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THE EFFECT OF DEXMEDETOMIDINE ON HEMODYNAMIC AND RECOVERY RESPONSES DURING TRACHEAL EXTUBATION IN PATIENTS UNDERGOING ELECTIVE GENERAL SURGICAL AND UROLOGICAL PROCEDURES

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ABSTRACT

Aims: To study the effects of dexmedetomidine in attenuating the hemodynamic response to extubation and emergence from anaesthesia. To study effect on the quality of extubation, postoperative sedation and any side effects. **Settings and Design:** Prospective, randomized, double‑blind study. **Subjects and Methods:** 80 patients of either sex between 20 and 50 years of age belonging to ASA-I and II, undergoing general surgical procedures and urological procedures were selected for the study .Patients were randomly allocated to two equal groups of 40 each to receive either dexmedetomidine 0.75 microgram/kg (Group A) or Normal Saline (Group B) over a period of 10 minutes, 10 minutes prior to anticipated extubation. Heart rate, systolic blood pressure, diastolic blood pressure, SpO2 was recorded at base line and at the start of drug injection, at 1, 5, 8 and 10 minutes after the start of drug infusion and thereafter at the time of extubation and at 1, 3 and 5 minutes after extubation, followed by every 5 minutes for 30 minutes. Quality of extubation was evaluated based on cough immediately after extubation using 5 point rating scale (extubation quality score). Post-operative sedation was evaluated on a Ramsay sedation scale (6 point scale) at extubation and thereafter at every 15 minutes for 1 hour. Occurrence of any event like laryngospasm, bronchospasm, desaturation, respiratory depression, vomiting was noted. **Results:** Heart rate, systolic, diastolic, mean arterial pressures were significantly higher in group B ($P < 0.05$). Extubation quality score of majority of patients was superior in group A than in group B. Sedation score of most patients was 3 in group A and 2 in group B. Bradycardia and hypotension incidences were higher in group A. The incidence of adverse effects was statistically insignificant between the two groups (p valve>0.05). No patient had any other side effects. **Conclusion:** Dexmedetomidine 0.75 microgram per kg intravenous infusion administered over a period of 10 minutes, just prior to extubation was effective in attenuating the haemodynamic stress response during tracheal extubation with minimal adverse effects.

KEYWORDS: dexmedetomidine, extubation, hemodynamics.

INTRODUCTION

Tracheal extubation is the discontinuation of an artificial airway when the indications for its placement like airway obstruction, protection of airway, suctioning, ventilatory failure and hypoxemia no longer exist. For a smooth extubation, there should be no straining, movement, coughing, breath holding or laryngospasm. Extubation at light levels of anesthesia or sedation can stimulate reflex responses via tracheal and laryngeal irritation. Various agents like lidocaine, opioids, esmolol, calcium channel blockers,[1,2] magnesium sulphate and propofol have been shown to attenuate these responses, but they all have limitations and side effects. Dexmedetomidine, an α2-adrenoreceptor agonist with a distribution half-life of approximately 6 minutes has been successfully used for attenuating the stress response to laryngoscopy.[3,4] 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.[5] We hypothesized that dexmedetomidine might be a useful agent to attenuate the response to extubation as it provides sedation, hemodynamic stability and does not depress respiration. We designed this prospective, randomized, double blind trial to determine if dexmedetomidine can serve as an effective alternative to the commonly used agents for

blunting the hemodynamic response to tracheal extubation. The aim of the study was to evaluate the effect of dexmedetomidine on hemodynamic and recovery responses during extubation, quality of extubation and postoperative sedation.

