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Original Research Article

Haemodynamic Effects of Esmolol versus Dexmedetomidine in Response to Extubation in Case of Elective Surgery under General Anaesthesia, A Randomized Double Blinded Interventional Study

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Abstract:

Introduction: Extubation is associated with awakening, pain, anxiety and airway irritation which may lead to haemodynamic responses similar to intubation, resulting in hypertension, tachycardia and arrhythmias. The present study was undertaken to evaluate the attenuating effects of dexmedetomidine and esmolol which belong to different pharmacological groups on haemodynamic changes with tracheal extubation in patients undergoing elective general surgery.

Material & Methods: 60 patients were randomized into 2 groups of 30 patients each to conduct a randomized double blind interventional study to compare the effects of i.v dexmedetomidine 0.5mcg/kg vs esmolol 1.5 mg/kg in attenuation of post extubation haemodynamics (SBP, DBP, HR and MAP) in patients undergoing elective general surgery under general anaesthesia and to note the side effects if any.

Observation & Results: After administration of study drug fall in HR was seen in both groups. But in group A fall in HR start at T1 and did not show rise compare to basal value during extubation and post extubation period(T3-T7). In group B fall in HR start at T3 and there was no increase in HR during extubation and post extubation period (T3-T7). Rise in MAP was seen in both the groups at T0 and T1 and the difference between group A and group B was statistically significant. Fall in MAP was seen in both the groups from T2-T7 that is after study drug administration. MAP was higher in group B as compare to group A.

Conclusion: We concluded that dexmedetomidine and esmolol both controls arterial pressure and heart rate, but dexmedetomidine is the preferred drug because of better quality of extubation due to sedation caused by dexmedetomidine.

Key Words: Extubation, General Anaesthesia, Esmolol, Dexmedetomidine

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Introduction

Tracheal extubation is an equally important part of general anaesthesia as intubation. Extubation is associated with awakening, pain, anxiety and airway irritation which may lead to haemodynamic responses similar to intubation, resulting in hypertension, tachycardia and arrhythmias. The haemodynamic changes are due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation [1].

There is a correlation between the magnitude of the pressor response and increase in the concentration of catecholamines [**2].** This sympathoadrenal response occurs very rapidly and last for few minutes. Various factors are responsible for this haemodynamic response like pain of surgery, emergence from anaesthesia or tracheal irritation. [3,4,5]

This reflex is triggered by sensory receptors in the glottic and subglottic mucosa and results in strong adduction of the vocal cords [**6].** An exaggerated, maladaptive manifestation of this reflex, referred to as laryngospasm, is a potential complication of airway management [7]. Irritation of the lower airway by a foreign substance activates a vagal reflex–mediated constriction of bronchial smooth muscle, resulting in bronchospasm [8].

Airway manipulation via laryngoscopy, endotracheal intubation and other airway devices act as a noxious stimulus.Central nervous system activity also increase in intracranial pressure in patients with decreased intracranial compliance**.** [9] Extubation during a light plane of anesthesia (stage II) can increase the risk for laryngospasm and other airway complications and should be avoided [10,11]. Bailey maneuver can be used in which Endotracheal tube is exchanged with a Supraglottic airway device (SGA) while the patient is under deep anesthesia. [12,13] Different pharmacological agents such as lidocaine [14], β- blockers [15], fentanyl citrate [16], calcium channel blockers [15], inhalational agents have been evaluated to eliminate or blunt this stress response seen during extubation.

The present study was undertaken to evaluate the attenuating effects of dexmedetomidine and esmolol which belong to different pharmacological groups on haemodynamic changes with tracheal extubation in patients undergoing elective general surgery.

Study was aimed to assess and compare the effects of iv dexmedetomidine or esmolol on haemodynamic responses during tracheal extubation.

Primary Objective was to evaluate difference in variation of haemodynamic parameters like heart rate, SBP, DBP, MAP from base line to just after extubation in both study groups. Secondary Objectives were to determine the difference in percentage of cases who develop adverse events in both groups There is increasing evidence of its protective effects against ischemic and hypoxic injury, including cardio-protection, neuro-protection and reno-protection. [17]

The hypnotic effect of dexmedetomidine is mediated by the hyperpolarization of noradrenergic neurons in the locus ceruleus of the brain stem, which is the primary site in modulating wakefulness [18,19].

