



COMPARATIVE EVALUATION OF ADMINISTRATION OF DEXMEDETOMIDINE AND FENTANYL FOR STRESS ATTENUATION DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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ABSTRACT **BACKGROUND:** During direct laryngoscopy & endotracheal intubation due to reflex sympathetic discharge haemodynamic changes like hypertension & tachycardia have been reported. These changes are well tolerated by healthy individuals but may be fatal in patients with hypertension, coronary artery diseases and intracranial hypertension. **MATERIALS AND METHODS:** – This randomized prospective double blind study was carried over in sixty patients, divided into two groups. **Group D** received 0.75 microgram/kg of dexmedetomidine in 100ml of normal saline over 10 mins and 5ml of normal saline given 5 mins prior to laryngoscopy and intubation. **Group F** received 100ml of normal saline over 10 mins and 2 microgram/kg of fentanyl in 5ml of normal saline, 5 mins prior to laryngoscopy and intubation. Anaesthesia was standardized in both groups and the baseline, 1 minute, 3 minute, 5 minute and 10 minutes after intubation values of HR, SBP, DBP and MAP were recorded. **RESULTS:** There was a statistically significant fall in SBP, DBP, MAP, HR in dexmedetomidine group in 1, 3, 5, 10 minutes after intubation when comparing with group F and it (p value less than 0.0001) is statistically significant. **CONCLUSION:** Dexmedetomidine in the dosage of 0.75 µg/kg given over ten minutes as an infusion in 100 ml normal saline, 5 minutes before intubation efficiently attenuates the haemodynamic response.

KEYWORDS: Dexmedetomidine, Fentanyl, Attenuation of Hemodynamic Response.

INTRODUCTION:

The hemodynamic response to laryngoscopy and endotracheal intubation have been recognised as early as 1951 by various studies.¹ During induction of anaesthesia, laryngoscopy, tracheal intubation and surgical stimuli evoke cardiovascular responses manifested as alteration in systemic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate and cardiac rhythm.² due to catecholamine release in response to sympathetic stimulation³. The response following laryngoscopy and intubation peaks at about 1 to 2 minutes and return to baseline within 5 to 10 minutes⁴ and causes little consequences in healthy patients. If this response is not suppressed it can be hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease, intracranial pathology and hyperactive airways^{5,6}.

Various systemic and topical agents have been used but they have only limited value in reducing these adverse hemodynamic responses. The commonest drugs used are narcotics, vasodilator agents, β -blockers, calcium channel blockers, lignocaine, α_2 agonists and other sympatholytics. In our study, we have compared dexmedetomidine and fentanyl. Dexmedetomidine is a highly selective α_2 receptor agonist having eight times higher affinity and α_2 selectivity compared to clonidine. α_2 to α_1 selectivity for dexmedetomidine is 1620:1 compared to 220:1 for clonidine. The various benefits of dexmedetomidine are anxiolysis, sedation, analgesia and much better haemodynamic control without any respiratory depression. Because of its short duration of action, it does not interfere much with recovery from anaesthesia¹⁰.

Fentanyl is a potent narcotic with rapid onset and short duration of action and it is routinely used in the context of balanced anaesthesia. Fentanyl given in a dose of 2 mcg/kg over 5 minutes before laryngoscopy and tracheal intubation attenuates the hemodynamic stress response²¹. Fentanyl is a synthetic opioid attenuating the cardiovascular response by its action on opioid receptors and by decreasing sympathetic outflow.

MATERIALS AND METHODS:

This is a randomized prospective double blind study. This was conducted in the Department of Anaesthesiology, Mahatma Gandhi Memorial Government Hospital, K.A.P.V. Government Medical College, Tiruchirappalli in sixty patients of both sex scheduled general anaesthesia. It was conducted after approval from Ethics Committee. The period of study was from

2. Patients with modified Mallampatti scores I & II
3. Men and Women aged between 18 and 60 years undergoing surgery under GA

EXCLUSION CRITERIA:

1. Patients with ASA PS III & IV
2. Patients with modified Mallampatti scores III & IV
3. Patients with Systemic Hypertension, CAD, H/O Cerebrovascular Accidents, CRF, Valvular Heart Diseases, patients on antihypertensives or cardiac drugs
4. Patients posted for emergency surgeries
5. Age <18 and >60 years
6. Hypotension and Bradycardia
7. Allergy to clonidine, dexmedetomidine or fentanyl
8. Patient refusal

