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Comparison of Dexmedetomidine Versus Esmolol in Attenuation of Sympathoadrenal Response to Tracheal Extubation After General Anaesthesia A Prospective Randomized Double Blind Study

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Abstract: Emergence from general anesthesia and tracheal extubation is associated with increased catecholamine secretion, leading to tachycardia, hypertension and increases oxygen consumption for about 5-15 min postextubation. We investigated and compared the efficacy of dexmedetomidine and esmolol to attenuate airway and circulatory reflexes during emergence from general anesthesia and tracheal extubation. This prospective randomized double blind study was conducted at Dr Sampurnanda Medical College Hospital, Jodhpur, after obtaining institutional ethical committee approval and informed written consent, 102 patients of ASA Grade I-II aged 20-60 years received standard general anesthesia. At the closure of skin incision, patients were randomly allocated to receive either dexmedetomidine 0.7 µg/kg (Group D) or esmolol 1.5mg/kg (group E) or saline placebo (Group C) intravenously over 10 minutes in a double-blind design. Heart rate, systolic, diastolic and mean arterial pressures were assessed before, during- and after extubation. Time to eye opening and extubation time were recorded, also extubation and sedation scores were recorded, complications such as coughing, laryngospasm, bronchospasm and desaturation if any were also tabulated. Analysis revealed that Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable till 5 minutes of study drugs infusion($p>0.05$) in all groups which became statistically highly significant at completion of study drugs infusion, during extubation($p<0.001$) and remained significantly higher till 30 minutes postextubation. Time to extubation and eye opening were prolonged in Group D. Incidence of coughing & Agitation was more in Group C.In dexmedetomidine group patients were more sedated post extubation. Extubation quality was better in dexmedetomidine group than esmolol and control. We concluded that single dose of dexmedetomidine 0.7µg/kg body weight given over 10 minutes before extubation is better than esmolol(1.5mg/kg) in attenuating the hemodynamic and airway reflexes during emergence from anesthesia without causing undue sedation, but may prolong time to extubation and eye opening.
Keywords: Airway reflexes, Dexmedetomidine, Esmolol, Hemodynamic responses.

INTRODUCTION

Tracheal intubation and extubation are often accompanied by increase in sympathetic and sympathoadrenal activity [1-3]. Emergence from general anesthesia (GA) and tracheal extubation is associated with increased catecholamine secretion, leading to tachycardia, hypertension and increases oxygen consumption for about 5-15 min postextubation[4]. Endotracheal extubation is the translaryngeal removal of a tube from trachea via nose or mouth,or is the discontinuation of an artificial airway.Complications that occur during and after extubation are three times more common than that occurring during tracheal intubation and induction of anesthesia[5-7]. Various drug regimens have been used from time to time for attenuating the stress response to laryngoscopy, intubation and extubation including opioids, lignocaine, magnesium, gabapentin, beta blockers, calcium channel blockers, vasodilators with variable response [8-14].

Dexmedetomidine, an α2-adrenoreceptor agonist with a distribution half-life of approximately 6 minutes has been successfully used for attenuating the

stress response to laryngoscopy [15]. Alpha-2 agonist decreases the sympathetic outflow and noradrenergic activity, there by counteracting the hemodynamic fluctuations occurring at the time of extubation due to increased sympathetic stimulation [16]. Esmolol, ultra-short acting beta-1adrenergic blocker, has prominent effect on $_{\beta}$-receptors. It has rapid onset and short duration of action. Use of this selective $_{\beta}$-adrenergic antagonist prevents the reflex sympathoadrenal discharge mediated tachycardia and hypertension during tracheal extubation [17].

Considering all these observations, the present study was designed to evaluate the hemodynamic changes associated with tracheal extubation and also the efficacy of dexmedetomidine versus esmolol in prevention of such hemodynamic changes.

