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Original Article

A Comparative Study of Effects of Three Different Doses of Dexmedetomidine on Extubation

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Abstract

Background and Aim: *Dexmedetomidine is a α_2 agonist with sedative, sympatholytic and analgesic properties and hence, it can be a very useful drug in anaesthesia to blunt the stress response to extubation, the smooth emergence of anaesthesia. We aimed primarily to evaluate the effects of three doses of dexmedetomidine on haemodynamic response to extubation in patients undergoing elective general surgery. The secondary aims were to observe the effects on extubation quality, sedation levels and occurrence of adverse effects.*

Methods: *90 patients of the American Society of Anaesthesiologists(ASA) physical grades I and II were randomly allocated into three groups. Group A patients 0.5mcg/kg, Group B 0.75mcg/kg and Group C 1.0 mcg/kg dexmedetomidine infusion, starting 15 minutes before extubation. Parameters noted were pulse rate, mean arterial pressure, oxygen saturation, post-operative sedation,coughing on extubation and any adverse effect .*

Results: *The three doses of dexmedetomidine were able to maintain hemodynamic stability on tracheal extubation. But significant changes in hemodynamic parameters were noted in group A at 3 and 15 minutes post extubation (P <0.05). The post extubation haemodynamically stability was statistically better in group A and group B as compared with group C (P<0.05). Time for extubation and eye opening was prolonged in Group C (P <0.001). The Incidence of hypotension and bradycardia were noted in group C (6.66% and 3.33%) but was transient. Incidence of coughing was lower in Group B (P <0.05). Patients in group C were more sedated for 30 minutesutes post extubation. No significant side effects were noted.*

Conclusion: *Dexmedetomidine 0.5 µg/kg,0.75 µg/kg and 1.0 µg/kg given before 15 minutes of extubation attenuates hemodynamic reflexes during emergence from anesthesia without causing undue sedation, but higher dose1.0 µg/kg were associated with more post extubation sedation and some undesirable adverse affect hypotension and bradycardia.*

Keywords: *Dexmedetomidine, general anesthesia, extubation, hemodynamic responses, quality of extubation.*

Introduction

Anaesthetic maneuvers like direct laryngoscopy, tracheal intubation and extubation involve severe sympathetic stimulation accompanied by increased plasma catecholaminutese levels, which cause tachycardia, increase myocardial contractility and systemic vascular resistance.[1,2]

For a smooth extubation, there should be no straining, movement, coughing, breath holding or laryngospasm. Extubation at light levels of anaesthesia or sedation can stimulate reflex responses via tracheal and laryngeal irritation.

Various agents like lidocaine[3], opioids[4], esmolol, and calcium channel blockers,[5] have been shown to attenuate these responses, but they all have limitations and side effects.

Dexmedetomidine is the most recent agent in this group approved by FDA in 1999 for use in humans for analgesia and sedation.

Dexmedetomidine, an alpha-2adrenoreceptor agonist with a distribution halflife of approximately 6 minutes has been successfully used for attenuating the stress response to laryngoscopy[6,7] and extubation.

Dexmedetomidine a useful agent to attenuate the response to extubation as it provides sedation, hemodynamic stability and does not depress respiration. The dose of Dexmedetomidine ranges from 0.5-1 mcg/kg[8]. Dexmedetomidine provides a unique quality of conscious sedation which resembles natural sleep. Its administration does not result in respiratory depression.The drug also acts as an anaesthetic-sparing agent and attenuate the pressor response to intubation.

Dexmedetomidine suppresses shivering, possibly due to agonism of α2B receptors in the hypothalamus. It also depresses the gag reflex and improves tracheal tolerance when compared with other sedatives [9]. Dexmedetomidine suitable for continuing infusion through the period of extubation in patients that deteriorate once sedatives are discontinued, allowing for a smooth and non-combative extubation.The primary aim of this study were therefore, to evaluate the effects of three different dose of dexmedetomidine on haemodynamic response to extubation in patients undergoing elective surgery. The secondary aims were to observe the quality of extubation, post extubation sedation levels, and occurrence of any adverse effects.