Dexmedetomidine induces sedation by decreasing activity of noradrenergic neurons in the locus ceruleus in the brain stem, thereby increasing the activity of inhibitory gamma-aminobutyric acid neurons in the ventrolateral preoptic nucleus. [20] Sedation by dexemeditomidine mirrors natural sleep. As such, dexmedetomidine provides less amnesia than benzodiazepines. [17]

Esmolol is a cardioselective beta$_1$ receptor blocker with rapid onset, a very short duration of action, and no significant intrinsic sympathomimetic or membrane stabilizing activity at therapeutic dosages and is only administered IV. It has been successfully used to prevent tachycardia and hypertension in response to perioperative stimuli, such as intubation, surgical stimulation and emergence.

Materials and Methods

The study was done in 60 patients undergoing elective general surgery after obtaining permission from the institutional ethical committee (No. 167-(12) MC/EC/2020) and review board.

Patients of either sex, ASA grade **I and II** aged between 20-50 years and posted for elective surgery requiring GA with endotracheal intubation were included. Patient with difficult airway, coagulation abnormalities, allergy to drugs, adrenal insufficiency, asthma, hypertension, psychiatric, endocrine illness, cardiovascular disease and other comorbidities were excluded from study.

All patients were explained about the anesthetic technique informed consent taken. A sample size of 30 cases in each group was adequate at 95% confidence and 80% power to verify the expected difference of 1.06(+0.53) in changes in MAP at 5 minutes post extubation period from baseline in both groups.

Group A (n=30)- Dexmedetomidine injection 0.5mcg/kg diluted in 10 ml NS as infusion over 10 minutes given prior extubation. Alongside 10ml NS also given as iv bolus for sake of blinding. Group B (n=30)-Esmolol injection 1.5 mg/kg i.v. as single bolus diluted in 10ml NS given before extubation. Along with this 10ml NS infusion will be given over 10 minutes for sake of blinding. In this study randomization was done by sealed envelope method.

Anesthesia Technique. Standard monitoring and iv access was secured**.** Inj. Ranitidine 1mg/kg + Inj. Metoclopramide 0.1 mg/kg +Inj. Glycopyrrolate 0.004 mg/kg+ Inj. Midazolam 0.02 mg/kg + Inj. Fentanyl 2 mcg/kg were given.

After preoxygenation with 100% O_2, anaesthesia was induced with inj. Thiopentone Sodium 5 mg/kg intravenously slowly and intubation was facilitated with Inj. Succinyl choline 2mg/kg. and then laryngoscopy and tracheal intubation was performed. Loading dose Inj. Atracurium 0.5 mg/kg was given. Anaesthesia was maintained with 40% O2+60% N2O and atracurium 0.1 mg/kg and sevoflurane 0.2-2%. Standard monitoring was done intra-operatively. At the beginning of skin suturing, sevoflurane was switched off and patient was received study drug, Group A was received dexmedetomidine 0.5mcg per kg body weight diluted in 10 ml NS as infusion over 10 minutes using an infusion pump, whereas Group B was

received 10ml normal saline over 10minutes. At this point nitrous oxide was discontinued at end of infusion. At the end of surgery HR, SBP, DBP, MAP was recorded, which serves as baseline values. Residual muscle relaxation was reversed with injection neostigmine 0.05mg/kg iv and injection glycopyrrolate 0.01mg/kg iv. After 2minutes of reversal, Group B was received esmolol 1.5mg/kg iv bolus diluted to 10 ml with normal saline over 1 minutes, whereas Group A was received 10 ml normal saline iv bolus. A thorough oropharyngeal suction was done before extubation. Then extubation was done after return of spontaneous respiration with adequate tidal volume, when patient was obeying verbal command, good hand grip and end tidal concentration of sevoflurane less than 0.1%

Immediately after tracheal extubation patient is given 100% oxygen by a facemask for 5minutes. All haemodynamic variables HR, SBP, DBP, MAP and SPO2 were noted at baseline, just before administering study drugs, just before extubation and then after extubation at 1, 3, 5 and 10minutes. Occurrence of any event like laryngospasm, bronchospasm, desaturation, respiratory depression, vomiting, hypotension, bradycardia or undue sedation was noted.