MATERIALS AND METHODS

After obtaining written informed consent from patients and approval from the institutional ethical committee, this prospective randomized comparative study was conducted on 102 patients of ASA grade I and II, in the age group of 20 years to-60 years of either sex, scheduled for various surgeries, under general anesthesia at Dr S N Medical College and attached group of Hospitals. Patients with cardiovascular or respiratory disorders, diabetes, hypertension, obesity, difficult airway, medications that effect heart rate (HR) or blood pressure (BP), pregnant, currently breast feeding women, history of sleep apnea, seizures disorder and those with history of allergy to study drugs were excluded.

A detailed preoperative check up including history, general physical and systemic examination of these patients was carried out. Routine investigations were done and whenever needed specific investigations like ECG, Chest x-ray, LFT, RFT, S.electrolytes etc. were also asked for. Patients were kept Nil by mouth for 6hrs. Tab. ranitidine 150 mg and tab.metoclopramide 10 mg was given as premedication at night before surgery. This study was conducted in a randomized prospective double blinded manner; Patients were randomized using opaque sealed envelope into three groups, each of 34 patients. Group D (dexmedetomidine), Group E (esmolol), Group C (control).The enrolling investigator prepared the drug solution to be given before extubation and had no role in patient's assessment.

On arrival in the operation theatre, the patients were connected to multi channel monitor which recorded heart rate, blood pressure ,$ETCO_2$, continuous ECG monitoring and O2 saturation. Under all aseptic conditions intravenous line was secured with 18/20G cannula and an infusion of RL solution was started. The following baseline parameters were recorded and monitored continuously: Heart rate, Blood pressure (systolic, diastolic), mean arterial pressure, SpO2 and rhythm.

Patients were uniformly premedicated with inj. Midazolam 0.01mg/kg iv, inj Fentanyl 2μg/kg iv, inj Ondansetron 0.1mg/kg iv and inj. Glycopyrolate 0.004mg/kg iv before induction. Baseline parameters were also recorded. In our study we took observations just before the study drug administration as basal value for comparison.

After preparing the patient,pre-oxygenation with 100% O_2 was done for 5mins,intravenous induction was done with inj propofol 2mg/kg body wt, inj succinylcholine 2mg/kg was administered and intermittent positive pressure ventilation was carried out with 100%O_2.After laryngoscopy endotracheal intubation was done with appropriate size(8/8.5mm for males and 7/7.5mm for females, high volume low pressure cuffed tube)of endotracheal tube, cuffed and confirmation was done by checking air entry bilateral, then was fixed at appropriate length(21cm) and taken on mechanical ventilation.

General anaesthesia was maintained with O_2+inhalational agent (isoflurane1-2%) and muscle relaxation was obtained with Atracurium besylate loading dose of 0.5mg/kg and 0.1mg/kg for maintenance. 10mins before the end of surgery the interventional drugs were given as follows:-

Group D (dexmedetomidine): Was given inj. Dexmedetomidine (0.7mcg/kg BW) in 20ml NS over 10 mins before the end of surgery.

Group E (esmolol): was given inj Esmolol (1.5mg/kgBW)in 20ml NS over 10mins before the end of surgery.
Group C (control): was given 20 ml of NS over 10 mins before the end of surgery.

Isoflurane was stopped at the end of surgery. Patient were reversed with injection neostigmine 0.05 mg/kg and Injection glycopyrolate 0.01mg/kg intravenously Oropharyngeal suction was performed immediately prior to extubation and endotracheal extubation was done once patients met following extubation criteria.

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

OBSERVATIONS

Patients were observed for;

- Haemodynamic response- HR, SBP, DBP, MAP and arrhythmias.
- Airway reflexes- coughing, breath-holding, laryngospasm and bronchospasm at extubation.
- Respiratory monitoring- RR and Spo2

HR, SBP, DBP, and MAP were recorded just prior to study drug administration/basal value (T_0) and at 1 min. (T_1), 3 min. (T_2), 5 mins. (T_3) and 10 mins. (T_4) of drug infusion, at extubation (T_5) and at 1min. (T_6), 5min. (T_7), 10 mins. (T_8) and 30 mins. (T_9), of extubation.