Methods

The present study was carried out from August 2013 to august 2015, after taking the approval from the Institutional ethical committee and the written informed consent from the patients. It was a randomized, double blind controlled clinical study. Ninety ASA physical grades I and II patients between 18 and 60 years, of either sex and posted for elective surgery under general anaesthesia were included in the study.Patients with coronary artery disease, hypertension, asthma, chronic obstructive pulmonary diseases,anticipated difficult intubation,Potentially full stomach patients (trauma, morbid obesity, pregnancy) , diabetes mellitus and neurosurgery patients were not considered for the study.Patients were randomly divided into three groups of 30 patients each by chit in box technique - Group A , Group B and Group C.All patients were receiving Dexmedetomidine 15 minutess before anticipated time of extubation.Patient in Group A, was receive 0.5mcg/kg intravenous (IV) in 10 ml normal saline(NS) over 10 minutes, Group B was receive 0.75mcg/kg intravenous(IV) in 10 ml normalsaline (NS) over 10 minutes, Group C was receive 1.00mcg/kg intravenous(IV) in 10ml normal saline (NS) over 10 minutes.

All patients were premedicated 20 minutes prior to transfer of the patient to the operation theatre with ondansetron 0.1 mg/kg, midazolam 0.03 mg/kg,tramadol 2 mg/kg intravenously. After that patients were pre-oxygenated with 100% oxygen for 3 to 5 minutes and then induced with thiopentone sodium 3-6 mg/kg (titrated dose) till the loss of eyelash reflex. Relaxation was achieved with inj succinylcholine 1.5 mg/kg following which laryngoscopy was attempted using standard technique. Patients were intubated by using an appropriate sized cuffed

ETT. Patients were subsequently maintained using 60% nitrous oxide with oxygen and isoflurane (0.8-1%). Heart rate (HR), systolic BP and diastolic BP was recorded at the start of slow bolus drug (Dexmedetomidine) injection. Residual neuromuscular blockade was reversed with neostigminutese 0.05mg/kg and glycopyrrolate 0.01mg/kg IV. When patient's spontaneous respiration is considered sufficient and patient is able to obey simple commands, suction of throat was done and trachea was extubated. Heart rate (HR) systolic BP,diastolic BP and mean BP was recorded at 1 minutesute, 3 minutesute and 5 minutesute after extubation followed by every 5 minutesutes for 15 minutesutes then every 15 minutes till 60 minutes. These values was also recorded 15 minutes before extubation and considered as control baseline value. Heart rate & SpO_2 was recorded from the pulse oximeter, while blood pressure was recorded using noninvasive electronic blood pressure measuring device inbuilt in multichannel monitor. Occurrence of any event like laryngospasm, bronchospasm, desaturation, respiratory depression, vomiting, hypotension, bradycardia or undue sedation were noted.Hypotension is defined as a decrease in systolic BP of more than 30 mmHg or a mean arterial pressure on less than 60 mmHg from baseline and was corrected with IV fluids and if required with small doses of mephenterminutese 6 mg IV. Bradycardia is defined as an HR of less than 50/minutes and will be corrected, if associated with hemodynamic instability, with atropine 0.6mg IV.Postoperative sedation was evaluated on a 6 point scale (Ramsay sedation score):[10] at 15 minutes, 30 minutes and 60 minutesutes.Grade 1 = Anxious or agitated and restless or both,Grade 2 = Cooperative, oriented and tranquil, Grade 3 = Drowsy but responds to commands, Grade 4 = Asleep, brisk response to light glabellar tap or loud auditory stimulus, Grade 5 = Asleep, sluggish response to light glabellar tap or loud auditory stimulus, Grade 6 =Asleep and unarousable.Quality of extubation were evaluated based on cough immediately after extubation, using a 5 point rating scale (Extubation Quality Score)[11] Score 1 =No coughing, Score 2 =Smooth extubation, minutesimal coughing (1 or 2 times), Score 3 =Moderate coughing (3 or 4 times),Score 4 =Severe coughing (5-10 times) and straining, Score 5=Poor extubation, very uncomfortable (laryngospasm and coughing >10 times).

