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Original Research Article

A Randomized Clinical Assessment of the Effect of 3-Different Doses of Dexmedetomidine on Hemodynamics and Anesthetic Depth

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Abstract

Aim: The aim of the present study was to evaluate and compare the effect of different doses of Dexmedetomidine on Heart rate, Blood pressure, oxygen saturation and depth of anaesthesia.

Methods: The present study was conducted in Department of Anaesthesiology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India for one year. 150 patients in the age group of 20 to 60 years. Patients were ASA I-II, scheduled for open cholecystectomy.

Results: The enrolled patients fulfilling all the inclusion and exclusion criteria were divided into three groups with 50 patients in each group. Group A (n=50) 0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml). Group B (n=50) 0.75µg/kg of Dexmedetomidine in NS (Total volume 10 ml) Group C (n=50) 1 µg/kg of Dexmedetomidine in NS (Total volume 10 ml). There were more females than male in all the three groups. Mean Age in group A, B and C were 42.18±11.19, 41.69± 11.20 and 43.67± 9.25 respectively. All the three groups were comparable with respect to age of the patients ($p>0.05$). The groups were also comparable in terms of Sex, BMI and ASA grade ($p>0.05$). The groups were comparable in terms of duration of surgery and interval between start of Dexmedetomidine infusion and Extubation ($p>0.05$).

Conclusion: The attenuation of Extubation response was almost similar with Dexmedetomidine in dose of 0.75µg/kg and 1µg /kg. However with increase in dose from 0.75µg/kg to1µg /kg there was significant increase in the side effects in the form of bradycardia ($p<0.05$). So we concluded that 0.75µg/kg is the single best dose of Dexmedetomidine for attenuation of Extubation response.

Keywords: Dexmedetomidine, Open Cholecystectomy, Tracheal Extubation

Introduction

When the reasons for maintaining an artificial airway, such as airway obstruction, protection of airway, suctioning, ventilator failure, and hypoxemia, no longer apply, tracheal extubation is performed. Extubation is commonly accompanied with bucking and coughing. If a person's lung volumes are lower than their vital capacity, they could develop negative pressure pulmonary oedema from bucking, which physiologically mimics the Valsalva manoeuvre. Patients are also put at danger because of the sudden rise in intra cavitary

pressures (in the eye, the lungs, the abdomen, and the brain). [1 , 2]

It is three times more common for respiratory problems to arise during tracheal extubation (4.6% vs 12.6%) than during tracheal intubation and induction of anesthesia. [3] Death or brain injury after induction of anesthesia reduced from 62% of perioperative claims in 1985-1992 to 35% in 1993-1999, according to a closed claims analysis of the American Society of Anesthesiologists database. This trend may be a result of the broad implementation of guidelines for managing a difficult airway, most of which focus on the administration of anesthesia. In contrast, there was hardly any change in the number of claims for death or brain injury connected to maintenance, Extubation, and rehabilitation. [4] Patient safety could be enhanced through the creation of individualized airway management regimens for use during these high-risk times.

Patients with hypertension may be harmed by the abrupt hemodynamic fluctuations that occur after extubation, which are well tolerated by healthy individuals. When considering the blunting of hemodynamic responses, tracheal extubation has traditionally been given less weight than intubation. Increases in plasma catecholamine levels produce a 10%-30% increase in BP and HR, which might exacerbate preexisting hypertension. [5 , 6] Myocardial ischemia and infarction can occur as a result of increased oxygen demand brought on by the aforementioned causes. Due to cardiac enlargement and decreased perfusion to coronary, hypertension patients frequently have an increased oxygen demand, putting them at an already high risk for adverse outcomes. [7] Consequently, it is sense to think about preventative measures to lessen the severity of these negative reactions after extubation.