Bradycardia was defined as HR < 60 /min and treated with rescue dose of injection atropine 0.6 mg intravenously, tachycardia being 20% increase from baseline, hypertension as either 20% increase from baseline or SBP > 180 mmHg and hypotension as 20% decrease from baseline or SBP < 80 mmHg. Extubation quality was rated using extubation quality 5-point scale, 1 = no coughing, 2 = smooth extubation, minimal coughing, 3 = moderate coughing (3 or 4 times), 4 = severe coughing (5 to 10 times) and straining, 5 = poor extubation, very uncomfortable (laryngospasm and coughing >10 times). Number of coughs per patient was monitored for 15 minute post extubation. Any incidence of laryngospasm, bronchospasm, breath holding or desaturation was noted. A decrease in peripheral arterial oxygen saturation >5% from baseline was defined as desaturation and holding breath for 20 seconds or more as breath holding.

Time to extubation and eye opening was recorded, sedation was evaluated using Ramsay Sedation Scale at 5 minutes after extubation 1 = anxious and agitated, restless, 2 = cooperative, 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.

For statistical analysis Statistical Package for Social Sciences (SSPS) version 22 was used. Descriptive data were presented as mean $\pm$ SD. Continuous data were analyzed by ANOVA and Chi-square test to assess the statistical difference between groups. P>0.05 not significant, P <0.05 significant P<0.001 highly significant.

Sample size: for comparison between esmolol and dexmedetomidine group immediately at extubation (as per previous study), required sample size is-keeping alpha error 0.1(1%) and power 95% (beta error 5%)- for MAP-grp E-116,grp D-95, pooled SD-13.5,sample size -15. For SBP-grp- E-159, grp D-125, pooled SD-15, sample size-8. For DBP-grp E-94, grp D-80, pooled SD-13, sample size-31.

RESULTS

Demographic profile and ASA physical status of the patients in all the three groups were comparable, and the differences between the three groups were statistically not significant (P > 0.05) (Table: 1).

Basal values of HR and BP were comparable in all the three groups, values of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure, from starting of study drugs infusion(T_1) till 5 minutes of study drugs infusion (T_3) showed no significant differences between the three groups(P>0.05),but their values during T_4(completion of study drugs infusion),T_5(at extubation),post extubation at T_6(1min), T_7(5min), T_8(10mins), T_9(30mins) showed significant decrease in the dexmedetomidine group in comparison to the esmolol and control group(P<0.0001)[Table 2,3,4,5]. The extubation time, ,time to awakening, time to orientation, were significantly prolonged in Dexmedetomidine group on comparison to Esmolol and Control group(P<0.001)[Table 5].

The extubation quality 5-point scale was lower in dexmedetomidine group on comparison to Esmolol and Control group(P<0.001)[Table 6],reflecting smoother extubation in dexmedetomidine group. And on comparison of the post operative sedation score (Ramsay Sedation Score) Dexmedetomidine group patients were significantly sedated on comparison to the other groups. Sedation scores at1min,5min,10mins post extubation were statistically significant increase in Group D as compared with Group E and C.(P<0.001)[Table 7].Two patients in dexmedetomidine group had bradycardia,but it was transient and responded to injection atropine.

Table-1: Demographic profile of the study group

	Dexmedetomidine(mean±SD)	Esmolol(mean±SD)	Control(mean±SD)	Pvalue
Age	31.23±7.11	36.02±10.59	36.41±9.95	>0.05
Weight	57.67±5.27	55.26±5.12	57.67±5.89	>0.05
Sex	19:15	14:20	17:17	
ASA(1:2)	21:13	26:08	28:06	