Monitoring was done at following intervals: Baseline values at the completion of surgery –T_0 (Prior to infusion), At the time of giving reversal-T_1, At the time of drug 2(iv bolus) -T_2, At the time of extubation —T_3, One minute after extubation-T_4, Three minute after extubation-T_5, Five minutes after extubation-T_6, Ten minutes after extubation-T7

Methodology (flow diagram)

Patient PAC, consent, Inclusion Criteria checked

⇩

Monitor vitals, Assess I.V. line and fluid, after preanaesthetic medication and pre oxygenation, induction and intubation was done as standard protocol

⇩

Anaesthesia maintained with 40 % O2 + 60% N_2O+ Inj. Atracurium + sevoflurane

Intraoperative monitoring of vital parameters (HR, SBP, DBP, MAP, SPO_2)

⇩

At beginning of skin suturing Group, A was received inj dexmedetomidine (.005mg/kg) in 10ml NS as infusion over 10min whereas Group B was received 10ml NS over 10min.

⇩

End of surgery and reversal. After 2min of reversal Group B was received esmolol 1.5mg/kg iv bolus diluted to 10ml with NS over 1min whereas Group A was received 10ml NS iv bolus over 1min.

⇩

Extubation done, HR, SBP, DBP, MAP, SpO2, recorded at extubation 1, 3, 5, 10, minutes post extubation.

Observation and Results

Statistical Analysis

Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, L, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by students t-test. Probability was considered to be significant if less than 0.05.

There was no significant difference in age and sex distribution between the group A and the group B.

Table 1 HR (bpm)

	Group A		Group B		Result (p value)
	Mean	SD	Mean	SD	
Pre Op.	79.83	2.44	79.80	3.50	0.965
T0	88.07	1.34	83.90	5.29	p<0.001
T1	86.87	2.76	87.10	1.90	0.704
T2	86.53	1.98	89.03	1.50	p<0.001
T3	93.57	1.65	97.77	1.99	p<0.001
T4	90.23	1.36	95.70	1.26	p<0.001
T5	88.47	0.86	89.40	0.93	0.0001
T6	87.20	1.00	87.13	1.01	0.797
T7	85.80	1.00	85.67	1.30	0.656

S = Significant ; NS = Non Significant

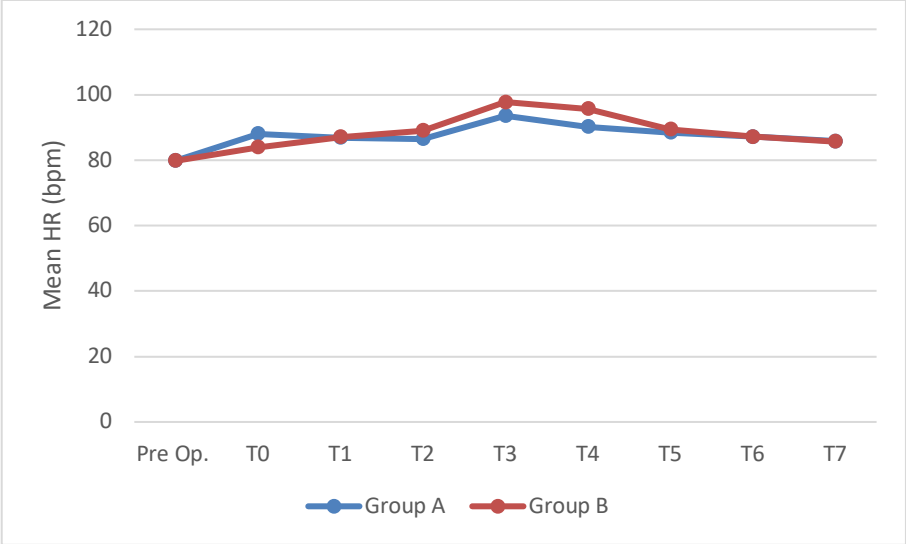

Diagram 1 HR

Baseline HR (Table1, Dia.1) was comparable in both groups. After administration of study drug fall in HR was seen in both groups. But in group A fall in HR start at T1 and did not show rise compare to basal value during extubation and post extubation period(T3-T7). In group B fall in HR start at T3 and there was no increase in HR during extubation and post extubation period (T3-T7).