Dexmedetomidine, an alpha 2-agonist with a distribution half-life of about 6 minutes that is indicated for sedation in the intensive care unit in mechanically ventilated patients [8], and for sedation of non-intubated patients before or during surgical and other procedures, has been used successfully to attenuate the stress response to laryngoscopy. [9] Dexmedetomidine alters sympathetic function and decreases HR and BP via activating receptors in the medullary vasomotor region, hence decreasing norepinephrine turnover and central sympathetic outflow. Dexmedetomidine's sedative effects, hemodynamic stability, and lack of respiratory depression make it a suitable drug for reducing the extubation response. Few studies have compared the efficacy of different dosages of dexmedetomidine in reducing the hypertensive tachycardiac response to tracheal Extubation, despite its widespread usage.

The aim of the present study was to evaluate and compare the effect of different doses of Dexmedetomidine on heart rate, blood pressure, oxygen saturation and depth of anaesthesia.

Materials and Methods

The current study was carried out on 150 patients aged 20 to 60 at the Department of Anaesthesiology at the Bhagwan Mahavir Institute of Medical Sciences in Pawapuri, Nalanda, Bihar, India for one year. Open cholecystectomy was planned for ASA I and ASA II patients.

Inclusion Criteria

1. Patients between the age group 20-60 years.
2. ASA class I-II.
3. BMI 18.5-29.9.
4. Undergoing open cholecystectomy.

Exclusion Criteria

1. Patient’s refusal for participation in the study.
2. Patients with ischaemic and/or congestive cardiac disease or abnormal ECG
3. Patients on Beta blockers, digoxin, anticonvulsant or psychotropic medicines.

4. Allergic to study drugs.
5. If Extubation did not occur within 10 minutes of starting infusion.
6. If bradycardia (HR < 50/min) or hypotension (SBP < 80 mm of Hg) occured anytime during study period, patient were excluded from the study.
7. If BIS > 60 anytime between starting of infusion and Extubation, patients were excluded from the study.

Methodology

Protocol review committee, institutional ethics committee, and signed informed patient consent were all obtained before the study could begin. All eligible patients who agreed to participate were randomly assigned to one of three groups.
Group A (n=50) 0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml)
Group B (n=50) 0.75µg/kg of Dexmedetomidine in NS (Total volume 10 ml)
Group C (n=50) 1 µg/kg of Dexmedetomidine in NS (Total volume 10 ml)

Procedure

The anesthetic procedure was explained to the patients enrolled for study and thereafter written consent was taken. Before commencing the surgery a case record form was filled for each patient. All patients were kept nil orally for at least eight hours before the procedure. They were given premedication in the form of tablet alprazolam 0.50mg and tablet ranitidine 150mg at HS on the day of surgery. On arrival to operation theatre, five lead ECG, NIBP, SpO2 and BIS were attached and baseline parameters noted along with starting of peripheral 18G I.V line. Anesthesia was induced with 5 mg/kg thiopentone and 2 µg/kg fentanyl and tracheal intubation was facilitated with 0.5 mg/kg Atracurium IV. Anesthesia was maintained with 0.5%-1.5% isoflurane and 60% nitrous oxide (N2 O) in oxygen. The end-tidal carbon dioxide pressure (ETCO2) was maintained between 30 and 35 mm Hg. Peripheral arterial oxygen saturation (SpO2) and the concentration of end-tidal isoflurane was monitored throughout from anesthesia machine monitor. BP was recorded immediately before the induction of anesthesia and every 10 min during anesthesia using automated noninvasive BP monitor. The HR was monitored by electrocardiography (ECG lead II). The BP and HR were maintained between 80% and 120% of the preoperative values by increasing or decreasing the concentration of isoflurane until completion of surgery. Muscle relaxation was maintained by intermittent boluses of atracurium (0.02 mg/kg). At the beginning of closure of rectus sheath, isoflurane was discontinued and Dexmedetomidine 0.5mcg/kg body weight diluted to 10 ml in normal saline was infused over 10 minutes using infusion pump in Group A patients. Similarly Group B and Group C patients received Dexmedetomidine 0.75µg/kg and 1µg/kg body weight diluted to 10 ml in normal saline over 10 minutes respectively using infusion pump. Nitrous oxide was discontinued before Extubation. BIS monitoring was continued till patient was extubated to ensure that depth of anaesthesia is adequate. Residual muscle relaxation was reversed with neostigmine 0.05 mg/kg and glycopyrolate 0.01 mg/kg IV. Patients were extubated when one or more of the following Extubation criteria were fulfilled-

