ORIGINAL RESEARCH PAPER

Anaesthesiology

COMPARISON OF THE EFFECTS OF INJ. DEXMEDETOMIDINE VERSUS INJ. FENTANYL ON AIRWAY REFLEXES AND HEMODYNAMIC RESPONSES TO TRACHEAL EXTUBATION IN PATIENTS UNDERGOING SURGERY FOR SUPRATENTORIAL SPACE OCCUPYING LESION(SOL):A RANDOMIZED, DOUBLE BLIND CONTROLLED STUDY

KEY WORDS:
dexmedetomidine, fentanyl, extubation,neurosurgery,SOL

Harish kumar	Junior Resident, Department of Anesthesia, RIMS
Usha Suwalka	Department of Anesthesia, RIMS
Mukesh Kumar	Department of Anesthesia, RIMS
Azizul Haque	Department of Anesthesia, RIMS
Rajesh Chandra	Department of Anesthesia, RIMS
Ranjit Kaur Arora	Department of Physiology, RIMS

ABSTRACT

Context: Extubation can stimulate reflex responses via tracheal and laryngeal irritation. Cardiovascular response includes tachycardia and hypertension. These transitory changes are of little consequences in ASA Grade I and II patients going for general surgical procedures, but could be of major concern for anesthesiologist in patients especially with intra cerebral space occupying lesions (ICSOL) where a sudden hypertension during or in immediate post extubation phase could lead to raised intracranial pressure (ICP) and decreased cerebral perfusion.

Aims: this randomized double blind study was designed to compare the effects of dexmedetomidine and fentanyl on airway reflexes and hemodynamic responses to tracheal extubation in patients undergoing surgery for supratentorial SOL.

Methods and Material: 75 patients ASA 1 AND 2 in the age group of 18 to 65 years were randomly divided into three groups including 25 patients in each group. Group C (n=25) for controls received isotonic saline 100 ml IV,Group F (n=25) received fentanyl 1 ğg/kg in 100 mL of isotonic saline IV Group D (n=25) received dexmedetomidine 0.5 ğg/kg in 100 mL of isotonic saline IV five minutes before extubation, patients received drugs intravenously over five minute. Hemodynamic monitoring (HR), (SBP), (DBP), and (SpO2) were recorded before anesthesia, 10, 5, and 1 minutes before and after tracheal extubation. Other parameters included Quality of extubation (extubation quality score), Postoperative sedation (ramsay scale).

Statistical analysis used: The t test was used for between-group comparisons of HR, SBP, DBP, and SpO2.Repeated-measures ANOVA was used for within-group comparisons. the Fisher exact test was used to analyze extubation and sedation scores, sex, and adverse events. $P < 0.05$ was considered statistically significant**.**

Results: Increase in mean arterial pressure was more significant in fentanyl and control group as compared to dexmedetomidine group. Smooth extubation was noticed more in dexmedetomidine group of patients as compared to fentanyl and control group

Conclusions: dexmedetomidine 0.5 ğg/kg IV, administered before extubation, was more effective in attenuating airway reflex responses to tracheal extubation and maintaining hemodynamic stability without prolonging recovery compared with fentanyl 1 ğg/kg IV in these patients undergoing surgery for supratentorial SOL.

Introduction:

Extubation can stimulate reflex responses via tracheal and laryngeal irritation. Complications of extubation eg., bucking, gagging caused by involuntarily resisting positive pressure ventilation in a patient with a endotracheal tube in place, breath holding, laryngospasm, pulmonary edema might occur. Cardiovascular response includes tachycardia and hypertension. For a smooth extubation, there should be no straining, movement, coughing, breath holding or laryngospasm. Extubation in light plane of anesthesia or sedation can stimulate reflex responses via tracheal and laryngeal irritation. These transitory changes are of little consequences in American Society of Anesthesiologists (ASA) physical status ASA classes I and II patients going for general surgical procedures, but could be of major concern for anesthesiologist in patients especially with intra cerebral space occupying lesions (ICSOL) where a sudden hypertension during or in immediate post extubation phase could lead to raised cerebral blood flow (CBF), intracranial pressure (ICP) and decreased cerebral perfusion pressure (CPP) resulting into increased intracranial bleeding, high morbidity and mortality.