Table-2: Heart rate

Heart Rate (min)	Group D (Mean±SD)	Group E (Mean±SD)	Control (Mean±SD)	Control vs Group D	Control vs Group E	Group D vs E
Before adm. of drugs	83.20±8.42	81.51±8.08	79.26±9.89	0.080	0.328	0.373
T1	80.11±9.26	80.41±8.19	78.47±9.34	0.323	0.366	0.908
T2	75.61±9.05	78.11±6.97	77.88±8.06	0.393	0.898	0.300
T3	71.11±8.66	74.47±6.55	76.91±7.97	0.008	0.172	0.108
T4	65.11±5.03	69.47±5.78	76.14±8.35	<0.0001	0.0003	0.001
T5	75.35±7.35	80.64±7.22	99.58±8.07	<0.0001	<0.0001	0.003
After extubation						
T6	76.02±7.16	80.67±6.95	96.20±7.90	<0.0001	<0.0001	0.008
T7	73.97±6.92	78.82±7. 55	92.97±6.61	<0.0001	<0.0001	0.007
T8	72.00±5.46	77.85±7.97	87.47±7.07	<0.0001	<0.0001	0.0008
T9	70.82±3.69	78.58±7.77	83.32±8.66	<0.0001	0.02	<0.001

Table-3: Shows the variations in the SBP

SBP (mmHg)	Group D	Group E	Control	Control vs Group D	Control vs Group E	Group D vs E
Before adm. of drugs	128.78±7.89	129.47±7.41	131.55±9.64	0.243	0.320	0.823
T1	126.70±7.50	128.26±7.26	129.91±9.30	0.122	0.418	0.387
T2	123.82±8.70	126.0±6.75	129.11±8.43	0.01	0.097	0.253
T3	117.76±8.71	123.85±7.20	127.64±9.10	<0.0001	0.06	0.005
T4	111.41±7.44	121.35±6.39	127.26±8.50	<0.0001	0.001	<0.0001
T5	124.76±7.25	130.76±7.51	156.47±7.98	<0.0001	<0.0001	0.004
After extubation						
T6	123.82±7.17	129.44±6.69	152.73±7.68	<0.0001	<0.0001	0.001
T7	119.91±7.49	128.47±6.61	146.97±6.79	<0.0001	<0.0001	<0.0001
T8	116.76±6.44	126.50±6.89	141.0±7.63	<0.0001	<0.0001	<0.0001
T9	116.82±6.07	127.70±6.95	134.23±8.59	<0.0001	0.0009	<0.0001

Table-4: Variations in diastolic blood pressure

DBP (min/	Group D	Group E	Control	Control vs Group D	Control vs Group E	Group D vs E
Before adm. of drugs	80.40±8.31	80.29±7.87	83.02±7.50	0.182	0.147	0.940
T1	79.05±8.04	79.26±7.66	82.20±7.41	0.098	0.112	0.914
T2	76.44±7.72	77.35±7.91	80.08±7.46	0.068	0.211	0.523
T3	73.38±8.29	75.91±7.41	78.73±7.64	0.007	0.126	0.189
T4	66.50±5.77	73.26±7.64	78.73±6.89	<0.0001	0.002	0.0001
T5	72.29±6.64	82.17±7.76	102.05±7.44	<0.0001	<0.0001	<0.0001
After extubation						
T6	73.05±5.65	79.38±7.03	98.52±7.37	<0.0001	<0.0001	0.0001
T7	72.20±5.31	78.17±6.66	93.26±6.93	<0.0001	<0.0001	0.0001
T8	71.26±6.85	78.23±6.93	88.70±6.67	<0.0001	<0.0001	<0.0001
T9	71.67±6.32	78.70±7.09	84.76±6.78	<0.0001	0.006	<0.0001

Table-5: Variations in mean arterial blood pressure

MAP	Group D	Group E	Control	Control vs Group D	Control vs Group E	Group D vs E
Before adm. of drugs	96.50±7.16	96.76±7.20	99.09±7.33	0.145	0.190	0.882
T1	94.62±7.11	95.61±8.84	97.97±7.13	0.056	0.182	0.562
T2	92.78±7.17	964.0±6.87	96.10±6.87	0.058	0.210	0.296
T3	88.69±7.66	91.38±5.43	95.04±6.81	0.001	0.02	0.09
T4	83.37±5.57	89.60±6.39	95.54±7.47	0.0008	<0.0001	<0.0001
T5	89.82±6.23	98.24±7.02	120.13±7.10	<0.0001	<0.0001	<0.0001
After extubation						
T6	90.07±4.78	96.09±6.01	116.55±6.96	<0.0001	<0.0001	<0.0001
T7	88.91±6.34	94.99±5.99	111.11±6.47	<0.0001	<0.0001	<0.0001
T8	85.93±6.88	94.31±6.37	106.13±6.57	<0.0001	<0.0001	<0.0001
T9	86.63±5.47	92.32±15.80	101.26±6.67	<0.0001	0.003	0.04

