ORIGINAL RESEARCH PAPER
Volume-8 | Issue-11 | November - 2019 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF INTRAVENOUS FENTANYL VS. INTRAVENOUS DEXMEDETOMIDINE TO ATTENUATE EXTUBATION RESPONSE IN ADULT PATIENTS UNDERGOING GENERAL ANAESTHESIA- A PROSPECTIVE RANDOMIZED DOUBLE BLINDED CONTROLLED TRIAL.

Anesthesiology

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ABSTRACT

Introduction: Complications during and after extubation are more common than during tracheal intubation and induction of anaesthesia. Hypertension and tachycardia are common events during extubation. Endotracheal extubation can be associated with arrhythmias, myocardial ischemia and raised intracranial pressures due to sympathetic stimulation.

Aim: To compare the effects of dexmedetomidine and fentanyl on airway reflexes and hemodynamic responses during tracheal extubation in patients undergoing surgeries under general anaesthesia.

Materials and Methods: 60 patients of either sex, ASA grade I -II normotensive, aged 20-60 years undergoing elective general surgeries under general anaesthesia were randomized into 2 groups comprising of 30 patients each- Group D (dexmedetomidine group) and Group F (Fentanyl Group). Anaesthetic technique was standardized. 15 min before the expected last surgical suture , patients received dexmedetomidine 0.75 µg/kg IV over 10 minutes (dexmedetomidine group) or fentanyl 1 µg/kg IV over 10 minutes (fentanyl group). HR, SBP, DBP, RR and SPO2 were recorded before, during and after extubation.

Results: Statistically significant lesser increase in HR, SBP, DBP, and RR were noted after extubation in the dexmedetomidine group than the fentanyl group. Dexmedetomidine group had better extubation quality than the fentanyl group. Bradycardia in one case observed with dexmedetomidine group than the fentanyl group but none required intervention.

Conclusion: Dexmedetomidine 0.75mcg/kg in 100 ml 0.9% normal saline administered 15 minutes before tracheal extubation was better compared to Inj. Fentanyl 1 mcg/kg in 100 ml 0.9% normal saline in attenuating the extubation response with comparable adverse effects. Hence, dexmedetomidine infusion can be a safer alternative to fentanyl infusion for attenuating extubation stress response.

KEYWORDS

Dexmedetomidine, Fentanyl, Extubation, Hemodynamic Response.

I. INTRODUCTION

It is well known factor that, after tracheal intubation, there is an increase in arterial blood pressure and heart rate associated with an increase in plasma concentrations of both noradrenaline and adrenaline[1,2]. Endotracheal extubation is the translaryngeal removal of a tube from trachea via nose or mouth[3]. An increase in heart rate and arterial pressure also occurs after tracheal extubation due to catecholamine release[4]. Arrhythmias, myocardial ischemia, raised intracranial and intraocular pressures can occur[5]. Respiratory complications resulting in serious consequences (hypoxic brain injury and death) following tracheal extubation have been thrice more common than those occurring during intubation (4.6% versus 12.6%)[6,7]. These transient but significant changes, which may be well tolerated by healthy individuals, may prove to be deleterious in patients with hypertension, coronary artery disease or intracranial pathologies[8]. The hemodynamic changes may have been influenced also by administration of neostigmine and glycopyrronium[9]. Laryngoscopy alone produces a significant pressor response, presumably because of stimulation of the supraglottic region[10].

Smooth tracheal extubation requires the absence of straining, movement, coughing, breath holding or laryngospasm[11]. Various techniques and antihypertensive drugs are available to attenuate airway and circulatory reflexes during extubation but none have been completely successful[12]. In our study, we compared the effects of dexmedetomidine and fentanyl on airway reflexes and hemodynamic responses during tracheal extubation in patients undergoing surgeries under general anaesthesia.