METHODOLOGY:

A total of 60 patients were scheduled for the study. After getting basic investigation results, pre-anaesthetic evaluation was done. The study was explained to all the patient and a written informed consent obtained from each patient on the day of surgery. All the patients were pre medicated with tablet ranitidine 150mg, tablet Diazepam 10 mg orally and kept in adequate starvation previous night (6-8 hours) before surgery. The patients were randomly allocated into two groups of 30 with the help of a computer generated table of random numbers to receive following drugs:

Group D: Patients in this group received 0.75 microgram/kg of dexmedetomidine in 100ml of normal saline over 10 mins and 5ml of normal saline given 5 mins prior to laryngoscopy and intubation

Group F: Patients in this group received 100ml of normal saline over 10 mins and 2 microgram/kg of fentanyl in 5ml of normal saline, 5 mins prior to laryngoscopy and intubation. After giving Inj Glycopyrolate 0.2mg IV and midazolam 1mg IV 30 minutes before surgery. Patients shifted to the operating room, an 18-gauge intravenous cannula was inserted in the forearm and infusion of ringer lactate was started. Standard multipara monitor was connected - ECG, NIBP and Pulse oximeter. Group D received 0.75mcg/kg of Inj. Dexmedetomidine in 100 ml of normal saline IV over 10 minutes and 5ml of normal saline 3 minutes before induction. Group F received 100 ml of normal saline over 10 minutes and Inj. Fentanyl 2mcg/kg in 5ml of normal saline 3 minutes before induction. These solutions of 100 ml and 5 ml were prepared by first anaesthesiologist. The second anaesthesiologist, who was not aware of the groups, administered the drug and monitored the patients recording vital parameters before intubation and 1min, 3min, 5 min and 10min after laryngoscopy and

INCLUSION CRITERIA:

1. Patients with ASA PSI & II

endotracheal intubation according to the group to which they were assigned. The laryngoscopy and intubation were performed by the third anaesthesiologist, who has 3 years of experience and was also blinded to the drug given. Patients were preoxygenated with 100% oxygen for 3 minutes. Patients were induced with Inj. Thiopentone 5mg/kg IV followed by Inj. Suxamethonium 1.5 mg IV. Laryngoscopy and intubation was then done and the time taken for the same was noted. Those that took > 15 seconds were excluded from the study. After confirming the position of the endotracheal tube, anaesthesia was maintained for the next 10 minutes with 66% nitrous oxide, 33% oxygen and 1% Sevoflurane. Inj. Vecuronium 0.1mg/kg is given IV bolus. No surgical stimulation was permitted for 10 minutes after intubation. The baseline, 1 minute, 3 minute, 5 minute and 10 minutes after intubation values of circulatory variables such as HR, SBP, DBP and MAP were recorded.

STATISTICAL ANALYSIS: was done by SPSS version 21.0 software and Student t test were applied for the interpretation of results. A P value < 0.05 was considered as statistically significant.

OBSERVATION AND RESULTS: DEMOGRAPHIC DATA

Out of 60 Subjects in the study, 30 subjects (50%) are in the Dexmedetomidine group and 30 subjects (50%) are in the Fentanyl group. Age group between 18 to 60 years was preferred. Thus, there is no significant difference between the two groups as their p=0.272 (p value of significance being < 0.05)

In the group D, the mean height was 157.40 ± 5.76 In the group F, the mean height was 160.13 ± 6.43 (p=0.088)

In the group D, the mean weight was 62.47 ± 6.93 In the group F, the mean weight was 64.83 ± 7.68 (p=0.215)

In the group D, the mean BMI was 25.21 ± 2.52 .In the group F, the mean BMI was 25.16 ± 3.10 . (p=0.94900)

The distribution of ASA Status in the study population was ASA I about 48 pts (80%) and ASA II WAS 12 pts (20%)

HEART RATE

Table 1: Baseline Heart Rate And Post Intubation Heart Rate At 1,3,5 And 10 Minutes In Both Groups

HR (per min)	Group	N	Mean	Std. Deviation	P value
BASELINE	Group D	30	88.53	11.69	0.52
	Group F	30	86.50	12.63	
1 MINUTE	Group D	30	87.97	10.44	<0.0001
	Group F	30	103.23	14.41	
3 MINUTES	Group D	30	82.63	8.86	<0.0001
	Group F	30	98.03	12.98	
5 MINUTES	Group D	30	78.83	7.87	<0.0001
	Group F	30	92.90	13.46	
10 MINUTES	Group D	30	75.17	7.17	<0.0001
	Group F	30	85.10	11.94	

The mean values of baseline heart rate in the groups Dexmedetomidine and Fentanyl were 88.53 and 86.50 respectively and p value 0.52 is statistically non-significant.