Table-6: Recovery parameters

	Dexmedetomidine	Esmolol	Control	Group D Vs Control	Group E Vs Control	Group D vs Group E
Extubation time	7.08±0.85	4.68±0.56	4.96±0.71	<0.0001	0.075	<0.0001
Time to awakening	6.73±0.83	4.19±0.56	4.37±0.60	<0.0001	0.216	<0.0001
Time to orientation	7.88±0.95	5.08±0.62	5.25±0.62	<0.0001	0.262	<0.0001
Extubation scores	1.32±0.47	2.32±0.47	2.67±0.47	<0.0001	0.003	<0.0001

Table-7: Postoperative sedation score (RAMSAY SCALE)

RAMSAY Score	Group D	Group E	Control	Control vs Group D	Control vs Group E	Group D vs E
1 min	2.5±0.50	2.0±0.0	1.73±0.0	<0.001	>0.05	<0.001
5 min	2.38±0.49	1.55±0.0	1.41±0.0	<0.001	>0.05	<0.001
10 min	2.26±0.44	1.58±0.23	1.38±0.0	<0.001	>0.05	<0.001
30 min	1.73±0.57	1.54±0.38	1.38±0.41	<0.05	>0.05	>0.05

DISCUSSION

Laryngoscopy and endotracheal intubation is considered to be the most crucial event while conducting general anesthesia. Likewise emergence from General Anaesthesia and tracheal extubation is often associated with sympathoadrenal response which is seen during tracheal intubation and is of equal concern. To circumvent these hemodynamic responses to tracheal extubation, this study was undertaken. In this study Dexmedetomidine (0.7mcg/kg), .Esmolol(1.5mg/kg) and Control groups were compared for attenuating stress response to tracheal extubation.

In our study we observed that in Dexmedetomidine group there was significant reduction in the Heart rate from 5mins of drug infusion and these continued at extubation, post extubation at all time intervals till 30mins.And this is in concordance to the study of *Barkha Bindu et al*.[18].in which they observed that there was significant reduction of HR from 5 minutes after starting administration of the agent till 20 minutes after extubation. Also *Ravi Shankar Goarya et al.* [19], in their study used dexmedetomidine at a dose of 0.75 mcg/kg, and concluded that, use of dexmedetomidine before extubation attenuates the tachycardia during and after extubation without affecting the emergence time.

While in the Esmolol group there was fall in the heart rate from 5mins of infusion, at extubation, post extubation at all intervals till 30mins, which is similar to the findings of *Anthony L Kovac et al.* [20], in their study with Esmolol @1.5mg/kg in comparison to Nicardipine @ 0.03mg/kg concluded with the result that Esmolol was better in attenuating the HR than nicardipine.

While in control group, there was a significant rise in HR compared to basal value. And in comparison to the Control group both the drugs came out to be effective in attenuating the HR changes during and post extubation. Only two patients in dexmedetomidine group developed bradycardia.

SBP, DBP and MAP values were significantly lower compared to baseline values at all times from the time of dexmedetomidine infusion to post extubation 30 minutes which is in concordance to the study of *Barkha Bindu et al*.[18] and *Ravi Shankar Goarya et al*.[19].Whereas in the Control group there was significant rise in the SBP,DBP,MAP at the time of extubation, post extubation till 30mins.

In the Esmolol group, SBP, DBP, MAP was also lower than its baseline values from 5mins of infusion, but at extubation the SBP, DBP was almost similar to its baseline values and thereafter was gradually reduced till 30 mins post extubation. And this is similar to the study of Nagrale *et al*. [21], with Esmolol 1.5mg/kg and found that it showed significant fall in SBP at 2minutes prior to extubation which was similar to our study where maximum fall in SBP was seen at completion of drug infusion.

