

A Comparative Study between Dexmedetomidine versus Fentanyl in Attenuation of Haemodynamic Response and Airway Reflex during Emergence from General Anaesthesia

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ABSTRACT

Background and aims: During and after extubation haemodynamic may be tolerated by healthy individuals but may prove to be deleterious in patients with cardiac, pulmonary or cerebrovascular disease. The aim of this study was to compare the effects of dexmedetomidine and fentanyl in attenuation of hemodynamic response and airway reflexes during emergence and extubation after general anaesthesia and to analyse the postoperative sedation.

Materials and Methods: 90 patients of either sex, ASA status I or II, aged 18 to 60 years undergoing surgeries with general anaesthesia were divided into 3 equal groups with 30 patients in each group. Group D (n=30) - was received Dexmedetomidine 0.5 µg/kg body weight in 100ml 0.9% normal saline over a period of 10 minutes. Group F (n=30) - was received Fentanyl 1 µg/kg body weight in 100ml 0.9% normal saline over a period of 10 minutes. Group C (n=30) - was received 100ml 0.9% normal saline over a period of 10 minutes. HR, SBP and DBP, values were recorded as baseline after inhalational agent stopped, just prior to extubation, immediate after extubation and then every 5 minutes for 30 minutes, thereafter every 30 minutes for 1 and half hour were recorded and quality of extubation was analyzed on a five point Extubation quality score based on the patient's comfort and response. Post Operative Sedation was evaluated using Ramsay Sedation Scale.

Result: Patients in the group D had significantly better controlled heart rate and blood pressure as compared to group F and group C. Smoothness in airway reflexes and a better sedation profile led to a superior quality of extubation in group D than with the group F and group C.

Conclusion: From the observation and results of our study it is concluded that I.V. Dexmedetomidine when given in the dose of 0.5 µg/kg over 10 mins prior to extubation effectively attenuates haemodynamic responses, airway reflexes with providing adequate sedation postoperatively thus allowing smoother extubation when compared to Fentanyl 1.0 µg/kg and control.

Keywords: Haemodynamic Response, Airway Reflex, Fentanyl, Dexmedetomidine.

INTRODUCTION

Extubation is one of the most uncomfortable state during general anaesthesia with the complications occurring during and after extubation being three times more common than that occurring during intubation and induction of anaesthesia.^[1] It is almost

always associated with hemodynamic changes and can stimulate airway reflexes by laryngeal and tracheal irritation. Hypertension and tachycardia are well documented events during extubation.

Laryngospasm is the commonest cause for upper airway obstruction after extubation.

For smooth extubation, patient should not have any straining, coughing, bucking, breath holding, laryngospasm or bronchospasm.^[2] Trials have been conducted to attenuate the hemodynamic and stressor responses during extubation by using various drugs like opioids^[3], inhalational agents^[4], local anaesthetics^[5], vasodilators, alpha blockers^[6], beta blockers^[7] and calcium channel blockers^{[8][9]}.

Studies have been carried out using fentanyl, sevoflurane, lignocaine, propofol, magnesium sulphate, nitroglycerine, clonidine, esmolol, labetalol, metoprolol, verapamil, nicardipine, diltiazem, etc., either as a sole agent or in comparison with each other.

Fentanyl, an opioid agonist, may blunt cardiovascular and airway reflexes during emergence without prolonging the recovery.^[10] Dexmedetomidine, an α 2-adrenoreceptor agonist with a distribution half-life of approximately 6 minutes has sedative, analgesic, sympatholytic and anxiolytic effect, reduces most of the cardiovascular responses in the perioperative period^[11]. Currently, dexmedetomidine is indicated for intensive care unit sedation in mechanically ventilated patients and for sedation of non-intubated patients before or during surgical and other procedures.^[12] So, it might be a useful agent to diminish the response to extubation as it provides sedation, haemodynamic stability and does not depress respiration.

