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Effect of Dexmedetomidine in Attenuating Hemodynamic Responses During Extubation

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Abstract

Introduction: Tracheal extubation produces unfavourable hemodynamic alterations which may result in life threatening. The present study was aimed to assess the effect of injection dexmedetomidine 0.5 µg/kg for attenuation of hemodynamic responses and airway reflexes during extubation following surgery under general anaesthesia. *Methodology:* Patients of ASA grade I & II posted for surgery under general anesthesia were randomized to receive either dexmedetomedine 0.5 µg/kg body weight diluted to 20 ml in normal saline, over 10 minutes or normal saline 20 ml over 10 minutes. Hemodynamic parameters were recorded during infusion, at the time of reversal and after extubation. Extubation quality, time to eye opening and time to extubation were noted as well. Post extubation sedation was evaluated using Ramsay Sedation Scale and possible side effects during and after the administration of dexmedetomedine and during postoperative period were recorded. *Results:* We observed the mean heart rate and blood pressures to be significantly lower among patients in the dexmedetomedine group as compared to the control group. Mean time to extubation and eye opening was statistically and clinically significantly prolonged in the dexmedetomedine group as compared to the control group ($p<0.01$). 93% in the dexmedetomedine group had smooth extubation as against 57% in the control group. The incidence of hypertension and tachycardia was significantly higher among patients in the dexmedetomedine group as compared to the control group. *Conclusions:* Single bolus dose of dexmedetomidine 0.5 µg/kg administered as infusion over 10 minutes, before tracheal extubation attenuates hemodynamic responses effectively during extubation.

Keywords: dexmedetomidine; extubation; preanesthetic dose.

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Introduction

Dexmedetomidine is a selective $\alpha_2$adrenoreceptor agonist that has been shown to have both sedative and analgesic effects [1]. Compared with clonidine, which is an α_2 agonist that has been used for the treatment of hypertension, dexmedetomidine has an α_2:α_1 adrenoreceptor ratio of approximately 1600 : 1 [2]. The α_2 agonists decrease central sympathetic outflow and modify intraoperative cardiovascular responses to surgical stimuli and laryngoscopy. The reduction in tachycardia, hypertension, and sympathetic activity may be of benefit in patients at risk of myocardial ischemia [3]. It has been

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suggested that tracheal extubation also produces unfavourable hemodynamic alterations which may compromise myocardial oxygenation in the postoperative period. Studies have shown that respiratory and hemodynamic changes after tracheal extubation are three times more common than those occurring during tracheal intubation and induction of anesthesia, which may result in life threatening complications like myocardial infarction [4]. Therefore, protection against hemodynamic responses during extubation are important to avoid these life threatening complications and improve patient outcomes. The present study was aimed to assess the effect of injection dexmedetomidine 0.5 µg/kg for attenuation of hemodynamic responses and airway reflexes during extubation following surgery under general anaesthesia.

Methodology

Study Design and Setting

A prospective randomized double blinded placebo controlled study was conducted in the Department of Anaesthesiology, MGM Medical College, Navi Mumbai from April 206 till August 2017, in which all adult patients in age group of 18 to 50 years of either sex belonging to American Society of Anesthesiologists (ASA) grade I & II posted for surgery under general anesthesia were included. Patients were randomized into two groups - dexmedetomedine and control group with 30 patients in each group. Randomization was done by picking lottery method. Patients were interviewed and examined one day before the scheduled surgery. Informed consent along with proper pre-operative evaluation and relevant investigations as per case record form were done. The study was approved by the institutional ethics committee.

