Section: Anaesthesia

Original Research Article

ATTENUATION OF CARDIOVASCULAR RESPONSE TO TRACHEAL EXTUBATION: DILTIAZEM VS ESMOLOL: A PROSPECTIVE RANDOMISED CONTROLLED STUDY

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Abstract

Background: Tracheal extubation is invariably associated with haemodynamic changes like tachycardia, hypertension mainly due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. Ideally, extubation of the trachea should be devoid of such complications. Our study aimed to investigate and compare the effects of esmolol and diltiazem on controlling haemodynamic response to extubation. **Materials and Methods:** This study population consisted of 90 patients undergoing elective surgery under general anaesthesia with endotracheal intubation. They were randomly divided into 3 groups each with 30 patients. Control group (Group C): 10 ml of normal saline (NS),Diltiazem group (Group D): 0.1mg/kg of Diltiazem, Esmolol group (Group E): 1mg/kg of Esmolol. These drugs were given 3 min after injection of neostigmine and glycopyrrolate and 2 minutes before tracheal extubation. Values of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) were recorded after completion of reversal at the time of administration of study drugs (3 mins after reversal taken as 0 min), 1 and 2 mins after administration of the drugs, and 1 min, 3 mins, 5 mins, 10 mins and 15 mins after extubation. **Result:** Demographic variables were compared in all the groups. Patients in Group D had lesser blood pressure variations, and patients in Group E had lesser heart rate variations. Patients in Group C had significant changes in heart rate and blood pressure. It is important to give intravenous diltiazem or esmolol at the time of extubation to decrease the incidence of any untoward haemodynamic and pharyngolaryngeal events. **Conclusion:** Diltiazem is more effective than Esmolol in attenuating blood pressure changes and Esmolol is more effective than Diltiazem in attenuating heart rate changes during tracheal extubation.

INTRODUCTION

Endotracheal extubation is one of the most frequently performed procedures in the practice of anaesthesia. Endotracheal extubation is the translaryngeal removal of a tube from the trachea via the nose or mouth1. Extubation from the trachea should be devoid of changes in haemodynamic parameters and adverse events such as coughing, breath-holding, laryngospasm, etc1. Endotracheal extubation almost always associated with haemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngo pharyngeal stimulation. This increase in sympathoadrenal activity may result in hypertension, tachycardia, and arrhythmias. This increase in blood pressure and heart rate is usually transitory, variable, and unpredictable. It is more hazardous to patients with hypertension, myocardial insufficiency, and cerebrovascular diseases. Therefore, this haemodynamic response to tracheal extubation such as hypertension, tachycardia, and arrhythmias has always been an interest to anesthesiologist.[1,2] Various techniques that are

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recommended to prevent this stress response associated with extubation include increasing the depth of anesthesia, limiting the duration of laryngoscopy, and the use of various pharmacological agents such as intravenous (IV) and topical lignocaine, opioids, beta-blockers such as esmolol, calcium channel blockers such as verapamil, diltiazem, and nicardipine, and other agents such as magnesium sulfate, labetalol, nitroprusside, and nitroglycerine.[2-4] None of the agents used so far is completely satisfactory and the quest for an ideal agent to attenuate the stress response due to extubation continues.[2-4] Esmolol is an ultrashort-acting, highly cardioselective beta-adrenergic receptor antagonist. Its rapid elimination is due to conversion to an inactive free acid metabolite by plasma esterases. It is Food Drug Administration (FDA)-approved for short-term duration use in the control of supraventricular tachycardia, such as a rapid ventricular rate in patients with atrial fibrillation or atrial flutter. It is also indicated in sinus tachycardia, where a rapid rate requires intervention secondary to other comorbidities.[5] Esmolol is further FDA-approved for tachycardia and hypertension induced by intubation. It is used for rate and rhythm control in aortic dissection, acute coronary syndrome, non-ST elevation myocardial infarction, hypertensive emergencies, thyrotoxicosis, refractory ventricular tachycardia, refractory to defibrillation ventricular fibrillation, and to decrease catecholamine response during electroconvulsive therapy.[6-8] Diltiazem is a Calcium channel blocker which reduce the influx of calcium into the cells. Inhibition of calcium channels in the vessels results in vasodilation and, consequently, a lowering of the blood pressure. In the heart, this blockage reduces cardiac contractility and slows atrioventricular conduction velocities.[9] Diltiazem has been used extensively to maintain perioperative haemodynamic stability. Diltiazem belongs to the non-dihydropyridine calcium channel blockers. This subclass presents more negative chronotropic and inotropic effects than the dihydropyridine subclass and induces a significant reduction of atrioventricular conduction rate; all of these make non-dihydropyridines useful for acute and chronic treatment as well as for prevention of atrial arrhythmias.[10] This drug is effective in blunting the haemodynamic responses associated with laryngoscopy and tracheal extubation as well as intubation.[11] The mechanism responsible for tachycardia and hypertension during tracheal extubation is unknown but these changes may be related to the release of catecholamines. The various pharmacological and non-pharmacological approaches mentioned for attenuation of haemodynamic responses to extubation are not entirely satisfactory.[12] Hence the present study was undertaken to evaluate and compare the ability of diltiazem and esmolol in attenuating the cardiovascular responses to tracheal extubation.

