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A Comparative Study of the Effects of Intravenous Esmolol and Sublingual Nitroglycerine Spray on Hemodynamic Response Following Tracheal Extubation

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Abstract

Background: Recovery from general anesthesia and tracheal extubation is associated with increased hemodynamic response due to reflex sympathoadrenal activity and can be dangerous in susceptible patients. Many pharmacological methods were used to attenuate hemodynamic response but none were ideal. *Aims:* The aim of this study was to compare the effects of intravenous Esmolol and sublingual Nitroglycerine spray on hemodynamic response following tracheal extubation in patients undergoing general anesthesia for various surgeries. *Methods:* 60 patients of ASA 1 and 2 of either sex undergoing elective surgeries under general anesthesia were placed randomly in either Group A (n = 30) or Group B (n = 30). Group A received intravenous Esmolol 1.5 mg/kg and Group B received Sublingual 0.8 mg NTG spray. Either of the study drug was administered after 1 minute of the reversal agents being given. Hemodynamic variables HR, SBP, DBP and MAP were monitored and noted during tracheal extubation. *Results:* Intravenous Esmolol group had better control over heart rate when compared to Sublingual NTG spray group during tracheal extubation. Sublingual NTG spray group had modest increase in heart rate (Mean of 122 bpm). With respect to Systolic, Diastolic and Mean arterial blood pressure both the groups were found to be statisticaly insignificant and had clinically significant control over hemodynamic response during tracheal extubation. *Conclusion:* Intravenously administered Esmolol in dose of 1.5 mg/kg attenuates tracheal extubation response by having better control on heart rate and blood pressure with minimal complications when compared to sublingual 0.8 mg NTG spray group.

Keywords: Nitroglycerin (NTG); Esmolol; Tracheal Extubation; Hemodynamic response.

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Introduction

Recovery from general anesthesia and extubation is a period of intense physiological stress for patients.[1] This increase in sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias.[1,2]

In order to control hemodynamic changes during tracheal intubation and extubation many pharmacological methods had been devised

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to reduce the extent of hemodynamic events[3] such as beta blockers, calcium channel blockers, opioids, local anesthetics and vasodilating drugs like nitroglycerine (NTG) but none were ideal.[1-4] Hence, the present study was under taken to compare the effect of intravenous Esmolol and sublingual NTG spray to attenuate the hemodynamic response during endotracheal extubation.

Materials and Methods

After obtaining approval from institutional ethical committee, written informed consent from patient belonged to ASA1 and 2 was taken, and routine preanesthetic evaluation was done. Patients were randomly allocated in to one of the two groups using numbers generated from www.random.org. Allocation concealment will be done using sealed envelope method.

Group A: Patients received a single dose of Inj. Esmolol 1.5 mg/kg diluted to 10 ml with Normal saline IV and 2 sprays of Normal saline sublingually;

Group B: Patients received two NTG sprays (2 sprays = 0.8 mg) through sublingual route and 10 ml of Normal saline by IV route.

Inclusion Criteria

1. Patients who have given written informed consent;
2. Patients with American Society of Anesthesiologists (ASA) Grade I & II;
3. Patients aged 20–60 years of either gender;
4. Patients with Body Mass Index (BMI) 19–28;
5. Patients scheduled for elective surgery lasting for 90–120 mins under general anesthesia.

Exclusion Criteria

1. Patients not willing to give written informed consent;
2. Patients with allergic to Esmolol or NTG;
3. Patients with anticipated difficult mask ventilation/Difficult intubation;
4. Patients with uncontrolled hypertension, diabetes mellitus, bronchial asthma, heart block, cerebrovascular disease and hepatic and renal disease;
5. Patients with BP below 90/60 millimeter of mercury (mm of Hg) or above 180/100 mm of Hg;
6. Patients using beta blockers, sympathomimetic agents, calcium channel blockers and vasodilator drugs;
7. Patients with chronic alcohol or drug abuse;
8. Pregnant women/Breastfeeding mothers.

Preanesthetic examination comprised of detailed history, systemic and thorough airway examination was conducted. Preoperative investigations comprised of Complete Blood Count (CBC), urine examination, blood sugar, serum electrolytes, coagulation profile, liver function tests, electrocardiography and echocardiography, Chest *X*-ray as indicated. All the patients were in fasting for 8 hours prior surgery.