All patients were preoxygenated with 100% oxygen for 3 minutes and were premedicated with glycopyrolate 0.2 mg, ondensetrone 4 mg, midazolam 1 mg and fentanyl 2 µg/kg intravenously. After preoxygenation for 3 minutes, they were induced with thiopentone 4-5 mg/kg or propofol 2 mg/kg intravenously till there was loss of eyelash reflex. Neuromuscular blockade was achieved with atracurium 0.75 mg/kg or vecuronium 0.1 mg/kg. Laryngoscopy was done after 3 minutes of muscle relaxant and intubated with 8 to 8.5 mm cuffed endotracheal tube for male and 7 to 7.5 mm for females. Correct placement of the tube was confirmed by auscultation and square wave capnography. Twenty minutes prior to the expected time of extubation, isoflurane was discontinued and patients were allocated randomly to either dexmedetomedine or normal saline. Dexmedetomedine was given as 0.5 µg/kg body weight diluted to 20 ml in normal saline, over 10 minutes with syringe pump. Control group received normal saline 20 ml over 10 minutes with syringe pump.

Sample population

We included all patients aged 18 to 50 years of ASA grade I and II undergoing surgery under general anesthesia. We excluded patients who had a known allergy to dexmedetomedine, showed dysrhythmias in the ECG, severe psychiatric disturbances or with history of drug abuse, cardiac and pulmonary disease, surgeries on neck and oral cavity, obese patients, with difficult airway or history of sleep apnea, haemodynamically compromised patients, pregnant and lactating patients.

Data Collection and Data Analysis

Parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation (SpO_2) were recorded prior to infusion and at the intervals 1, 3, 5, 7 and 10 minutes during infusion of the study drug /normal saline and at the time of reversal. Extubation quality was rated using extubation quality 5-point scale: 1- no coughing; 2- smooth extubation, minimal coughing; 3- moderate coughing (3 or 4 times); 4- severe coughing (5 to 10 times) and straining and 5- poor extubation, very uncomfortable (laryngospasm and coughing > 10 times). Time to eye opening and Time to extubation i.e. interval between cut off of nitrous oxide to eye opening and extubation respectively were recorded. Number of coughs per patient was monitored for 15 minutes post extubation. Any incidence of laryngospasm, bronchospasm or desaturation were noted for a period of 15 min post extubation. All the hemodynamic parameters were recorded again after extubation at 1 minutes, 3 minutes, 5 minutes, 7 minutes, 10 minutes, 13 minutes and 15 minutes after extubation. Post extubation, sedation was evaluated using Ramsay Sedation Scale. Possible side effects during and after the administration of dexmedetomedine and during postoperative period were noted as well. The data were analysed in SPSS version 21. Quantitative data were described as mean and standard deviation and qualitative data as frequency distribution. For categorical data chi

square test or Fisher's exact probability test and for continuous data student's t test were used. For this study p value of less than 0.05 was considered statistically significant.

Results

A total of 60 patients were included in the present study, half of which recived dexmedetomedine and the other half placebo (normal saline). We observed that the mean age, gender distribution, ASA grade and body mass index were similar in the two groups (Table 1). We observed the mean heart rate to be significantly lower among patients in the dexmedetomedine group as compared to the control group 3 minutes and later after infusion (Fig. 1). Mean systolic, diastolic and mean arterial blood pressures was significantly lower in the dexmedetomedine group 1 minute after infusion and in the post-intubation phase (Figs. 2, 3 and 4 respectively). We observed that SpO_2 values were comparable in both the groups with no incidence of desaturation. Mean time to extubation and eye opening was statistically and clinically significantly prolonged in the dexmedetomedine group as compared to the control group ($p<0.01$). Also the number of bouts of cough per patient was significantly lower in the dexmedetomedine group (mean 0.46 ± 0.17) compared to the control group (mean 1.60 ± 1.10) with $p<0.01$ (Table 2). Furthermore, 93% in the dexmedetomedine group had smooth extubation (scale 1) as against 57% in the control group. Two patients in the dexmedetomedine group had minimal coughing (scale 2) as compared to 8 patients patients in the control group. In addition, patients in the dexmedetomedine group were calm and tranquil compared to control group at extubation, and post extubation period (Fig. 5). The incidence of hypertension and tachycardia was significantly higher among patients in the dexmedetomedine group as compared to the control group (Table 3). However, both the conditions were transient and did not necessitate treatment. Cases of laryngospasm, bronchospasm and desaturation were not observed in either of the groups.

