Original Research Article

Dexmedetomidine versus Esmolol to attenuate the extubation response following surgeries under general anaesthesia - A comparative study

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Abstract

Background: Extubation of trachea always brings about acute, transient, undesirable hemodynamic and airway response which is sometimes fatal in susceptible patients. To attenuate this undesirable extubation response Dexmedetomidine and esmolol have been used. In present study we have compared the efficiency of two drugs in attenuation of hemodynamic and airway response during tracheal extubation. **Methods:** A Prospective, randomized, double blinded controlled study was carried in our hospital, After obtaining ethical clearance and written informed consent from the patients, 100 patients aged 18-50 years of ASA 1 and ASA 2 were randomly allocated into 2 groups. Group D received 1mcg/kg of dexmetomidine over 10 mins prior to extubation. group E received 1.5mg/kg of esmolol 2mins prior to extubation. **Results:** significant attenuation of hemodynamic and airway reflexes observed ingroup D when compared to group E. **Conclusion:** When compared to Esmolol (1.5mg/kg), Dexmedetomidine(1mcg/kg) effectively suppresses cough and attenuates hemodynamic responses to tracheal extubation without causing clinically significant delayed emergence.
Key Word: Dexmedetomidine; Esmolol; Extubation response;

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INTRODUCTION

Endotracheal extubation is one of the most common day-to-day performed procedure in the practice of anaesthesia. Translaryngeal removal of a tube from the trachea via the nose or mouth is endotracheal extubation. It is well known that endotracheal intubation is associated with adverse hemodynamic and circulatory effects due to catecholamine surge. Likewise, epipharyngeal and laryngo pharyngeal stimulation[1,2] during endotracheal extubation causes catecholamines release into circulation, resulting in acute, transient, significant and undesirable hemodynamic changes. The cardiovascular reflexes might range from tachycardia, hypertension, arrhythmias, left ventricular failure to myocardial ischemia or infarction in susceptible patients[3,4]. 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%)[5, 6] varies from coughing, laryngospasm to negative pressure pulmonary edema, Therefore, this haemodynamic response to tracheal extubation such as hypertension, tachycardia and arrhythmias have always been an interest to anesthesiologist. Considerable Pharmacological and non pharmacological interventions are enumerated in literature to attenuate these hemodynamic responses, which includes extubating in the deeper plane of anaesthesia and using drugs such as Esmolol[7,8], labetalol[9] (beta blockers), Verapamil[10], Diltiazem[10], Nicardipine[11]

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(Ca2+ channel blockers), propofol[12,13], lignocaine (topical or IV)[14,15], Opioids like Fentanyl[16], alfentanil, sufentanil, Nitroglycerine (vasodialator), clonidine[17] etc,each having their own merits and demerits. Dexmedetomidine is a new generation centrally acting highly selective potent alpha 2 agonist selectivity of alpha2 : alpha1 is 1600:1), which has sedative, amnestic, analgesic, anxiolytic, symapatholytic properties, cardiovascular stabilizing effects, reduced anesthetic requirements, and preservation of respiratory function[18,19].

OBJECTIVES OF THE STUDY

1. To study the effect of dexmedetomidine and esmolol on haemodynamic responses during tracheal extubation.
2. To study the effect of dexmedetomidine and esmolol on airway reflexes during tracheal extubation.
3. To study the side effects of the drugs if any.

MATERIALS AND METHODS

Design of the study: case control study, power of study being 80% and 95%confidence limit, for a period of 2 years.

Duration of study: 2 years, from October 2016 to September 2018.

Sample size: 100

Formula: $n = 2(Z\alpha + Z1\text{-}\beta)$

$2\sigma\ 2\ d\ 2$

Where, σ= standard deviation

Z=constant 1 =type1 error β= type 2 error

d=allowable error

n=sample size

After obtaining institutional ethical clearance and written informed consent from the patients, 100 patients of ASA I and ASA II grade aged 18-50 years undergoing various surgeries done under general anaesthesia at Navodaya Medical College Hospital and Research Centre, Raichur are included in the study.