Monitoring included Heart Rate (HR), Systolic Arterial Pressure (SBP), Diastolic Arterial Pressure (DBP), Mean Arterial Pressure (MAP), Peripheral Oxygen Saturation (SpO_2), and End-tidal CO_2 ($EtCO_2$).

Anesthetic procedure

Patients were premedicated with Inj. Glycopyrolate 0.005 mg/kg intravenously (IV), Inj. Midazolam 0.02 mg/kg IV and Inj Fentanyl 2 μg/kg IV. Induced with Inj. Propofol 1–2.5 mg/kg IV and Inj. Vecuronium 0.10–0.12 mg/kg IV given to facilitate tracheal intubation, anesthesia was maintained with 40:60 mixture of oxygen and air, and maintained with Isoflurane. Controlled mechanical ventilation was adjusted to maintain $EtCO_2$ pressure between 30 and 35 mm Hg. Hemodynamic parameters HR, SBP, DBP, MAP, $EtCO_2$ and SpO_2 were maintained every 5 minutes intraoperatively.

The BP and HR were maintained between 80% and 120% of the preoperative values by altering the concentration of Isoflurane and giving additional doses of Inj. Fentanyl until completion of surgery. Muscle relaxation was maintained by intermittent boluses of Inj Vecuronium 0.02 mg/kg IV After induction Inj. Paracetamol 1 gm intravenously administered to both the groups. Isoflurane will be stopped after completion of surgery.

Residual muscle relaxation was reversed with Inj Neostigmine 0.05 mg/kg IV and Inj. Glycopyrrolate 0.01 mg/kg IV on appearance of spontaneous ventilation. After 1 minute of the reversal agents being given, either of the study drug was administered.

Group A: Patients was received a single dose of Inj. Esmolol 1.5 mg/kg diluted to 10 ml with normal saline IV and 2 sprays of Normal saline sublingually;

Group B: Patients were received two NTG sprays (2 sprays = 0.8 mg) through sublingual route and 10 ml of Normal saline by IV route.

Study drugs were prepared before hand by an assistant and their identity was unknown to the anesthesiologist who was involved in the study. Thorough oropharyngeal suction was done before extubation. Then tracheal extubation was done once criteria for extubation were met. Return of spontaneous respiration with adequate tidal volume, obeying verbal commands, spontaneous eye opening, and good hand grip were the criteria for extubation. Immediately after tracheal extubation patient were given 100% oxygen by a facemask for 5 minutes.

Parameters like HR, Systolic, Diastolic and Mean arterial Blood Pressures were monitored at the completion of surgery – Baseline, Isoflurane stopped-T0, at the time of giving reversal-T1, 1 min after giving study medication-T2, during extubation-T3, One minute after extubation-T4, Two minute after extubation-T5, Five minutes after extubation-T6, Ten minutes after extubation-T7 and Fifteen minutes after extubation-T8. Events like coughing, bucking and breath holding were monitored. Excessive secretions, bronchospasm, laryngospasm, postoperative nausea and vomiting and any other untoward events were monitored.

Need for Inj. Atropine 0.01 mg/kg IV (HR < 60/min) or Inj. Ephedrine 5mg IV (SBP < 90 mm Hg) or additional dose of Nitroglycerine or Esmolol (SBP > 200 mm Hg, DBP > 120 mm Hg or HR > 150/min) was recorded.

Efficacy parameters

Hemodynamic parameters assessed were HR, SBP, DBP and MAP.

H. Statistical Analysis

Datas were entered in Microsoft excel and exported into SPSS Version 21.0. Datas were analyzed by descriptive Statistics; Student's *t*-test was used to compare the significant difference between two means. ANOVA was used to compare the significant difference between three or more groups. $p < 0.05$ is considered significant.

Results

In Esmolol group, 46.7% were females and 53.3% were males. In nitro-glycerine group, 70% were females and 30% were males. There was no significant difference in gender distribution between two groups, as shown in Table 1 and 2.

Table 1: Gender distribution comparison between two groups

		Groups			
		Group A (Esmolol)		Group B (Nitro-glycerine)	
		Count	%	Count	%
Sex	Female	14	46.7%	21	70.0%
	Male	16	53.3%	9	30.0%

$p = 0.067$.