With this background, this study was considered to analyse & compare the effect of sedation with single-dose dexmedetomidine and fentanyl on the attenuation of circulatory and airway response to extubation.

AIMS AND OBJECTIVES

- 1) To compare the effects of dexmedetomidine and fentanyl on hemodynamic responses during emergence from general anaesthesia.
- 2) To compare the effects of dexmedetomidine and fentanyl on airway reflexes during extubation after general anaesthesia.
- 3) To compare Post-operative sedation with the study drug.

- 4) To analyse the complication and side effect if any.

MATERIAL AND METHODS:-

The present study was conducted in a prospective randomized manner on 90 patients of ASA I and II of age group 18 to 60 years of either sex posted for elective surgeries under General anaesthesia after taking informed consent and approval of the institutional ethics committee. Patients with history of cardiopulmonary, neurological, renal disease, active hepatic disease, psychiatric disorders, coagulation disorders and patients with history of drug allergy were excluded from our study.

After obtaining institutional ethics committee approval, the study was conducted in 90 patients undergoing surgeries in general anaesthesia. A detailed history of all selected patients was taken. All relevant investigations like Complete Blood Picture, Fasting/Random blood sugar, Renal Function Test, Chest X-ray and ECG was carried out. The entire procedure was explained to the patient and proper informed written consent was taken. All patients were undergo pre anaesthetic evaluation on the previous day of surgery.

Patients were randomly divided into three equal groups by closed envelope method.

Group F (n=30) - Intravenous bolus infusion of Fentanyl 1µg/kg body weight in 100ml 0.9% normal saline over a period of 10 minutes.

Group D (n=30) Intravenous bolus infusion of Dexmedetomidine 0.5µg/kg body weight in 100ml 0.9% normal saline over a period of 10 minutes.

Group C (n=30) - Intravenous bolus infusion of 100ml 0.9% normal saline over a period of 10 minutes.

All patients were thoroughly investigated and proper pre anaesthetic check up was done. The entire procedure was explained to the patient and proper informed written consent was taken. Patients were kept nil orally for 8 hrs before surgery. In O.T. baseline preoperative parameters were recorded.

All the patients were pre-medicated with Inj. Glycopyrrolate 0.005mg/kg BW IV, Inj. Midazolam 0.03mg/kg BW IV, inj. Ondansetron 0.1mg/kg IV, and Inj. Pentazocine 0.6mg/kg body weight IV. After pre-oxygenation with 100% oxygen

for 3 minutes and anaesthesia was induced with Inj. Propofol 2- 2.5mg/ kg body weight IV and Inj. Succinylcholine 1.5- 2mg/kg body weight IV. After one minute of giving Inj. Succinylcholine, laryngoscopy was performed and oro-tracheal intubation was done. The correct placement of endotracheal tube was confirmed by auscultation and end tidal carbon dioxide (Et CO₂) values. The cuff of the endotracheal tube was inflated with air. Anaesthesia was maintained with O₂ 40%, N₂O 60%, Isoflurane 0.2% - 1% , and intermittent dose of Inj. Atracurium at the dose of 0.1mg/kg body weight was used for maintenance of muscle paralysis as per requirement. The concentration of isoflurane was increased or decreased during surgery to maintain BP and HR between 80% and 120% of the preoperative values. Hypotension (a decrease in SBP >25% from baseline or an SBP <90 mm Hg) was controlled by increasing the fluid infusion rate and decreasing gas concentrations.

At the beginning of closure of skin incision, isoflurane was discontinued and fentanyl 1.0mcg/kg

body weight diluted to 100 ml in normal saline was infused over 10 minutes in Group F patients. Group D patients received iv dexmedetomidine 0.5mcg/kg diluted to 100 ml in normal saline was infused over 10 minutes, and Group C patients received 100ml normal saline infused over 10 minutes. After onset of spontaneous breathing , intravenous neostigmine 0.05mg/kg body weight and glycopyrrolate 0.01mg/kg body weight was administered to antagonize the effect of muscle relaxants. Patient was extubated when the extubation criteria fulfilled likes spontaneous breathing , obeys simple commands, lift the head and hold for 30 Second .