Dexmedetomidine, a potent alpha2-adrenoceptor agonist, activates receptors in the medullary vasomotor center, reducing norepinephrine turnover and decreasing central sympathetic outflow, resulting in alterations in sympathetic function and decreased HR, and BP. Fentanyl is a proven drug to attenuate the intubation and extubation response. Fentanyl is a potent, synthetic narcotic analgesic with a rapid onset and short duration of action. It is extremely lipid soluble, has a low molecular weight and which is popularly used as intravenous analgesic supplement, component of inhalation anaesthesia, balanced anaesthesia and neuroleptic analgesia and also as a sole anaesthetic. Fentanyl has been reported to reduce the prevalence of coughing during and after extubation and to suppress the sneezing reflex after abdominal hysterectomy and periocular injections. Fentanyl has also been reported to attenuate the cardiovascular responses to tracheal extubation in elective gynecologic surgery.

II. MATERIALS AND METHODS

Following ethical committee approval patients were thoroughly explained regarding the nature of the study. A written informed consent was obtained from all the patients.60 patients belonging to both sexes and aged between 20-60 years of ASA -1 & 2 Physical status were randomly taken for the study. They were divided into two groups, comprising of 30 patients each- Group D (Dexmedetomidine group) and Group F (Fentanyl Group) using sealed envelope method. Patients were interviewed and examined a day before surgery in the pre-operative assessment room. A detailed history was taken and systemic examination done. Vital monitoring was done. Basic investigations as per the case record form were taken.

Exclusion criteria:

1. Patients less than 20 years of age
2. Patients more than 60 years of age
3. Hemodynamically unstable patients
4. Patients with cardiorespiratory disorders [medications that effect heart rate]
5. Patients with history of sleep apnea

Patients were shifted into the operation theatre and ASA standard monitoring was carried out. IV fluid normal saline started in peripheral line via a 20-gauge cannula in each patient. HR, SpO2, noninvasive SBP and diastolic BP (DBP), and end-tidal carbon dioxide (ETCO2) were monitored throughout the anesthetic period. For all patients, anaesthesia was induced with propofol 1.5-2mg/kg IV and fentanyl 2 µg /kg IV. Rocuronium 1 mg/kg IV laryngoscopy done and endotracheal intubation done.. The internal diameter of the endotracheal tube was 7 to 7.5 mm for women and 8 to 8.5 mm for men. Anaesthesia was maintained with sevoflurane 1% to 2% in 66% nitrous oxide in oxygen. Patients were ventilated to an ETCO2 of 30-40mmHg. Opioids were given after induction every hourly if HR and BP crossed greater than 20% of baseline values. Dexmedetomidine and fentanyl were prepared in 100 mL of isotonic saline in bottles that were numbered and named by the anaesthesiologist not involved in the study before the study began. The drugs were identical in appearance. Before extubation, an anaesthesiologist who was involved in the study administered the study drugs. Extubation quality, postoperative

sedation, time to extubate, time to emergence and adverse events were assessed by an anaesthesiologist who also was involved in the study. 15 min before the expected last surgical suture , patients received dexmedetomidine 0.75 µg/kg IV over 10 minutes (dexmedetomidine group) or fentanyl 1 µg/kg IV over 10 minutes (fentanyl group).

Sevoflurane and nitrous oxide were discontinued when surgery was complete. Oropharyngeal secretions were aspirated and throat pack will be removed if used by using laryngoscope. A residual neuromuscular block was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg. The endotracheal tube was removed smoothly after spontaneous ventilation had returned. All patients were extubated by anesthesiologists who was involved in the study.

Extubation quality was rated using a 5-point scale:

1. No coughing;
2. Smooth extubation, minimal coughing (1 or 2 times);
3. Moderate coughing (3 or 4 times);
4. Severe coughing (5–10 times) and straining; and
5. Poor extubation, very uncomfortable (laryngospasm and coughing >10 times).

The postoperative sedation level was rated using a 3-point scale:

1. Awake and alert
2. Responds to voice
3. Not arousable.

An anesthesiologist who was involved in the study assessed all patients.

Breath holding was defined as desaturation and not breathing for ≥20 seconds, resulting in a decrease in SpO2 >5% from baseline. HR, SBP, DBP, and SpO2 were recorded before anesthesia, after drug administration, after skin incision, at the completion of surgery, and 1, 5, 10 and 15 minutes before and after tracheal extubation.

Any laryngospasm, bronchospasm, or desaturation was recorded. Extubation time (from end of sevoflurane administration until extubation), emergence time, and duration of surgery were noted. Awakening time was assessed using the patient's response to verbal commands. Prompt responses were graded as awake and the time from extubation was recorded. Orientation was assessed by the patient's response to questions regarding time, place, and person, and the time from extubation was recorded.