Table 2: Profile of subjects in the two groups

	Groups				*p* - value
	Group A (Esmolol)		Group B (Nitro-glycerine)		
	Mean	SD	Mean	SD	
Age	37.43	11.11	38.90	11.49	0.617
Height	1.58	0.05	1.60	0.07	0.255
Weight	58.93	4.98	57.93	5.36	0.457
BMI	23.46	1.17	22.54	1.41	0.325

Demographic parameters which were comparable in both the groups.

ASA Grading 1 and 2 which were comparable in both the groups, as shown in Table 3.

Table 3: ASA Grade comparison between two groups

	Groups				
	Group A (Esmolol)		Group B (Nitro-glycerine)		
	Count	%	Count	%	
ASA Grade	Grade 1	22	73.3%	25	83.3%
	Grade 2	8	26.7%	5	16.7%

$p = 0.347$

Baseline HR which are comparable in both the groups. After giving reversal agent, in Nitrglycerine group there was significant increase in HR before and after extubation when compared to Esmolol group and p – value (< 0.001) also showed to be statistically significant between the groups, as shown in Table 4 and Figure 1.

Table 4: Heart rate comparison between two groups at different time intervals

Heart rate	Groups						p - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	p - value	Mean	SD	p - value	
Base line	87.50	12.83		92.50	15.79		0.183
T0	100.33	19.30	< 0.001	96.97	19.75	0.201	0.507
T1	110.67	18.41	< 0.001	115.03	20.88	< 0.001	0.394
T2	99.30	14.99	0.001	122.70	22.72	< 0.001	< 0.001
T3	93.37	12.33	0.056	121.17	21.33	< 0.001	< 0.001
T4	88.77	10.17	0.611	113.47	21.96	< 0.001	< 0.001
T5	85.90	10.25	0.559	103.6	17.83	0.006	< 0.001
T6	81.00	7.50	0.009	94.53	19.13	0.620	0.001
T7	76.40	8.50	< 0.001	84.73	20.40	0.111	0.043
T8	74.60	9.34	< 0.001	80.80	18.04	0.016	0.100

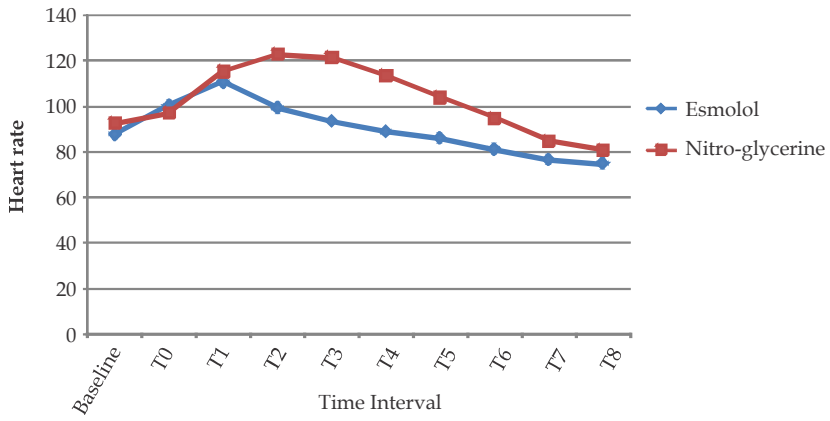

Fig. 1: Heart rate comparison between two groups at different time intervals.

Baseline systolic blood pressure values were comparable in both the groups. After giving reversal agent systolic blood pressure was found to be comparable in both the groups and there was significant decrease in SBP compared to baseline in both the groups. There was no statistical significance between Esmolol group and Nitrglycerine group before and after extubation, as shown in Table 5.