MATERIALS AND METHODS

This prospective, randomized, double blind, controlled study was conducted in the Department of Anaesthesiology and Critical Care at Sher-i-Kashmir Institute of Medical Sciences Srinagar Kashmir from June 2013 to June 2015. After institutional ethical committee approval, 80 patients of either sex between 20 and 50 years of age belonging to ASA-I and II, undergoing general surgical procedures and urological procedures were selected for the study. Patients were excluded from the study with ischemic heart disease, 2nd and 3rd degree heart block, uncontrolled hypertension, uncontrolled diabetes, any medication that affect heart rate or blood pressure, pregnant and breast feeding women, expected difficult intubation and history of allergy to study drugs. During the pre-operative visit, all patients were clinically evaluated, assessed and investigated. The study protocol was explained to the patients and a written informed consent was taken. No patient was given any premedication. Routine anesthetic technique was used using propofol, fentanyl, atracurium, nitrous oxide-oxygen and isoflorane. Standard monitoring with electrokardiography (EKG), pulse oximetry (SpO_2) and noninvasive BP was done. About 10 minutes before the estimated time of end of surgery, inhalation agent was cut off and patients in each group received the specified solution intravenously over 10 minutes. In order to attain double blinding, the person who was not involved in recording the data prepared the dexmedetomidine 0.75 microgram/kg or Normal Saline to a total of 50 ml volume infused. Patients were randomly allocated to two equal groups of 40 each by means of a computer generated table of random numbers to receive either dexmedetomidine 0.75 microgram/kg (Group A) or Normal Saline (Group B) over a period of 10 minutes, 10 minutes prior to extubation.

HR, systolic BP and diastolic BP were recorded at the start of bolus drug injection and thereafter at 1, 3, 5, 8 and 10 minutes. Residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg IV. When patients' spontaneous respirations were considered sufficient and patients were able to obey simple commands, suction of throat was done and trachea was extubated. The anesthesiologist performing the extubation was blinded to the study drugs. HR, systolic BP and diastolic BP were recorded at the time of extubation and thereafter at 1, 3 and 5 minutes after extubation followed by every 5 minutes for 30 minutes. Occurrence of any event like laryngospasm, bronchospasm, desaturation, respiratory depression, vomiting, hypotension, bradycardia or undue sedation was noted.

Quality of extubation was evaluated by means of Extubation Quality Score[6] using 5 point rating scale. 1 = No coughing; 2=Smooth extubation, minimal coughing (1 or 2 times); 3=Moderate coughing (3-4 times); 4=Severe coughing and straining (5-10 times); 5=Poor extubation, very uncomfortable (laryngospasm and cough 10 times).

Post operative sedation was evaluated using Ramsay sedation scale[7] (6 point scale) at extubation and thereafter at every 15 minutes for 1 hour. 1=Anxious or agitated and restless or both; 2=Cooperative, oriented and tranquil.; 3=Drowsy but responds to commands; 4=Asleep, brisk response to light glabellar tap or loud auditory stimulus; 5=Asleep, sluggish response to light glabeller tap or loud auditory stimulus; 6=Asleep and un arousabe.

Table 1 Demographic profile of two groups

	Group A (Mean± SD)	Group B (Mean± SD)	p value
Age	35.5±7.147	36.7±7.741	0.492
Weight	60.2±6.92	60.6±6.258	0.761
Sex	17/23	19/21	0.653

Statistical software SPSS (version 16.0) and Microsoft Excel were used to carry out the statistical analysis of data. Data was analysed by means of descriptive statistics viz, means, standard deviations and percentages. Chi-square test or Fisher's exact test, whichever appropriate, was used for qualitative data. Student's independent t-test was employed for inter group analysis. Graphically the data was presented by bar and line diagrams. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The patients in the two groups were comparable for age, weight and male: female ratio and the difference between the two groups was not statistically significant ($P > 0.05$) Table 1.

We observed a statistically significant difference ($P < 0.05$) in HR between the two groups from 5 minutes after starting administration of the agent till 60 minutes after extubation Table 2. A statistically significant difference was observed in systolic BP between the two groups ($P < 0.05$) from 8 minutes after start of administration of the agent and continued till the time observations were made Table 2. Our study showed a significant difference in diastolic BP between the two groups ($P < 0.05$) from 8 minutes after starting the administration of the agent and continued till the time observations were made Table 2. The mean arterial pressure between the two groups showed statistically significant difference ($P < 0.05$) from 8 minutes after starting administration of the agent and continued till the time observations were made Table 2.