MATERIALS AND METHODS

This prospective, randomised, controlled study was conducted in department of Anaesthesiology, D Y Patil University School of Medicine & Hospital, Nerul, Navi Mumbai. Patients belonging to ASA (American society of Anaesthesiologists) I and II between age group 18 to 60 years undergoing surgery under general anaesthesia were included for this study. The patients who refused to participate, having allergy to trial drugs, pregnant patient, patients with cardiac, respiratory diseases, patients on antihypertensive medication and patient with difficult intubation were excluded from study. This study was a prospective, randomized controlled study, which was carried out after obtaining approval of the ethical committee of the institution and informed consent from the patients. Selected ninety patients were randomly divided into 3 groups using random number tables. The groups were organized as follows: Control group (Group C, n=30): 10 ml of normal saline (NS) Diltiazem group (Group D, n=30): 0.1mg/kg of Diltiazem diluted with NS to make total 10 ml. Esmolol group (Group E, n=30): 1mg/kg of Esmolol diluted with NS to make total 10 ml. These drugs were given 3 min after injection of neostigmine and glycopyrrolate and 2 minutes before tracheal extubatioon. In the operation theatre, standard monitors including electrocardiograph (ECG), noninvasive blood pressure (NIBP), pulseoxymetry (SpO2) were attached and baseline values noted. All the patients received injection (inj) midazolam 0.02mg/kg intravenous (iv) and inj fentanyl 1-2 mcg/kg i.v. preinduction. General Anaesthesia was induced with 2mg/kg of propofol, after confirming bag mask ventilation, inj vecuronium 0.1mg/kg was given. After successful and confirmed intubation, maintenance of anaesthesia was done with 50% O2 and 50% air each and sevoflurane 1-2 % and intermittent top up of vecuronium (0.02mg/kg). Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) and peripheral oxygen saturation (SpO2) were monitored every 5 minutes (min) throughout anaesthesia. At the end of surgery, all anaesthetics discontinued and patients were ventilated with 100% oxygen. Neuromuscular block was reversed with neostigmine (0.04mg/kg) and inj. glycopyrrolate(0.01mg/kg) i.v. Three minutes after reversal, and 2 minutes before tracheal extubation, 1mg/kg esmolol or diltiazem 0.1 mg/kg or saline was injected iv. The trachea was extubated 2 mins after administration of these drugs. Just before extubation, it was confirmed that the patients can breathe spontaneously and can open their eyes on command and oropharyngeal secretions were sucked out. Immediately after extubation, 100% oxygen was given via face mask for 5 mins. Values of HR, SBP, DBP, MAP were recorded after completion of reversal at the time of administration of study drugs (3 mins after reversal taken as 0 min), 1 and 2 mins

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after administration of the drugs and 1 min, 3 mins, 5 mins, 10 mins and 15 mins after extubation.

Statistical anlaysis: Sample size calculation was derived from a previous study by Singh et al.

All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software. Results were presented as mean difference (MD), and 95 % confidence interval for continuous variables. Qualitative data was compared using the Chi- square test and Fishers exact tests. The student t test was used for evaluation of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

Control group (Group C, n=30): 10 ml of normal saline (NS)

Diltiazem group (Group D, n=30): 0.1mg/kg of Diltiazem diluted with10 ml NS.