Inclusion criteria

- Patients scheduled for various surgeries under general anaesthesia
- ASA grade I and II.
- Age between 18-50 yrs.
- Patient given valid informed consent.

Exclusion criteria

- Patients cardiac and pulmonary co-morbidities.
- ASA grade III and IV
- Surgeries on neck and oral cavity.
- Patients with history of drug abuse or psychiatric disorder.
- Patients with h/o hypersensitivity
- Obese patients with difficult airway or history of sleep apnea.

After obtained informed written consent, patients were randomly allocated into 2 groups.

Group D: Dexmedetomidine group

Group E: Esmolol group

Monitoring of all patients was done using electrocardiography(ECG), Oxygen saturation(Spo2), non invasive blood pressure(NIBP), end-tidal carbon-di-oxide(Etco2) and premedicated with injection glycopyrolate 4mcg/kg; injection midazolam 0.03mg/kg and injection fentanyl 2mcg/kg intravenously. After preoxygenation, patients are induced with injection propofol 2mg/kg and intubation facilitated with injection atracurium 0.5mg/kg intravenously. Patients are maintained on 66% nitrous oxide in oxygen and Isoflurane 1-2% and atracurium. At the commencement of closure of skin incision, halothane is discontinued and inj Dexmedetomidine 1mcg/kg body weight diluted to 10ml in normal saline is infused over 10minutes using infusion pump in Group D patients. Group E patients received inj Esmolol 1mg/kg body weight diluted to 10ml normal saline 2min prior to extubation. Nitrous oxide is discontinued at the end of infusion. Residual neuromuscular blockade is reversed using injection neostigmine 0.05mg/kg and injection glycopyrolate 8mcg/kg intravenously.

Patients are extubated when the following extubation criteria are fulfilled.

1. Sustained head lift for 5 seconds.
2. Sustained hand grip for 5 seconds.
3. Adequate level of consciousness.
4. Maximum inspiratory pressure 40 to 50 cm H2O or greater.

Any occurance of cough, laryngospasm, bronchospasm or desaturation will be documented for a period of 15 min after extubation Emergence and extubation times were documented which were defined as emergence time – time interval between discontinuation of anesthetic and patient following verbal commands and Extubation time – time interval between termination of anesthetic agents and tracheal extubation. Delayed emergence was defined as emergence time more than 15 min after discontinuing anesthetics and reversal of neuromuscular blockade. Sedation is evaluated using Ramsay Sedation Scale.

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

RESULTS

Table 1: Comparison of Demographic and other Characterics between the two Study Groups.

Demographic and other Characterises	Group E (esmolol) n=50	Group D (demedetomidine) n=50	p-value
Age(mean±SD)	34.78(±8.34)	34.44(±9.02)	=0.85,NS
Gender (male/female)	25/25	26/24	
Weight(mean±SD)	47.16(±10.8)	49.62(±11.29)	=0.27,NS

Table 2: showing the age distribution of groups E and D

Age (years)	Group E		Group D	
	No. of patients	%	No. of Patients	%
<20	2	4	3	6
21-30	17	34	16	32
31-40	16	32	17	34
41-50	15	30	14	28
Total	50	100	50	100
Mean age (±SD)	34.78(±8.34)		34.44(±9.02)	
Maximum age	50		19	
Minimum age	19		50	
	t-value=0.1958	p-value=0.8452	Result=NS	

Table show age distribution of the patients in both the groups. The minimum age in group D and group E were 19 years and 19 years respectively. The maximum age group D and group E was 50 years and 50 years respectively The mean age in group D and group E was 34.44 and 34.78 years respectively. It is seen that group D had 26 males and 24 females, group E had 25 males and 25 females there was no statistical difference between two groups (p>0.05).

Table 3: Types of surgical procedures.

