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A comparison among different doses of dexmedetomidine in attenuating extubation response in patients undergoing open cholecystectomy

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Abstract
To evaluate and compare the effect of different doses of Dexmedetomidine on Heart rate, Blood pressure, oxygen saturation and depth of anaesthesia. This study was done in the Department of Anaesthesiology, Dr. RPGMC, Kangra at Tanda, Himachal Pradesh.
This study was carried out on 90 patients in the age group of 20 to 60 years. Patients were ASA I-II, scheduled for open cholecystectomy. Study design–It was a prospective, double blind randomised study. The patients were allocated into one of the three groups by random number chart. The study drug solution was prepared and given to the investigator by a non-participant staff. As a result we concluded that Dexmedetomidine effectively attenuates the Extubation response in dose of 0.75µg/kg and 1µg /kg whereas in dose of 0.5µg/kg the Extubation response was not effectively attenuated.
However the quality of Extubation was comparable with Dexmedetomidine in dose of 0.75µg/kg and 1µg /kg (p>0.05). So we conclude that 0.75µg/kg is the single best dose of Dexmedetomidine for attenuation of Extubation response.

Keywords: Dexmedetomidine, Open Cholecystectomy, Tracheal Extubation

Introduction
Tracheal Extubation refers to the discontinuation of an artificial airway when the indications for its placement like airway obstruction, protection of airway, suctioning, ventilator failure and hypoxemia no longer exist. Bucking and coughing frequently occur during Extubation. Bucking physiologically mimics Valsalva manoeuvre and can cause negative pressure pulmonary oedema if lung volumes are less than vital capacity. It also cause abrupt increase in intra cavitary pressures (intraocular, intrathoracic, intra-abdominal and intracranial) which can put patients at high risk [1-2].
Respiratory complications after tracheal Extubation are three times more common than complications occurring during tracheal intubation and induction of anaesthesia (4.6% *vs* 12.6%) [3]. A closed claims analysis of the American Society of Anesthesiologists database revealed that death or brain damage with induction of anaesthesia decreased from 62% of perioperative claims in 1985–1992 to 35% in 1993–1999. This may reflect widespread adoption of difficult airway guidelines which predominantly address induction of anaesthesia. In contrast, the claims for death or brain damage associated with maintenance, Extubation and recovery remained almost the same.[4] Development of specific airway management plans addressing these periods of risk should improve patient safety.
It is a well-known fact that both after tracheal intubation and Extubation there is increase in arterial blood pressure and heart rate due to increased plasma concentration of both noradrenaline and adrenaline [5-7]. Physiologic responses to emergence from anaesthesia and tracheal Extubation occur due to lighter planes of anaesthesia and may be due to inadequate analgesia, resulting in tachycardia, hypertension, coughing, bucking, laryngospasm and bronchospasm [8-10]. For a smooth Extubation, there should be no straining, movement, coughing, breath holding or laryngospasm. Extubation at lighter levels of anesthesia or sedation can stimulate reflex responses via tracheal and laryngeal irritation.

Endotracheal Extubation has become an integral part of the anaesthetic management and critical care of the patient.

The change in catecholamine concentration associated with tracheal Extubation occurs rapidly and lasts for only about five minutes [7]. These cardiovascular changes during Extubation and emergence from anaesthesia may lead to myocardial ischemia in patients with coronary heart disease. The sudden increase in blood pressure and heart rate associated with tracheal Extubation can aggravate the already increased blood pressure and heart rate, which commonly occur towards the end of anaesthesia with the possibility of increased anaesthetic morbidity and mortality. Myocardial ischaemia has been reported both during tracheal intubation and Extubation [11], even cerebral hemorrhage and pulmonary oedema have been known to occur. Patients with pre-existing hypertension exhibit an increase in blood pressure at the time of tracheal intubation and Extubation due to non-compliant vasculature, elevated peripheral vascular tone, high level of baseline endogenous sympathetic nervous system activity and impaired baroreceptor control of heart rate. Tracheal Extubation has always received less emphasis than intubation with respect to attenuation of haemodynamic response.