Sample size was calculated using MedCalc Software version 11.5.0.0. (MedCalc Software bvba, Acacialaan 22, 8400 Ostend, Belgium) Based on minutesimum mean difference in 25% in parameters with α =0.01 and β =0.20, sample size of each group was estimated as 28. Rounding up this figure, we took 30 patients in each group. The results were tabulated and statistically analysed using SPSS (Statistical Package for Social Sciences) Software version 17.0, Chi-square test was used for qualitative data (sex, ASA grade). PR, blood pressure etc, (quantitative) data were compared with the group of baseline values using paired t-test. ANOVA test was used for three group comparisons of continuous variables; if ANOVA was found significant, tuckey post-hoc test was used for comparing two groups and the results were expressed as mean ± standard deviation. P <0.05 was considered as statistically significant.

Result

The three groups were similar with respect to demographic data and ASAphysicalstatus Table 1.

Table 1: Comparison of demographic parameters among the groups

Parameter assessed	Group A (n=30)	Group B (n=30)	Group C (n=30)	P Value
Male: female ratio	10:20	13:17	12:18	0.5959
Age (years) Mean±SD	38.26±11.38	35.53±11.74	36.58+11.86	0.3642
Body mass index (kg/m^2) Mean±SD	23.19±2.27	23.61±2.29	24.78+2.86	0.4784
ASA I/II	16/14	13/17	18/12	0.3835
Weight (kg.)Mean±SD	56.36±6.67	56.16±12.27	55.26±22.17	0.278

There was less fluctuation in heart rate in Group C as compared to Group A and Group B after extubation (Figure 1) but the major changes in heart rate was in first 10 minutes after extubation in all the three group however, they were found to be not statistically significant (P>0.05) Table 2.

