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Original Research Article

A COMPARATIVE STUDY OF DILTIAZEM AND LIGNOCAINE IN ATTENUATING HEMODYNAMIC RESPONSES DURING TRACHEAL EXTUBATION: A RANDOMISED CLINICAL TRIAL

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Abstract

Background: Because of the rise in sympatho-adrenergic activity generated by epipharyngeal and laryngopharyngeal stimulation, endotracheal extubation induces transitory hemodynamic stimulation, increasing blood pressure and heart rate (HR). To reduce hemodynamic reactions, sodium channel blocker lignocaine and calcium channel blocker diltiazem are utilised. The study aims to assess the efficacy of intravenous Diltiazem and intravenous Lignocaine in blunting hemodynamic responses to tracheal extubation. **Materials and Methods:** This randomised controlled study included 90 patients from the Department of Anaesthesiology and Critical Care, Rajiv Gandhi Govt, for one year. General Hospital, between the ages of 20 and 65, had physical status ASA Classes I of both sexes. Diltiazem 0.2 mg/kg injection and preservative-free lignocaine 1 mg/kg injection were given to Group D. Diltiazem 2% mg/kg injection was given to Group L, and normal saline 5ml IV was given to Group N 2 minutes before extubation. Heart rate and blood pressure parameters were determined at baseline post-surgery and 5 minutes post-extubation. **Result:** The heart rate in the Diltiazem group was lower at baseline and after extubation than in the Lignocaine group, which was statistically significant ($p<0.05$). Similarly, group D had lower blood pressure (MAP, SBP, and DBP) than group L ($p<0.05$). **Conclusion:** Diltiazem reduced the rise in mean Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), and Heart Rate (HR) more efficiently than lignocaine. Diltiazem, a calcium channel blocker, provided superior protection against changes in cardiovascular reactivity than lignocaine.

INTRODUCTION

As a scientific endeavour, surgery is a constantly developing and evolving field. In the practice of anaesthesia, general anaesthesia with endotracheal intubation and intermittent positive pressure breathing is commonly used.[1] Endotracheal intubation (insertion of an ETT into the trachea) and extubation (Trans laryngeal removal of an ETT) are procedures performed during general anaesthesia and are related to hemodynamic responses.[2] Prolonged mechanical ventilation during endotracheal intubation increases the risk of pulmonary problems such as ventilator-associated pneumonia (VAP), increased risk of deep vein thrombosis, bed sores, longer hospital stays, and poor clinical results.[3]

Extubation, or removing an endotracheal tube (ETT), is the final step in removing a patient from artificial ventilation.[4] Endotracheal extubation is linked to reflex sympathetic discharge induced by epi-pharyngeal and laryngopharyngeal stimulation, which results in hypertension, tachycardia, and arrhythmias. Coughing during tracheal extubation can cause tachycardia, arterial hypertension (AHT), a rise in intracranial pressure (ICP) and intraocular pressure (IOP), and surgical wound dehiscence.[5]
The imbalance between myocardial oxygen demand and supply occurs when blood pressure and heart rate rise, even if these rises are transient, fluctuating, and unexpected.[6] This might be dangerous for those suffering from hypertension, cardiac insufficiency, or cerebrovascular illness. Tracheal extubation is just as

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risky as tracheal intubation. It can cause severe hypertension, tachycardia, arrhythmias, coughing, laryngospasm, bronchospasm, and cerebrovascular accidents, particularly in patients with hypertension, coronary artery disease, and cerebrovascular illness.[7] Various strategies can be used to modulate the cardiovascular reactions following extubation. Non-pharmacological approaches include smooth and gentle extubation with a shorter period of laryngoscopy, extubation of the patient in the deep plane with spontaneous respiration, and extubation of the patient in a deep plane with spontaneous breathing have been examined to lessen the hemodynamic stress response and cough during extubation.[8]

The primary downside of these approaches is that they result in cardiovascular depression and insufficient upper airway reflexes. To minimise the severity of hemodynamic episodes, drugs such as esmolol, fentanyl, Diltiazem, verapamil, and local anaesthetics such as lignocaine have been used alone or in combination.[9,10] Extubation of the trachea with the patient under a deep plane of anaesthesia using inhalation or IV anaesthetic drugs has also been shown to reduce cardiovascular reactions to tracheal extubation.[11] Lignocaine, a centrally depressant and antiarrhythmic action, has been administered as a bolus or peri-operative infusion to reduce the pressor response following extubation. Diltiazem maintains hemodynamic stability during extubation due to its calcium channel antagonistic effect, vasodilation, and negative inotropic action.[11] Diltiazem, a calcium channel blocker, reduces hemodynamic responsiveness in smooth and cardiac muscle by blocking voltage-sensitive L-type channels and decreasing calcium entry-mediated action potentials. It also can increase peripheral vasodilation. Diltiazem's onset and duration of action are quick and brief.10 The MAP begins to fall 20-40 seconds after i.v. Diltiazem administration, with a peak impact at 1.5-2 seconds. In 70% of patients, tracheal extubation causes increases in HR and SBP of 20% or higher. The precise cause of these cardiovascular responses is unknown. Still, it is thought to be related to the release of catecholamines, which increases heart rate (HR), myocardial contractility, and systemic vascular resistance starting at 1 minute and lasting until 10 minutes after tracheal extubation. This is because there is a significant rise in the plasma concentration of adrenaline after tracheal extubation, not noradrenaline.[11]