HR, SBP, DBP, MAP, and SPO₂ values were recorded as baseline after inhalational agent stopped, then at just prior to extubation , immediate after extubation and then every 5 minutes for 30 minutes , thereafter every 30 minutes for 1 and half hour were recorded and quality of extubation was analyzed on a five point score (Extubation quality score) based on the patient's comfort and response.

EXTUBATION QUALITY SCORE ^[15]

EXTUBATION QUALITY SCORE	EXTUBATION RESPONSE
1	Patient is having no cough
2	Endotracheal extubation is smooth and the patient is having cough - one or two times (minimal)
3	Patient is having cough - three or four times (moderate)
4	Patient is having cough - five to ten times (severe)
5	Patient is having cough - more than ten times or laryngospasm or breath holding. Extubation is poor and the patient is restless.

Post Operative Sedation was evaluated using Ramsay Sedation Scale.

RAMSAY SEDATION SCALE^[16]

SCORE	RESPONSE
1	Patient anxious and agitated or restless or both
2	Patient cooperative, oriented, and tranquil
3	Patient drowsy but responds to commands
4	Brisk response to light glabellar tap or loud auditory stimulus
5	Sluggish response to light glabellar tap/loud auditory stimulus
6	No response to light glabellar tap or loud auditory stimulus

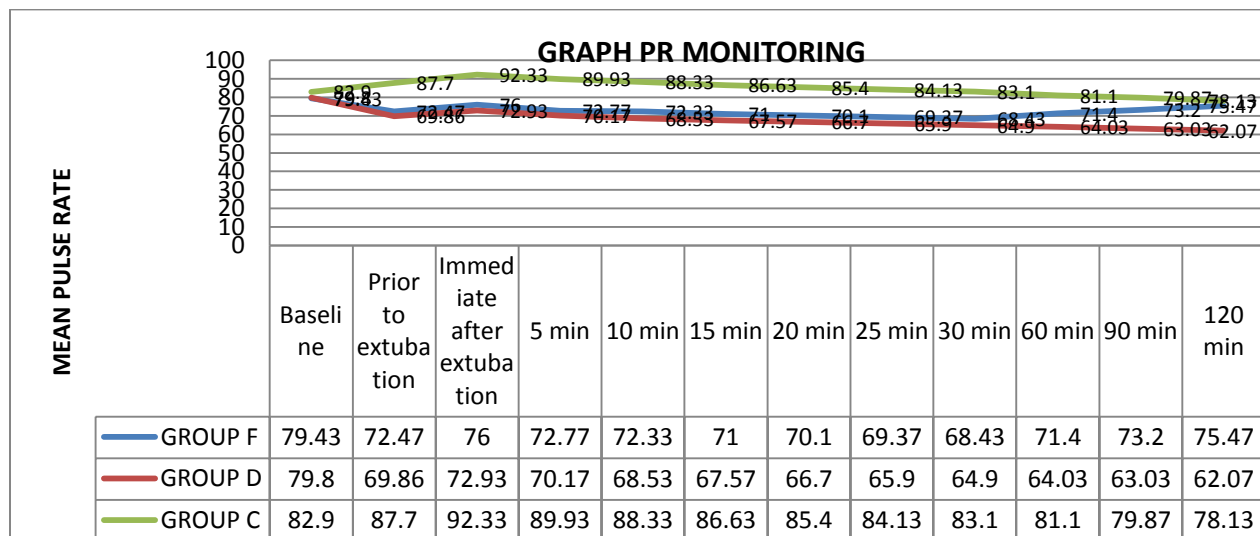
Adverse events such as bradycardia, hypotension, hypertension, nausea, vomiting, shivering, cough, laryngospasm, bronchospasm or desaturation if any were noted.