Table 1: Baseline characteristics of the patients included in the study

	Dexmedetomidine group	Control group	p value
Mean age (SD) in years	31.53 (9.19)	32.19 (10.85)	0.7
Gender distribution			
Male	22	21	1.0
Female	8	9	
ASA grade			
I	23	22	1.0
II	7	8	
Mean BMI (SD) in kg/m2	21.44 (3.21)	21.47 (2.91)	0.8

Table 2: Comparing extubation related variables among patients in the two groups

	Dexmedetomidine group	Control group	p value
Mean time to extubation (SD) in minutes	18.27 (1.89)	14.57 (2.2)	<0.01
Mean time to eye opening (SD) in minutes	17.73 (2.2)	13.70 (1.89)	<0.01
Mean number of bouts of cough per patient (SD)	0.46 (0.17)	1.60 (1.1)	<0.01
Extubation quality on a 5 point scale			
Scale 1	28	17	<0.01
Scale 2	2	8	
Scale 3	0	4	
Scale 4	0	1	
Scale 5	0	0	

Table 3: Complication among patients in the two treatment groups

Complications	Group		Total	p- value
	Dexmedetomidine	Control		
Hypotension	0 0.0%	4 13.3%	4 6.7%	0.112
Hypertension	25 83.3%	0 0.0%	25 41.7%	<0.01
Bradycardia	0 0.0%	2 6.7%	2 3.3%	0.492
Tachycardia	26 86.7%	0 0.0%	26 43.3%	<0.01
Agitation	6 20.0%	0 0.0%	6 10.0%	0.024
Laryngospasm	0 0.0%	0 0.0%	0 0.0%	NA
Bronchospasm	0 0.0%	0 0.0%	0 0.0%	NA
Desaturation	0 0.0%	0 0.0%	0 0.0%	NA
Coughing	11 36.7%	4 13.3%	15 25.0%	0.072