Sl.No	Type of surgical procedures	Group E (esmolol) No.of Patients	Group D (demedetomidine) No.of Patients
1	FESS	2	2
2	Excision	6	10
3	hernioplasty	2	1
4	incision anddrainage	2	1
5	laminectomy	2	1
6	lap appendicectomy	6	5
7	lap cholecystectomy	3	2
8	lap tubectomy	4	4
9	laparotomy	1	1
10	LSCS	3	4
11	lymphnode excision	1	1
12	ORIF	2	1
13	pedicle screw fixation	2	3
14	Plating	6	5
15	septoplasty	2	2
16	TAH	1	1
17	Tonsillectomy	1	1
18	tympanoplasty	4	5
Total		50	50

Table 4: Mean heart rate(HR)in both study groups.

Mean heart rate(HR)in both study groups.	Group E (esmolol) n=50	p-value	Group D (demedetomidine) n=50	p-value	p- value(b/w E and D)
drug will be give(T-0)	89.32(±2.97)		102.12(5.47)		0.0001***
Before Extubation (T-	87.14(3.62)	0.0001***	85.24(5.52)	0.0001***	0.0446*
extubation (T- 2)	84.54(4.19)	0.0001***	81.92(5.45)	0.0001***	0.0083**
3 min after extubation (T-3)	82.34(4.23)	0.0001***	79.24(4.83)	0.0001***	0.0009***
5 min after extubation (T-4)	80.62(4.13)	0.0001***	77.64(4.71)	0.0001***	0.0011**
10 min after extubation (T-5)	79.24(4.35)	0.0001***	75.96(4.76)	0.0001***	0.0005***

The changes in the Heart rate between the two groups at various time interval as mentioned in the table 4 shown to be significant (p value< 0.05)

Table 5: Mean SBP in both study groups.

Mean SBP in both study groups.	Group E (esmolol) n=50	p-value	Group D (demedetomidine) n=50	p-value	pvalue(b/w E and D)
Before study drug will be give(T-0)	129.88(±4.11)		130.28(±4.35)		0.6376,N S
Before extubation(T-1)	118.28(8.48)	0.0001**	103.44(±3.28)	0.0001**	0.0001***
1 min after extubation(T-2)	117.38(7.94)	0.0001**	105.02(±3.45)	0.0001**	0.0001***
3 min after extubation(T-3)	117.48(6.22)	0.0001**	110.66(±3.48)	0.0001**	0.0001***
5 min after extubation(T-4)	118.26(4.42)	0.0001**	115.94(±3.36)	0.0001**	0.0039**
10 min after extubation(T-5)	118.46(4.11)	0.0001**	117.64(±3.52)	0.0001**	0.2869,N S

The changes in the systolic blood pressure between the two groups at various time interval as mentioned in the table 5 shown to be significant (p value< 0.05).

Table 6: Mean DBP in both study groups.

Mean DBP in both study groups.	Group E (esmolol) n=50	p-value	Group D (demedetomidine) n-50	p-value	p- value(b/w E and D)
Before study drug will be give(T-0)	89.44(±2.52)	0.0001***	89.36(2.54)		0.8748,N S
Before Extubation(T-1)	74.16 (±10.09)	0.0001***	65.08(3.94)	0.0001***	0.0001***
1 min after extubation(T-2)	70.34 (±5.94)	0.0001***	67.08(3.99)	0.0001***	0.0018**
3 min after extubation(T-3)	73.32 (±4.34)	.0001***	71.64(3.98)	0.0001***	0.0466*
5 min after extubation(T-4)	77.12 (±4.52)	0.0001***	75.5(3.58)	0.0001***	0.0498*
10 min after extubation(T-5)	80.84 (±3.21)	0.0001***	78.6(3.47)	0.0001***	0.0011**

The changes in the diastolic blood pressure between the two groups at various time interval as mentioned in the table 6 shown to be significant (p value< 0.05)

Comparision of SPO2 between the groups didn't show any statistically significant: In Group D 34 patients(64%) had grade 1, 15 patients (30%) had grade 2 and 1 patient (2%) had grade 3 extubation quality. In group E 10 patients (20%) had grade 1, 12 patients (24%) had grade 2 and 28 patients (56%) had grade 3 extubation quality.