To blunt the hemodynamic and cough responses to Extubation, several pharmacological strategies and Extubation in deeper planes of anaesthesia have been studied [12]. Each one has its own merits and demerits. As per Difficult Airway Society basic Extubation guidelines, cardiovascular and airway factors need to be optimized before Extubation.

Various techniques and antihypertensive drugs are available to attenuate airway and circulatory reflexes during Extubation but none have been completely successful. Attempts have been made to attenuate the pressor response by the use of drugs such as narcotic analgesics, deep anaesthesia induced by inhalational anaesthetics, local anaesthetics, adrenoceptor blockers and vasodilator agents[11]. Studies have been carried out with use of diltiazem[13], lignocaine [14], labetalol [15], nicardipine [16] and opioids [17] as sole agent or in comparison with each other.

Dexmedetomidine is a FDA approved α_2-adrenoreceptor agonist with a distribution half-life of approximately 6 minutes indicated for intensive care unit sedation in mechanically ventilated patients [18] and for sedation of non-intubated patients before or during surgical and other procedures has now been successfully used for attenuating the stress response to laryngoscopy [19]. 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. Thus Dexmedetomidine is a useful agent to attenuate the response to Extubation as it provides sedation, hemodynamic stability and does not depress respiration.

Although Dexmedetomidine has been used with varying success to attenuate hypertensive tachycardiac response to tracheal Extubation, yet not many studies have evaluated different doses of Dexmedetomidine to attenuate the Extubation response. There is a need to study the effectiveness of Dexmedetomidine in obtunding the hemodynamic response to Extubation.

Therefore we designed this prospective, randomized, double blind trial to determine the optimal dose of Dexmedetomidine which can serve as an effective alternative to the commonly used agents for blunting the hemodynamic response to tracheal Extubation and improve the quality of Extubation.

Aim and Objectives

Aim

Comparison among different doses of Dexmedetomidine in attenuating Extubation response in patients undergoing open Cholecystectomy.

Objectives

1. To evaluate and compare the effect of different doses of Dexmedetomidine on Heart rate, Blood pressure, oxygen saturation and depth of anaesthesia.
2. To study and compare the quality of Extubation response with three different doses of Dexmedetomidine.
3. To study and compare the duration of post-operative analgesia and requirement of post-operative analgesics with three different doses of Dexmedetomidine.
4. To observe any side effect of Dexmedetomidine.

Material and Methods

Study area– Department of Anaesthesiology, Dr. RPGMC, Kangra at Tanda, Himachal Pradesh.

Study population– After approval by institutional ethics committee this study was carried out on 90 patients in the age group of 20 to 60 years. Patients were ASA I-II, scheduled for open cholecystectomy.

Study design–It was a prospective, double blind randomised study. The patients were allocated into one of the three groups by random number chart. The study drug solution was prepared and given to the investigator by a non-participant staff.

Sample size –Total 90 patients who fulfilled our inclusion and exclusion criteria were included in the study.

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

The study commenced after obtaining approval from protocol review committee, institutional ethics committee and written informed patient consent. The enrolled patients fulfilling all the inclusion and exclusion criteria were divided into three groups.

Group A (n=30) 0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml)
Group B (n=30) 0.75µg/kg of Dexmedetomidine in NS (Total volume 10 ml)
Group C (n=30) 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 *al*prazolam 0.50mg and tablet ranitidine 150mg at HS, 6:00 am on the day of surgery.

On arrival to operation theatre, five lead ECG, NIBP, SpO_2 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 (N_2 O) in oxygen. The end-tidal carbon dioxide pressure ($ETCO_2$) was maintained between 30 and 35 mm Hg. Peripheral arterial oxygen saturation (SpO_2) 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 was 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 monitoing 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 H_2O or greater

Outcome Parameters

A. Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation (SpO_2) and BIS were noted every 10 minutes during surgery, every 30 seconds after start of infusion till Extubation. Thereafter hemodynamic parameters (PR, BP), SpO_2 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)

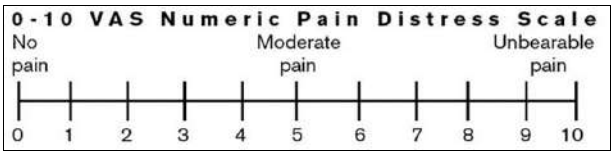
Any incidence of cough, laryngospasm, bronchospasm or desaturation was noted for a period of 15 min post Extubation.