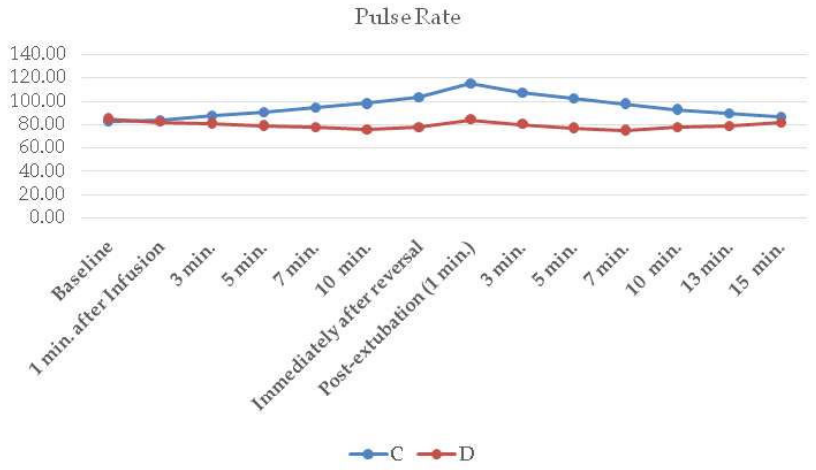

Fig. 1: Comparing the study groups based on mean heart rate change

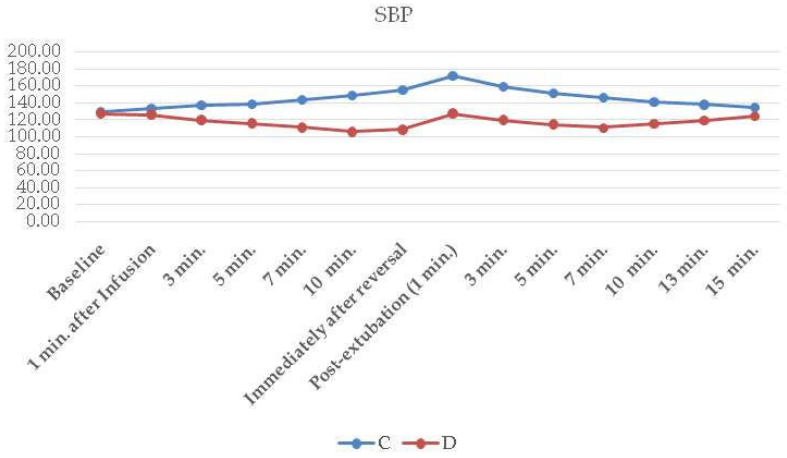

Fig. 2: Comparing the study groups based on mean change in systolic blood pressure

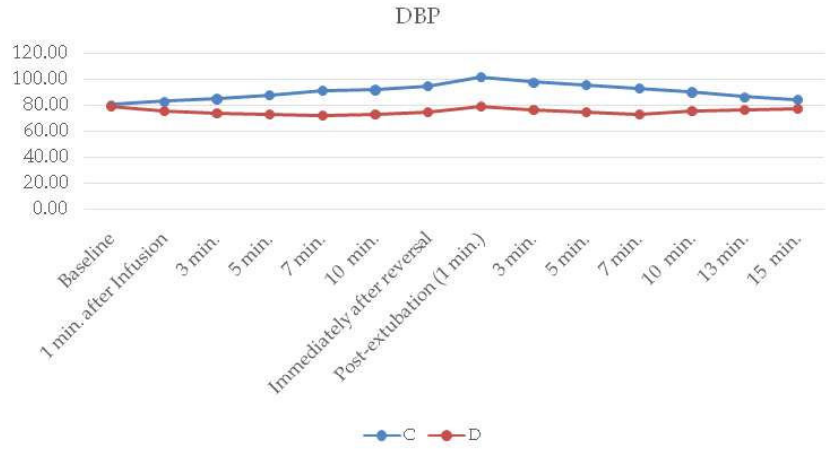

Fig. 3: Comparing the study groups based on mean change in diastolic blood pressure

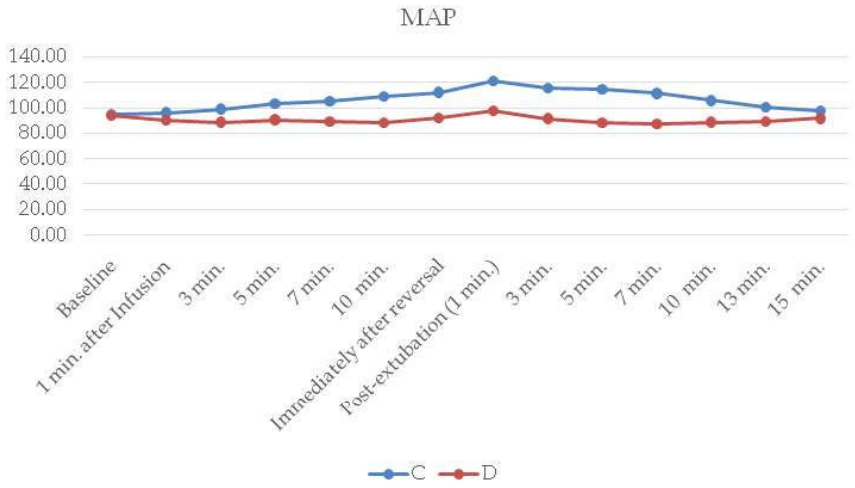

Fig. 4: Comparing the study groups based on mean change in mean arterial blood pressure