Esmolol group (Group E, n=30): 1mg/kg of Esmolol diluted with 10 ml NS.

These drugs were given 3 min after injection of neostigmine and glycopyrrolate, 2 minutes before tracheal extubation.

The following results were obtained:

Mean heart rate in the Group E was significantly lower in comparison to both Group C and Group D at extubation, 1 minute after extubation, 3 minutes after extubation, 5 minutes after extubation, 10 minutes after extubation and 15 minutes after extubation. Mean heart rate in the Group D was significantly lower in comparison to Group C at extubation, 1 minute after extubation, 3 minutes after extubation and 5 minutes after extubation.

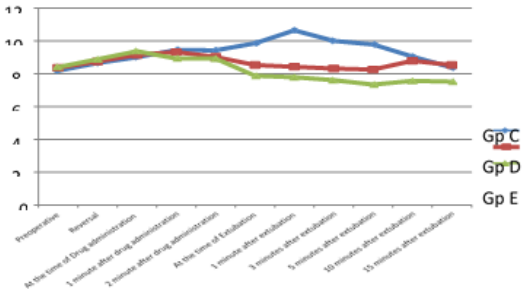

Figure 1: Heart rate at different time intervals.

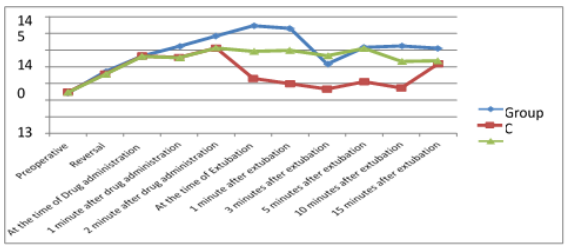

Figure 2: SBP at different time interval.

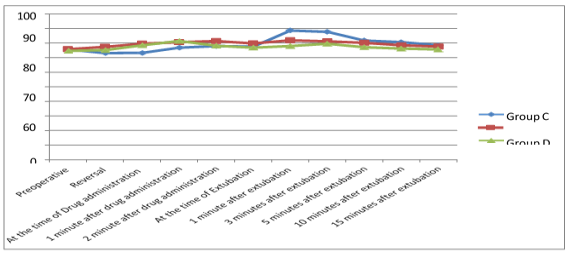

Figure 3 show the comparison of p value of SBP at different time intervals.

Mean SBP was significantly lower among patients of Group D at extubation, 1 minute after extubation, 3 minutes after extubation, 5 minutes after extubation, 10 minutes after extubation and 15 minutes after extubation.

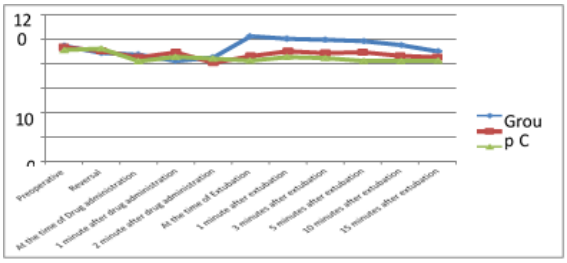

Figure 4: MAP at different time intervals.

[Table 3] shows the comparison of mean arterial pressure at different time intervals. Mean arterial pressure was significantly higher among patients of the Group C in comparison to Group D and Group E respectively at extubation, 1 minute, 3 minutes,5 minutes, 10 minutes and 15 minutes after extubation.

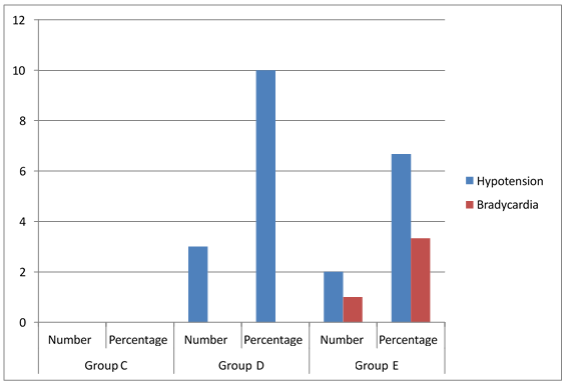

Figure 5: Adverse events

Hypotension was seen in 10 percent of the patients of the Group D while it was seen in 6.67 percent of the patients of the Group E. Bradycardia was seen in 3.33 percent of the patients of group E.

