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COMPARISON OF INTRAVENOUS LIGNOCAINE VERSUS COMBINATION OF LIGNOCAINE WITH DILTIAZEM ON ATTENUATION OF HAEMODYNAMIC RESPONSES TO TRACHEAL EXTUBATION IN PATIENTS UNDERGOING ABDOMINAL SURGERIES UNDER GENERAL ANAESTHESIA: A RANDOMIZED DOUBLE BLIND INTERVENTIONAL STUDY

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Lignocaine, diltiazem, attenuation, hemodynamic response, tracheal extubation

ABSTRACT

Background: Tracheal intubation is frequently associated with cardiovascular stress response characterized by hypertension, tachycardia and increased serum concentration of catecholamines and similar phenomenon is also seen during extubation. During Endotracheal extubation increase in sympathoadrenergic activity is caused by epipharyngeal and laryngopharyngeal stimulation. **Objective:** The aim and objectives of this study are to compare the effect of combination of intravenous (i.v.) diltiazem 0.1 mg/kg and i.v lignocaine 1.0 mg/kg vs intravenous lignocaine alone to attenuate haemodynamic extubation responses and airway reflexes during extubation. **Material and method**: This study was undertaken with 72 patients belonging to the age group 20–60 years with physical status ASA Classes I and II of either sex. Group A received injection diltiazem 0.1 mg/kg and lignocaine 1 mg/kg. Group B received injection lignocaine 1 mg/kg with normal saline. In this study, the drug dosage was fixed based on the previous studies. **Result**: The baseline values of heart rate,systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were statistically comparable between the two groups. The heart rate, SBP, DBP, and MAP was significantly high in group A (lignocaine) as compared to group B (diltiazem with lignocaine) at extubation and till 1 min, 3 min, 5 min, and 10 min post extubation (pvalue<0.05). **Conclusion:** Combined diltiazem and lignocaine provides more effective prophylaxis than lignocaine alone for attenuating the cardiovascular responses to tracheal extubation

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INTRODUCTION

Endotracheal extubation is one of the frequently performed procedures in the practice of anaesthesia. Complications after tracheal extubation are 3 times more common than complications occurring during tracheal intubation and induction of anaesthesia. Hypertension and tachycardia are well-documented events during extubation [1]. Both tracheal intubation and extubation are frequently associated with cardiovascular stress response because of increased serum concentration of catecholamines characterized by hypertension and tachycardia [2]. There is a correlation between the magnitude of the pressor response and increase in the concentration of catecholamines [3].

This sympathoadrenal response occurs very rapidly and lasts for few minutes. The increase in catecholamines leads to increased cardiac workload, heart rate and myocardial contractility which may lead to increased myocardial oxygen demand and could prove fatal particularly in patients suffering from coronary artery disease. Various factors are responsible for this haemodynamic response like pain of surgery, emergence from anaesthesia or tracheal irritation [1,4]. Many pharmacological drugs have been used to reduce the extent of haemodynamic events, including esmolol, alfentanil, fentanyl, diltiazem, high dose of opioids, local anesthetics like lignocaine and vasodilating drugs like nitroglycerine [5,6]. Esmolol acts by blocking the action of adrenergic activity of epinephrine and norepinephrine. It decreases inotropic contractility, heart rate and conduction. So it is associated with bradycardia and hypotension. Nitroglycerine works as a vasodilator and reduces haemodynamic responses to extubation, but it may lead to hypotension. Fentanyl, an opioid agonist, may blunt cardiovascular and airway reflexes during emergence but large doses may lead to sedation, muscular rigidity, bradycardia, nausea and vomiting. Topical anaesthesia with lignocaine applied to the larynx and trachea in a variety of ways remains a popular method used alone or in combination with other techniques [7].

Intravenous lignocaine with its well established centrally depressant and antiarrhythmic effect was found to be a more suitable alternate method to minimize this pressor response [8]. Recently several studies have shown that calcium channel antagonist like diltiazem, with its direct vasodilation and direct negative chronotropic and dromotropic properties is also effective [5,6,9].

The non-pharmacological methods like, smooth and gentle extubation with a shorter duration of laryngoscopy and blocking the glossopharyngeal nerve and superior laryngeal nerve have been used to attenuate the cardiovascular responses to endotracheal extubation [7].