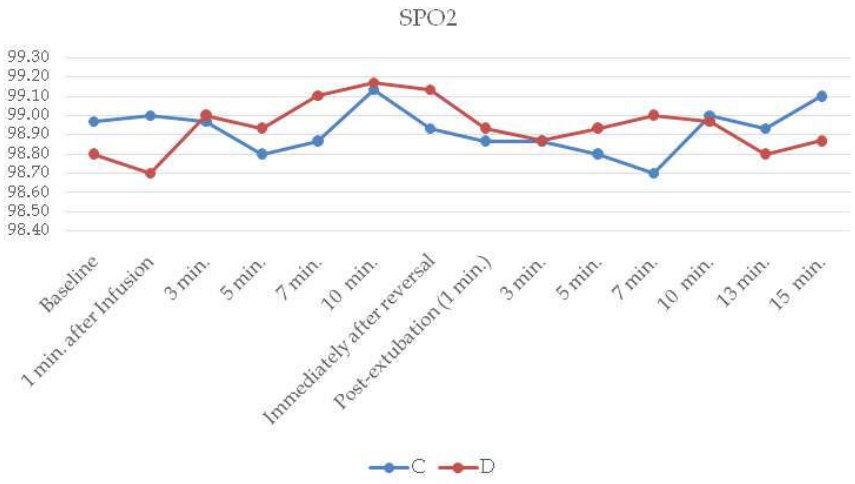

Fig. 5: Comparing the study groups based on mean change in SpO_2

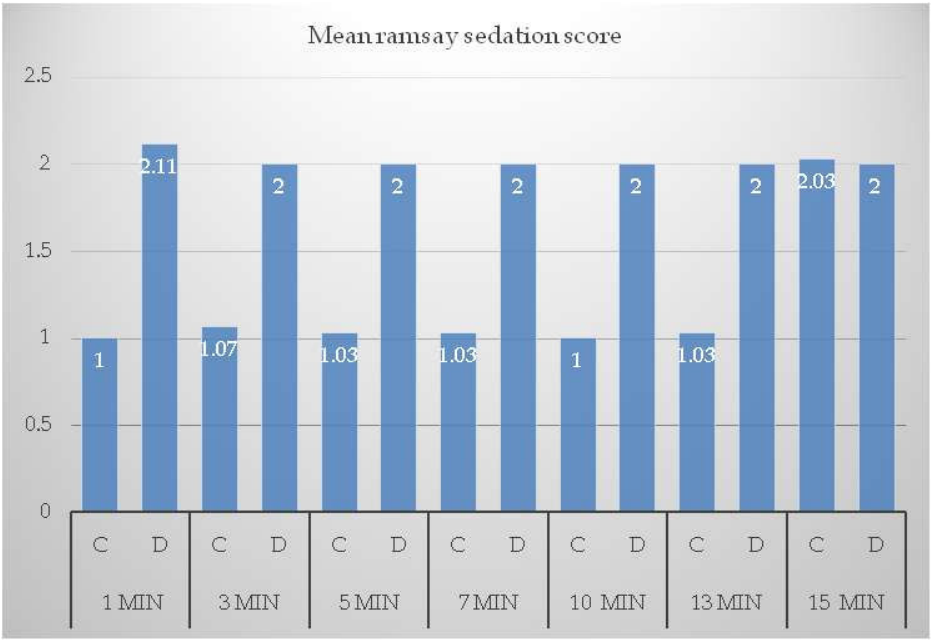

Fig. 6: Comparing post-extubation mean Ramsay Sedation Score in the two study groups