The concentration of sevoflurane 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. Atropine (0.5-mg IV bolus) was given for bradycardia (HR <45 beats/min). Adverse events (eg, bradycardia, hypotension, hypertension, nausea, vomiting, shivering) were recorded by an anesthesiologist who was involved in the study.

III. OBSERVATIONS & RESULTS.

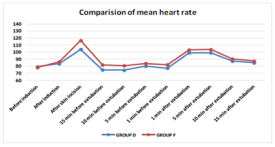
Patient data were represented as mean and standard deviations (S.D) for continuous measurements and categorical measurements were represented in number (%). Significance was assessed at 5% level of significance. Data was entered in Microsoft Excel worksheet 2013 and data analysis was done by using SPSS software (trial version 21).Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups .Chi-square test has been used to find significance of categorical measurements. In the present study statistical significance of difference between group D (Dexmedetomedine) and group F (Fentanyl) were analyzed.

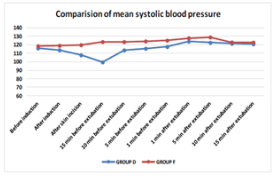
P value <0.05 was taken to be statistically significant.

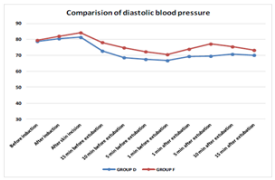
The groups were demographically similar in all respects [Table 1].

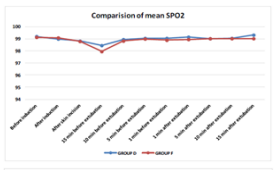
Table 1. Dermographics

	Group D	Group F	P value
Age	34.83±11.14	33.06±9.83	0.51
Weight	65.33±9.06	66.40±9.93	0.66
Duration of surgery(min)	154.0±76.43	174.33±79.77	0.31
ASA I/II	27/3	26/4	0.68
Sex (M/F)	11/19	10/20	0.78









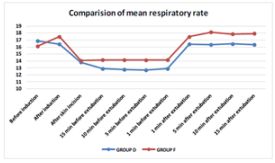


Table 2. DISTRIBUTION OF PATIENTS BASED ON POST OPERATIVE SEDATION GRADES

POST OPERATIVE SEDATION	GROUP D	GROUP F	P VALUE
GRADE I	28(93.33%)	27(90%)	1.0
GRADE II	2(6.66%)	3(10%)	
GRADE III	0(0%)	0 (0%)	

Table 3.DISTRIBUTION OF PATIENTS BASED ON SMOOTHNESS OF EXTUBATION

SMOOTHNESS OF EXTUBATION	GROUP D	GROUP F	P VALUE
GRADE I	10(33.33%)	4(13.33%)	**0.001 Significant**
GRADE II	18(60%)	11(36.66%)	
GRADE III	2(6.6%)	15(50%)	

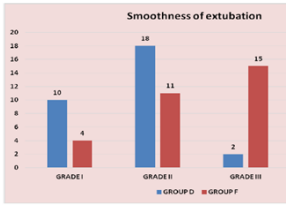
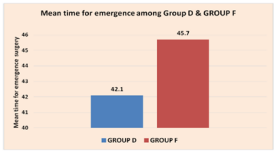


Table 4. DISTRIBUTION OF STUDY PARTICIPANTS BASED ON ADVERSE DRUG REACTIONS

ADVERSE DRUG REACTIONS	GROUP D	GROUP F
Nasal pruritis	0(0%)	2(6.66%)
Respiratory depression	0(0%)	1(3.33%)
Delayed arousal	0(0%)	1(3.33%)
Bradycardia	1(3.33%)	0(0%)
No reactions	29(96.66%)	26(86.66%)

Table 5. DISTRIBUTION OF STUDY PARTICIPANTS BASED ON MEAN TIME TO EMERGENCE IN GROUP D & GROUP M

GROUP	Mean±S.D. (time)	P value	Significance
GROUP D (DEXMEDETOMIDINE)	42.10±7.30	**0.04**	**Significant**
GROUP F (FENTANYL)	45.70±7.30		



