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EFFECT OF BOLUS DOSE OF DEXMEDETOMIDINE ON HEMODYNAMIC RESPONSES AND AIRWAY REFLEXES DURING TRACHEAL EXTUBATION: DOUBLE BLIND, RANDOMIZED, CONTROLLED TRIAL STUDY

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ABSTRACT

Background: To study the effect of bolus dose of dexmedetomidine on hemodynamic responses and airway reflexes during extubation. **Methods:** After obtaining institutional ethical committee approval and informed written consent 60 patients of ASA grade I and II in the age group of 18–50 years of either sex undergoing elective surgeries were included. At the closure of skin incision, patients received either dexmedetomidine 0.5 µg/kg (Group D) or saline (Group C) intravenously over 10 minutes. Hemodynamic parameters were assessed before, during and after extubation. Time to eye opening and extubation, side effects recorded. Extubation quality rated using 5-point scale. Sedation rated using Ramsay Sedation Scale. **Results:** Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were increased more in Group C. Time to extubation and eye opening were prolonged in Group D. Incidence of coughing & Agitation was more in Group C, hypotension was more in Group D. In dexmedetomidine group patients were more sedated post extubation. Extubation quality was better in dexmedetomidine group. **Conclusions:** We conclude that single- dose of dexmedetomidine 0.5 µg/kg body weight given over 10 minutes before extubation attenuates the hemodynamic and airway reflexes during emergence from anesthesia without causing undue sedation, but may prolong time to extubation and eye opening.

KEYWORDS: Airway reflexes, Dexmedetomidine, Extubation, Hemodynamic responses.

INTRODUCTION

Laryngoscopy and tracheal intubation in adults are commonly accompanied by increase in arterial blood pressure (BP) and heart rate (HR).[1] Emergence from general anesthesia and tracheal extubation are also often accompanied by tachycardia and hypertension and is of equal concern as intubation response. [2]

Tracheal intubation and extubation are accompanied by raised sympathoadrenal activity with an increased plasma catecholamine levels which cause an increase in HR, BP, myocardial contractility and increased systemic vascular resistance.[3,4] The peak changes are noticed about 1 minute following extubation and may continue until 10 minutes. Majority of the patients tolerate these changes without any significant clinical consequences[5] but patients suffering from diseases like hypertension and diabetes may not tolerate these responses.

Alpha2-agonists simultaneously potentiate the effects of general anesthetics, reduce their dose requirements, and attenuate sympathoadrenal responses to noxious stimuli encountered during anesthesia and surgery, thus providing improved hemodynamic, metabolic, and hormonal stability [9] Clonidine has been studied in this aspect.

Dexmedetomidine, a newer drug in this class is a highly selective alpha2-adrenergic agonist. It has sedative, anxiolytic and analgesic actions as well. It is known to exhibit dose dependent attenuation of stress response to intubation. [10]

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. Aim of our study was to study the effect of bolus dose of dexmedetomidine on hemodynamic responses and airway reflexes during extubation of trachea following surgery under general anesthesia and to study the side effects of the drug if any.

MATERIALS AND METHODS

This clinical study was carried out in 60 patients admitted for various surgeries, done under general anesthesia at RL Jalappa Hospital and Research center, Tamaka Kolar, during the period of December 2011 to May 2013. Patients of American Society of Anesthesiologist (ASA) Grade I and II in the age group of 18 years to 50 years of either sex, admitted for various surgeries, done under general anesthesia, were selected for study. Patients suffering

from cardiac, pulmonary disease, history of drug allergy to dexmedetomidine, obese patients, with difficult airway or history of sleep apnoea and history of drug abuse or psychiatric disorder were excluded.

Patients were randomly divided into 2 groups of 30 each. Randomization was done by computer generated table. Group D-Dexmedetomidine group, Group C-Control group. Ethical committee approval was taken for use of the drug. An informed consent was taken from the patients. Complete hemogram, bleeding time, clotting time, blood sugar level, blood urea, serum creatinine, chest radiograph and ECG investigations were done.

All patients were examined a day before surgery. All were kept fasting overnight after 10 : 00 pm and received tab. Ranitidine 150 mg orally and tab, Alprazolam 0.5 mg orally as premedication at night before surgery and at 7 : 00 am in the morning on the day of surgery. On OT table all patients were monitored with electrocardiography, oxygen saturation, noninvasive blood pressure, end-tidal carbon-di-oxide. Base line blood pressure, pulse rate were recorded. An intravenous line was secured and all were given Ringer lactate 5 ml/kg. Premedicated with injection glycopyrrolate 5 µg/kg, injection fentanyl 2 µg/kg intravenously. Patients were preoxygenated with 100% O_2 for 3 minutes and induced with injection thiopentone 5 mg/kg and intubation facilitated with injection suxamethonium 2 mg/kg intravenously.