Intracranial local anesthetic instillation, intracuff lidocaine, intravenous lignocaine, short acting opioids such as Fentanyl and Remifentanyl, Esmolol, Labetalol, Diltiazem, Prostaglandin – E_1 and Verapamil have been used to attenuate these hemodynamic and respiratory responses during extubation in the past but with certain limitations.[1]

Dexmedetomidine is a highly selective α_2-adrenoreceptor agonist that induces sedation and analgesia without affecting respiratory status. Administered after induction, dexmedetomidine was found to reduce the prevalence of emergence agitation. It has also been reported to reduce the hemodynamic response following rise in plasma catecholamine level during intubation and extubation in ophthalmic and vascular surgeries.[2]

Fentanyl, a short acting synthetic opioid, 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.[3]

MATERIAL AND METHODS

Study eligibility included patients aged 18 to 65 years who were classified physical status ASA classes I and II posted for elective surgery for supratentorial space occupying lesion(SOL).paient with systemic illnesses (eg, hypertension [systolic BP (SBP) >160 mm Hg], cardiac disease [congestive heart failure, congenital heart disease, history of myocardial infarction, and arrhythmia],diabetes mellitus, asthma) were excluded.

This was a double-blind, randomized, controlled study. HR, peripheral arterial oxygen saturation by pulse oximetry (SpO2), noninvasive SBP and diastolic BP (DBP), and end-tidal carbon dioxide (ETCO2) were monitored (AS/3 Anesthesia
Monitor, Datex Engstrom, Helsinki, Finland) throughout the anesthetic period.

For all patients, anesthesia was induced with thiopental 4 $mg.kg^{-1}$ i.v and fentanyl 1 $g.kg^{-1}$ i.v. ,Vecuronium 0.1 $mg.kg^{-1}$ i.v was used to relax muscles for insertion of the endotracheal tube (high-volume/low-pressure endotracheal tubes)of appropriate size. Anesthesia

was maintained with isoflurane 1% to 2% in 66% nitrous oxide in oxygen. Patients were ventilated to an ETCO2 of 30 – 40 mmhg.

Dexmedetomidine and fentanyl were prepared in 100 mL of isotonic saline in bags that were numbered by the anesthesiologist before the study began. The drugs were identical in appearance. The patients were randomized into 3 groups (25 patients per group)as GROUP C(control),GROUP D(dexmedetomidine),GROUP F(fentanyl) via the sealed-envelope method. Extubation quality, postoperative sedation, and adverse events were assessed by a different anesthesiologist who also was blinded to treatment.

Before extubation, patients received dexmedetomidine 0.5 $g.kg^{-1}$ i.v over 5 minutes (group D) or fentanyl 1 $g.kg^{-1}$ i.v over 5 minutes (group F). isoflurane and nitrous oxide were discontinued when surgery was complete. A residual neuromuscular block was antagonized with neostigmine 0.05 $mg.kg^{-1}$ i.v and atropine 0.02 $mg.kg^{-1}$ i.v. Oropharyngeal secretions were aspirated before extubation. The endotracheal tube was removed smoothly after spontaneous ventilation had returned.

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).18 The postoperative sedation level was rated using a 5 point scale: 1=anxious or agitated and restless or both 2=cooperative,oriented and tranquil 3=drowsy but responds to command 4=asleep,brisk response to light glabellar tap or loud auditory stimulus 5=asleep,sluggish response to light glabellar tap or loud auditory stimulus. HR, SBP, DBP, and SpO2 were recorded before anesthesia, after drug administration, after skin incision, at the completion of surgery, and 1, 5, and 10 minutes before and after tracheal extubation. Any laryngospasm, bronchospasm, or desaturation was recorded. Extubation time (from end of isoflurane administration until extubation), duration of anesthesia, 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 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.

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.

STATISTICAL ANALYSIS

The t test was used for between-group comparisons of HR, SBP, DBP, and SpO2.

Repeated-measures ANOVA was used for within-group comparisons. the Fisher exact test was used to analyze extubation and sedation scores, sex, and adverse events. $P < 0.05$ was considered statistically significant.

The primary outcome measure of this study was the effect of dexmedetomidine and fentanyl on extubation quality in surgery for supratentorial SOL. The secondary outcome measures were hemodynamic responses to extubation, postoperative sedation scores, extubation time, awakening time, orientation time, and prevalence of adverse events.