Table 5: SBP comparison between two groups at different time intervals

SBP	Groups						*p* - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	*p* - value	Mean	SD	*p* - value	
Baseline	127.57	10.64		131.60	15.29		0.240
T0	138.07	14.79	0.002	142.43	14.34	< 0.001	0.140
T1	147.67	17.69	< 0.001	153.97	24.93	< 0.001	0.264
T2	140.60	9.98	< 0.001	145.77	27.48	0.004	0.337
T3	135.13	10.56	0.004	140.70	24.11	0.058	0.251
T4	130.67	8.21	0.091	127.57	18.02	0.239	0.395
T5	125.43	8.64	0.252	119.97	27.15	0.033	0.298
T6	121.93	7.10	0.006	119.97	16.01	< 0.001	0.541
T7	118.27	7.55	< 0.001	118.30	14.48	< 0.001	0.991
T8	115.23	7.75	< 0.001	119.10	12.30	< 0.001	0.151

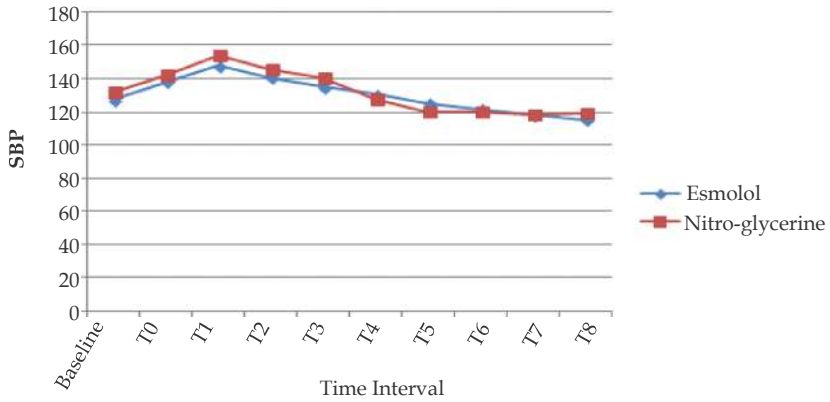

Fig. 2: Line diagram showing SBP comparison between two groups at different time intervals.

Baseline diastolic blood pressure values were comparable in both the groups. After giving reversal agent diastolic blood pressure was found to be comparable in both the groups and there was significant decrease in DBP compared to baseline in both the groups. At T0, T2, T4, T5 intervals DBP were higher in NTG group compared to Esmolol group but at T5 there was statistically significant decrease in DBP values in Esmolol group copmpared to NTG group, as shown in Table 6.

Table 6: DBP comparison between two groups at different time intervals

DBP	Groups						*p* - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	*p* - value	Mean	SD	*p* - value	
Baseline	80.83	11.68		81.27	6.90		0.862
T0	81.57	10.97	0.767	90.57	11.72	< 0.001	0.003
T1	93.77	16.66	<0.001	98.93	14.06	<.001	0.199
T2	83.80	17.30	0.345	91.53	7.46	<.001	0.028
T3	79.57	14.83	0.654	84.47	11.13	0.181	0.153
T4	73.57	14.12	0.011	82.83	9.37	0.418	0.004
T5	69.13	12.82	<.001	79.33	7.21	0.332	<.001
T6	72.60	13.06	0.002	76.70	7.64	0.014	0.143
T7	71.73	11.66	0.001	74.97	6.83	0.001	0.195
T8	72.27	8.71	<.001	73.30	7.32	<.001	0.621

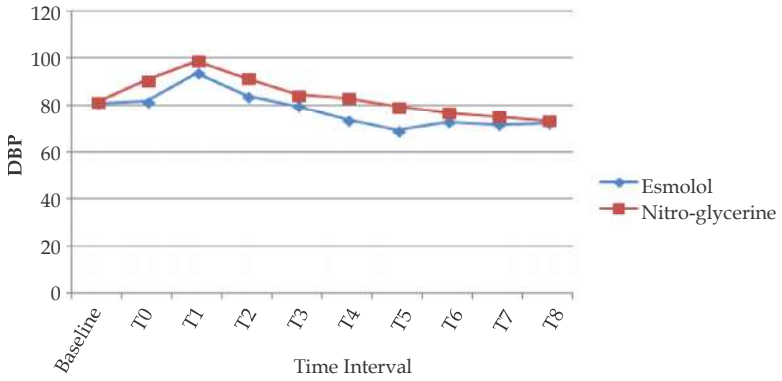

Fig. 3: Line diagram showing DBP comparison between two groups at different time intervals.

Baseline mean arterial pressure values were comparable in both the groups. After giving reversal agent mean arterial blood pressure was found to be comparable in both the groups and there was decrease in mean arterial blood pressure compared to baseline in both the groups. And there was no statistical significance between Esmolol group and Nitrglycerine group before and after extubation, as shown in Table 7.