None of these above mentioned approaches have proved entirely satisfactory. Hence, the search for an ideal agents to attenuate the haemodynamic responses is still continuing. With this background, the present study was undertaken to compare the effect of intravenous lignocaine versus combination of intravenous diltiazem with intravenous lignocaine on blunting the haemodynamic responses to endotracheal extubation in patients undergoing abdominal surgeries under general anaesthesia. The aim of this study is to compare the effect of intravenous lignocaine with combination of lignocaine with diltiazem on attenuation of haemodynamic responses to tracheal extubation in patients undergoing abdominal surgeries under general anaesthesia. The objective of this work is to determine the difference in change in heart rate HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) from base line to 1,3,5 and 10 min following tracheal extubation in both the groups. This also aims to determine the difference in cough response to tracheal extubation as per Eshak's grading. This also determine the difference in % of cases who develop side effects in both the groups (hypotension, bradycardia etc.)

MATERIALS AND METHODS

Study location

The hospital based prospective double blind interventional study was conducted in a tertiary care center after due permission from the Institutional Ethics Committee and Research Review Board and a written informed consent.

Sample size

The sample size of 36 in each group was needed at 95% confidence & 80% power to verify the expected minimum difference of 7.7% ($\pm$8.4%) in change in heart rate from baseline to 1 minute post extubation period. This sample size was adequate to cover all other study variables also [1]

Procedure

Eligible cases were assigned into two interventional groups using computer generated random number table.

Blinding: Similar sterile syringes containing equal volume of the study drug were prepared by other anaesthesiologist. The administration of the study drug and intraoperative and postoperative observations were recorded by anaesthesiologist participating in the study who was unaware of the contents of the syringes.

Study groups

Patients were randomly allocated into 2 groups (36 in each group).

Group A (n=36): received Inj. Lignocaine 1mg/kg i.v with normal saline (total volume=10ml)

Group B (n=36): received Inj. Diltiazem 0.1 mg/kg i.v and Inj. lignocaine 1 mg/kg i.v (total volume=10ml)

Eligibility Criteria

Inclusion criteria included patients of either sex, between 20-60 years of age, belonging to ASA Grade I & ll and seheduled for abdominal surgeries under general anaesthesia.

Exclusion criteria included patients not willing to participate in study ,Uncooperative patients patients with history of drug allergy ,patients suffering from cardiac diseases (ischemic heart disease, arrhythmias, angina, previous myocardial infarction, hypertension, and pulmonary diseases), any contraindication to study drugs administration,patients posted for emergency surgeries,patients with psychiatric and neurovascular disorders and Pregnant/Lactating women.

Patient was kept overnight fasting after 10 PM. Patient's written informed consent and PAC was checked. In operating room 18 gauge peripheral venous cannula was inserted and R.L drip was started. Monitoring in the operation theatre included electrocardiogram, pulse oximeter and non-invasive blood pressure (NIBP). Then patient was premedicated with Inj. Ranitidine (1mg/kg) i.v, Inj. Metoclopramide (0.1mg/kg) i.v, Inj. Glycopyrrolate (0.004mg/kg) i.v, Inj. Midazolam (1mg) i.v, Inj. Fentanyl 2mcg/kg i.v. Patient was preoxygenated with 100% oxygen for 3-5 minutes. General anaesthesia was induced with Inj. propofol 1.5 mg/kg i.v and Inj. scoline 1.5 mg/kg i.v to facilitate intubation. Intubation was done with appropriate size ET tube, bilateral air entry was checked, cuff inflated and tube was fixed. Maintenance was done with N_2O:O_2 in 60: 40, isoflurane (0.8-1 MAC) and Inj. Atracurium (loading dose 0.5mg/kg i.v and intermittent doses of 0.1 mg/kg i.v) throughout the surgical procedure. After completion of procedure, isoflurane was discontinued. On return of spontaneous respiratory efforts, nitrous oxide was discontinued and neuromuscular block was reversed with Inj. neostigmine (0.05 mg / kg) i.v and glycopyrrolate (0.01 mg /kg) i.v. and after 1 min. The study drug was given as bolus, by slow intravenous injection by the anaesthesiologist who was unaware of the group allocation .The haemodynamic parameters including HR, SBP, DBP, MAP was recorded just before the study drug injection. Extubation was done once following criteria were met (criteria for extubation): return of spontaneous respiration with adequate tidal volume,Patient obeying verbal commands (eye opening) and good hand grip.