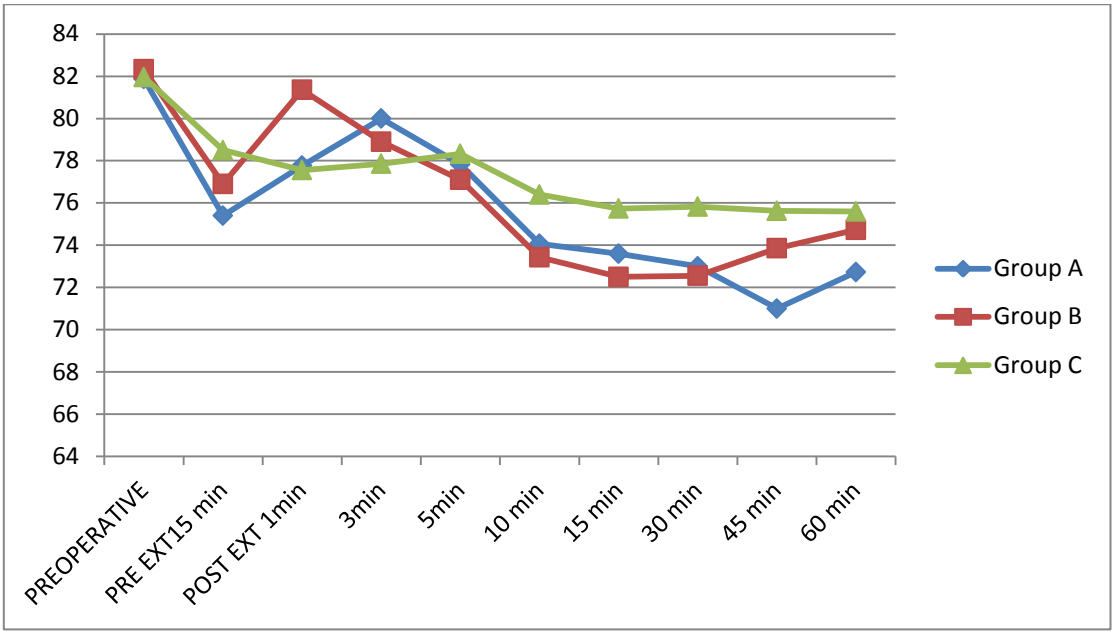

Figure 1: Changes in heart rate at various time intervals in the three groups

Table 2: Changes in heart rate among the three groups

HEART RATE	Mean ± SD			P value
	A (N = 30)	B (N = 30)	C (N = 30)	
PREOPERATIVE	81.87±8.46	82.33±8.21	81.96±10.76	0.9792
PREEXTUBATION 15min	75.40±10.79	76.90±12.45	78.50±14.38	0.6376
POSTEXTUBATION 1min	77.77±12.92	81.36±15.47	77.56±12.15	0.4795
3 min	80.00±12.72	78.90±15.86	77.86±12.47	0.8346
5 min	77.83±12.78	77.10±15.49	78.33±16.10	0.9494
10 min	74.07±11.45	73.43±13.06	76.40±13.65	0.6387
15 min	73.60±10.32	72.50±14.58	75.74±12.96	0.6070
30 min	73.00±11.64	72.56±14.85	75.83±12.37	0.5751
45 min	71.00±11.00	73.86±13.83	75.63±12.18	0.3487
60 min	72.73±11.03	74.73±13.45	75.60±11.61	0.6419

There was no significant difference between Group A, Group B and Group C for the means of MAP from the preextubation values.MAP was significantly lower in Group C at 3 min and most probably at 15 minutes in Group B and Group C differed from Group A.All patients in three groups were hemodynmically stable after postextubation as shown in Table 3 and Figure 2.

Table 3: Changes in mean arterial blood pressure among the three groups

MAP	Mean ± SD			P value
	A (N=30)	0.844B (N=30)	C (N=30)	
PREOPERATIVE	93.37±7.81	94.13±8.37	92.90±8.55	0.844
PRE-EXTUBATION 15 min	94.17±10.13	95.96±11.99	95.43±11.12	0.844
POST-EXTUBATION 1min	96.27±13.28	98.20±13.45	90.06±10.62	0.815
3 min	95.97±15.87	93.70±10.17	88.53±9.68	0.036
5 min	93.97±11.99	94.73±10.94	89.23±10.86	0.060
10 min	95.03±10.97	92.70±11.73	88.23±10.28	0.088
15 min	92.70±14.02	85.16±14.29	86.30±11.83	0.019
30 min	89.47±12.70	91.86±11.42	87.36±14.14	0.070
45 min	88.10±12.13	84.20±10.19	89.30±13.42	0.236
60 min	88.17±9.96	83.83±11.08	91.10±14.16	0.232

