clonidine or dexmedetomidine attenuate these potentially harmful events during induction of anaesthesia. In our study, we compared dexmedetomidine, a newer α-2 agonist with opioid, fentanyl for attenuating hemodynamic response to laryngoscopy and tracheal intubation.

Dexmedetomidine has a unique pharmacological profile with sedation, analgesia, sympatholysis, cardiovascular stability and a great advantage to avoid respiratory depression. Dexmedetomidine increases hemodynamic stability by altering the stress induced sympatho adrenal responses to intubation during surgery and during emergence from anaesthesia.[13,14,15]

In the present study, the induction dose of thiopentone was significantly reduced in patient receiving dexmedetomidine which is inconsistent with previous studies.[16,17] demonstrating the anaesthesia potentiating effect of the drug.

According to previous study, tracheal intubation is associated with increases in heart rate, arterial pressure and plasma catecholamine concentrations.[18] Various studies reported the effects of dexmedetomidine on attenuation of stress response to endotracheal intubation.[19,20] In the present study pre-treatment with dexmedetomidine 1µg/kg attenuated, but did not totally obtund the cardiovascular responses to tracheal intubation after induction of anaesthesia. In all the patients, heart rate and mean arterial pressure increased after laryngoscopy and tracheal intubation, and these hemodynamic changes were greater with fentanyl as compared to dexmedetomidine.

In addition to the beneficial property of alpha-2 agonists, authors have reported increase in the risk of hypotension and bradycardia.[21]

These effects have often been noticed in young healthy volunteers on rapid bolus administration of the drug.[21] The present study findings corroborate with those of the previous studies.[22,23,24] Bradycardia, a possible consequence of administration of α-2 agonist, was counteracted by the use of atropine. Post-operative sedation scores were assessed using Ramsay sedation score. Patients in Group D were more sedated compared to their counterpart (Group F), well oriented and cooperative without any significant respiratory depression.

CONCLUSION: Preoperative infusion of 1μg/kg of both dexmedetomidine and fentanyl are effective in attenuating the sympathetic responses to laryngoscopy and tracheal intubation however, dexmedetomidine blunts this response more effectively than fentanyl. In addition dexmedetomidine has significant anaesthetic sparing effect.

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