Immediately after tracheal extubation patient was given 100% O_2 by facemask for 5 min. Values of HR, SBP, DBP, MAP were recorded at the end of surgery, at the time of reversal, before giving study drug, at the time of extubation and 1, 3, 5, 10 min after extubation. Cough response was noted using ESHAK grading and adverse effects (if any) were noted

Outcome Variables

1. Haemodynamic variables (Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean Arterial Pressure (MAP).
2. Post-operative cough response to tracheal extubation by ESHAK grading.
3. Adverse effects (if any)

Statistical Analysis

All the statistical analysis of data was done with statistical programming software – SPSS (Statistical Package for the Social Science) version 21.0.0 (SPSS Inc., Chicago, Illinois, USA). The continuous variables (quantitative data) like age, weight, blood pressure, pulse rate, time were presented as mean and standard deviation and analyzed by applying t- test. The categorical variables (qualitative data) like ASA grade were presented in frequency and percentage and were analyzed with Chi-Square test (for nominal data). P value of <0.05 was considered statistically significant in all the analysis.

RESULTS

As per our study to compare intravenous lignocaine alone or combination of lignocaine with diltiazem on attenuation of haemodynamic responses to tracheal extubation in patients undergoing abdomen surgeries under general anaesthesia, data and results obtained are tabulated and analysed

Table: 1. Age, weight, sex wise distribution of patients (mean±SD)

		Group A			Group B			P value	Significance
		Mean	SD	%	Mean	SD	%		
Age (Yrs)		40.31	11.92		41.64	11.35		0.625	NS
Weight (kg)		59.25	6.75		61.15	3.83		0.292	NS
SEX	**Male**			41.66			44.44	1.00	NS
	Female			58.33			55.55		