Trachea was intubated with a soft seal cuffed sterile poly vinyl chloride endotracheal tube of appropriate size. Endotracheal tube cuff was filled with the minimal volume of room air required to prevent an audible leak.

Anesthesia was maintained with 66% nitrous oxide in 33% oxygen and isoflurane. Muscle relaxation was achieved with injection, vecuronium 0.1 mg/kg (initial dose) and 0.02 mg/kg (repeat doses) later intravenously.

At the beginning of closure of skin incision, isoflurane was turned off and dexmedetomidine 0.5 µg/kg body weight diluted to 10 ml in normal saline was infused over 10 minutes in Group D patients. Group C patients were received a bolus of 10 ml normal saline over 10 minutes. Nitrous oxide was turned off at the end of infusion.

Residual neuromuscular blockade was reversed using injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.01 mg/kg intravenous. Patients were extubated when extubation

criteria, 1) Sustained head lift for 5 seconds, 2) Sustained hand grip for 5 seconds, 3) Obeys commands, 4) Tidal volume > 6 ml/kg were fulfilled.

Pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation -basal, prior to drug or placebo infusion, and 1, 2, 5, 7 and 10 minutes during infusion, following reversal administration, post extubation every 5 min for 15 min, thereafter every 30 min for next 2 hours.

Bradycardia was defined as HR < 60 /min and treated with rescue dose of injection atropine 0.6 mg intravenously, tachycardia being 20% increase from baseline, hypertension as either 20% increase from baseline or SBP > 180 mmHg and hypotension as 20% decrease from baseline or SBP < 80 mmHg. Extubation quality was rated using extubation quality 5-point scale, 71 = no coughing, 2 = smooth extubation, minimal coughing, 3 = moderate coughing (3 or 4 times), 4 = severe coughing (5 to 10 times) and straining, 5 = poor extubation,very uncomfortable (laryngospasm and coughing >10 times). Number of coughs per patient was monitored for 15 minute post extubation. Any incidence of laryngospasm, bronchospasm or desaturation was noted.

Time to extubation and eye opening was recorded, sedation was evaluated using Ramsay Sedation Scale. [8] At 5 minutes after extubation 1 = anxious and agitated, restless, 2 = co-operative, oriented, tranquil, 3 = responsive to verbal commands, drowsy, 4 = “asleep”, responsive to light stimulation (loud noise, tapping), 5 = asleep, slow response to stimulation, 6 = no response to stimulation.

With the power of study being 80% and confidence limits at 95% minimum sample size required to detect 30% reduction in hemodynamic parameters was 24 patients in each group. We conducted study with 30 patients in each group to make it more authentic. The parameters were recorded and data was entered into Statistical Package for Social Sciences (SPSS 15.0). Statistical analysis was done using paired-samples t-test for between-group comparisons. The χ_2 test or the Fisher exact test was used to analyze extubation quality, sedation scores, and adverse events. $P < 0.05$ was considered as statistically significant.

RESULTS

The patients in the two groups were comparable for age, weight and male:female ratio, ASA physical status, Mallampatti class, nature of surgery and the difference between the two

groups was not statistically significant (P > 0.05).

Basal HR was comparable in both groups. But it was statistically and clinically lower in study group from 2nd minute of drug infusion till the end of infusion; at reversal administration; extubation and post extubation 5, 10, 15, 30 minutes compared to basal value. SBP, DBP, MAP values were statistically and clinically significantly lower in Group D during study drug infusion; at reversal administration; extubation and post extubation 5, 10, 15, 30, 60 and 90 minutes compared to basal values.

Patients in dexmedetomidine group were significantly sedated compared to Control group at extubation and post extubation 5 and 10 minutes. Extubation quality 5- point scale was lower in study group implying smoother extubation as compared to control group, 7 patients in study group had hypotension which was statistically significant. This responded to intravenous fluids administration. In 22 patients in control group hypertension was observed which was statistically very significant. One patient in dexmedetomidine group had bradycardia, but this was transient and responded to injection atropine. Tachycardia was observed in 2 in study group as against 23 in Control group which was statistically very significant. Two patients in study group had Coughing post extubation as against 9 patients in control group which was statistically significant. Laryngospasm and desaturation (SpO_2 < 92%) was not observed in either of the groups (Table 3).