1. Sustained head lift for 5 seconds.
2. Sustained hand grip for 5 seconds.
3. Sustained leg lift for 5 seconds
4. Sustained ‘tongue depressor test’
5. Maximum inspiratory pressure 40 to 50 cm H2O or greater

Outcome Parameters

A. Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation (SpO2) and BIS were noted every 10 minutes during surgery, every 30 seconds after start of infusion till

Extubation. Thereafter hemodynamic parameters (PR, BP), SpO2 were recorded every 30 seconds till 5 min and thereafter every 15 min till 2 hours.

B. Extubation time was noted and Extubation quality was rated using Extubation quality 5-point scale.

Extubation quality 5-point scale

1- No coughing
2- Smooth Extubation, minimal coughing
3- Moderate coughing (3 or 4 times)
4- Severe coughing (5 to10 times) and straining
5- Poor Extubation, very uncomfortable (laryngospasm and coughing >10 times)

Any incidence of cough, laryngospasm, bronchospasm or desaturation was noted for a period of 15 min post Extubation.

C. Sedation was evaluated using Ramsay Sedation Scale at 5 minute interval uptill 30 min and thereafter at 30 min interval for next 90 minutes.

Ramsay sedation scale

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

D. Pain was assessed using VAS scale at 5 minute interval up till 30 min and thereafter at 30 min interval for next 90 minutes. Patients were asked to rate the pain on a scale ranging from 0 to 10.

Statistical analysis

Data was collected and entered in MS Excel 2007. Statistical analysis was performed using Epi info.

Results

Table 1: Group Wise Distribution of Patients

Groups	Description	No. of Patients	Percentage
A	0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml)	50	33.33
B	0.75µg /kg of Dexmedetomidine in NS (Total volume 10 ml)	50	33.33
C	1 µg /kg of Dexmedetomidine in NS (Total volume 10 ml)	50	33.33

The enrolled patients fulfilling all the inclusion and exclusion criteria were divided into three groups with 50 patients in each group. Group A (n=50) 0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml). Group B (n=50) 0.75µg/kg of Dexmedetomidine in NS (Total volume 10 ml) Group C (n=50) 1 µg/kg of Dexmedetomidine in NS (Total volume 10 ml).

Table 2: Demographic profile of the three Groups (mean ± SD)

Parameter	Group A	Group B	Group C	P value
Age(years)	42.18±11.19	41.69±11.20	43.67± 9.25	.630
Sex(M/F)	8:42	10:40	7:43	.250
BMI(kg/m^2)	25.45±2.15	25.35±2.20	25.70±1.85	.555
ASA I/ASA 2	24:26	25:25	26:24	.830

There were more females than male in all the three groups. Mean Age in group A, B and C were 42.18±11.19, 41.69± 11.20 and 43.67± 9.25 respectively. All the three groups were comparable with respect to age of the patients (p>0.05). The groups were also comparable in terms of Sex, BMI and ASA grade (p>0.05).