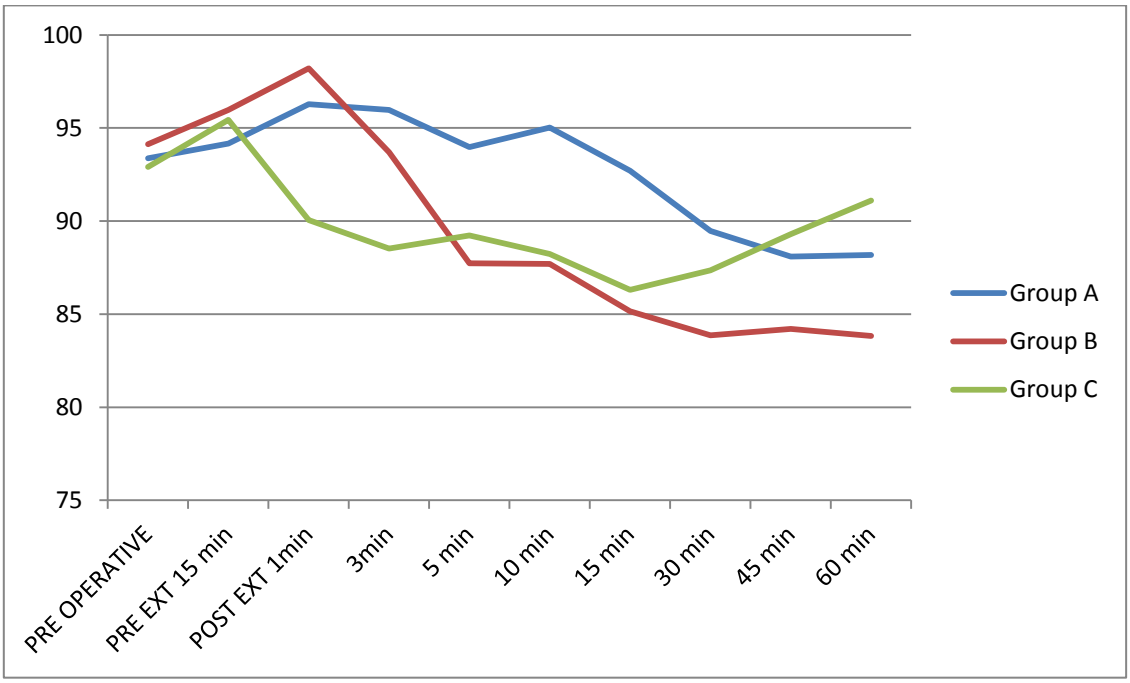

Figure 2: Changes in mean arterial pressure at various time intervals in the three groups

By comparing the Ramsey sedation scoreTable 4, we found that patients were more sedated in group C as compared to group A and group B,but least sedation was found among the group A.Sedation score was statistically significant at 15 and 30 minutesute post extubation among the study groups.But at 60 minutes postextubation sedation scores observedwere not statistically significant (P>0.05).

Table 4: Distribution of Ramsay sedation score between the three groups

RAMSAY SEDATION SCORE	Mean ± SD			P value
	A (N=30)	B (N=30)	C (N=30)	
15 min	2.6±0.72	2.93±0.52	3.5±0.57	<0.001
30 min	2±0.45	2.06±0.52	2.5±0.57	<0.001
60 min	1.6±0.49	1.6±0.498	1.83±0.37	0.085

There was statistically significant differences in extubation score between Group A &Group B , Group A & Group C $P \leq 0.05$ but not significant between Group B & Group C (P>0.05).The Extubation quality score was best in Group B as no cough was observed on extubation Table 5.Only one patient in Group C had bradycardia that was managed with Atropine 0.6 mg i.v. and two patient undergone hypotension that was managed successfully with i.v bolus normal saline 500ml. Other adverse effects such as laryngo-spasm, brochospasm, respiratory depression were not observed in any of the three groups. None of patient had respiratory depression and desaturation among the three groups as described in Table 5.

Table 5: Comparison of post extubation complication and quality of extubation score amongthe three groups

Parameter assessed	Group A (n=30)	Group B (n=30)	Group C (n=30)	P Value
Extubation quality score (Mean±SD)	1.33±0.34	1.1±0.30	1.22+0.01	0.02
Hypotension Y/N	0/30	0/30	2/28	0.129
Bradycardia Y/N	0/30	0/30	1/29	0.478
Desaturation Y/N	0/30	0/30	0/30	NA*
Laryngospasm Y/N	0/30	0/30	0/30	NA
Bronchospasm Y/N	0/30	0/30	0/30	NA