RESULTS

Seventy five patients (21 male, 54 female) were included in the study. All completed the study with no study protocol violations. Demographic data, duration of surgery, and duration of anesthesia were not significantly different between the 3 groups

Table I. DEMOGRAPHIC CHARACTERSTICS OF THE STUDY PATIENTS(N=75).DATA ARE EXPRESSED AS MEAN(SD) UNLESS OTHERWISE SPECIFIED.

Characteristic	Dexmedetomidine Group(D)	Fentanyl Group(F)	control Group(C)	P
AGE	36.3±11.2	35.6±12.5	35.9±13.1	0.983,NS
SEX(m/f)	6/19	8/17	7/18	0.82,NS
WEIGHT	63.60±12.7	59.68±11.8	53.32±9.4	0.008,Sig.

The saturation was 97.4% in control group, 97.5% in the Fentanyl group and 97.9% in the dexmedetomidine group before the induction of anesthesia.

In the control group, the mean pulse rate before the anesthesia was 86.76 beats/min and 10 minutes after extubation was 90.72 beats/ min. In Fentanyl group, the mean pulse rate was before induction of anesthesia was 90.72 beats/min and the increase in pulse rate was noticed 10 minutes before extubation and 10 minutes after extubation. The mean pulse rate before the anesthesia was 87.08 beats/ min which was increased at 10 minutes before the extubation and after drug administration in Dexmedetomidine group.

In control group, there was increase in the mean arterial pressure at 5 minutes before extubation, 1 minute before extubation, 5 minutes after extubation and 10 minutes after extubation. In Fentanyl group, there was increase in mean arterial pressure at 5 minutes before extubation,immediately after drug administration, 1 minute before extubation and 5 minutes after extubation. In Dexmedetomidine group also there was an increase in mean arterial pressure 5 minutes before extubation, after drug administration, 1 minute before extubation and 5 minutes after extubation.

Table 1. comparison of the study groups according to mean arterial pressure

Mean arterial pressure	Groups	Mean ± SD	P values		
			C:F	**F:D**	**C:D**
Before anesthesia	**Group C**	89.65 ± 3.34	0.619, NS	0.908, NS	0.635, NS
	Group F	90.37 ± 6.4			
	Group D	90.19 ± 4.57			
10 minutes before extubation	**Group C**	86.33 ± 5.05	0.56, NS	0.715, NS	0.872, NS
	Group F	87.22 ± 5.63			
	Group D	86.6 ± 6.37			
5 minutes before extubation	**Group C**	88.62 ± 4.68	0.681, NS	0.219, NS	0.234, NS
	Group F	87.8 ± 8.73			
	Group D	90.38 ± 5.62			
After drug administration	**Group C**	88.38 ± 5.12	0.948, NS	0.178, NS	0.171, NS
	Group F	88.28 ± 5.63			
	Group D	90.71 ± 6.85			
1 minute before extubation	**Group C**	88.47 ± 5.25	0.18, NS	0.732, NS	0.087, NS
	Group F	90.68 ± 6.21			
	Group D	91.28 ± 6.1			

1 minute after extubation	**Group C**	86.83 ± 4.42	0.086, NS	0.39, NS	0.007, Sig
	Group F	89.21 ± 5.14			
	Group D	90.39 ± 4.45			
5 minutes after extubation	**Group C**	88.17 ± 5.24	0.317, NS	0.464, NS	0.071, NS
	Group F	89.73 ± 5.66			
	Group D	90.85 ± 5.04			
10 minutes after extubation	**Group C**	88.43 ± 4.19	0.776, NS	0.19, NS	0.089, NS
	Group F	88.8 ± 4.96			
	Group D	90.62 ± 4.7			

The comparison of mean arterial values had shown that there was no significant difference between the mean arterial values of C and F group, F and D group and C and D group except at 1 minute after extubation.

Chart 1. Distribution of the study groups according to quality of extubation

NS-not significant sig-significant p value=0.624, NS
No coughing after extubation was noticed in 60% of the C, 76% of F and D group patients. Smooth extubation was noticed in 12% of C group, F group and 16% of D group of patients. Moderate coughing was noticed in 8% of C and F group of patients and 4% of D group of patients. Severe coughing was noticed in 16% of C, 4% of F and D group of patients. Poor extubation was noticed in 4% of the C. This difference in quality of extubation was not statistically significant between the three groups.