Table 1: Comparison of p value of heart rate at different time intervals.

Time-interval	p-value: Group C VS Group D	p-value: GroupD VS Group E	p-value: Group C VS Group E
Preoperative	0.28	0.22	0.74
Reversal	0.54	0.84	0.25
At the time of Drug administration	0.36	0.75	0.46
1 minute after drug administration	0.85	0.25	0.82

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2 minute after drug administration	0.46	0.33	0.34
At the time of Extubation	0.01*	0.03*	0.01*
1 minute after extubation	0.02*	0.02*	0.02*
3 minute after extubation	0.03*	0.01*	0.01*
5 minutes after extubation	0.02*	0.01*	0.02*
10 minutes after extubation	0.22	0.02*	0.04*
15 minutes after extubation	0.12	0.01*	0.03*

*: Significant

Table 2: Comparison of p value of SBP at different time intervals.

Time-interval	p- value: Group C VS group D	p- value: Group D VS group E	p- value: Group C VS group E
Preoperative	0.12	0.84	0.27
Reversal	0.88	0.36	0.13
At the time of Drug administration	0.92	0.41	0.34
1 minute after drug administration	0.65	0.28	0.19
2 minute after drug administration	0.12	0.79	0.28
At the time of Extubation	0.02*	0.00*	0.19
1 minute after extubation	0.04*	0.01*	0.28
3 minutes after extubation	0.00*	0.03*	0.34
5 minutes after extubation	0.01*	0.02*	0.85
10 minutes after extubation	0.02*	0.02*	0.74
15 minutes after extubation	0.03*	0.03*	0.46

*: Significant

Table 3: Comparison of p value of Mean arterial pressure at different time intervals

Time-interval	p-value: Group C VS group D	p- value: Group D VS group E	p- value: Group C VS group E
Preoperative	0.42	0.47	0.22
Reversal	0.39	0.69	0.36
At the time of Drug administration	0.15	0.58	0.43
1 minute after drug administration	0.28	0.66	0.61
2 minute after drug administration	0.33	0.49	0.58
At the time of Extubation	0.01*	0.84	0.02*
1 minute after extubation	0.02*	0.28	0.04*
3 minutes after extubation	0.04*	0.46	0.02*
5 minutes after extubation	0.04*	0.27	0.04*
10 minutes after extubation	0.03*	0.39	0.01*
15 minutes after extubation	0.02*	0.88	0.02*

DISCUSSION

Extubation of the trachea should be devoid of changes in haemodynamic parameters and adverse events such as coughing, breath holding, and laryngospasm. The hemodynamic changes at extubation are due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. This increase in sympathoadrenal activity may result in hypertension, tachycardia, and arrhythmias which are transient, variable, and unpredictable.[12] It is more hazardous to patients with hypertension, myocardial insufficiency, and cerebrovascular disease.[13] Many pharmacological methods have been devised to reduce the extent of haemodynamic events accompanying extubation, including esmolol, alfentanil, fentanyl, diltiazem, high dose of opioids, local anesthetics like lignocaine.[14-16]

Esmolol is an ultrashort-acting, highly cardioselective beta-adrenergic receptor antagonist and Diltiazem, a calcium channel blocker has been used extensively to maintain perioperative hemodynamic stability. This drug is effective in blunting the haemodynamic responses associated with laryngoscopy and tracheal extubation as well as intubation. The mechanism responsible for tachycardia and hypertension during tracheal extubation is unknown but these changes may be related to the release of catecholamines.[17-19]

In the present study, 60 percent, 50 percent, and 53.33 percent of the patients of Group C, Group D, and Group E were of ASA grade I while the remaining were of ASA Grade II. All three study groups were comparable in terms of ASA Grade-wise distribution of patients. Demographic parameters were comparable in all three groups. In the present study, mean heart rate in the Group E was significantly lower in comparison to both Group C and Group D at extubation, 1 minute, 3 minutes, 5 minutes, 10 minutes and 15 minutes after extubation. Mean heart rate in the Group D was significantly lower in comparison to Group C at extubation, 1 minute, 3 minutes and 5 minutes ,10 minutes and 15 minutes after extubation.