Baseline values were comparable in both groups. The SBP at T0 and T1 was comparable in both groups. SBP fell from T2 to T7 in both groups i.e. after administration of study medication. The SBP was higher in group B than group A and the difference was statistically significant.

Baseline DBP was comparable in both the groups. Rise in DBP was seen at T0 and T1 in both the groups and the difference between group A and group B was statistically significant. Fall in DBP was seen in both the groups after study drug administration(T2-T7).

Table 2 MAP (mmHg)

	Group A		Group B		Result (p value)
	Mean	SD	Mean	SD	
Pre Op.	93.52	0.82	94.13	1.80	0.095
T0	92.87	1.01	94.29	1.10	p<0.001
T1	93.18	0.78	95.16	1.46	p<0.001
T2	97.47	1.71	101.00	0.84	p<0.001
T3	92.33	1.43	95.69	1.36	p<0.001
T4	91.80	0.81	96.02	1.09	p<0.001
T5	91.27	1.27	94.60	1.29	p<0.001
T6	90.80	1.24	93.27	1.00	p<0.001
T7	90.82	0.52	92.29	0.78	p<0.001

S = Significant ; NS = Non Significant

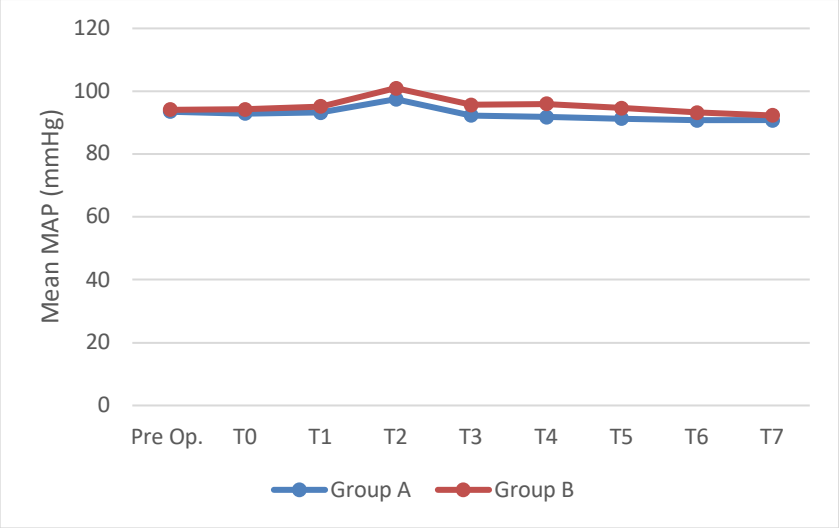

Diagram 2

Baseline MAP (Table 2, Dia. 2) was comparable in both the groups. Rise in MAP was seen in both the groups at T0 and T1 and the difference between group A and group B was statistically significant. Fall in MAP was seen in both the groups from T2-T7 that is after study drug administration. MAP was higher in group B as compare to group A.

In group A, 2 patients (6.67%) had episode of nausea, 1 patient (3.33%) had episode of vomiting and 1patient (3.33%) had episode of hypotension.In group B, 2patients(6.67%) had episode of nausea, 2patients(6.67%) had episode of vomiting and 2patients(6.67%) had coughing episode which was not seen in group A.