OBSERVATION AND RESULT

All data were compiled and the chi square test was used for the statistical analysis. P value less than 0.05 was considered as statistically significant.

Demographic profiles were similar in all the three groups in our study.

Mean heart rate: in our study the mean HR immediately after extubation was found to be 76.00 ± 5.34 in group F, 72.93 ± 3.52 in group D, and 92.33 ± 5.36 in group C, there is significant difference in mean HR before and after extubation between the group F and D ($p < 0.05$), between group F and C ($p < 0.0001$), and between group D and C ($p < 0.0001$), there after a significant difference in HR were recorded between the groups at different time interval indicated.



Mean arterial pressure: in our study the mean of MAP immediately after extubation was found to be 92.30 ± 1.95 in group F, 85.90 ± 3.32 in group D, and 99.13 ± 3.63 in group C. Statistical analysis shows that there is a significant difference in Mean of MAP before and after extubation between the group F and D ($p < 0.0001$), between group F and C ($p < 0.0001$), and between group D and C ($p < 0.0001$), there after a significant difference in MAP were recorded between the groups at different time interval indicated. MAP was well controlled in group D immediately after extubation, at 5 min and whole observation period postoperatively, group F also

decreases MAP prior and after extubation but is less than group D and. MAP was significantly increased after extubation in group C as compared to group D and group F.