S=Significant; NS = Non significant

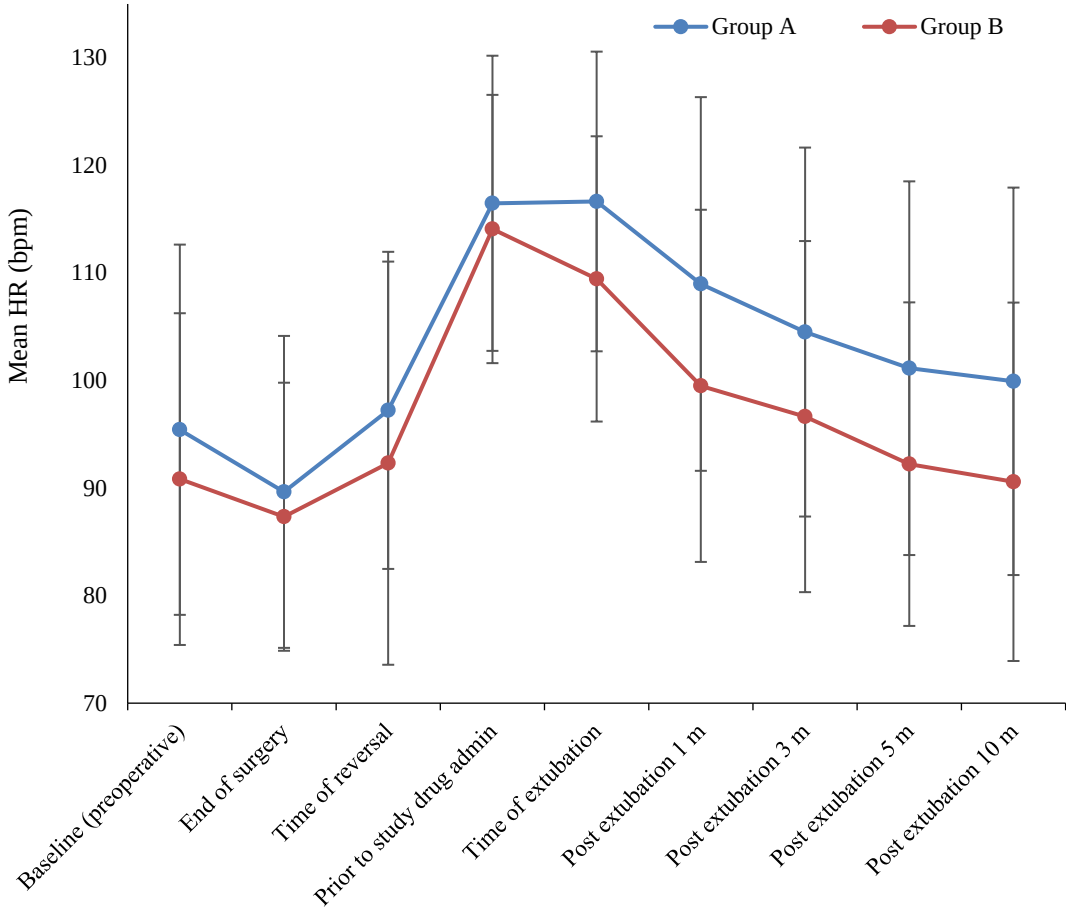

Figure 1 Comparison of mean heart rate with standard deviation in the two groups at different time intervals

Table 1 shows that both groups were statistically comparable with respect to mean age, gender mean weight, of patients and no statistically significant difference in terms of age, gender and weight of patients.

Baseline HR was more in Group A as compared to Group B but the difference was not statistically significant. The HR was higher in Group A as compared to Group B at the time of extubation (P=0.027) and till 1min, 3min,5 min and 10 minute post extubation (P- value < 0.05) which was statistically significant.

Inter group comparison was done using student t test. Baseline value of SBP was (122.28±8.37 and 119.86±8.38) in Group A and Group B respectively. The difference between the groups was statistically non-significant (P-value =0.225).

The SBP was significantly higher in Group A as compared to Group B at the time of extubation (P=0.033) and till 1min, 3min,5 min and 10 minute post extubation (P- value < 0.05) which was statistically significant Inter group comparison was done using student t test.