Sedation: In group D, no patients had grade 1, 15 patients (30%) had grade 2, 34 patients (68%) had grade 3 and 1 patient(2%) had grade 4 sedation. In group E, 5 patients (10%) had grade 1, 40 patients (80%) had grade 2 and 5 patients (10%) had grade 3 sedation.

DISCUSSION

Drug selected for the study: Dexmedetomidine according to several authors is known to diminish the haemodynamic response for laryngoscopy and intubation. Dexmedetomidine is a novel drug to India (introduced in 2009). Small number of studies are done on mitigating extubation response in india. As a consequence we have selected it as our study drug. G. Guler, A. Akin *et al*[19] conducted a study to evaluate the effect of single dose Dexmedetomidine in attenuating airway and circulatory reflexes during extubation which revealed single dose intravenous Dexmedetomidine bolus before tracheal extubation attenuates heart rate and circulatory reflexes during extubation. Esmolol, being cardio-selective beta blocker, attenuates the hemodynamic response to extubation by blocking the beta 1 adrenergic receptors. On account of its rapid onset and short duration of action and lesser number of studies being available in comparision with dexmedetomidine, it instigated us to study its effect on extubation response.

Dose selection: Different doses of dexmedetomidine have been used to attenuate the stress response to emergence from general anaesthesia. Guler *et al*[9] (0.5 µg/kg over 5 mins), Aksu *et al*[10] (0.5 µg/kg over 10 mins.), Jain *et al*[11] (1 µg/kg over 10 mins.), Sriranga Rao *et al*[12] (0.5 µg/kg over 10 mins), Kwon Hui Seo *et al*[13] (0.5 µg/kg, 0.7 µg/kg, 1 µg/kg), Bindu *et al*[14] (0.7 µg/kg over 10 mins) have used different doses of dexmedetomidine. D Jain *et al*[18]conducted a study on effect of dexmedetomidine on stress response to extubation and inferred that a bolus dose of Dexmedetomidine 1mcg/kg over 10mins, prior to reversal provided hemodynamic stability associated with extubation which may prove beneficial for cardiac patients. Hence, we selected dose of 1mcg/kg dexmedetomidine, which is the dose effective with very less side effects. Turan *et al*[20]observed the effects of dexmedetomidine at the end of procedure to prevent hyperdynamic response during extubation and concluded that without interference in recovery time, Dex 0.5mcg/kg administered 5 min before end of surgery allows easy extubation, more comfortable recovery. In our study we have used 1mcg/kg Dexmedetomedine with same results without any adverse effects

Method of administration: In the current study dexmedetomidine was diluted in 10 mL of normal saline

and with the aid of a syringe pump infused it intravenously over 10 minutes. As and when dexmedetomidine is administered as a single bolus dose, transient rise in blood pressure and fall in heart rate was observed. This initial change of hemodynamics of dexmedetomidine can be refered to its stimulation of peripheral alpha-2B receptors located in smooth muscles of blood vessels and this change can be diminished by a slow infusion. Thereby, in our study we administered the bolus dose of dexmedetomidine over 10 minutes intravenously. Esmolol is administered after diluting 1.5mg/kg with NS upto 10ml and infused as slow bolus.

Timing of administration: From the pharmacokinetic profile, it is seen that the distribution half-life of intravenous dexmedetomidine is approximately 6 minutes. Jain *et al*[18], Sriranga Rao *et al*[21], and Bindu *et al*[22] have administered dexmedetomidine 10 minutes before extubation. Accordingly, in the current study, dexmedetomidine was administered 10 minutes before extubation to hamper stress response to extubation.

Esmolol hydrochloride is an ultra-short-acting, beta-one selective adrenergic receptor blocker with a distribution halflife of 120 seconds and an elimination half-life of 540 seconds. Therefore, we administered the bolus dose of esmolol 2minutes before extubation.