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.



0-No pain and 10-worst pain ever experienced by the patient Inj. Diclofenaic sodium 75mg intramuscular was given to the patient when VAS > 4 as rescue analgesia and Inj. Tramadol 2mg/kg intramuscular as a second line rescue analgesic.

Statistical analysis

Data was collected and entered in MS Excel 2007. Statistical analysis was performed using Epi info. Normally distributed data was analyzed using a repeat-measures general linear model analysis of variance (ANOVA), whereas non-normally distributed data were analyzed using the Mann–Whitney U-test and categorical data was analyzed using the Chi-square test. For comparison between two groups unpaired t test was applied in normally distributed data. The Bonferroni correction was used to correct for multiple testing at different time points.

1. Level of significance: "P" is level of significance
P > 0.05 not significant
P <0.05 Significant
P <0.01 highly significant
P <0.001 Very highly significant

Observation and results

The study commenced after obtaining approval from protocol review committee, institutional ethics committee and written informed patient consent. The enrolled patients fulfilling all the inclusion and exclusion criteria were divided into three groups with 30 patients in each group.

Group A (n=30) 0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml)

Group B (n=30) 0.75µg/kg of Dexmedetomidine in NS (Total volume 10 ml)

Group C (n=30) 1 µg/kg of Dexmedetomidine in NS (Total volume 10 ml).

The relevant data of each patient was entered in master chart and results were analysed statistically after recording the observations.

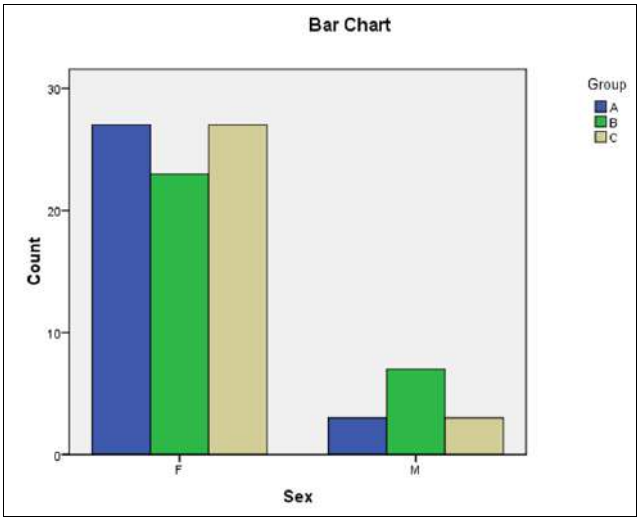
Table 1: Group Wise Distribution of Patients

S. No	Group	Description	No. of Patients	Percentage
1	A	0.5µg /kg of Dexmedetomidine in NS (Total volume 10 ml)	30	33.33
2	B	0.75µg /kg of Dexmedetomidine in NS (Total volume 10 ml)	30	33.33
3	C	1 µg /kg of Dexmedetomidine in NS (Total volume 10 ml)	30	33.33

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

Parameter	Group A	Group B	Group C	P value
Age(years)	43.27±11.209	40.87±11.968	42.77± 9.198	.666
Sex(M/F)	3:27	7:23	3:27	.237
BMI(kg/m^2)	25.6377±2.02116	25.1933±2.06691	25.6900±1.96521	.580
ASA I/ASA 2	14:16	15:15	16:14	.875

Mean Age in group A, B and C were 43.27±11.209, 42.77± 9.198 and 42.77± 9.198 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).