Table 7: MAP comparison between two groups at different time intervals

MAP	Groups						*p* - value b/w two groups
	Group A (Esmolol)			Group B (Nitro-glycerine)			
	Mean	SD	*p* - value	Mean	SD	*p* - value	
Baseline	96.53	15.31		95.90	8.66		0.844
T0	97.47	12.44	0.734	107.43	12.00	< 0.001	0.003
T1	113.80	21.05	<.001	115.70	14.17	< 0.001	0.683
T2	102.33	20.15	0.073	108.13	6.54	< 0.001	0.139
T3	100.57	18.06	0.172	101.03	9.46	0.035	0.901
T4	91.37	14.03	0.065	98.90	9.23	0.136	0.017
T5	86.70	14.13	0.001	94.27	7.73	0.433	0.013
T6	86.57	12.95	<.001	91.30	7.04	0.017	0.084
T7	85.33	11.52	<.001	89.13	6.52	0.001	0.121
T8	85.83	9.08	<.001	86.53	7.06	<.001	0.740

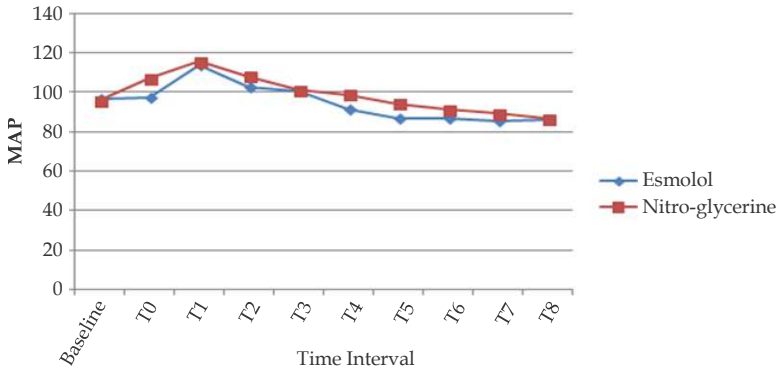

Fig. 4: Line diagram showing MAP comparison between two groups at different time intervals.

In NTG Group 3 patients (10%) had complications like hypotension, laryngospasm, headache and in Esmolol Group 1 patient (3.3%) had complications like hypotension and bradycardia and were treated immediately. There was no significant difference in complications between two groups, as shown in Table 8.

Table 8: Complications

	Groups				
	Group A (Esmolol)		Group B (Nitro-glycerine)		
	Count	%	**Count**	%	
Complications	Absent	29	96.7%	27	90.0%
	Present	**1**	**3.3%**	**3**	**10.0%**

Discussion

Endotracheal intubation and extubation is commonly associated with increase in hemodynamic changes due to reflex sympathetic discharge[1] and stimulation of laryngopharynx[2] which leads to increased plasma catecholamine levels causing tachycardia, increased SVR, hypertension and increased myocardial contractility.[3] These hemodynamic changes leads to serious consequences in patients with hypertension, coronary artery disease, diabetes, preeclampsia, and cerebrovascular disease which may leads to perioperative or postoperative myocardial ischemia and acute heart failure in susceptible patients.[4]

The known factors responsible for such untoward hemodynamic response during extubation are lighter plane of anesthesia, mechanical irritation to airway,[5] pain due to surgery and during emergence from general anesthesia.[6] The study by Miyazaki et al. had shown that extubation increases heart rate and systolic blood pressure by 20 % in more than 70% of patients.[7]

There are various agents which are used to attenuate these hemodynamic changes like intravenous Lignocaine,[8] Topical Lignocaine spray,[9] narcotic opioids like Fentanyl,[10] Alfentanyl,[11] calcium channel blockers like Diltiazem,[3] vasodilators like Nitroglycerine both intravenous[5] and sublingual sprays,[1,2] alpha agonists like Clonidine,[12] Demeditomidine,[13] and Betablockers like Esmolol.[3–5] By controlling the hemodynamic changes that occur during endotracheal extubation which can reduce mortality and morbidiy attributable to anesthesia especially in vulnerable patients.[3]