Comparative analysis of haemodynamic data between Dexmedetomidine and esmolol groups at various intervals

I. Changes in heart rate after Dexmedetomidine and esmolol administration

Our study revealed dexmedetomidine and esmolol injections minimized the increase of HR before extubation and upto 10 mins post extubation ($p< 0.001$), but there was considerable decrease in HR with Dexmedetomidine (1mcg/kg) when compare to esmolol (1.5mg/kg). Before extubation (T1) there is statistically significant fall in heart rate from the baseline value, i.e., before giving study drugs, in dexmedetomidine group (16%) when compare to esmolol group (3%). (p value= 0.044). At One minute after extubation (T2) we have noticed that there is 20% reduction in heart rate in dexmedetomidine group when compared to esmolol group which is about 6%. This is statistically significant with p value of 0.0083. At 3 minutes after extubation (T3) there is statistically significant reduction in heart rate in dexmedetomidine group (22%) when compared to esmolol group (8%) with p value 0.0009. At 5minutes after extubation we observed that there is statistically significant 24%fall in heart rate in group D when compare to group E which is about 10%. (p value 0.0011). At 10 minutes of extubation there is statistically significant fall in heart rate in groupD (25%) when compare to group E (11%) with p value 0.005.

These analysed values are in accordance with the study done by Jain D *et al*[18], Sriranga Rao *et al*[21], Wang YQ *et al*[23], kovac AL *et al*[11] and vanish priya *et al*[24]. Vanish Priya *et al*[24] conducted a study on comparative evaluationof attenuation of post- extubation hyperdynamic responses with single dose dexmedetomidine or esmolol and concluded that Both the drugs, dexmedetomidine and esmolol were effecient in controlling rise of pulse and blood pressure during extubation phase, however dexmedetomidine proves to be better due to its ancillary analgesic , sedative and anti – emetic actions. Our findings are in congruence to this study. Bradycardia was not seen in any of the patients. This conclusion which is also found in other studies, did not observe statistically significant incidence of bradycardia.

II. Changes in systolic blood pressure (SBP)

Our study illustrated dexmedetomidine and esmolol injections reduced systolic blood pressure before extubation and upto 10 mins post extubation ($p<0.001$), but there was comparatively more decrease in blood pressure with Dexmedetomidine (1mcg/kg) when compare to esmolol (1.5mg/kg). Before extubation (T1) there is statistically significant fall in blood pressure from the base line value, i.e., before giving study drugs, in dexmedetomidine group (21%) when compare to esmolol group (9%). (p value= 0.0001). At One minute after extubation (T2) we have noticed that there is 19% reduction in SBP in dexmedetomidine group when compare to esmolol group which is about 10%. This is statistically significant with p value of 0.0001. At 3 minutes after extubation (T3) there is statistically significant decrease in SBP indexmedetomidine group (14%) when compare to esmolol group (9%) with p value 0.0001. At 5minutes after extubation (T4) we observed that there is statistically significant10% fall in SBP in group D when compare to group E which is about 8.5%. (p value 0.0001) which continued to be same even after 10 minutes post extubation.

III. Changes in diastolic blood pressure (DBP)

Our study showed dexmedetomidine and esmolol injections reduced diastolic blood pressure prior to extubation and upto 10mins post extubation ($p< 0.001$), but there was significant decrease in blood pressure with Dexmedetomidine (1mcg/kg) to esmolol (1.5mg/kg). Before extubation (T1) there is statistically significant fall in diastolic blood pressurefrom the base line value, i.e., before giving study drugs, in dexmedetomidine group (26%) when compare to esmolol group (17%). (p value= 0.0001). At One minute after extubation (T2) we observed that there is 24% fall in DBP in dexmedetomidine group when compared to esmolol

group which is about 21%. This is statistically significant with p value of 0.0018.

At 3 minutes after extubation (T3) there is statistically significant fall in DBP in dexmedetomidine group (20%) when compare to esmolol group (18%) with p value 0.0466. At 5minutes after extubation (T4) we observed that there is statistically significant16% fall in DBP in group D when compare to group E which is about 13.5%. (p value 0.0498). At 10 minutes of extubation(T5) there is statistically significant fall in DBP ingroup D (12%) when compare to group E (9%) with p value 0.0011.