Table 3: Quality of extubation and hemodynamic parameter at extubation of the three groups

	Group A	Group B	Group C	*P*
Quality of extubation, *n* (%)				
1-2	26 (52)	44 (88)	45 (90)	0.003
3-4	24 (48)	6 (12)	5 (10)	<0.001
Time of extubation (min), mean±SD	8.32±0.50	8.50±0.40	9.45±0.44	0.055
Heart rate (bpm), mean±SD	90.85±11.45	80.70±11.99	65.8±7.65	<0.001
SBP (mmHg), mean±SD	124.66±10.52	110.40±9.60	102.90±9.50	<0.001
DBP (mmHg), mean±SD	84.72±7.70	72.10±7.00	64.06±6.40	<0.001
MAP (mmHg), mean±SD	100.50±6.60	86.44±6.40	78.96±6.50	<0.001
SpO_2 (%), mean±SD	98.40±1.12	98.15±0.80	98.95±1.16	0.100
BIS, mean±SD	76.74±5.04	70.80±3.16	71.29±4.15	<0.001

After extubation, the overall difference between the three groups is statistically significant (P < 0.001). After 10 min from extubation, there was no difference in HR between Groups A and B (P = 0.025); however, there was significant difference between Groups B and C (P < 0.001). SBP, DBP, and MAP were significantly higher in Group A as compared to Groups B and C. This shows that good attenuation of pressor response was done with higher doses as compared to lower dose, and Group B had more stable hemodynamic without any undue variations.

Table 4: Duration of Surgery (mean ± SD) and interval between start of Dexmedetomidine Infusion and Extubation (mean ± SD)

Group A	Group B	Group C	P value
60.20±9.11	61.3333±8.22	55.05±7.94377	.110
Interval between start of Dexmedetomidine Infusion and Extubation			
8.85± 0.52	8.72± .54	8.70± .55	.065

The groups were comparable in terms of duration of surgery and interval between start of Dexmedetomidine infusion and Extubation (p>0.05).

Table 5: Quality of Extubation

Group A	Group B	Group C
12	24	25
18	20	20
20	6	5

In group C 25 patients had no coughing at the time of Extubation as compared to 24 patients in group B and 12 in group A. Both in group B & group C 20 patients had smooth Extubation with minimal coughing whereas 18 patients in group A had smooth Extubation with minimal coughing. The difference in quality of Extubation was significant between group A & group B and between group A & group C whereas it was comparable between group B & group C.

Table 6: Time of 1st Rescue Analgesia after Extubation in min (mean± SD) and Total No of Rescue Analgesic used

Time of 1st Rescue Analgesia after Extubation in min			
Group A	**Group B**	**Group C**	**P value**
45±15.17	48±16.18	55±15.75	.040
Total No of Rescue Analgesic used			
2.38±0.370	2.35±0.450	2.25±0.420	.540

Interval between Extubation and use of 1st rescue analgesic was least in group A and maximum in group C. However, statistically the difference were only significant between group A and group C ($p<0.05$). Total number of rescue analgesics used was comparable in all the three groups.

Discussion

It is a well-established fact that when compared to intubation complications are three times higher in frequency during and after extubation. [5,10,11] There is a strong recommendation to maintain hemodynamic during extubation within 20% of normal awake value particularly in high-risk patients. The cardiovascular changes to these critical points are more brisk in poorly controlled hypertensives than do normotensives or well-controlled hypertensives. [5] Laparoscopic surgeries under general anesthesia are associated with unique hemodynamic changes in the form of decreased venous return and increased systemic vascular resistance leading to systemic hypertension. This increases the need for deepening the plane of anesthesia and requires the use of vasodilators to counteract the rising blood pressures. IAPs higher than 10 mmHg due to peritoneal insufflation with CO2 induce significant alterations in hemodynamic, characterized by decrease in venous return, increase in arterial pressure, and elevation of systemic and pulmonary vascular resistance and HR. [12,13] These hemodynamic changes are even more pronounced and challenging in hypertensive patients than normotensive patients during general anesthesia and require more anesthetic interventions to get hemodynamic stability. [14]

In the past, various pharmacological agents have been used for the attenuation of intubation and Extubation response. Extubation has always received less emphasis than Intubation in past studies. Various agents which have been used for attenuation of Extubation response include diltiazem [15], lignocaine [16], labetalol [17], nicardipine [18] and opioids [19] as sole agent or in comparison with each other. Dexmedetomidine is a newly emerging drug which has been extensively studied for attenuation of both intubation and Extubation response. Dexmedetomidine is a highly selective α2 agonist that has been shown to have sedative, analgesic and anaesthetic sparing effects. It causes a dose-dependent decrease in arterial blood pressure and heart rate, associated with decrease in serum norepinephrine concentration.