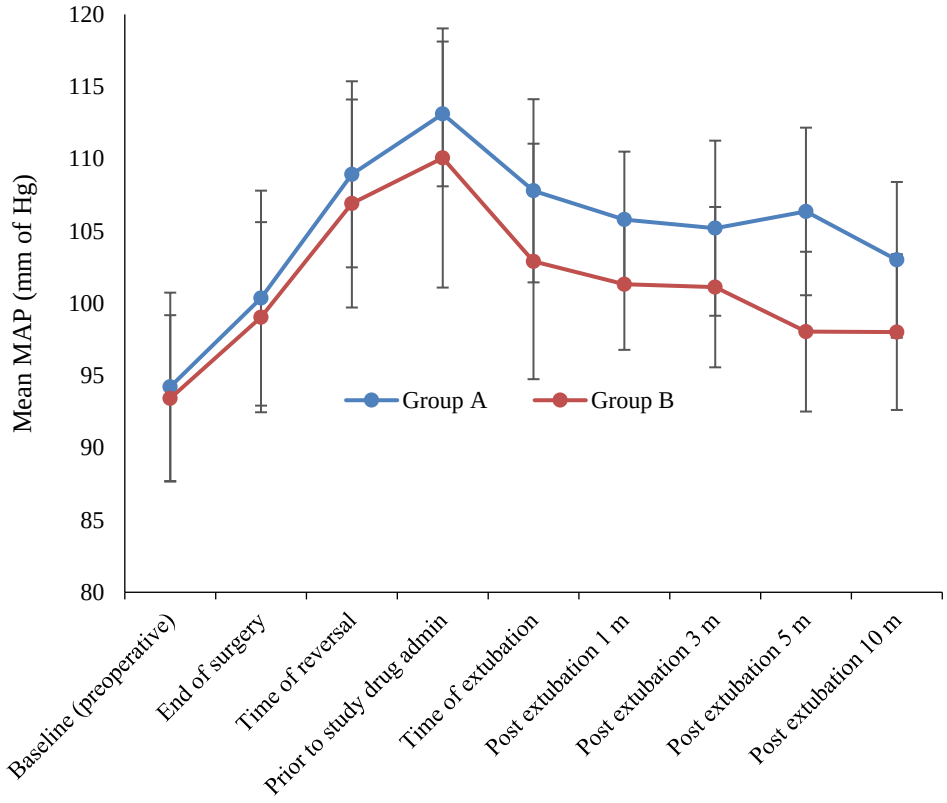

Figure 2 Comparison of mean arterial pressure (mm of Hg) between study groups

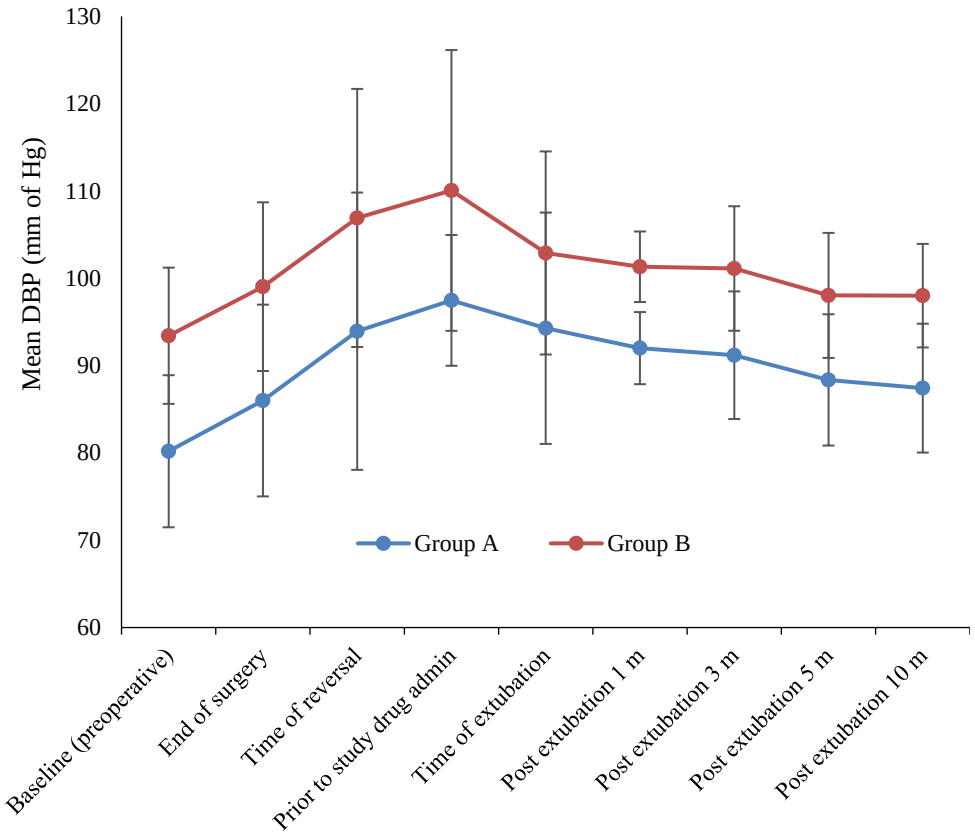

Figure 3 Comparison of mean diastolic blood pressure between study groups

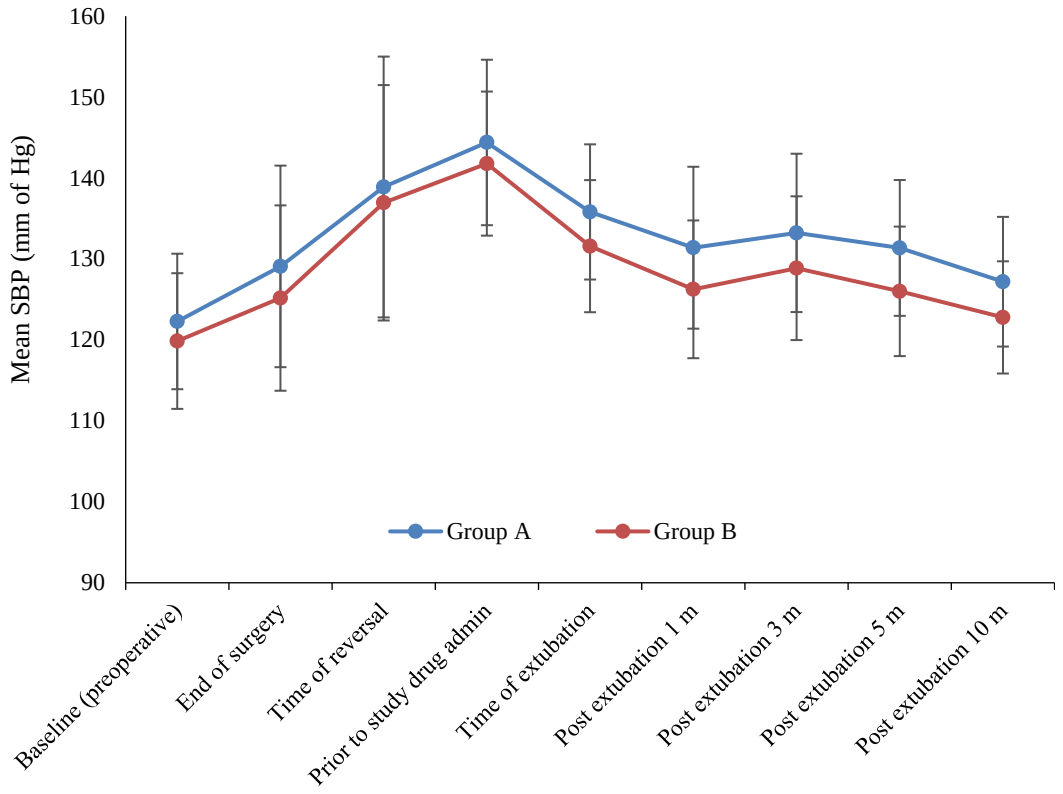

Figure 4 Comparison of mean systolic blood pressure between study groups

Baseline value of DBP was (80.19±8.71 and 77.19±7.80) in Group A and Group B respectively. The difference between the groups was statistically non-significant (P-value > 0.05). The DBP was significantly higher in Group A as compared to Group B at the time of extubation (P=0.047) and till 1min, 3min,5 min and 10 minute post extubation (P- value < 0.05) which was statistically significant. Inter group comparison was done using student t test.

Baseline value of MAP was (94.22±6.52 and 93.42±5.76) in Group A and Group B respectively. The difference between the groups was statistically non-significant (P-value > 0.05). The MAP was significantly higher in Group A as compared to Group B at the time of extubation (P=0.020) and till 1min, 3min,5 min and 10 minute post extubation (P- value < 0.05) which was statistically significant. Inter group comparison was done using student t test.

Table: 2. Post extubation cough grading (ESHAK grading)/post-operative complications

		Group A		Group B		P value	Significance
		No.	%	No.	%		
Post extubation cough	**Grade 0**	32	88.88	36	100	0.123	NS
	Grade 1	4	11.11	0	0		
	Grade 2	0	0	0	0		
	Grade 3	0	0	0	0		
Hypotension		0	0	0	0		
Bradycardia		0	0	0	0		
Desaturation episodes		0	0	0	0		
Any adverse effects		0	0	0	0		
Total		36	100.00	36	100.00		