Attenuating this increased hemodynamic response to extubation is more challenging than that of intubation because we cannot deepen the plane of anesthesia,[15,16] When we use any drug for attenuating the hemodynamic response to tracheal extubation its peak effect should correspond to that of the stimulus, so, there should be two to three minutes time gap between administration of drug and tracheal extubation.[2] Thus, the choice of the drug, route of administration and the timing used in the present study seems to be justified. The study by Dyson A et al.,[17] on Esmolol with doses of 1.5 mg/kg and 2 mg/kg controlled both systolic blood pressure and heart rate but larger dose produced significant decrease in systolic blood pressure. Hence, in our study we have used dose of 1.5 mg/kg of intravenous Esmolol. And the study by Tagalpallewar A et al.,[2] on Nitroglycerine showed satisfactory blood pressure control with 0.8 mg of sublingual dose of NTG spray. Hence, in our study we have used 0.8 mg sublingual NTG spray. But there was no study comparing these drugs, hence this study was undertaken. Because of immediate action, shorter half life and lack of sedative properties of intravenous Esmolol[5] and sublingual NTG spray,[2] we planned to do a prospective randomized controlled double blind study to compare the effects of these drugs on hemodynamic response following tracheal extubation.

In our study, we found intravenous Esmolol significantly attenuated the tachycardia response to extubation when compared to sublinlual NTG group. In intravenous Esmolol group control of heart rate was observed within 1 minute of administration and maintaining upto 15 minutes after extubation, where as in NTG group there was increase in mean heart rate upto 122 beats per minute during and after extubation. Hence, we found intravenous Esmolol has better control over heart rate when compared to sublingual NTG group. Various studies by Acharya N et al.,[3] Vachhani et al.[4] and Kotambkar V et al.[5] on comparison of Intravenous Esmolol and Intravenous NTG showed, Intravenous Esmolol has better control over heart rate during extubation when compared to Intravenous NTG.

Nitroglycerine is known to reduce blood pressure with increase in heart rate.[18] And we found only few studies on sublingual NTG spray to attenuate hemodynamic response to tracheal extubation. The study by Tagalpallewar A et al.[2] found that at the time of extubation there was modest increase in heart rate following sublingual NTG spray which correlates with our study. In present study, the baseline value of systolic, diastolic, mean

arterial pressure were comparable between the groups during intraoperative period. At the time of extubation mean arterial pressure was lower in Esmolol group when compared to NTG group which was found to be statistically significant following extubation and this is in similar to study done by Ersin et al.[19]

However, in a study done by Kotambkar V et al.,[5] systolic, diastolic, mean arterial pressure were significantly lower in NTG group as compared to Esmolol group at the time of extubation this is in contrary to our study. Tagalpallewar A et al.[2] reported that sublingualy administered NTG spray in a dose of 0.8 mg prior to extubation resulted in stable hemodynamics, and allows easy extubation and comfortable recovery.

Complications

In the present study, heart rate less than 60 bpm and blood pressure less than 90/60 mm of hg was considered dangerous and injection Atropine 0.01 mg/kg IV and injection Ephidrine 6mg IV were used as rescue drug for bradycardia and hypotension respectively. In NTG Group 3 patients had complications like hypotension, laryngospasm and headache and in Esmolol group one patient had bradycardia which were treated immediately and there was no significant differences in complications between the two groups.

Limitations

Our study has some limitations like invasive monitoring was not done so evaluation of cardiac output during extubation could not be assessed and effects of these drug in high risk patients needs validation.

Conclusion

We conclude from this study that administration of intravenous Esmolol in a dose of 1.5 mg/kg and sublingual NTG spray in a dose of 0.8 mg prior to extubation in ASA1 and ASA 2 patients are effective and relatively safe method of protecting patients from the complications related to hypertension and tachycardia and allows easy extubation with stable hemodynamics with smooth and comfortable recovery. Increase in Systolic, Diastolic and Mean arterial pressures were controlled by both intravenous Esmolol and sublingual NTG spray but intravenous Esmolol also controlled heart rate during extubation. Hence, we conclude intravenous Esmolol attenuates extubation response by having better control on heart rate and blood pressure with minimal complications when compared to sublingual NTG spray group.