The mean heart rate at 1,3,5,10 minutes after intubation in the groups Dexmedetomidine and Fentanyl were (87.97 and 103.23), (82.63 and 98.03), (78.83 and 92.90), (75.17 and 85.10) respectively and p value less than 0.0001 is statistically significant.

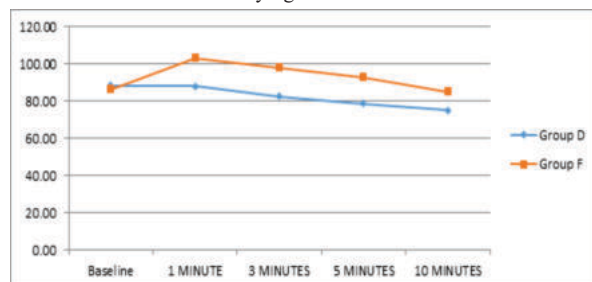


Chart 1: Trend Chart Showing Baseline Heart Rate And Post Intubation Heart Rate At 1,3,5 And 10 Minutes In Both Groups

SYSTOLIC BLOOD PRESSURE (SBP)

Table 2 : Baseline Sbp And Post Intubation Sbp At 1,3,5 And 10 Minutes In Both Groups

SBP (mm Hg)	Group	N	Mean	Std. Deviation	P value
BASELINE	Group D	30	121.23	8.05	0.18
	Group F	30	124.40	9.94	
1 MINUTE	Group D	30	122.10	7.46	<0.0001
	Group F	30	136.80	9.37	
3 MINUTES	Group D	30	116.63	7.18	<0.0001
	Group F	30	130.13	9.57	
5 MINUTES	Group D	30	112.67	8.10	<0.0001
	Group F	30	125.20	9.58	
10 MINUTES	Group D	30	109.93	6.80	<0.0001
	Group F	30	120.07	9.53	

The mean values of baseline SBP in the groups Dexmedetomidine and Fentanyl were 121.23 and 124.40 respectively and p value 0.18 is statistically non-significant.

The mean SBP at 1 minute after intubation in the groups Dexmedetomidine and Fentanyl were 122.10 and 136.80, at 3 minutes 116.63 and 130.13, at 5 minutes 112.67 and 125.20 at 10 minutes, 109.93 and 120.07 respectively and p value less than 0.0001 is statistically significant.

DIASTOLIC BLOOD PRESSURE (DBP)

Table 3: Baseline Dbp And Post Intubation Dbp At 1,3,5 And 10 Minutes In Both Groups

DBP (mm Hg)	Group	N	Mean	Std. Deviation	P value
BASELINE	Group D	30	79.10	6.01	0.755
	Group F	30	79.60	6.33	
1 MINUTE	Group D	30	78.23	5.68	<0.0001
	Group F	30	87.00	5.53	
3 MINUTES	Group D	30	73.83	5.25	<0.0001
	Group F	30	82.77	5.52	
5 MINUTES	Group D	30	72.33	4.48	<0.0001
	Group F	30	80.00	5.81	
10 MINUTES	Group D	30	70.20	4.42	<0.0001
	Group F	30	77.33	5.77	

The mean values of baseline DBP in the groups Dexmedetomidine and Fentanyl were 79.10 and 79.60 respectively and p value 0.755 is statistically non-significant.

The mean DBP at 1 minute after intubation in the groups Dexmedetomidine and Fentanyl were 78.23 and 87.00 respectively and at 3 minutes after intubation 73.83 and 82.77, at 5 minutes 72.33 and 80.00, at 10 minutes, 70.20 and 77.33 respectively. p value less than 0.0001 and it is statistically significant.