It was observed that in Group B none of the patients had Grade 1, Grade 2, Grade 3 cough whereas in Group A, 11.1% patient had Grade 1 cough during extubation which is statistically non-significant with a P-value of 0.123. None of the patients in either group experienced hypotension, bradycardia, desaturation episodes or any other adverse effects.

DISCUSSION

The haemodynamic and airway responses during intubation have been discussed at length as compared to extubation in literature. Many theories have been proposed to explain this sudden increase in heart rate and blood pressure during extubation such as a rise in catecholamines[10], airway irritation due to suction, and intense pain from surgical wound and emergence [11].

Tracheal extubation is performed usually with the patient in a light stage of anaesthesia and produces significant increases in heart rate and arterial pressure which persist into the recovery period. . Although the exact mechanism of these cardiovascular responses in man is unknown, but it is believed to be associated with the release of catecholamines causing increases in heart rate, myocardial contractility and systemic vascular resistance [12].

The haemodynamic responses and coughing during tracheal extubation can be attenuated by various methods such as extubation with the patient in a deep plane of anaesthesia achieved by inhalational anesthetic agents or by using drugs like fentanyl, labetalol, propofol etc at the time of extubation. But this may lead to various adverse effects like respiratory depression, delayed recovery, cardiovascular system instability or difficulty in maintaining the upper airway [13].