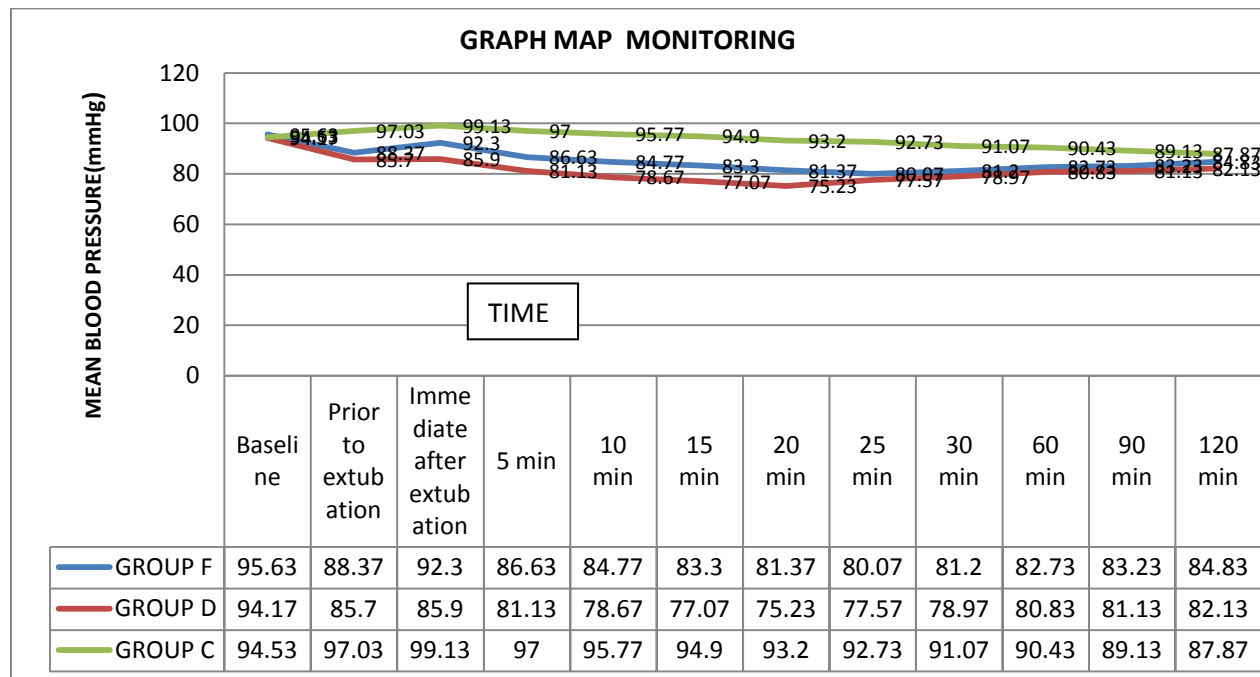


TABLE-1: COMPARISON OF EXTUBATION QUALITY SCORE BETWEEN GROUPS

Quality score	GROUP D	GROUP F	GROUP C	Total	P value
1	11 (37%)	4 (13%)	2 (7%)	17	p<0.0001
2	18 (60%)	5 (17%)	3 (10%)	26	
3	1 (3%)	20(67%)	8 (26%)	29	
4	0 (0%)	1 (3%)	17(57%)	18	
5	0 (0%)	0 (0%)	0 (0%)	0	
Total	30	30	30	90	

When we compared extubation quality score we found that, in the Dexmedetomidine group, 37 % of the patients had no cough during extubation whereas 60 % of the patients were extubated smoothly with minimal cough and 3% of them had moderate cough. In the Fentanyl group, 13% of the patients had no cough, 17% of the patients had minimal cough and 67 % patients had moderate cough whereas 3% of the patients had severe cough during extubation. In the control group, 7 % of the patients had no cough during extubation , 10 % had minimal cough and 26 % patients had moderate cough whereas 57% of the patients had severe cough during extubation. Statistical analysis of the Extubation Quality score shows a P value of <0.0001 which is statistically significant.

TABLE -2: COMPARISON OF SEDATION SCORE BETWEEN GROUPS

Sedation score	GROUP D		GROUP F		GROUP C		P Value
	N	%	N	%	N	%	
1	1	3 %	2	7 %	18	60 %	P<0.0001
2	10	33 %	17	57 %	8	27 %	
3	19	64 %	11	36 %	4	13 %	
4	0	0.00 %	0	0.00 %	0	0.00 %	
5	0	0.00 %	0	0.00 %	0	0.00 %	
6	0	0.00 %	0	0.00 %	0	0.00 %	

In our study, when we compared sedation score we found in the dexmedetomidine group, 33% of the patients were tranquil, oriented and co- operative (grade 2) and 64% of the patients were drowsy (grade 3) but responded to commands and 3% of the patients were anxious and restless (grade 1). In the Fentanyl group, 57% of the patients were tranquil, oriented and co – operative (grade 2) and 36% of the patients were drowsy and responded to commands (grade 3) and 7 % of the patients were apprehensive and restless (grade 1). In the control group, 27% of the patients were tranquil, oriented and co – operative (grade 2) and 13 % of the patients were drowsy and responded to commands (grade 3) and 60 % of the patients were apprehensive and restless (grade 1). There were statistically significant difference among the groups. ($p<0.0001$)

DISCUSSION

Extubation is associated with wide fluctuations in the hemodynamics that can lead to tachycardia, hypertension and arrhythmias. It is also associated with reflex increases in airway reactivity leading to stress responses and airway irritation.

In our study we used Intravenous bolus infusion of Fentanyl $1\mu\text{g/kg}$ body weight in 100ml 0.9% normal saline over a period of 10 minutes and Intravenous bolus infusion of Dexmedetomidine $0.5\mu\text{g/kg}$ body weight in 100ml 0.9% normal saline over a period of 10 minutes.

In our study mean heart rate just prior to extubation in the group D was 69.86 ± 3.85 , in the group F was

72.47 ± 5.76 and in the group C it was 87.70 ± 6.62 which increases immediately after extubation to mean heart rate of 72.93 ± 3.52 in the group D and 76.00 ± 5.34 in group F, in the group C it was 92.33 ± 5.36 respectively. Then later on no significant increase in HR after extubation was observed when compared with pre-extubation values in the dexmedetomidine group. HR in the fentanyl group was mildly higher at 5 and 10 minutes after extubation compared with preextubation. HR in the control group was significantly higher at 5 and 10 minutes after extubation compared to preextubation, duration of tachycardia was significantly longer in control group. Guler et al^[13], Nishina et al^[3], P Rani^[10] and D Jain et al^[14] also found similar results.