Discussion

Attenuating stress response during extubation has been attempted by numerous pharmacological and non-pharmacological methods. Dexmedetomidine, an imidazole derivative, is a full adrenoceptor agonist with high selectivity for α_2- compared with α_1-adrenergic receptors [5]. In the present study, a total of sixty patients were allocated randomly to receive either dexmedetomedine 0.5 µg/kg body weight diluted to 20 ml in normal saline, over 10 minutes with syringe pump or normal saline 20 ml over 10 minutes with syringe pump. We observed the mean heart rate to be significantly lower among patients in the dexmedetomedine group as compared to the control group 3 minutes and later after infusion. Similarly, the mean systolic, diastolic and mean arterial blood pressures was significantly lower in the dexmedetomedine group 1 minute after infusion and in the post-intubation phase. Variations in heart rate and blood pressures have been reported by various authors and seems to be affected by the dose of dexmedetomedine used in the study. Aantaa showed that dexmedetomidine 1 µg/kg decreased heart rate by 18%, but they observed no changes in heart rate with doses of 0.5 µg/kg [6]. In addition, infusion speed, premedication and fluid infusion before drug administration also affect the outome, as has been demonstrated by Antaa. Lawrence and Lange did not observe any change in systolic blood pressure after laryngoscopy and endotracheal intubation with dexmedetomidine 2 µg/kg, but diastolic pressure increased by 1% [7]. They also showed that if the effects of different doses of dexmedetomidine were evaluated with respect to heart rate, 0.67 µg/kg and 1 µg/kg doses significantly decreased heart rate. It appears from this data that the haemodynamic responses to endotracheal intubation is reduced with dexmedetomidine, i.e. a small increase in heart rate causes a small increase in arterial pressure.

α_2-adrenoceptors do not have an active role in the respiratory centre [8]. The minimal ventilatory effects of dexmedetomidine indicate that α_2-adrenergic agonists may be useful drugs for providing sedation and analgesia without ventilatory depression in healthy young patients. However, dexmedetomedine in doses up to 2 µg/kg has been shown to cause mild ventilatory depression, but this was not significantly different from that seen with placebo [9]. Hall et al. [15] showed that SpO_2 did not decrease below 95% with dexmedetomidine 0.2 µg/kg and 0.6 µg/kg infusions for 50 minutes after a 10-minute infusion of dexmedetomidine 6 µg/kg. Moreover, though not studied in the present study, the effects of dexmedetomedine on the central nervous system has been shown to reduce the anaesthetic drug requirement [10]. Aho et al. showed that, in patients who were scheduled for abdominal hysterectomy, a dexmedetomidine infusion reduced the isoflurane requirement by 90% [11]. Even in animal models, the induction dose of thiopental was reduced due to the effect of dexmedetomedine [10]. Aantaa et al.

also reported a decrease in thiopental requirement by 55% with dexmedetomidine 1 µg/kg and by 37% with a dexmedetomidine dose of 0.5 µg/kg [12].

We observed that the mean time to extubation and eye opening was statistically and clinically significantly prolonged in the dexmedetomedine group as compared to the control group. Guler et al. reported similar results [13]. In addition, 93% in the dexmedetomedine group had smooth extubation (scale 1) as against 57% in the control group and only two patients in the dexmedetomedine group had minimal coughing (scale 2) as compared to 8 patients patients in the control group. This is similar to that reported by Guler et al. [13], who found that dexmedetomedine facilitated tolerance of the endotracheal tube and significantly reduced coughing during extubation without affecting the emergence time. The incidence of hypertension and tachycardia was significantly higher among patients in the dexmedetomedine group as compared to the control group. However, both the conditions were transient and did not necessitate treatment. In the study by Guler et al., bradycardia occurred in one patient and hypotension in three, within 3 min of dexmedetomidine administration. Some studies have also shown dry mouth, fatigue, anxiety and mild headache to be frequent adverse effects of dexmedetomidine [14].

Conclusion

The results of our study demonstrate that single bolus dose of dexmedetomidine 0.5 µg/kg body weight administered as infusion over 10 minutes, before tracheal extubation attenuates the airway reflexes and hemodynamic responses effectively during emergence from anaesthesia providing smooth extubation. Future studies are required to compare the effect of different doses and modes of administration of dexmedetomedine.

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