It was observed that Dexmedetomidine used in premedication supresses the sympathetic activation which is due to the endotracheal intubation. [20] Güler et al. found that the increase in blood pressure and heart rate during the Extubation is decreased and the quality of Extubation is increased by Dexmedetomidine. [21] The enrolled patients fulfilling all the inclusion and exclusion criteria were divided into three groups with 50 patients in each group. Group A (n=50) 0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml). Group B (n=50) 0.75µg/kg of Dexmedetomidine in NS (Total volume 10 ml) Group C (n=50) 1 µg/kg of Dexmedetomidine in NS (Total volume 10 ml). There were more females than male in all the three groups. Mean Age in group A, B and C were 42.18±11.19, 41.69± 11.20 and 43.67± 9.25 respectively. All the three groups were comparable with respect to age of the patients ($p>0.05$). The groups were also comparable in terms of Sex, BMI and ASA grade ($p>0.05$).

We found that Dexmedetomidine in doses of 0.75µg /kg and 1µg /kg effectively attenuated the Extubation response where as in dose of 0.5µg /kg the response was not effectively attenuated. There was decrease in HR, SBP, DBP and MAP with Dexmedetomidine in doses of 0.75µg /kg and 1µg /kg during infusion upto Extubation whereas all these parameters increased in group A in which

Dexmedetomidine was used in dose of 0.5 µg /kg. In a study done by Celik et al. [22] similar results were obtained where they concluded that to control haemodynamic responses to tracheal intubation, Dexmedetomidine 1 µg.kg-1 is more effective than Dexmedetomidine 0.5 µg.kg-1. Martina et al. [23] studied the effect of 2 doses of Dexmedetomidine 0.3ug/kg & 0.6ug/kg, fentanyl 2ug/kg & saline to attenuate the intubation response. They found that in all groups BP & HR increased after tracheal intubation. However increase in BP & HR was significantly less in Dexmedetomidine group which received 0.6µg/kg than in saline group.

In group C 25 patients had no coughing at the time of Extubation as compared to 24 patients in group B and 12 in group A. Both in group B & group C 20 patients had smooth Extubation with minimal coughing whereas 18 patients in group A had smooth Extubation with minimal coughing. The difference in quality of Extubation was significant between group A & group B and between group A & group C whereas it was comparable between group B & group C. Bindu et al. [24] studied the effect of intravenous Dexmedetomidine infusion 0.75 mcg/kg given 15 min prior to Extubation and concluded that Dexmedetomidine stabilises hemodynamics' and facilitates smooth Extubation, but there was bradycardia in 13 patients out of 25 patients. Aksu R et al. [25] compared the effects of Dexmedetomidine (0.5 mcg/kg) and fentanyl (1 mcg/kg) in patients undergoing rhinoplasty and concluded that Dexmedetomidine was more effective in attenuating airway reflex responses to tracheal Extubation and maintaining haemodynamic stability compared to fentanyl but was associated with bradycardia in two patients out of 20 patients.

Conclusion

The attenuation of Extubation response was almost similar with Dexmedetomidine in dose of 0.75µg/kg and 1µg /kg. However with increase in dose from 0.75µg/kg to1µg /kg there was significant increase in the side effects in the form of bradycardia ($p<0.05$). Also the quality of Extubation was much better with Dexmedetomidine in dose of 0.75µg/kg and 1µg /kg as compared to Dexmedetomidine in dose of 0.5µg/kg ($p<0.05$). So we concluded that 0.75µg/kg is the single best dose of Dexmedetomidine for attenuation of Extubation response.

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