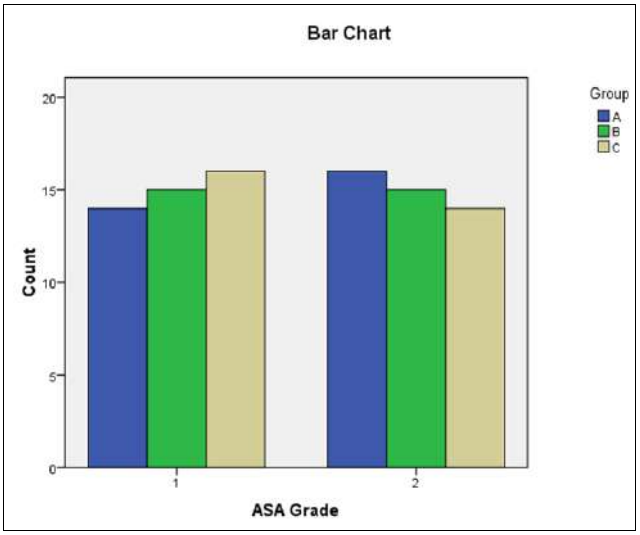


Table 3: Duration of Surgery (mean ± SD)

Group A	Group B	Group C	P value
60.6667±9.07187	61.3333±8.19307	57.0000±7.94377	.106

Table 4: Interval between start of Dexmedetomidine Infusion and Extubation (mean ± SD)

Group A	Group B	Group C	P value
8.900± 0.4807	8.833± .5142	8.600± .5153	.058

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
	Quality		
1	8	14	15
2	10	12	12
3	12	4	3

Group wise comparison of Quality of Extubation

Inter group comparison of Patients with no coughing or smooth Extubation with minimal coughing (Quality of Extubation 1 or 2)

Group A	Group B	P value
18	26	0.0195

Group B	Group C	P value
26	27	0.6876

Group A	Group C	P value
18	27	0.0072

In group C 15 patients had no coughing at the time of Extubation as compared to 14 patients in group B and 8 in group A. Both in group B & group C 12 patients had smooth Extubation with minimal coughing whereas 10 patients in group A had smooth Extubation with minimal coughing. The difference in quality of Extubation is significant between group A & group B and between group A & group

C whereas it is comparable between group B & group C.

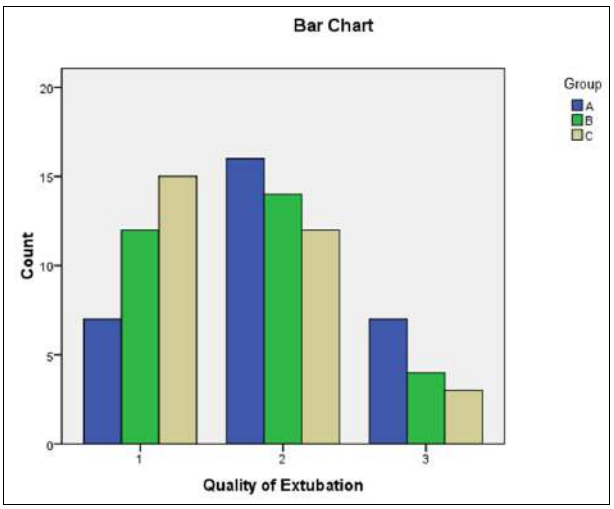


Table 6: Time of 1st Rescue Analgesia after Extubation in min (mean± SD)

Group A	Group B	Group C	P value
44±14.166	49±14.166	54±16.989	.043

Interval between Extubation and use of 1st rescue analgesic was least in group A and maximum in group C. However statistically the difference was only significant between group A and group C ($p<0.05$).

Table 7: Total No of Rescue Analgesic used

Group A	Group B	Group C	P value
2.37±0.490	2.33±0.479	2.23±0.430	.519

Total number of rescue analgesics used were comparable in all the three groups.

Discussion

Anesthesiologists are more concerned about the problems associated with Extubation, recovery and emergence. The problems at Extubation are more common than problems at intubation. Tracheal Extubation is associated with a 10–30% increase in arterial pressure and HR lasting 5–15 min. Respiratory complications after tracheal Extubation are 3 times more common than complications occurring during tracheal intubation and induction of anaesthesia (4.6% vs. 12.6%) [22]. Hence, we decided to do a comparative study on attenuation of Extubation response with three different doses of Dexmedetomidine.

In 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 [13], lignocaine [14], labetalol [15], nicardipine [16] and opioids [17] 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 α_2 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.