Table 3 E Quality Score

	Group A (N=30)		Group B (N=30)	
	No.	**%**	**No.**	**%**
Score 1	**27**	**90.00**	**19**	**63.33**
Score 2	**3**	**10.00**	**5**	**16.67**
Score 3	**0**	**0**	**5**	**16.67**
Score 4	**0**	**0**	**1**	**3.33**
Result (p value)	**0.063 (NS)**			

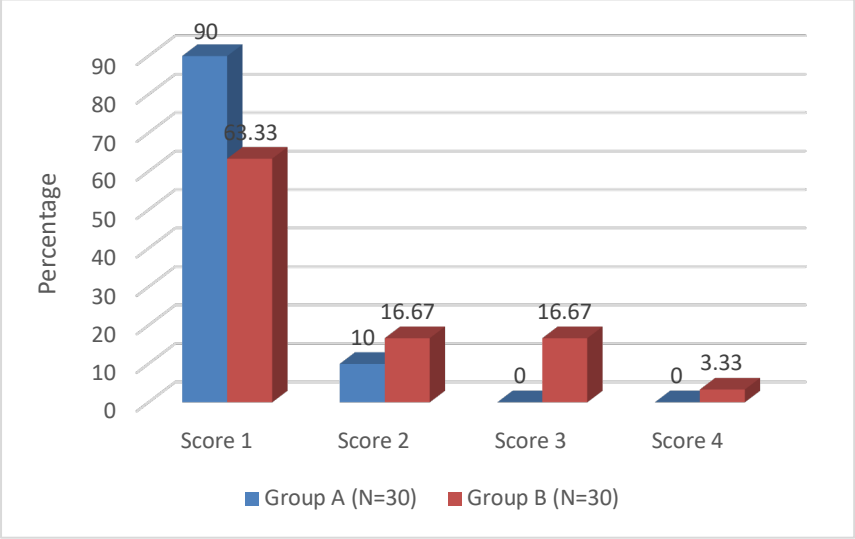

Diagram 3

The quality of extubation (Table 3, Dia. 3) was better with group A as compared to group B and comparison was statiscally insignificant. But lower score of extubation quality was seen with group B as compared to group A.

Table 4 Ramsay sedation score

	Group A		Group B		Result (p value)
	Mean	SD	Mean	SD	
T0	3.47	0.51	2.80	0.41	p<0.001 (S)
T30	3.00	0.59	2.40	0.50	p<0.001(S)
T60	2.43	0.50	2.20	0.41	0.053(NS)
T90	2.27	0.45	1.77	0.43	p<0.001(S)
T120	2.20	0.41	1.80	0.41	0.0003(S)
T150	2.03	0.18	1.60	0.50	p<0.001(S)
T180	1.80	0.41	1.63	0.49	0.157 (NS)
T210	1.80	0.41	1.60	0.50	0.093 (NS)
T240	1.60	0.50	1.43	0.50	0.202 (NS)

S = Significant ; NS = Non Significant

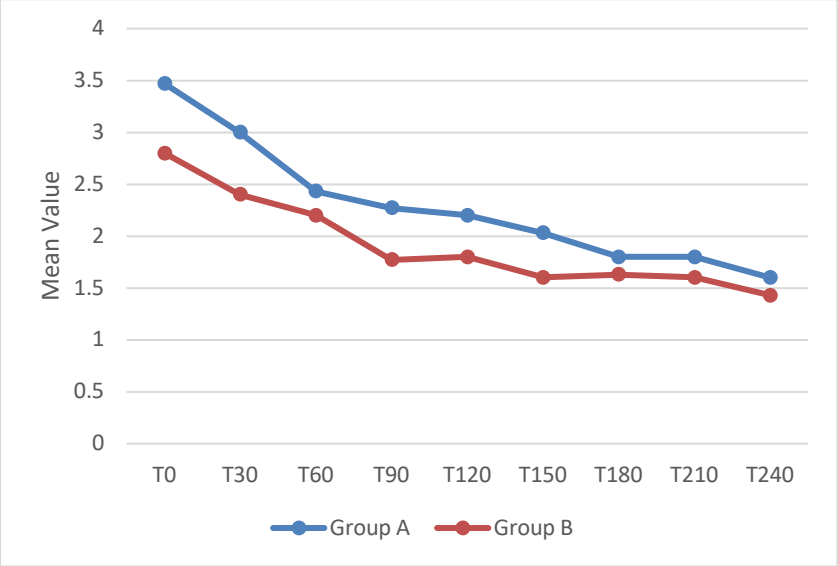

Diagram 4

The patients in the group A were significantly sedated as compared to group (Table 4, Dia. 4)