Lignocaine has been used with apparent good effect to suppress not only the cardiovascular response to extubation but also the coughing associated with the presence of an endotracheal tube [14]. However, the mechanism by which lignocaine works remains unclear. It may be caused by deepening of anaesthesia or by local anaesthesia of the airway. Neither of these effects is desirable at the conclusion of anaesthesia. Diltiazem, a calcium channel blocker, attenuates haemodynamic response by blocking voltage sensitive L-type channels and inhibiting calcium entry mediated action potential in smooth and cardiac muscle [15].

Demographic variables

There was clinically no significant difference between the two groups in terms of demographic data like age, sex and weight and ASA grade

Haemodynamic parameters

The baseline values of heart rate,systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were statistically comparable between the two groups. The heart rate, SBP, DBP, and MAP was significantly high in group A (lignocaine) as compared to group B (diltiazem with lignocaine) at extubation and till 1 min, 3 min, 5 min, and 10 min post extubation (pvalue<0.05). Our results are consistent with the study done by Khan et al on the circulatory changes during extubation of the trachea with or without prior xylocaine (1 mg/kg IV) in patients having coronary artery disease or 2 or more cardiac risk factors. They observed that the circulatory changes in xylocaine group were statistically insignificant as compared to highly significant rise in rate pressure product in the control group [16].

Another study done by Savitha et al, compared the haemodynamic and cough response to orotracheal tube extubation among three groups -saline (control group), I.V lignocaine 0.5mg/kg and I.V lignocaine 1mg/kg. They concluded that lignocaine 1mg/kg was better than 0.5 mg/kg in attenuating the haemodynamic responses to extubation [17]. Therefore we selected lignocaine 1mg/kg for our study

Another study was done by Nishina et al in 1995 to examine the effects of intravenous diltiazem (0.1 or 0.2 mg/kg) on haemodynamic changes during tracheal extubation and emergence of anaesthesia. The effect of diltiazem was compared with that of lignocaine or saline. They concluded that a bolus dose of i.v diltiazem 0.1 or 0.2 mg/kg given before extubation was of value in attenuating the cardiovascular changes occurring in association with tracheal extubation and emergence from anaesthesia. This alleviating effect of diltiazem was equal or superior to that of i.v lignocaine 1 mg/kg [11]. Our study demonstrated that combination of diltiazem and lignocaine was better in attenuating the increase in SBP, MAP, and HR than lignocaine alone.

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Similar to our study Abhilasha Thanvi et al conducted a study to compare the effects of intravenous diltiazem and intravenous

lignocaine on blunting the haemodynmic responses to endotracheal extubation in patients undergoing elective laparoscopic cholecystectomy. They concluded that pressor responses and tachycardia could be blocked by a bolus dose of 1 mg/kg lignocaine iv or 0.2 mg/kg diltiazem iv However use of diltiazem attenuated these responses more than lignocaine [17].

Our results validate the findings of a study done by Sowmya et al who evaluated the impact of tracheal extubation on haemodynamic changes in 105 patients. Group A received injection diltiazem 0.1 mg/kg and preservative free lignocaine 1mg/kg. Group B received injection diltiazem 0.2mg/kg and lignocaine 1 mg/kg. Group C received injection lignocaine 1mg/kg with normal saline. These drugs were given 2 min before tracheal extubation. Values of HR SBP, DBP and MAP were recorded at 1,2,3,5 and 10 min after extubation. They concluded that combination of diltiazem and lignocaine is more effective than lignocaine alone in attenuating cardiovascular responses to tracheal extubation [1]

Post extubation cough grading (ESHAK grading)

The incidence of post extubation cough was evaluated using a 4-point rating scale suggested by Eshak [18] Grade 0 = no coughing or straining, Grade 1= moderate coughing, Grade 2 = marked coughing, straining and Grade 3 = poor extubation with laryngospasm. In our study, in lignocaine group only four patients had grade 1 cough in lignocaine plus diltiazem group none of the patients had cough during extubation. The results were statistically non-significant. So, the quality of extubation was good in both groups. Intravenous lignocaine is known to suppress the cough reflex in both awake and anaesthetized patients. The exact mechanism of action of the antitussive effect of intravenous lignocaine is not known but could be either due to local anaesthetic effect in the pharynx or due to an action in the central nerve

Postoperative Complications

None of the patient had hypotension,bradycardia, breath holding, laryngospasm, bronchospasm or episodes of desaturation.