Dexmedetomidine has been studied extensively for attenuation of intubation and Extubation response. In most studies Dexmedetomidine has been compared with other pharmacological agents in dose of 0.5 to 1 μg/kg. Very few studies have compared different doses of Dexmedetomidine in attenuation of Extubation response. We conducted this prospective randomised study in an attempt to find out the minimum effective dose of Dexmedetomidine for attenuation of Extubation response with minimum side effects.

We randomly divided the patients into three groups of 30 patients each with group A receiving 0.5µg /kg of Dexmedetomidine in NS, group B receiving 0.75µg /kg of Dexmedetomidine in NS and group C receiving 1µg /kg of Dexmedetomidine in NS over 10 minutes.

The main findings of our study are as follows:

- During Infusion of Dexmedetomidine upto Extubation there was increase in heart rate in group A whereas in group B & C the increase in heart rate was attenuated. The decrease in heart rate was more in group C than in group B. 2 patients in group A, 3 patients in group B and 10 patients in group C had bradycardia during Dexmedetomidine infusion.
- There was increase in SBP, DBP and MAP in group A whereas the SBP, DBP and MAP decreased in group B and group C.
- The SPO_2 during Dexmedetomidine infusion was lower in group B & C as compared to group A.However the mean saturation remained above 97 all the times in the three groups and the lower oxygen saturation is not clinically significant.
- The BIS during Dexmedetomidine infusion was comparable in all the three groups.
- Patients in group B & group C had better Extubation quality than patients in group A.In group B & group C the quality of Extubation was comparable. In group C 15 patients had no coughing at the time of Extubation as compared to 14 patients in group B and 8 in group A. Both in group B & group C 12 patients had smooth Extubation with minimal coughing as compared to 10 patients in group A. Only 3 patients had moderate coughing in group C as compared to 4 in group B and 12 in group A.
- Immediately after Extubation heart rate significantly differed in three groups. Heart rate was maximum in group A and minimum in group C. However after 30 minutes of Extubation and thereafter the heart rate was comparable in all the groups.
- Immediately after Extubation SBP, DBP and MAP was significantly higher in group A as compared to group B and group C. SBP, DBP and MAP in group B & group C were comparable. However 30 minutes after Extubation and thereafter the SBP, DBP and MAP were comparable in all the three groups.
- Immediately after Extubation SPO_2 was lower in group B and group C as compared to group A.However mean saturation remained above 97 all the times in three groups and the lower saturation is not clinically significant. 30 minutes after Extubation and thereafter SPO_2 was comparable in all the groups.
- Post operatively pain was judged by The Visual Analogue Score. Patients in group A experienced more pain as compared to group B & group C. Pain score in

group B & group C were comparable.

- Mean Interval between Extubation and use of 1st rescue analgesic was 44±14.166 min in group A, 49±14.166 min in group B and 54±16.989 in group C.
- Post operatively patients in group C were more sedated. Sedation score was maximum in group C and minimum in group A. The difference in sedation score was only significant in group A & C and difference was insignificant between group A & group B and between group B & group C.However after 1 hour sedation scores were comparable in all the three groups.
- Total number of rescue analgesics used were comparable in all the three groups.

The α_2 receptors are involved in regulating the autonomic and cardiovascular systems. α_2 receptors are located on blood vessels, where they mediate vasoconstriction, and on sympathetic terminals where they inhibit norepinephrine release. α_2 receptors are also located within the central nervous system and their activation leads to sedation, a reduction of tonic levels of sympathetic outflow and an augmentation of cardiac-vagal activity. This can result in a decrease in heart rate and cardiac output. The use of α_2 agonists in the perioperative period has been associated with reduced anesthetic requirements and attenuated heart rate and blood pressure responses to stressful events. In addition,α_2 receptors within the spinal cord modulate pain pathways, thereby providing some degree of analgesia [23-25].