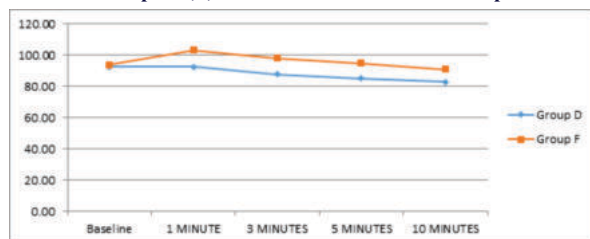
MEAN ARTERIAL PRESSURE (MAP)

Table 4 : Baseline Map And Post Intubation Map At 1,3,5 And 10 Minutes In Both Groups

MAP (mm Hg)	Group	N	Mean	Std. Deviation	P value
BASELINE	Group D	30	92.73	5.98	0.529
	Group F	30	93.80	7.01	
1 MINUTE	Group D	30	92.57	5.80	<0.0001
	Group F	30	103.33	6.29	
3 MINUTES	Group D	30	87.60	5.52	<0.0001
	Group F	30	98.23	6.27	
5 MINUTES	Group D	30	85.27	5.06	<0.0001
	Group F	30	94.70	6.31	
10 MINUTES	Group D	30	82.93	4.61	<0.0001
	Group F	30	91.10	6.40	

The mean values of baseline MAP in the groups Dexmedetomidine and Fentanyl were 92.73 and 93.80 respectively and p value 0.529 is statistically non-significant.

The mean MAP at 1 minute after intubation in the groups Dexmedetomidine and Fentanyl were 92.57 and 103.33 respectively and p value less than 0.0001 is statistically significant. At 3 minutes 87.60 and 98.23, at 5 minutes 85.27 and 94.70, at 10 minutes 82.93 and 91.10 respectively and p value less than 0.0001 is statistically significant.

Chart 2 : Trend Chart Showing Baseline Map And Post Intubation Map At 1,3,5 And 10 Minutes In Both Groups**DISCUSSION :**

In the present study, heart rate was significantly decreased in the dexmedetomidine group when compared to fentanyl group. There was statistically significant reduction in heart rate for up to 10 min after intubation in the dexmedetomidine group. In fentanyl group, heart rate increased following laryngoscopy and endotracheal intubation and returned back to normal only after 3 minutes. The attenuation in systolic, diastolic and mean arterial pressure was significantly better in the dexmedetomidine group than the fentanyl group.

This finding was also observed by Laha et al., and Bloor et al., [7,19,20]. In dexmedetomidine group, systolic and diastolic blood pressure following laryngoscopy and endotracheal intubation, mean systolic and diastolic blood pressure returned to baseline value within 1 minute after intubation, whereas in fentanyl group it was 2 minutes.

Scheinin et al., performed a study on the effect of dexmedetomidine on tracheal intubation and dose of thiopentone and fentanyl needed for the surgery [12]. They observed that dexmedetomidine not only attenuates the haemodynamic responses to intubation but also reduces the doses of thiopentone and fentanyl. The plasma catecholamine concentration was measured in this study and it was found lesser in the dexmedetomidine group during all phases of induction.

Sulaiman et al., studied the efficacy of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off pump coronary artery bypass grafting surgery [13].

Lawrence et al., performed a study with a single dose of 2mcg/kg of dexmedetomidine and observed that it attenuated the haemodynamic response to both intubation and extubation [22]. Jaakola et al. (21), and Saraf et al., studied the effect of dexmedetomidine with a dose of 0.6mcg/kg before induction obtunds stress response in both adult and paediatric patients [23].

Gandhi et al., performed a study comparing dexmedetomidine in a dose of 0.6mcg/kg with fentanyl 2mcg/kg for stress attenuation. They observed that dexmedetomidine was effective in attenuating heart rate and blood pressure for up to 10 minutes after intubation [18]. In our study heart rate control was achieved for 10 minutes, but there was a statistically significant difference in blood pressure control for 1min only.

There were no intra operative complications like bradycardia, hypotension, arrhythmia during the study in any patients. The findings of several studies which used dexmedetomidine in a dose of 0.5mcg/kg to 1mcg/kg is effective in obtunding haemodynamic stress response following laryngoscopy and intubation were comparable to our study. One of the limitation of our study is that we did not measure plasma catecholamine levels which was not feasible in our institute.

CONCLUSION:

We conclude that dexmedetomidine in the dosage of 0.75 µg/kg given over ten minutes as an infusion in 100 ml normal saline, 5 minutes before intubation efficiently attenuating the haemodynamic changes and also proved to keep the haemodynamics in stable manner during laryngoscopy and endotracheal intubation than Fentanyl (2 µg/Kg) which was not fully effective in reducing the increase in heart rate and blood pressure.

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