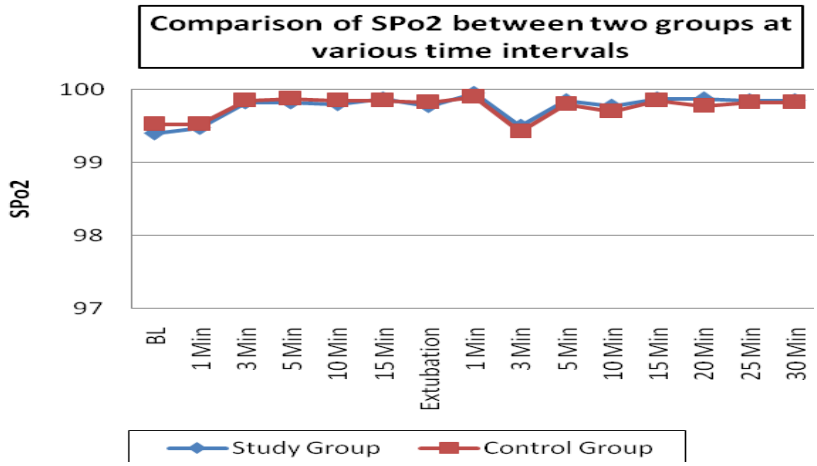

Fig.1: comparison of spo_2 between two groups.

In Group A, 82.5% patients had extubation quality score of 2, 12.5% patients had extubation quality score of 3 and 5% patients had extubation quality score of 1. In Group B, 75% patients had extubation quality score of 3, 12.5% patients had extubation quality score of 4, 10% patients had extubation quality score of 2 and 2.5% patients had extubation quality score of 1 table3.

TABLE 3: Comparison of Extubation quality score between two groups

Score	Group A (n=40)		Group B (n=40)	
	No. of Patients	%age	No. of Patients	%age
1(No coughing)	2	5	1	2.5
2(Smooth extubation, minimal coughing (1 or 2 times)	33	82.5	4	10
3(Moderate coughing (3-4 times)	5	12.5	30	75
4(Severe coughing and straining (5-10 times)	0	0	5	12.5
5(Poor extubation, very uncomfortable (laryngospasm and cough 10 times).	0	0	0	0
P-value<0.001 (Sig.)				

We did not observe statistically significant difference in any adverse effects between the two groups with a p value of > 0.05 Table 4.

Table 4: Comparison of Adverse Effects between two groups:

Adverse effects	Group A(n=40)		Group B(n=40)		P-value	Remarks
	No. of Patients	%age	No. of Patients	%age		
Bradycardia	2	5	0	0	0.494	NS
Hypotension	3	7.5	0	0	0.241	NS
Vomiting	1	2.5	1	2.5	1.000	NS
Larynogospasm	0	0	0	0	1.000	NS
Bronchospasm	0	0	0	0	1.000	NS
Desaturation	0	0	0	0	1.000	NS
Respiratory Depression	0	0	0	0	1.000	NS

DISCUSSION

Tracheal extubation is a critical step during emergence from general anaesthesia. Major airway complications, increased morbidity and mortality occur during extubation and emergence or during recovery in approximately one third of the reported closed claimed cases relating to anaesthesia.[8,9] These complications are due to circulatory and airway responses because of reflex sympathetic activity following stimulation of epipharyngeal and laryngo-pharyngeal structures leading to coughing, agitation, bronchospasm, tachycardia, hypertension, arrhythmias, myocardial ischemia and raised intracranial and intraocular pressures.[10] 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. Respiratory complications resulting in serious consequences (hypoxic brain injury and death) f.