Our results were in concordance with the results obtained by Singh A et al,[1] who also reported similar findings in their respective study. They reported that the heart rate in the esmolol group was significantly lower than saline group and diltiazem group at extubation and 1, 3, 5, 10 minutes after extubation.

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Similar findings were reported in the studies conducted by Lee et al,[20] and Talwar et al.[21] Lee et al found that diltiazem (0.3 mg/kg) did not attenuate the increase in HR, when administered alone. Talwar et al, in their study, reported that Diltiazem alone was no different from control as both were associated with a significant rise in HR till 3 min after laryngoscopy.

Sharma MV et al,[22] in another study, reported that heart rate in the group E was found to be significantly lower than those in group S and group D during extubation and 1,3 and 5 minutes after extubation. This was due to that, diltiazem causes sympathoadrenal reflex stimulation by hypotension. In the present study, mean SBP was significantly lower among patients of Group D at extubation, 1 minute, 3 minutes, 5 minutes, 10 minutes and 15 minutes after extubation compared to Group E and Group C.

Our results were in concordance with the results obtained by Singh A et al1 who also reported similar findings in their respective study. They reported that the SBP in diltiazem group was found to be significantly lower than in esmolol group and saline group at extubation and 1, 3,5,10 minutes after extubation. Statistical evaluation between the groups showed that decrease in SBP observed in diltiazem group was statistically highly significant when compared to SBP in esmolol group. In another study conducted by Sharma MV et al,[22] authors reported that the SBP in the group D was found to be significantly lower than those in group E and group S during extubation and 1,3 and 5 minutes after extubation. In the present study, mean DBP was significantly higher among the patients of the Group C in comparison to Group D and Group E respectively. Our results were in concordance with the results obtained by Singh A et al,[1] who also reported similar findings in their respective study.

Esmolol was used by Andrew Dyson et al,[11] in 1990 to attenuate the cardiovascular responses associated with extubation in a dose of 1mg/kg, 1.5mg/kg and 2 mg/kg. They have concluded that increase in heart rate that occurs during extubation can be successfully attenuated by bolus injection of 1mg/kg esmolol, although this dose is insufficient to effectively block increase SBP which corelates with present study finding.

Nam DH et al,[23] in 1996 used esmolol in the dose of 1.5 mg/kg and diltiazem in the dose of 0.2mg/kg to attenuate cardiovascular responses to tracheal extubation, which concluded that esmolol was more effective than diltiazem in attenuating the heart rate changes and diltiazem was more effective than esmolol in attenuating the systolic blood pressure changes, similar to present study findings.

Sharma MV et al,[22] reported that the DBP in the group D was not found to be significantly lower than those in group E and group S during extubation and at 1, 3 and 5 minutes after extubation.

In another study conducted by Talwar et al,[21] authors reported that all the study groups were associated with a significant fall in the SBP, DBP, and MAP after induction as compared to the baseline. The control group was associated with a significant rise in SBP till 2 min after laryngoscopy. As compared to the control, esmolol group was effective in preventing a rise in SBP till 5 min and the diltiazem group till 1 min after extubation. This is consistent with study done by Kumar et al,[25] who showed that esmolol in a dose of 2 mg/kg, blunts the SBP response. Mikawa et al showed that diltiazem in a dose of 0.2-0.3 mg/ kg, successfully suppresses the pressor response to intubation, and its action is rapid and short. Fujii et al4 similarly showed that esmolol and diltiazem attenuate the rise in SBP after laryngoscopy, as compared to control. Vacevic et al,[26] found that 100 mg of esmolol decrease SBP significantly at 1.5 minutes after intubation.

In the present study, mean arterial pressure was significantly higher among patients of the Group C in comparison to Group D and Group E respectively at extubation, 1 minute, 3 minutes, 5 minutes, 10 minutes and 15 minutes after extubation. In the present study, Hypotension was seen in 10 percent of the patients of the Group D while it was seen in 6.67 percent of the patients of the Group E. Bradycardia was seen in 3.33 percent of the patients of group E. Non-significant results were obtained while comparing the incidence of complications among the two study groups.In a study conducted by Sharma et al,[22] bradycardia was seen in 2 percent of patients of esmolol group while tachycardia was seen in 6 percent of the patients of the Diltiazem group. Kumar et al, in another study, also reported non-significant difference while comparing the incidence of complications among the esmolol group and Diltiazem.