Limitations of this study

Our Study was done on only 72 patients so, a larger study population would be required to get a more definitive result. As depth of anaesthesia was not monitored, so it was difficult to maintain uniformity in timing of extubation. Also this study was conducted in ASA I and II patients so result cannot be generalized in the whole population.

CONCLUSION

The present study was conducted in 72 ASA grade I and II patients between 20-60 years of age scheduled for elective abdomen surgeries under general anaesthesia and it was concluded that attenuation of exaggerated haemodynamic responses to extubation was better with combination of Inj. Diltiazem (0.1mg/kg) and Inj. Lignocaine (1mg/kg) as compared to Inj. Ligncaine(1 mg/kg) alone.

FINANCIAL ASSISTANCE

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTION

Kanchan Chauhan contributed in conception of work and study design. Vivek Gupta performed experimental work and collected data. Sunil Chauhan performed statistical analysis of data. Manoj Soni contributed in interpretation of collected data. All the authors helped in proofreading and reviewing the final manuscript.

REFERENCES

[1] Swamy SN, Madhusudhana R. Attenuation of Hemodynamic Responses to Endotracheal Extubation with Different Doses of Diltiazem with Lignocaine: A Placebo-Controlled Study. *Anesth Essays Res* **12**, 428-433 (2018)

[2] Dyson A, Isaac PA, Pennant JH, Giesecke AH, Lipton JM. Esmolol attenuates cardiovascular responses to extubation. *Anesth Analg* **71**, 675-678 (1990)

[3] 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. *J Clin Anesth* **4**, 444-447 (1992)

[4] Nishina K, Mikawa K, Shiga M, Maekawa N, Obara H. Prostaglandin E1 attenuates the hypertensive response to tracheal extubation. *Can J Anaesth* **43**, 678-683 (1996)

[5] Hagberg CA, Artime CA. Airway management in the adult. In: Miller RD, ed. Miller's anaesthesia, 8th edn, New York: Elsevier Churchill Livingstone

[6] 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* **85**, 1005-10 (1997)

[7] Mandai P. Lignocaine for prevention of laryngospasm during extubation in smokers. *Indian Journal of Anaesthesia* **49(5)**, 395-402 (2005)

[8] Farooq SU, Rani BS, Acharya A. Attenuation of haemodynamic responses to endotracheal extubation-diltiazem versus lidocaine. *International Journal of Clinical Trials* **7(2)**, 77 – 82 (2020)

[9] Baraka A. Intravenous lidocaine controls extubation laryngospasm in children. *Anesth Analg* **57**, 506-507 (1978)

[10] Lowrie A, Johnston PL, Fell D, Robinson SL. Cardiovascular and plasma catecholamine responses at tracheal extubation. *Br J Anaesth* **68**, 261-263 (1992)

[11] Nishina K, Mikawa K, Maekawa N, Obara H. Attenuation of cardiovascular responses to tracheal extubation with diltiazem. *Anesth Analg* **80**, 1217-22 (1995)

[12] Prys-Roberts C, Greene LT, Meloche R, Foëx P. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. *Br J Anaesth* **43**, 531-547 (1971)

[13] 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* **2(1)**, 24-28 (2012).

[14] Bidwai AV, Bidwai VA, Rogers CR, Stanley TH. Blood-pressure and pulse-rate responses to endotracheal extubation with and without prior injection of lidocaine. *Anesthesiology* **51**, 171-173 (1979)

[15] Flood P, Rathmell JP, Shafer S (Editors). Stoelting's Pharmacology & Physiology in Anesthetic Practice—5th Edition. Wolters Kluwer, Philadelphia, USA, 2015

[16] Savitha KS, D'Souza JS, Kothari AN. Attenuation of haemodynamic response to extubation with i.v. lignocaine: A randomized clinical trial. *Journal of Evolution of Medical and Dental Sciences* 3(4), 838-846 (2014)

[17] Thanvi A, Tak ML, Naithani U. Comparison of diltiazem and lignocaine in attenuating haemodynamic responses during extubation in patients undergoing laparoscopic cholecystectomy. *International Journal of Health Sciences and Research* **6(7)**, 82 – 89 (2016)

[18] Eshak Y, Khalid A, Bhatti TH. Small dose propofol attenuates cardiovascular responses to tracheal extubation. *Anesthesia & Analgesia* 86(2S), 5S (1998)