IV. DISCUSSION

Extubation is frequently done procedure in anesthesia .This study was conducted to know the smooth extubation at postoperative period. In this 30 patients were given Dexameditomide (group D), 30 patients were given Fentanyl(Group F).The mean age of study participants who received Dexmedetomedine was 33.2±12.09 whereas the mean age of study participants who received Fentanyl was 33.07±11.18 However almost similar findings in the study done by Rani, et al[13] where they took 25 patients in each group and mean age and standard deviation was 35.96 (31.07-40.85) in dexameditomide group and 39.04 (34.08-44) in fentanyl group similarly in Jayshree P Vaswani et al[14] also.

In the present study among the study participants male:female ratio in dexmedetomidine group was 11:19 and fentanyl group was 10:20, mean weight of the study population who received Dexmedetomidine was 64.57±13.04 kgs and who received Fentanyl was 71.43±16.53 kgs. Among total 60 patients, 27 patients belongs to grade1 and 3 patients belong to grade 2 in Group D and , 26 patients belongs to grade 1 and 4 patients belongs to grade 2 in group F according to American Society of Anesthesiologists (ASA) grading. Mean duration of surgery in group D was 94.28±21.04 and in group F was 83.12±17.79.Dexmedetomidine took more time than Fentanyl. This difference was not statistically associated.

In the present study Inj. Fentanyl 1 mcg/kg in 100 ml 0.9% normal saline was given over 10 mins for group F and Inj. Dexemedetomidine 0.75 mcg/kg in 100 ml 0.9% normal saline was given over 10 mins, similar to P.rani et al[13] However in Jayshree P Vaswani et al[14]. dexmedetomidine 0.5 µg/kg was given and Group-F (N=30) fentanyl 0.5 µg/kg was given although in R.Aksu et al[15] patients received dexmedetomidine 0.5 µg/kg IV over 5 minutes (dexmedetomidine group) or fentanyl 1 µg/kg IV over 5 minutes (fentanyl group), but in Lovinaneil et al[16] Group F received fentanyl 0.5 µg/kg as loading dose over 10 minutes prior to induction followed by 0.2-0.7 µg/kg/hr as maintenance dose and Group D received Dexmedetomidine 0.5 µg/kg as loading dose over 10 minutes prior to induction followed by 0.2 µg/kg/hr-0.7 µg/kg/hr as maintenance dose till surgery was over.

HEART RATE:

The present study revealed that there was not much difference in the heart rates before induction but after induction there was constant significant difference between the groups and also there was Tachycardia of more than 100bpm was found in 1min and 5min after extubation in Fentanyl group although at the time of incision there was increase in heart rates in most of the patients (>100) in both groups. Overall in fentanyl group patients the mean heart rates were higher than Dexameditomide group patients this difference was significantly associated (p<0.05). our results were comparable with R.Aksu et al[15] and Jayshree P Vaswani et al[14].

SYSTOLIC BLOOD PRESSURE:

The present study revealed that mean systolic blood pressure, after skin incision, 15,10,5&1 min before extubation, and 1,5,10,15 min after extubation was higher in Fentanyl group when compared to Dexameditomide group, this difference between two groups was statistically significant (p>0.05). None were in hypertension during the surgery (>140mm of Hg) and none of the patients developed hypotension (SBP<60mmHg). Similar findings were found in other studies like Jayshree P Vaswani et al[14], Aksu et al[15] and R Amutharani et al[3].

DIASTOLIC BLOOD PRESSURE:

The present study revealed that mean diastolic blood pressure, after skin incision, 15,10,5&1 min before extubation, and 1,5,10,15 min after extubation was higher in Fentanyl group when compared to Dexameditomide group, this difference between two groups was statistically significant (p>0.05). However there was increase in DBP from the baseline, at the time of skin incision in both groups but there was considerably more increase in Fentanyl group. Similar findings were found in other studies like Lovina Neil et al[16], Aksu et al[15], Jayshree P Vaswani et al[14] and R. Amutharani et al[3].