Vucevic and Purdy et al,[26] found that Esmolol causes a less rise in systolic blood pressure than the control group. Diltiazem caused greater fall in diastolic blood pressure post-induction than Esmolol and blunted pressor response better than Esmolol. The rise in rate-pressure product with Esmolol was greater than in diltiazem group, thus showing that diltiazem controls myocardial oxygen demand better than Esmolol. Mikawa et al reported attenuation by diltiazem 0.3 mg/kg, and Hasegawa et al,[27] with 0.2 mg/kg. A continuous infusion of diltiazem is also known to suppress this pressor response as shown by Shimada et al (1991).[28]

CONCLUSION

Under the light of above obtained data, following conclusion can be withdrawn:

- It is important to give intravenous diltiazem or esmolol, so as to decrease the incidence of any untoward haemodynamic and pharyngolaryngeal events, at the time of extubation.
- Diltiazem is more effective than esmolol in attenuating blood pressure changes and esmolol is

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more effective than diltiazem in attenuating heart rate changes during tracheal extubation.

- Hence further studies are recommended for comparing the results if both drugs are given together in appropriate doses to balance effectiveness of both with less adverse effects.

REFERENCES

1. Singh A, Aphale S, Bhosale J. Comparison of diltiazem and esmolol in attenuating the cardiovascular responses to tracheal extubation. Innovative Journal of Medical and Health Science. 2015; 5(1): 1- 5.
2. Smith JE, King MF, Yanny HF, Pottinger KA, Pomirska MB: Effect of Fentanyl on circulatory responses to orotracheal fibreoptic intubation. Anaesthesia 1992; 47(1): 20-3
3. Mikawa K, Nishina K, Maekawa N, Obara H. Attenuation of cardiovascular responses to tracheal extubation: verapamil Vsdiltiazem.Anaesthesia Analgesia 1996; 82: 1205-10
4. Fujii Y, Yuhjisakoh, Takahashi S. Combined diltiazem and lignocaine reduces cardiovascular responses to tracheal extubation and anaesthesia emergence in hypertensive patients.Canadian Journal of anaesthesia 1999;46:952-956.
5. Ellenbogen KA, Dias VC, Cardello FP, et al. Safety and efficacy of intravenous diltiazem in atrial fibrillation or atrial flutter. Am J Cardiol. 1995;75:45–49.
6. National Center for Biotechnology Information. PubChem Compound Summary for CID 59768, Esmolol. https://pubchem.ncbi.nlm.nih.gov/compound/Esmolol. Accessed Dec. 13, 2020.
7. Poveda-Jaramillo R, Monaco F, Zangrillo A, Landoni G. Ultra-Short-Acting β-Blockers (Esmolol and Landiolol) in the Perioperative Period and in Critically Ill Patients. J Cardiothorac Vasc Anesth. 2018 Jun;32(3):1415-1425.
8. Pevtsov A, Kerndt CC, Fredlund KL. Esmolol. [Updated 2020 May 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK518965/
9. National Center for Biotechnology Information. PubChem Compound Summary for CID 39186, Diltiazem. https://pubchem.ncbi.nlm.nih.gov/compound/Diltiazem. Accessed Dec. 13, 2020.
10. Nishina K, Mikawa K, Maekawa N, Obara H. Attenuation of cardiovascular responses to tracheal extubation with diltiazem. Anesth Analg. 1995 Jun;80(6):1217-22.
11. Singh S, Laing EF, Owiredu WK, Singh A. Comparison of esmolol and lidocaine for attenuation of cardiovascular stress response to laryngoscopy and endotracheal intubation in a Ghanaian population. Anesth Essays Res. 2013 Jan-Apr;7(1):83-8.
12. Alshami A, Romero C, Avila A, Varon J. Management of hypertensive crises in the elderly. J Geriatr Cardiol. 2018 Jul;15(7):504-512.