IV. Changes in mean arterial pressure (MAP): Before extubation (T1) there is statistically significant reduction in mean blood pressure from the base line value, i.e., before giving study drugs, in dexmedetomidine group (25%) against esmolol group (12%). (p value= 0.0001). At One minute after extubation (T2) we observed that there is 23% of MBP reduction in dexmedetomidine group to esmolol group which is about 16%. This is statistically significant with p value of 0.0001. At 3 minutes after extubation (T3) there is statistically significant fall in MBP indexmedetomidine group (18%) in comparision to esmolol group (14%) with p value 0.0001. At 5minutes after extubation (T4) we observed that there is statistically significant14% fall in MBP in group D when seen with to group E which is about 11%. (p value 0.0013). At 10 minutes of extubation(T5) there is statistically significant fall in MBP ingroup D (11%) when noticed to group E (10%) with p value 0.0001. SBP, DBP and MAP values were significantly lower in dexmedetomidine in comparision with baseline values, when observed everytime since dexmedetomidine infusion to post extubation 10 minutes. This observations are in accordance with the study done by Sriranga Rao *et al*[21], Wang YQ *et al*[23], kovac AL *et al*[11], vanish priya *et al*[24] andJain D *et al*[18]in which study group patients received 1 µg/kg of dexmedetomidineand there was no significant change (p value < 0.005) in the blood pressure in dexmedetomidine group throughout the study tenure. In the same manner, the SBP, DBP and MAP values in esmolol group was lower than the pre-drug values.

Comparision of airway reflexes: Our study also found that postextubation cough is considerably suppressed by in the dexmedetomidine group than in the esmolol group. No cough noted in 34 patients (68%) in dexmedetomidine when compare to 10 patients(20%) in esmolol group. Mild cough noted in 15 patients(30%) in group D to 12 patient (24%) among esmolol group. Moderate cough noted in 1(2%) patient in group D when seen against 28(56%) in group E. None of the patient presented severe coughing or poor extubation in the two groups. This notable distinction may be due to the sedative action of dexmedetomidine and also by the reason that it relaxes the bronchial smooth muscle and prevents airway irritation. It may be additional advantage as it helps in the reduction of incidence of the postoperative hoarseness and irritation due to tracheal tube. Our observations are in concurrence with A Luthra *et al*[25] where they drawn conclusions that Dexmedetomidine infusion suppresses cough and reduces hemodynamic responses to tracheal extubation in comparison to placebo without causing delay in emergence.

Delayed emergence: Only 6% of the patients presented with delayed emergence in group E when compared to 20% of group D patients which was statistically, but not clinically significant. Shukry *et al.*[26]studied effects of infusions of dexmedetomidine (0.2 µg/kg/h)during surgery on the incidence of emergence delirium in 50 children aged 1–10 years scheduled for sevoflurane-based general anesthesia. After induction of the children with inhalational agent, they were allocated randomly to dexmedetomidine or placebo groups, respectively. The infusion of 0.2 µg/kg/h dexmedetomidine or equal volume of saline was started after securing the airway. The investigators analysed and showed that there was reduction of incidence of emergence agitation from 61% to 26%.

Sedation: We witnessed that significant number of the patients in group D were sedated after extubation without compromising airway or breathing and were responsive to verbal commands and none of them showed agitation, emergence delirium, restless. Where as in group E 5% of patients were anxious and agited. Time of extubation and eye opening were similarly obtained among the two groups. Our findings are similar with Ankur Luthra *et al* who surveyed alleviating stress response to tracheal extubation in neurosurgical patients : a comparative study of two infusion doses of dexmedetomidine which showed that Dexmedetomidineinfusion did not show delaying emergence, delayed extubation when compared to placebo.

CONCLUSION

When compared to Esmolol (1.5mg/kg), Dexmedetomidine (1mcg/kg) effectively suppresses cough and attenuates hemodynamic responses to tracheal extubation without causing clinically significant delayed emergence.

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