TIME	HR (Mean ± SD)			SBP(Mean ± SD)			DBP(Mean ± SD)			MAP(Mean ± SD)		
	Group A	Group B	P Value	Group A	Group B	P Value	Group A	Group B	P Value	Group A	Group B	P Value
Baseline	80.13±3.75	79.43±3.94	0.418	121.35±3.68	122.30±3.02	0.187	80.90±5.42	81.80±2.67	0.349	94.38±3.60	95.31±2.05	0.160
1 Min	79.45±3.93	78.78±3.84	0.439	120.08±5.09	122.13±7.03	0.139	80.95±4.67	81.68±3.09	0.415	93.97±3.36	95.16±2.75	0.093
3 Min	78.97±4.25	80.23±4.02	0.084	122.53±4.24	123.90±5.38	0.108	80.85±6.71	82.20±6.06	0.348	94.75±4.69	96.25±4.17	0.131
5 Min	71.70±4.51	81.05±5.90	<0.001	121.78±5.01	124.01±6.75	0.087	79.53±6.55	82.18±7.42	0.094	93.61±5.84	96.14±6.09	0.062
8 Min	69.28±4.04	81.25±3.10	<0.001	116.48±3.30	129.60±3.62	<0.001	76.13±2.48	85.90±2.18	<0.001	89.58±1.99	100.42±2.08	<0.001
10 Min	65.05±5.10	85.33±3.83	<0.001	112.15±3.11	131.33±3.39	<0.001	73.83±4.08	89.90±4.25	<0.001	86.60±3.13	103.71±2.97	<0.001
Reversal	72.08±5.23	99.55±3.23	<0.001	119.20±2.97	149.40±3.55	<0.001	76.90±4.30	101.00±3.68	<0.001	90.99±3.23	117.15±2.69	<0.001
Extubation	81.78±3.46	119.85±3.89	<0.001	127.30±3.42	165.80±8.72	<0.001	83.28±3.12	109.68±3.16	<0.001	97.97±2.15	128.39±3.16	<0.001
1 Min	82.23±4.57	110.78±4.24	<0.001	126.38±3.34	155.48±2.91	<0.001	82.60±4.41	103.85±2.82	<0.001	97.21±3.04	121.06±2.12	<0.001
3 Min	80.83±4.29	100.10±3.66	<0.001	122.08±2.03	144.03±2.62	<0.001	75.25±4.17	93.40±4.18	<0.001	90.87±2.99	110.28±2.82	<0.001
5 Min	77.38±4.37	92.73±3.86	<0.001	117.03±3.27	134.30±3.25	<0.001	70.50±3.54	85.93±2.26	<0.001	86.02±2.88	102.07±1.80	<0.001
10 Min	73.20±4.34	86.10±3.29	<0.001	113.60±3.02	125.20±2.88	<0.001	69.30±3.44	84.08±3.72	<0.001	84.07±2.41	97.78±2.95	<0.001
15 Min	69.48±3.06	79.05±3.90	<0.001	110.30±4.57	122.83±2.45	<0.001	69.78±3.87	82.55±4.19	<0.001	83.30±3.15	95.98±3.10	<0.001
20 Min	70.38±3.91	78.90±4.07	<0.001	107.38±5.26	122.55±3.00	<0.001	66.28±5.50	82.98±4.06	<0.001	79.97±4.58	96.18±2.84	<0.001
25 Min	68.88±5.02	78.93±3.75	<0.001	107.93±4.84	121.70±2.54	<0.001	65.50±1.96	81.08±1.91	<0.001	79.64±1.81	94.62±1.57	<0.001
30 Min	68.35±4.32	79.18±3.84	<0.001	107.80±3.67	121.43±2.16	<0.001	65.10±3.67	81.83±4.55	<0.001	79.37±2.96	95.02±3.16	<0.001
Overall Mean±SE	74.33±1.74	88.26±1.49	<0.001	117.11±1.15	132.29±1.46	<0.001	74.79±1.53	88.13±1.40	<0.001	88.89±1.07	102.85±0.95	<0.001

following tracheal extubation have been thrice more common than those occurring during intubation (4.6% versus 12.6%).[13-19]

Dexmedetomidine has been successfully used to attenuate the hemodynamic responses to tracheal intubation. Basing on its characteristics of sedation, hemodynamic stability and lack of respiratory depression, along with its relatively short half-life and analgesic effects, the present study was conducted to evaluate the effect of dexmedetomidine in a dose of 0.75 mcg/kg on hemodynamic responses during extubation, the quality of extubation, the level of postoperative sedation and the prevalence of complications.