*NA: Not applicable

Discussion

The present study shows that administration of 0.5 µg/kg,0.75 µg/kg and 1.0 µg/kg of dexmedetom-idine as an infusion over 10 minute before 15 minute of extubation will attenuate hemodynamic responses to extubation and provides smooth extubation. Complications at extubation include hypertension, tachycardia, dysrhythmias, myocardial ischemia; coughing; laryngospasm and bronchospasm; impaired laryngeal competence and pulmonary aspiration and hypoventilation[12] were prevented using dexmeditomidine before extubation . Untreated tachycardia or hypertension from the increased sympathoadrenal activity will result in increased myocardial oxygen consumption, resulting in myocardial ischemia in patients at risk (patients with diabetes mellitus, cardiac disease, pre-eclampsia and those undergoing intracranial, intraocular or vascular surgeries)[13]. So the technique or drug chosen at extubation should attenuate hemodynamic disturbance and provide smooth extubation with minimal or no side effects. Extubation of trachea with patients in a deeper plane of anesthesia avoids cardiovascular stimulation. This can be achieved by inhalation or intravenous anaesthetic agents, opioids or both, however it carries the highest risk of hypoventilation and upper airway obstruction[12]. Coughing may be particularly troublesome during “light anesthesia” extubation and cannot be entirely prevented[13].

Dexmedetomidine by its alpha2 agonist action at multiple sites not only results in decrease in heart rate and blood pressure, by central sympatholysis but also in analgesia, sedation, and anxiolysis[14-15]. Dexmedetomidine has been found to be superior to fentanyl and lignocaine in blunting hemodynamic changes to extubation[15-16]. In the current study,the heart rate and blood pressures remained below baseline in the post-extubation period among all three group but in group A fluctuation were less as compared to group B and group C and the incidence of tachycardia and hypertension were lower following adminutesi-stration of dexmedetomidine which is concurrent with the observation of earlier studies[17-18]. The incidence of bradycardia was higher when a higher dose of dexmedetomidine was used[18].

Also in our study the incidence of bradycardia ,hypotension was 3.33% and 6.66% respectively among the group C patient but none of the patient in group A and group B suffered hypotension and bradycardia. It signifies that higher dose of dexmedetomidine is associated with cardiovascular instability. Incidence of coughing was significantly lower in the group B receiving dexmedetomidine,which is in accordance with observations of Aksu R et al [15]. Alpha2 agonist activity of dexmedetomidine is known to reduce secretions of mucus glands, glands of oral and tracheobronchial tree in particular. Reduction in secretions may result in decreased incidence of coughing and other complications such as laryngospasm and bronchospasm. However, none of the patients in the present study complained of dry mouth. Thirty eight percent of patients receiving dexmedetomidine were drowsy but responded to oral commands following 15 minutes of extubation in group C. However, after 60 minutes of extubation sedation scores were not significant among three groups. Time from extubation to orientation with time, place and person were significantaly prolonged among group C.This observation is in agreement with a study conducted by by Guler G and colleagues on emergence agitation whereas time to extubation and emergence were prolonged significantly[18].It explained that higher dose of dexmedetomidine 1.0 µg/kg is associated with more post operative sedation.

The major limitation of our study was that it is rather focused on the general population and post-operative analgesia was not studied. Future studies may be done in specific patient populations such as geriatric, pediatric neurosurgical and cardiovascular patients where extubation responses are equally critical to that of intubation responses.

Conclusion

All the three doses of dexmedetomidine (0.5mcg/kg, 0.75mcg/kg, 1.0 mcg/kg) were able to maintain hemodynamic stability on tracheal extubation. Patients developed more sedation in Group C.Quality of extubation was best in Group B as there is no cough on extubation.Advese effect of dexmedetomidine such as hypotension , bradycardia could be avoided by restricting ourself to lower dose 0.5mcg/kg and 0.75mcg/kg dexmedetomidine.

However, further comparative studies with larger sample size in the clinical context particularly in hypertension, cardiac disease, neurosurgical patient and in patients with co- existing morbidities need to be evaluated.

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