Chart 2.comparison of the study groups according to Ramsay sedation scale

p value=0.818, NS

The Ramsay sedation score had shown that about 8% of the controls, 4% of the fentanyl group and 12% of the D group were anxious and agitated, 40% of C and F group and 44% of D group were cooperative, 32% of C, 36% of F and D group patients were responding to commands, 20% of C, 16% of F and 8% of D group were asleep with brisk response and about 4% of F group were asleep with sluggish response to glabellar tap. There was no statistically significant difference in the ramsay sedation score of the three groups.

Chart 3. Distribution of the study groups according to side effects

NS-not significant sig-significant p value=0.202, NS

Bradycardia was found in 8% of the fentanyl group F. Hypotension was noticed in 16% of the group C, 4% of the F and D group each. Nausea/ vomiting was noticed in 8% of the C, 12% of the F group and 4% of the D group. No side effects were noticed in 76% of the C and F group patients and 92% of the D group patients. This difference in adverse effect was statistically significant between the groups.

DISCUSSION

A randomized controlled study was conducted among the 75 patients aged between 18 to 65 year of physical status ASA classes I and II undergoing surgery for SOL**.**

Using fentanyl during the induction of anesthesia might have been a limitation of this study, although it has been reported that fentanyl administered during the induction of anesthesia does not affect extubation, because surgery for supratentorial SOL requires >3 hours. Additionally, use of fentanyl during anesthesia induction might have also been a limitation because of its intraoperative hemodynamic stabilization effects and its reported ability to reduce intraoperative bleeding in surgical areas during supratentorial SOL requires further study. Timing of administration and dosage of drugs may also affect the final outcome.

Changes in Saturation

The saturation was 97.4% in group C, 97.5% in the group F and 97.9% in the group D before the induction of anesthesia. There was significant difference between the saturation at 5 minutes after extubation and 10 minutes after extubation. A study by **Kothari et al** has observed no statistically significant difference in SPO_2 in the dexmedetomidine group and in control group.[7] In a study by **Shruthi et al**, the saturation was comparable in control and dexmedetomidine group.[10]

Changes in pulse rate

In the control group, the mean pulse rate before the anesthesia was 86.76 beats/min and 10 minutes after extubation was 90.72 beats/ min. In group F, the mean pulse rate was before induction of anesthesia was 90.72 beats/min and the increase in pulse rate was noticed 10 minutes before extubation and 10 minutes after extubation. The mean pulse rate before the anesthesia was 87.08 beats/ min which was increased at 10 minutes before the extubation and after drug administration in group D. In a study by **Bindu et al**, the heart rate was significantly different between the two groups from 5 minutes after starting the administration of the agent till 20 minutes after extubation. [6] **Kothari et al** have observed that, during and immediately after extubation stages the patients in dexmedetomidine group and lignocaine group showed a statistically significant increase in the Heart rate.[7] In a study by **Ali et al**, tachycardia response was seen in 84% of the normal saline group, 36% of the fentanyl and 8% in the dexmedetomidine group.[8] **Gosai et al** have observed a statistically significant difference in heart rate between the dexmedetomidine group and lignocaine group.[9] In a study by **Shruthi et al**, the heart rate was lower than the basal value during post extubation till 30 minutes in dexmedetomidine group. In control group, the heart rate was steadily increased compared pre operative values.[10]

Changes in mean arterial pressure

In group C, there was increase in the mean arterial pressure at 5 minutes before extubation, 1 minute before extubation, 5 minutes after extubation and 10 minutes after extubation. In group F, there was increase in mean arterial pressure at 5 minutes before extubation, after drug administration, 1 minute before extubation and 5 minutes after extubation. In group D also there was an increase in mean arterial pressure 5 minutes before extubation, after drug administration, 1 minute before extubation and 5 minutes after extubation.

Increase in mean arterial pressure was more significant in group F and C as compared to dexmedetomidine group.