The dose of dexmedetomidine ranges from 0.5-1 mcg/kg.[11] A pilot study, using three different doses (0.5 µg/kg, 0.75 µg/kg and 1 µg/kg) of dexmedetomidine, was conducted. In this pilot study, a dose of 1 mcg/kg resulted in hemodynamic instability while a dose of 0.5 mcg/kg gave insignificant results. The present study was therefore, conducted with a dose of 0.75 mcg/kg, although there is evidence in favor of a dose of 0.5 mcg/kg.[12]

In the present study, the hemodynamic parameters in the study group were significantly stable during extubation when compared to the control group. Dexmedetomidine 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. Dexmedetomidine 0.5 mcg/kg administered 5 minutes before the end of surgery has been shown to stabilize hemodynamics, allow easy extubation, provide a more comfortable recovery and allow early neurological examination following intracranial operations.[13] Dexmedetomidine 0.5 mcg/kg, given 5 minutes before extubation has been found to be more effective than fentanyl 1 mcg/kg in attenuating airway reflex responses to tracheal extubation and maintaining hemodynamic stability without prolonging recovery.[14] In patients undergoing vascular surgery, dexmedetomidine (plasma concentrations in the range of 0.18 to 0.35 ng/ml) attenuated the increase in HR and plasma norepinephrine concentrations during emergence from anesthesia and did not attenuate postoperative increases in HR or BP after emergence from anesthesia or affect intraoperative anesthetic or postoperative analgesic requirements.[15] An infusion of dexmedetomidine started 20 minutes before anesthesia and continued until the start of skin closure in patients undergoing supratentorial brain tumor surgery was found to blunt tachycardic response to intubation and the hypertensive response to extubation.[16]

We found that most patients in study group were drowsy but responding to verbal commands (Ramsay Sedation Scale 3) after extubation when compared to control group, where most patients belonged to Ramsay Sedation Scale 2. Central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus coeruleus in the brainstem plays a prominent role in the sedation and anxiolysis produced by dexmedetomidine. Decreased noradrenergic output from the locus coeruleus allows for increased firing of inhibitory neurons including the g-amino butyric acid system resulting in anxiolysis and sedation. Dexmedetomidine 0.25 mcg/kg/hour has been used for sedation during mechanical ventilation in pediatric patients and found to be as effective as midazolam 0.22 mg/kg/hour.[17] The quality of sedation is better and the need for rescue sedation is less with dexmedetomidine use as compared with midazolam and there is no significant adverse effect on hemodynamic or respiratory function.[18]

In our study, the incidence of bradycardia and hypotension was higher in study group than in control group. The activation of α2 adrenoceptors, imidazoline-preferring receptors, or both in the ventrolateral medulla and especially in the solitarius nucleus tract by dexmedetomidine causes bradycardia. Dexmedetomidine 2.5mcg/kg followed by 0.2-2.5mcg/kg/hour has been found to reduce HR in patients.[19] A higher frequency of postoperative hypotension has been reported when patient controlled analgesia with dexmedetomidine is administered.[20]

Our study found insignificant difference in the incidence of vomiting between the two groups. However, others have found a higher, though not statistically significant, prevalence of adverse events (i.e., hypotension, bradycardia, and perioperative nausea and vomiting) with use of dexmedetomidine.[21] In our study, none of the patients in either group developed respiratory depression, laryngospasm, bronchospasm, undue sedation or desaturation. Similar findings have been made by Guler et al.[22] Dexmedetomidine use in morbidly obese patients has been found not to induce respiratory depression at clinical doses although it improved quality of postoperative analgesia.[17]

To conclude, use of dexmedetomidine before extubation attenuates the hemodynamic response to extubation. It enables smooth extubation of the trachea and provides adequate sedation postoperatively. Dexmedetomidine increases the incidence of bradycardia and hypotension, but does not cause side effects like respiratory depression, laryngospasm, bronchospasm, undue sedation and desaturation.

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