OXYGEN SATURATION:

The present study revealed that mean oxygen saturation, before induction, after skin incision, 15,10,5&1 min before extubation, and 1,5,10,15 min after extubation there is no significant difference between two groups (p>0.05). Desaturation was not observed in any of the patients in both groups. Similar findings were reported in Jayshree P Vaswani et al[14] and in Lovina Neil et al[16], Aksu et al[15], Bajwa et al[17] and Yildiz et al[18].

RESPIRATORY RATES:

The present study revealed that mean Respiratory rates, 15,10,5&1 min before extubation, and 1,5,10,15 min after extubation was higher in Fentanyl group when compared to Dexameditomide group, this difference between two groups was statistically significant (p>0.05). other studies which compared the parameters between dexameditomide and Fentanyl did not comment on respiratory rates.

SMOOTHNESS OF EXTUBATION:

After an ideal extubation, patients should exhibit adequate ventilatory drive, a normal breathing pattern, a patent airway with intact protective reflexes, normal pulmonary function, and the absence of any mechanical perturbation. In the present study, Dexmedetomine group had grade 1 and grade 2 smooth of extubation and in fentanyl group majority had grade 3 smoothness of extubation. This difference was found to be statistically significant.

In R. Amutharani et al[3] most of the patients of Dexameditomide group were in GRADE I, II and for Fentanyl in grade II and III, for he normal saline group patients were almost equally present in all 4 groups, this difference was significantly associated. Dexmedetomidine group had a better quality of extubation compared to the fentanyl group. Aksu et al[15] observed that dexmedetomidine 0.5 µg/kg IV before tracheal extubation was associated with significantly less coughing and better quality of extubation than was fentanyl. In Rani et al[13], both groups (group D& group F), none of the patients had breath holding or difficulty in tolerating the endotracheal tube. Smoothness during extubation without coughing on tube was comparable between the two groups. Moreover Dexmedetomidine group showed better airway response during oral suctioning and laryngoscopy when compared to fentanyl which correlated well with better sedation score in dexmedetomidine group.

SEDATION SCORE:

In the present study both group D and group F the sedation scores were grade 1 and grade 2 and were almost similar, so this was not statistically associated also Rani et al observed the smoothness of extubation was comparable between the two groups and better sedation score in dexmedetomidine group. Similar findings were found in other studies like Liyakath et al[8] and R. Amrutharani et al[3].

ADVERSE DRUG REACTIONS:

In the present study majority had no adverse reactions in Dexmedetomidine group except one case presented with bradycardia where as in fentanyl group 2 cases had nasal pruritis, 1 case had respiratory depression and 1 case had delayed arousal.

In Aksu et al[15], the fentanyl group had a similar prevalence of cough (70%), 20% of which was severe. The lower prevalence of cough (15%) found with dexmedetomidine compared with fentanyl suggests that dexmedetomidine was more effective for improving the quality of extubation. In R.Amrutharani et al[3] Adverse effects like respiratory depression, laryngospasm, bronchospasm or desaturation were not observed in both the groups. Recovery profile is similar in dexmedetomidine and fentanyl group.

MEAN TIME TO EMERGENCE:

In the present study mean time to emergence from surgery in Dexameditomide group was lower (42.10±7.30) when compared to Fentanyl group (45.70±7.30) this difference was statistically significant(p=0.04).

MEAN TIME TO EXTUBATE:

In the present study mean time to extubate in Dexameditomide group was higher (23.28±4.08) when compared to Fentanyl group (27.36±2.84) this difference was not statistically associated (p=0.34). Lovina Neil et al study showed a significant attenuation of HR at the time of extubation in dexmedetomidine group.

Therefore Single-dose of Inj. Dexemedetomidine 0.75 mcg/kg in 100 ml 0.9% normal saline will be given over 10 mins before extubation produced better attenuation of airway response to laryngoscopy and airway suctioning. This resulted in smooth tracheal extubation without prolonging recovery when compared to fentanyl.

V. CONCLUSION

Dexmedetomidine 0.75 mcg/kg in 100 ml 0.9% normal saline administered 15 minutes before tracheal extubation was better compared to Inj. Fentanyl 1 mcg/kg in 100 ml 0.9% normal saline in attenuating the hemodynamic stress response with comparable adverse effects. Hence, dexmedetomidine infusion can be a safer alternative to fentanyl infusion for attenuating extubation stress response.

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