Acknowledgment: Nil

Conflict of Interest: Nil

References

1. Singh D, Sundrani O, Tagalpallewar A, et al. The effects of Nitroglycerine (NTG) sublingual spray to slunt the hemodynamic response to endotracheal extubation in lumbar disc surgery. Journal of Evolution of Medical and Dental Sciences 2015;4(81):14233–14239.
2. Tagalpallewar A, Ambare B, Agrawal J, et al. Efficacy of sublingual Nitroglycerine spray in attenuation of hemodynamics to tracheal extubation. International Journal of Research in Medical Sciences 2017;5(8):3560–565.
3. Narayan Acharya. Comparative evaluation of esmolol, nitroglycerine and diltiazem on attenuation of cardiovascular responses to tracheal extubation: A prospective randomized study. Sch J App Med Sci Jan 2017;5(1C):188–94.
4. Vachhani R, Gulati Rahul. A comparative study to evaluate the effects of nitroglycerine and esmolol on hemodynamic parameters in controlled hypertensive patients during emergence from anesthesia and extubation. Int J Med Res Prof 2017;3(3):90–93.
5. Kotambkar V, Katdare M. A comparative study of effects of intravenous Nitroglycerine and intravenous Esmolol on hemodynamic response following tracheal extubation. Indian Journal of Basic and Applied Medical Research 2015 June;4(3): 344–56.
6. Shirasaka T, Iwasaki T, Hosokawa N, et al. Effects of landiolol on the cardiovascular response during tracheal extubation. Journal of anesthesia 2008 Aug 1;22(3):322–25.
7. Miyazaki M, Kadoi Y, Saito S. Effects of landiolol, a short-acting beta-1 blocker, on hemodynamic variables during emergence from anesthesia and tracheal extubation in elderly patients with and without hypertension. Journal of Anesthesia 2009 Nov 1; 23(4):483–88.
8. Bidwai AV, Bidwai VA, Rogers CR, et al. Blood-pressure and pulse-rate responses to endotracheal extubation with and without prior injection of lidocaine. Anesthesiology. 1979 Aug;51(2):171–73.
9. Jee D, Park SY. Lidocaine sprayed down the endotracheal tube attenuates the airway-circulatory

reflexes by local anesthesia during emergence and extubation. Anesthesia & Analgesia 2003 Jan 1;96(1):293–97.

10. Nishina K, Mikawa K, Maekawa N, et al. Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta Anesthesiol Scand 1995 Jan 1;39(1):85–89.
11. Fuhrman TM, Ewell CL, Pippin WD, et al. Comparison of the efficacy of esmolol and alfentanil to attenuate the hemodynamic responses to emergence and extubation. Journal of Clinical Anesthesia 1992 Dec 31;4(6):444–47.
12. Zalunardo MP, Zollinger A, Spahn DR, et al. Preoperative clonidine attenuates stress response during emergence from anesthesia. Journal of Clinical Anesthesia 2000 Aug 31;12(5):343–49.
13. Guler G, Akin A, Tosun Z, et al. Single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. Acta Anesthesiol Scand 2005 Sep 1;49(8):1088–91.
14. Mikawa K, Nishina K, Takao Y, et al. Attenuation of cardiovascular responses to tracheal extubation: Comparison of verapamil, lidocaine, and verapamil-lidocaine combination. Anesthesia and Analgesia 1997 Nov 1;85(5):1005–10.
15. Heartley M, Vaughan RS. Problem associated with tracheal extubation. Br J Anesth 1993:71:561–68.
16. Bostan H, Eroglu A. Comparison of the clinical efficacies of fentanyl, esmolol and lidocaine in preventing the hemodynamic responses to endotracheal intubation and extubation. Journal of Current Surgery 2012;2(1):24–28.
17. Dyson A, Isaac PA, Pennant JH, et al. Esmolol attenuates cardiovascular responses to extubation. Anesth Analg 1990;71:675–78.
18. James P Rathmell, Shafer Steven. Vasodilators, chapter 20. Pamella Flood, Stoelting's handbook of pharmacology and physiology in anesthetic practice. 5th edition. New Delhi: Wolters Kluwer; 2013.p.309.
19. Ersin Y, Çelik M, Besler M, et al. Comparing the effects of esmolol and diltizem to depressing the hemodynamic response against tracheal extubation. The Medical Journal of SSK Göztepe Educational Hospital. 2005;20(4):193–96.