Bindu et al have observed that, the mean arterial pressure significantly different from 10 minutes after starting administration of the agent and continued till the time observations were made.[6] In a study by **Ali et al**, the magnitude of increase above baseline in groups N, F and D was 27, 13 and 11 mm of Hg respectively in normal saline, fentanyl and dexmedetomidine groups respectively.[8] **Gosai et al** have observed that the mean arterial pressure between the two groups showed a statistically significant difference between the dexmedetomidine group and lignocaine group from 5 mins after starting the administration of the agent and continued till the time observations were made.[9]

Quality of extubation

Smooth extubation was noticed in 12% of the controls, 12% of the fentanyl group and 16% of the dexmedetomidine group of patients. Moderate coughing was noticed in 8% of the controls,

8% of the fentanyl group of patients and 4% of the dexmedetomidine group of patients. Severe coughing was noticed in 16% of the controls, 4% of the fentanyl and 4% of the dexmedetomidine group of patients. Poor extubation was noticed in 4% of the controls. In a study by **Bindu et al**, 84 percent of the patients in dexmedetomidine group could be extubated smoothly with minimal coughing, whereas 16 percent patients showed moderate coughing at the time of extubation. Eighty four percent patients in control group showed moderate coughing at the time of extubation whereas 16 percent patients could be extubated smoothly.[6] In a study by **Kothari et al**, only 5 patients in lignocaine group had grade 1 cough during extubation as against none in dexmedetomidine group. No patients had breath holding/ laryngospasm/ bronchospasm during or after extubation in both the study groups.[7] In a similar study, **Gosai et al** have observed a statistically significant difference in the quality of extubation between the two groups. Sixty percent of the patients in dexmedetomidine group could be extubated smoothly with minimal coughing, whereas 36% patients showed moderate coughing at the time of extubation. Fifty two percent of the patients in lignocaine group showed moderate coughing at the time of extubation and 36% of the patients could be extubated smoothly.[9]

Ramsay sedation score

The Ramsay sedation score had shown that about 8% of group C, 4% of the group F and 12% of group D were anxious and agitated, 40% group C and F , 44% group D were cooperative, 32% of group C, 36% group F and D patients were responding to commands, 20% of the group C, 16% of group F and 8% of group D were asleep with brisk response and about 4% of the group F were asleep with sluggish response to glabellar tap. Eighty four percent of the patients in group D were drowsy, but responding to commands with a sedation score of 3 on the Ramsay scale whereas in group C 80 percent were cooperative, oriented and tranquill with a sedation score of 2 on the Ramsay scale.[6] **Gosai et al** have observed that, 44% of the patients in the dexmedetomidine group were drowsy, but responding to the commands with a sedation score of 3, 1 patients had sedation score of 6 on the Ramsay scale; whereas in lignocaine group 56% of the patients were cooperative, oriented and tranquill with a sedation score of 2 on the Ramsay scale.[9] In a study by **Shruthi et al**, the Ramsey sedation scale was significantly higher in patients of Group D compared to group C at the time of extubation and at 5, 10, 15 and 30 minutes post extubation.[10]

Side effects

Bradycardia was found in 8% of the group F. Hypotension was noticed in 16% of the group C, 4% of the group F and D each. Nausea/ vomiting was noticed in 8% of group C, 12% of the group F and 4% of th group D. In a study by **Bindu et al**, the incidence of bradycardia and hypotension was higher in the dexmedetomidine group compared to control group. Most of the patients in dexmedetomidine group developed braydcardia as compared to the control group. One patient in dexmedetomidine group and two patients in control group had vomiting.[6] In a study by **Gosai et al**, the incidence of bradycardia was higher in dexmedetomidine group compared to lignocaine group. Hypertension and vomiting was higher in lignocaine group than the dexmedetomidine group.[9] In a study by **Shruthi et al**, the incidence of hypotension was higher in Group D compared to controls. The incidence of hypertension, tachycardia, agitation and coughing were higher in control group.[10] Intraoperative and post operative adverse effect like hypotension, bradycardia and nausea vomiting was observed in dexmedetomidine group.

Conclusion

The findings in the present study suggest that dexmedetomidine 0.5 µg/kg IV, administered before extubation, was more effective in attenuating airway reflex responses to tracheal extubation and maintaining hemodynamic stability without prolonging recovery compared with fentanyl 1 µg/kg IV in these patients undergoing surgery for supratentorial SOL..

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Conflicts of interest There are no conflicts of interest

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