Table 1: Demographic profile of two groups

	Group=D (Mean±SD)	**Group=C (Mean±SD)**
Age(in yrs)	31.07±9.20	33.70±9.04
Male:female	14:16	10:20
Weight	56.70±9.34	56.47±7.31
ASA	I/II	I/II
MP class	I/II	I/II

Table 2a: Haemodynamic parameters

	Systolic Blood Pressure			**Diastolic Blood Pressure**		
	Group D	**Group C**	**P value**	**Group D**	**Group C**	**P value**
Base line	125.03±15.01	126.67±8.39	0.605	75.90±9.56	77.97±7.83	0.363
Prior to infusion	125.60±12.53	124.63±8.83	0.731	77.67±9.94	78.33±9.80	0.795
1 min	123.47±11.38	129.50±8.41	0.023	77.37±8.89	81.07±9.14	0.117
2 min	121.97±9.65	134.77±9.64	<0.001	75.43±8.89	83.90±8.38	<0.001
5 min	119.87±11.05	138.67±9.29	<0.001	74.47±11.62	86.00±8.41	<0.001
7 min	117.50±9.28	141.07±8.48	<0.001	72.33±7.96	88.17±8.28	<0.001

10 min	115.17±8.95	142.53±9.07	<0.001	71.20±7.98	89.63±9.04	<0.001
At reversal	119.57±10.39	146.13±9.92	<0.001	74.67±7.30	92.30±10.04	<0.001
Extubation	124.10±11.54	158.27±15.02	<0.001	78.77±10.71	99.73±11.32	<0.001
5 min	114.80±10.37	149.03±12.10	<0.001	70.53±8.79	92.73±10.19	<0.001
10 min	111.20±9.71	144.23±11.63	<0.001	67.50±8.74	90.20±9.08	<0.001
15 min	111.67±9.80	137.83±9.33	<0.001	67.57±6.78	87.00±8.98	<0.001
30 min	112.60±10.02	132.30±8.25	<0.001	69.37±6.54	83.90±9.63	<0.001
60 min	118.63±8.67	128.60±7.99	<0.001	74.00±8.35	81.77±9.41	0.001
90 min	123.17±8.20	127.53±6.75	0.028	76.17±6.72	80.17±8.38	0.046
120 min	123.63±8.83	125.27±6.77	0.425	78.37±7.07	78.40±8.30	0.987

Table 2b: Haemodynamic parameters

	Heart rate			Mean Arterial Pressure		
	Group D	**Group C**	**P value**	**Group D**	**Group C**	**P value**
Base line	85.60±11.60	83.77±7.61	0.472	95.07±8.59	95.17±6.20	0.959
Prior to infusion	87.40±13.72	84.63±5.26	0.307	94.77±9.21	93.00±9.37	0.465
1 min	85.27±13.55	87.60±4.87	0.378	92.40±8.25	96.27±7.87	0.068
2 min	83.10±13.09	90.97±7.27	0.006	90.57±7.83	99.33±7.46	<0.001
5 min	78.20±12.88	95.07±8.99	<0.001	90.73±9.98	103.03±8.78	<0.001
7 min	75.27±11.79	97.80±9.25	<0.001	87.47±7.67	104.87±7.63	<0.001
10 min	73.83±12.43	99.97±10.32	<0.001	86.00±8.16	106.80±9.18	<0.001
At reversal	78.73±12.90	104.77±8.28	<0.001	90.43±8.04	109.87±10.57	<0.001
Extubation	85.53±14.12	115.97±8.72	<0.001	94.93±10.71	118.17±12.17	<0.001
5 min	77.83±14.29	105.80±8.83	<0.001	86.10±9.06	110.63±12.23	<0.001
10 min	73.87±13.71	96.90±8.48	<0.001	81.27±7.67	106.10±9.74	<0.001
15 min	74.40±12.59	93.47±6.96	<0.001	81.83±6.67	101.70±10.04	<0.001
30 min	73.93±11.56	89.63±6.72	<0.001	83.93±7.23	98.53±9.69	<0.001
60 min	77.53±10.72	84.30±6.28	0.004	89.67±8.24	95.90±9.01	0.007
90 min	80.53±11.09	83.37±5.03	0.208	91.57±5.85	95.60±7.21	0.021
120 min	83.27±11.46	83.03±7.08	0.925	92.93±7.36	94.60±6.56	0.359