13. Stones JG, Foex P, Sear JW, et al. Risk of myocardial ischaemia during anaesthesia in treated and untreated hypertensive patients. Br.J.Anaesth 1988; 61:675-9.
14. Bidwai AV, Bidwai VA, Rogers CR, Stanley TH. Blood pressure and pulse rate responses to endotracheal extubation with or without prior injection of lidocaine Anesthesiology 1979; 51:171-3.
15. Efe EM, Bilgin BA, Alanoglu Z, Akbaba M, Denker C. Comparison of bolus and continuous infusion of esmolol on hemodynamic response to laryngoscopy, endotracheal intubation and sternotomy in coronary artery bypass graft. Braz J Anesthesiol. 2014 Jul-Aug;64(4):247-52.
16. Cakırgöz MY, Taşdöğen A, Olguner C, Korkmaz H, Oğün E, Küçükebe B, Duran E. Efeito de diferentes doses de esmolol sobre a resposta hemodinâmica, BIS e resposta de movimento durante a intubação orotraqueal: estudo prospectivo, randômico e duplo- cego [The effect of different doses of esmolol on hemodynamic, bispectral index and movement response during orotracheal intubation: prospective, randomized, double- blind study]. Rev Bras Anestesiol. 2014 Nov-Dec;64(6):425-32.
17. Alkaya MA, Saraçoğlu KT, Pehlivan G, Eti Z, Göğüş FY. Effects of Esmolol on the Prevention of Haemodynamic Responses to Tracheal Extubation after Craniotomy Operations. Turk J Anaesthesiol Reanim. 2014;42(2):86-90.
18. S. J. B. Shubhada Aphale, "Comprison of diltiazem and esmolol in attenuating the cardiovascular responses to tracheal extubation.", ijmhs, vol. 5, no. 1, pp. 1-5, Feb. 2015.
19. 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; 4(1): 65- 69.
20. Lee KH, Jun ES, Chae YJ, Park GS, Choi JC, Lim HK. Effect of diltiazem and lignocaine on cardiovascular response to tracheal intubation. Korean J Anesthesiol 2002;43:710‐5.
21. Talwar V, Ganeriwal V, Aggarwal S, Gupta A. Efficacy of combination of esmolol and diltiazem for attenuating hemodynamic response to laryngoscopy and intubation: A prospective randomized study. Anesth Essays Res 2018;12:674-9
22. Sharma MV, Sharma T, Chauhan D. Comparison of The Effect of Diltiazem and Esmolol in Attenuating The Cardiovascular Responses To Endotracheal Extubation and Emergence From Anaesthesia. Indian Journal of Applied Research, Jan-2018;8:23-29Selvaraj V, Manoharan KR. Prospective randomized study to compare between intravenous dexmedetomidine and esmolol for attenuation of hemodynamic response to endotracheal intubation. Anesth Essays Res. 2016 May-Aug;10(2):343-8.
23. Nam DH, Park BS, Kang HS. Cardiovascular response of esmolol and diltiazem to tracheal extubation.Korean J. anaesthesiology 1996; 31: 43-48.
24. Acharya N, Routray D. Comparative Evaluation of Esmolol, Nitroglycerine and Diltiazem on Attenuation of the Cardiovascular Responses to Tracheal Extubation: A Prospective Randomized Study. Scholars Journal of Applied Medical Sciences (SJAMS), 2017; 5(1C):188-194.
25. Kumar KS, Laxminarsaiah G. Attenuation of Cardiovascular Responses to Tracheal Extubation: Esmolol versus Propofol. Journal of Medical Science and Clinical research. 2018; 6(1): 56- 59.
26. Vacevic M, Purdy GM, Ellis FR. Esmolol hydrochloride for management of the cardiovascular stress response to laryngoscoy and tracheal intubation. Br. J. Anaesth 1992; 68: 529-30.
27. Hasegawa J, Mitsuhata H, Matsuhata S, Enzan K: Attenuation of cardiovascular responses to laryngoscopy and tracheal intubation with bolus injection of diltiazem. Masui 1992; Mar: 41(3): 356-62
28. Shimada T, Mitsuhata H, Matsumoto S, Ohtaka K, Hasegawa J: Effect of continuous infusion of diltiazem on cardiovascular responses to laryngoscopy and intubation. Masui 1991; Oct-40 (10):1507-12..

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