Similarly, Anthony *L Kovac et al*. [20],in their study with Esmolol found that there was rise in diastolic BP for the initial 1 to 2minute time periods post study drug infusion and at extubation which is similar to our studies as there was rise in DBP at extubation and 1min post extubation.

Regarding the extubation time, time to orientation, time to awakening, Group Dexmedetomidine took a longer time on comparison to Esmolol and Control group. And these were similar to the findings of *Guinay et al.* and *Guler, A. Akin et al.*[22,23]. In the extubation quality, it was better in the Dexmedetomidine group on comparison to Esmolol and Control group and this was in concordance to the study of *Recep Aksu, Aynur Akin, et al*. [24].

Sedation in our study was assessed using Ramsay Sedation Scale. Significant numbers of patients in Dexmedetomidine group were drowsy but responded to oral commands as compared to Esmolol and Control group. And this was in concordance to the study of *Arpino C et al.* [25], and *Siobal et al.* [26] that dexmedetomidine produces sedation and anxiolysis without any respiratory depression.

Regarding the side-effects, there was no such events in our study and this was similar to the study of Guler *et al*. [22] and Barkha Bindu *et al.* [18] and Nagrale *et al*. [13] and Anthony L Kovac *et al*. [20].

CONCLUSION

From our study, we conclude that, IV Dexmedetomidine in a dose of 0.7mcg/kg given over 10minutes before extubating can be recommended to attenuate the sympathoadrenal response to extubation and better quality of extubation without any significant side effects of the drugs.

REFERENCES

1. Reid and Brace. Irritation of respiratory tract and its reflexes effect on heart Surgery Gynaecology Obstetrics.1940; 70:157.
2. Burstein CL, Lopinto FJ, Newman W, Electrocardiographic studies during endotracheal intubation. I Effects during usual routine techniques Anaesthesiology 1950; 11(2):224-37.
3. Wycoff endotracheal intubation effects on BP and heart rate. Anaesthesiology, 1960; 21:1553-8.
4. Lowrie A, Johnston PL, Fell D, Robinson SL. Cardiovascular and plasma catecholamine responses at tracheal extubation. Br J Anaesthesiology 1992; 68: 261-3.
5. Wellwood M, Aylmer A, Teasdale S Extubation and myocardial ischemia. Anesthesiology 1984; 61:A132.
6. Elia S, Liu P, Chrusciel C, Hilgenberg A, Skourtis C, Lappas D. Effects of tracheal extubation on coronary blood flow, myocardial metabolism and systemic haemodynamic responses. Canadian journal of anaesthesia. 1989 Jan 1;36(1):2-8.
7. Paulissian R, Salem MR, Joseph NJ, Braverman B, Cohen HC, Crystal GJ, Heyman HJ. Hemodynamic responses to endotracheal extubation after coronary artery bypass grafting. Anesthesia and analgesia. 1991 Jul;73(1):10-5.
8. Fuhrman TM, Ewell CL, Pippin WD, Weaver JM. Comparison of the efficacy of esmolol and alfentanil to attenuate the hemodynamic responses to emergence and extubation. Journal of clinical anesthesia. 1992 Nov 1;4(6):444-7.
9. Mikawa K, Nishina K, Takao Y, Shiga M, Maekawa N, Obara H. Attenuation of Cardiovascular Responses to Tracheal Extubation: Comparison of Verapamil, Lidocaine, and Verapamil Lidocaine combination. Anesth Analg 1997; 87: 1005-10.
10. Kovac AL, Masiongale A. Comparison of nicardipine versus esmolol in attenuating the hemodynamic responses to anesthesia emergence and extubation. Journal of cardiothoracic and vascular anesthesia. 2007 Feb 1;21(1):45-50.
11. Arar C, Colak A, Alagol A, Uzer SS, Ege T, Turan N, Duran E, Pamukcu Z. The use of esmolol and magnesium to prevent haemodynamic responses to extubation after coronary artery grafting. European journal of anaesthesiology. 2007 Oct;24(10):826-31.
12. Chakravorty N, Chakravarty D, Vachhani R, Shidhaye RV. Comparison of esmolol and nitroglycerine on hemodynamic parameters during extubation in obese patients following laparoscopic cholecystectomy: a prospective randomized study. Anaesth Pain & Intensive Care 2015;19(4):437-443.
13. Nagrale MH, Indurkar PS, Pardhi CS. Comparative study on Haemodynamic response to extubation: Attenuation with Lignocaine, Esmolol, Propofol. International Journal of Research in Medical Sciences. 2016 Dec 24;4(1):144-51.
14. Aouad MT, Al-Alami AA, Nasr VG, Souki FG, Zbeidy RA, Siddik-Sayyid SM. The effect of low-dose remifentanil on responses to the endotracheal tube during emergence from general anesthesia. Anesth Analg. 2009;108:1157–60.
15. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S. Effect of dexmedetomidine on haemodynamic responses to