Table 3: Comparison of side effects

Side effects	**Group D (n=30)**		**Group C (n=30)**		**P value**
	No	**%**	**No**	**%**	
1.Hypotension	7	23.3	0	0.0	0.011*
2.Hypertension	0	0.0	22	73.3	<0.001**
3.Bradycardia	1	3.3	0	0.0	1.000
4.Tachycardia	2	6.7	23	76.7	<0.001**
5.Agitation	0	0.0	5	16.7	0.052+
6.Coughing	2	6.7	9	30.0	0.020*
7.Laryngospasm	0	0.0	0	0.0	-
8.Bronchospasm	0	0.0	0	0.0	-
9.Desaturation	0	0.0	0	0.0	-

DISCUSSION

Emergence from general anesthesia and tracheal extubation are also often accompanied by tachycardia and hypertension and is of equal concern as intubation response.[2] These responses may produce myocardial ischemia or infarction in susceptible patients. Alpha2-agonists decrease the sympathetic outflow and noradrenergic activity, thereby counteracting hemodynamic fluctuations occurring at the time of extubation due to increased sympathetic stimulation. [11] This study was designed to assess the degree of attenuation of hemodynamic responses and airway reflexes to extubation of trachea by administration of dexmedetomidine at the dosage of 0.5 μg/kg body weight.

In our study in the study group we observed that HR did not show a significant rise compared to basal value from 2nd minute of drug administration, during reversal, at extubation and any period post extubation. But in control group, there was a significant rise in HR compared to basal value. Incidence of tachycardia was 77% in control group vs. 7% in study group. The rise in HR in control group was more persistent than study group.

This observation is in concurrence with the study done by Jain et al. [11] where the pulse rate in study group remained below the pre-DEX values (baseline value) at all times intervals following extubation.

Bradycardia was observed in 1 patient (3%) in study group which responded to injection atropine. This is in conjunction with the observation by Aksu et al. [12]

SBP, DBP and MAP values were significantly lower in study group compared to baseline values at all times from the time of dexmedetomidine infusion to post extubation 30 minutes. This is in conjunction with the study conducted by Bindu et al. [13] in which study group patients received 0.75 μg/kg of dexmedetomidine and they did not observe any significant change ($P < 0.05$) in the blood pressure in dexmedetomidine group throughout the study period.

Dexmedetomidine by virtue of its analgesic and sedative properties is known to blunt airway reflexes. 93% patients in study group had smooth extubation as against only 67% patients in control group. Incidence of coughing was significantly higher in control group than when compared to study group (33 vs. 7% respectively). This is in accordance with study done by Aksu et al. [12] Guler et al. [14] noted the effect of dexmedetomidine on children undergoing

adenotonsillectomy where in dexmedetomidine group had significantly decreased incidence and severity of agitation and a smooth extubation without any increase in incidence of side effects.

SpO_2 values were comparable in both the groups with no incidence of desaturation. Also, no bronchospasm or laryngospasm was observed in either of the groups. These observations are in concurrence with study conducted by Aksu et al. [12]

Sedation in our study was assessed using Ramsay Sedation Scale. Significant number of patients in study group (46%) were drowsy but responded to oral commands (score of 3) following extubation as against 80% of patients in control group were co-operative and oriented (score of 2). This observation is in agreement with the comparative study done between dexmedetomidine and fentanyl in those undergoing rhinoplasty by Basar et al. [10] But, in contrast to Jain et al. [11] who did not notice sedation in both the groups probably because of the difference in the anesthetic technique employed by the authors.

Agitation was observed in 5 patients (17%) in Group C following extubation whereas none were agitated in Group D. This is statistically and clinically significant ($P < 0.001$). This observation is in conjunction with study done by Guler et al. [14] who conducted a study on the effect of single- dose dexmedetomidine in reducing the agitation and providing smooth extubation after pediatric adenotonsillectomy.

Guler et al. [14] in their study on emergence agitation in children undergoing adenotonsillectomy observed that time to extubation and emergence were prolonged significantly when compared to control group with $P < 0.05$. (5.03 ± 2.3 vs 3.30 ± 1.3 minutes and 9.30 ± 2.9 vs 7.20 ± 2.7 minutes, respectively).

This observation is in agreement with our study conducted wherein time to extubation and eye opening (i.e, interval between cut off of nitrous oxide to extubation and eye opening respectively) were significantly prolonged in dexmedetomidine group when compared to control group. (19.03 ± 3.90 vs 15.23 ± 1.74 minutes and 17.47 ± 3.63 vs 14.03 ± 1.75 minutes, respectively).

We conclude our study demonstrates that single- dose of dexmedetomidine 0.5 µg/kg body weight administered over 10 minutes, before tracheal extubation attenuates the airway and hemodynamic reflexes during emergence from anesthesia providing smooth extubation

without causing undue sedation.

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