In our study, the mean SBP just prior to extubation in the group D was 114.60 ± 5.64 in the group F was 117.93 ± 4.86 and in the group C it was 128.73 ± 4.56 which increases immediately after extubation to mean SBP of 122.40 ± 4.34 in the group D, in group F 116.27 ± 5.09 and 131.60 ± 4.38 in group C respectively. SBP was significantly increased after extubation in group C as compared to group D and group F, SBP was well controlled in group D immediately after extubation, at 5 min and whole observation period postoperatively, group F also decreases SBP prior and after extubation but is less than group D.

The MAP just prior to extubation in the group D was 85.70 ± 3.79 in the group F was 88.37 ± 2.19 and in the group C was 97.03 ± 3.25 which increases immediately after extubation to MAP of $85.90 \pm$

3.32 in the group D in the group F it was 92.30 ± 1.95 and 99.13 ± 3.63 in group C respectively. Then later on as trend shows it was better controlled in the group D than group F and it was not controlled in group C. The findings observed were in accordance with **Aksu et al**^[17] and also **Talke et al**^[20]

In our study extubation quality score was better in Dexmedetomidine group as compared to others. In Dexmedetomidine group 37 % of the patients had no cough during extubation whereas 60 % of the patients were extubated smoothly with minimal cough and 3% of them had moderate cough. In the Fentanyl group, 13% of the patients had no cough, 17% of the patients had minimal cough and 67 % patients had moderate cough whereas 3% of the patients had severe cough during extubation. In the control group, 7 % of the patients had no cough during extubation, 10 % had minimal cough and 26 % patients had moderate cough whereas 57% of the patients had severe cough during extubation. This was in accordance with the study conducted by **Kim and Bishop**^[4] also **Guler et al**^[13] and **Fan Q et al**^[19]

Sedation profile of Dexmedetomidine is better as it leads to central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus coeruleus in the brainstem playing a prominent role in the sedation and anxiolysis. Noradrenergic output from the locus coeruleus is decreased allowing increased firing of inhibitory neurons including the GABA system contributing in anxiolysis and sedation. In our study, when we compared sedation score we found that in the dexmedetomidine group, 33% of the patients were tranquil, oriented and co-operative (grade 2) and 64% of the patients were drowsy (grade 3) but responded to commands and 3% of the patients were anxious and restless (grade 1). In the Fentanyl group, 57% of the patients were tranquil, oriented and co-operative (grade 2) and 36% of the patients were drowsy and responded to commands (grade 3) and 7 % of the patients were apprehensive and restless (grade 1). In the control group, 27% of the patients were tranquil, oriented and co-operative (grade 2) and 13 % of the patients were drowsy and responded to commands (grade 3) and 60 % of the patients were apprehensive and restless (grade 1). There was statistically significant difference among the groups. ($p < 0.0001$). There was a statistically significant

difference among both groups which was in accordance with the study conducted by **Barkha Bindu et al.**^[18] and **Koroglu A et al**^[21]

In present study, none of the patients in either of the group developed any complications such as respiratory depression, laryngospasm, bronchospasm, undue sedation or desaturation. Similar findings have been made by **Guler et al**^[13]

CONCLUSION

From the observation and results of our study it is concluded that I.V. Dexmedetomidine when given in the dose of $0.5 \mu\text{g/kg}$ prior to extubation effectively attenuates haemodynamic responses, airway reflexes with providing minimal sedation postoperatively thus allowing smoother extubation when compared to Fentanyl $1.0 \mu\text{g/kg}$.

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