laryngoscopy and intubation. Drugs in R & D. 2006 Jan 1;7(1):43-52.
16. Jain D, Khan R, Maroof M. Effect of dexmedetomidine on stress response to extubation. The Internet Journal of Anesthesiology. 2009;21(1).
17. Dyson A, Isaac PA, Pennant JH, Giesecke AH, Lipton JM. Esmolol attenuates cardiovascular responses to extubation. Anesthesia and analgesia. 1990 Dec;71(6):675-8.
18. Bindu B, Pasupuleti S, Gowd UP, Gorre V, Murthy RR, Laxmi MB. A double blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation. Journal of anaesthesiology, clinical pharmacology. 2013 Apr;29(2):162.
19. Goarya RS, Mathur A. I/V bolus dexmedetomidine attenuates the airway reflexes and hemodynamic responses during extubation following general anaesthesia. Journal of Evolution of Medical and Dental Sciences. 2014 Nov 27;3(65):14114-29.
20. Anthony L Kovac,Amy Masiongale. Comparison of Nicardipine Versus Esmolol in Attenuating the Hemodynamic Responses to Anesthesia Emergence and Extubation: Journal of Cardiothoracic and Vascular Anaesthesia, 2007;21(1)P 45-60.
21. Nagrale MH, Indurkar PS, Pardhi CS. Comparative study on Haemodynamic response to extubation: Attenuation with Lignocaine, Esmolol, Propofol. International Journal of Research in Medical Sciences. 2016 Dec 24;4(1):144-51.
22. Guler G, Akin A, Tosun Z, Eskitascoglu E, Mizrak A, Boyaci A. Single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. Acta anaesthesiologica scandinavica. 2005 Sep 1;49(8):1088-91.
23. Guler G, Akin A, Tosun Z, Ors S, Esmaoglu A, Boyaci A. Single-dose dexmedetomidine reduces agitation and provides smooth extubation after pediatric adenotonsillectomy. Pediatric Anesthesia. 2005 Sep 1;15(9):762-6.
24. Aksu R, Akin A, Biçer C, Esmaoğlu A, Tosun Z, Boyaci A. Comparison of the effects of dexmedetomidine versus fentanyl on airway reflexes and hemodynamic responses to tracheal extubation during rhinoplasty: A double-blind, randomized, controlled study. Current therapeutic research. 2009 Jun 1;70(3):209-20.
25. Arpino PA, Kalafatas K, Thompson BT. Feasibility of dexmedetomidine in facilitating extubation in the intensive care unit. Journal of clinical pharmacy and therapeutics. 2008 Feb 1;33(1):25-30.
26. Siobal MS, Kallet RH, Kivett VA, Tang JF. Use of dexmedetomidine to facilitate extubation in surgical intensive-care-unit patients who failed previous weaning attempts following prolonged mechanical ventilation: a pilot study. Respiratory care. 2006 May 1;51(5):492-6.