Hemodynamic effects

It was observed that Dexmedetomidine used in premedication supresses the sympathetic activation which is due to the endotracheal intubation [26]. 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 [27].It was found in the study by Jaakola *et al*. that, during the intubation blood pressure and heart rate is significantly reduced by 0.6 µg.kg1Dexmedetomidine [28]. In Scheinin's study these parameters were also reduced by equal doses of Dexmedetomidine [29]. In the other study which was done by Tezer *et al*. it is concluded that sympathetic responses during laryngoscopy and intubation were effectively reduced by Dexmedetomidine 1 $\mu g.kg^{-1}h^{-1}$ and esmolol 250 $\mu g.kg^{-1}min^{-1}$ [30]. Khan *et al*. demonstrated that heart rate, systolic and diastolic blood pressures were reduced by Dexmedetomidine [31]. In another study on the patients undergoing vascular surgery, it was observed that in the recovery period Dexmedetomidine infusion led to supression of heart rate and plasma cathecholamine levels [32].

Similar results were obtained in our study. 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 where as 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*. [33] similar results were obtained where they concluded that to control haemodynamic responses to tracheal intubation, Dexmedetomidine 1 $\mu g.kg^{-1}$ is more effective than Dexmedetomidine 0.5 $\mu g.kg^{-1}$. Martina *et al*. [21] 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. Similarly in our study we found that BP and HR increased in the group A with Dexmedetomidine 0.5 $\mu g.kg^{-1}$.We cannot comment on the attenuation of the haemodynamic response in group A as we had no control group.

Quality of Extubation

Bindu *et al*. [20] 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*. [36] 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. Fan *et al*. [34] compared two doses of Dexmedetomidine with remifentanil for tracheal Extubation in deeply anesthetized adult patients after otologic surgery. They concluded that Dexmedetomidine in dose of 0.7 mcg/kg was associated with a higher percentage of patients with a smooth Extubation as compared to Dexmedetomidine in dose of 0.5 mcg/kg. Similar results were obtained in our study. The quality of Extubation increased with increase in dose of Dexmedetomidine. In group C 15 patients had no coughing at the time of Extubation as compared to 14 patients in group B and 8 in group A.

Adverse effects

Dexmedetomidine has been used in dose of 0.1 to 10 µg/kg/h. The studies with higher infusion rates had more incidences of adverse effects like hypotension and bradycardia. Bindu *et al*. [20] and Aksu R *et al*. [36] found that Dexmedetomidine led to higher incidence of bradycardia. Similar results were obtained in our study where we found that with increase in dose of Dexmedetomidine from 0.75µg /kg to 1µg /kg the side effects also increased as 10 patients in group C had bradycardia during Dexmedetomidine infusion as compared to 3 patients in group B and 2 patients in group A.The BIS was comparable in all the three groups during Dexmedetomidine infusion.

Recovery from anesthesia

Post Extubation the HR, SBP, DBP and MAP was much higher in group A as compared to group B & group C. However after 30 minutes of Extubation these parameters were comparable in all the three groups. The mean saturation remained above 97 all the times in the three groups. There was decrease in post- operative pain with increase in dose of Dexmedetomidine. Pain as determined by VAS was much more in group A as compared to group B & group C. The pain scores were comparable in group B & group C. Mean Interval between Extubation and use of 1st rescue analgesic was 44±14.166 min in group A, 49±14.166 min in group B and 54±16.989 in group C. However total number of rescue analgesics used were comparable in all the

groups. Post-operative sedation also increased with increase in dose of Dexmedetomidine. Sedation score was maximum in group C and minimum in group A. However after 1 hour sedation scores were comparable in all the three groups. The findings are similar to that of Bindu *et al* who also concluded that Dexmedetomidine in dose of 0.75µg /kg led to higher sedation scores as compared to placebo.

Summary and conclusion

We concluded that Dexmedetomidine effectively attenuates the Extubation response in dose of 0.75µg/kg and 1µg /kg whereas in dose of 0.5µg/kg the Extubation response was not effectively attenuated. 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 ($p<0.05$). However the quality of Extubation was comparable with Dexmedetomidine in dose of 0.75µg/kg and 1µg /kg ($p>0.05$). So we conclude that 0.75µg/kg is the single best dose of Dexmedetomidine for attenuation of Extubation response.

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