Discussion

Tracheal extubation is many times associated with major cardiovascular and respiratory system complications. Though it seems to be a benign procedure, multiple studies have shown that it provokes hypertension and tachycardia as does tracheal intubation due to pharyngeal and laryngeal stimulation. The stimulation of these tracheal and laryngeal receptors results in release of catecholamines leading to increase in heart rate and blood pressure which may persist till the recovery period. [5]

Esmolol hydrochloride is an ultra-short-acting, beta-one selective adrenergic receptor blocker quite suitable for use during a short-lived stress such as tracheal intubation and extubation. [21,22]

The effect of different strength bolus doses of esmolol 0.5 mg/kg, 1 mg/kg, 1.5 mg/kg. 2 mg/kg) was studied by Wang, YQ et al in 2003 who found that high doses of esmolol (2 mg/kg) cause bradycardia and hypotension and lower doses do not control stress responses so he concluded that 1.5 mg/kg, not only controlled cardiovascular responses but also had no side effects. [23]

Therefore, we chose 1.5 mg/kg as a bolus dose of esmolol at reversal to attenuate the haemodynamic effects at extubation. In our study, we used esmolol 1.5 mg/kg slow bolus 2 minutes prior to extubation, which was effective in blunting haemodynamic response with no side effects. The heart rate reduced gradually and remained stable till we observed the patients, upto 10 minutes post extubation. SBP, DBP and MAP also showed attenuation upto 10minutes post extubation. [24]

Fuhrman et al [2] and Muzzi DA et al in 1990 concluded that an esmolol bolus dose followed by an esmolol infusion significantly attenuated the hemodynamic response to extubation which were similar to our study although doses were different. [25]

Dexmedetomidine is a highly selective α2 adrenoreceptor agonist (α1:α2 - 1:1620). α2 agonists, decreases the sympathetic outflow and noradrenergic activity thereby counteracting

haemodynamic fluctuations occurring at the time of extubation.

A study conducted in 2009 by Aksu R et al to compare the effects of dexmedetomidine and fentanyl on airway reflexes and hemodynamic responses and suggested that dexmedetomidine 0.5 µg/kg IV, administered before extubation, was more effective than fentanyl 1 µg/kg IV in patients undergoing rhinoplasty. [29] Barkha Bindu et al in 2013 concluded that Dexmedetomidine 0.75 mcg/kg administered 15 minutes before extubation, stabilizes hemodynamics and facilitates smooth extubation.

Kwon Hui Seo et al conducted a study to investigate the optimal dose of dexmedetomidine and concluded that intravenous infusion of 0.5 µg/kg dexmedetomidine 30 min before the end of surgery attenuated the haemodynamic responses during emergence without prolonging the extubation time.

Hence, we selected dose of 0.005 mg/kg dexmedetomidine, which is the dose effective with minimal side effects. We diluted the required dose of dexmedetomidine in 10 mL of normal saline and with the help of a syringe pump infused it intravenously over a period of 10 minutes.

In our study, we observed that MAP did not show a significant rise compared to basal value during reversal, at extubation and any period post extubation in dexmedetomidine group. SBP, DBP and MAP were well controlled during extubation and post extubation in dexmedetomidine. This observation is in concurrence with the study done by Malvika Prasad Tendulkar et al done a prospective comparison of pressure and airway response to iv esmolol and dexmedetomidine during emergence from general anaesthesia.

The cough grading and quality of extubation was better with group dexmedetomidine as compared to group esmolol.

Conclusions

In our study we compared the effects of dexmedetomidine 0.5mcg/kg iv infusion over 10 minutes and esmolol 1.5mg/kg i.v. bolus over 1minute in patients posted for elective general surgeries under general anaesthesia which was given before extubation.

We found that dexmedetomidine 0.5mcg/kg and esmolol 1.5mg/kg both was effective in controlling the SBP, DBP and HR at extubation and post extubation period and We concluded that dexmedetomidine and esmolol both controls arterial pressure and heart rate, but dexmedetomidine is the preferred drug because of better quality of extubation due to sedation caused by dexmedetomidine resulting in less agitation so less coughing, bucking and straining.

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