The study aims to compare the effects of intravenous Diltiazem and intravenous Lignocaine on tracheal extubation hemodynamic responses and to look for any negative effects or difficulties when studying in groups.

MATERIALS AND METHODS

The one-year randomised controlled trial (January-December, 2021) comprised all patients undergoing elective general surgery under general anaesthesia at the Department of Anaesthesiology and Critical Care, Institute of Anaesthesiology and Critical Care, Rajiv Gandhi Govt. General Hospital, Madras Medical College. Before the study began, the Institutional Ethical Committee approved it. Each subject provided informed written permission.

Inclusion Criteria

The study comprised patients of both genders aged 18 to 60, undergoing elective procedures under general anaesthetic, belonging to ASA class I, and providing valid informed permission.

Exclusion Criteria

Patients with known allergies to study medicines, difficult airways, ASA class II-IV, requiring post-operative ventilation, basal heart rate of 60 bpm, and basal systolic pressure of 100 mm Hg were excluded. The sample size was determined using the data from the previous study.12 Using the following calculation, the sample size is determined using the mean and standard deviation of MABP at the 5th minute in the Diltiazem group as 86.2 3.15 and the mean and standard deviation of MABP at the 5th minute in the Lignocaine group as 89.47 4.97 at 95% confidence interval with 80% power. As a result, the sample size of 90 patients was designated equally into three groups (30 in each).

After accounting for the non-responsive rate, the sample size necessary for each group is 30; the overall sample size required is 90. Preoperatively, all consenting patients scheduled for surgery were evaluated. Anaesthesia was administered in the same manner to all patients according to the usual protocol. Selected patients were randomly assigned to one of three groups: Diltiazem, Lignocaine, or normal saline (control group) [Table 1].

All patients were given injections of 0.2 mg glycopyrrolate and 2mcg/kg fentanyl. 100% oxygen was used to preoxygenate the patients. Induction was accomplished with a 5 mg/kg thiopentone injection, and tracheal intubation was aided by a 0.5 mg/kg atracurium injection. The anaesthesia was maintained using a mixture of 60% nitrous oxide and oxygen. Monitoring was carried while during anaesthesia. Suctioning was done thoroughly after surgery. Nitrous oxide was stopped after sufficient spontaneous respiration, and remaining muscular relaxation was reversed with 43 Inj Neostigmine 50mcg/kg and Inj Glycopyrrolate 10mcg/kg iv. Diltiazem (Group D), Lignocaine (Group L), or normal saline (Control Group) were administered three minutes later, depending on the patient's group. The trachea was then extubated 2 minutes after the research medicines were administered. HR, SBP, DBP, and MAP values were recorded immediately after extubation at 1, 2, 3, 4, and 5 minutes.

Statistical Analysis

Age, HR, SBP, DBP, and MAP are numerical variables with mean and standard deviation. Frequencies and percentages are used to indicate categorical variables such as gender. When suitable, pie charts and bar graphs are employed. When a

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category Variable is linked to another variable, the variables are represented using tables and bar graphs. The chi-square test is used to determine significance. Fisher's exact test is applied when more than 20% of the cell values have an anticipated cell value of less than 5.

A one-way analysis of variance (ANOVA) is performed to see if there are any statistically significant differences in the means of two or more independent (unrelated) groups. The mean difference in HR, SBP, DBP, and MABP between the Diltiazem, Lignocaine, and normal saline groups was computed. Statistical significance was defined as P-values less than 0.05. The data was imported into an MS Excel spreadsheet and evaluated with SPSS software version 16.

RESULTS

The sample size of 90 patients was designated equally into three groups (30 in each). The man age of patients in groups D, L and N was 42.03, 38.57 and 37.97, respectively. Group D had a higher number of males (14), followed by Group L (13) and N (6). Group N had a higher number of females (24), followed by Group L (17) and Group D (16). No significant differences in mean age and gender were observed among the groups [Table 2].

The mean HR at baseline after surgery was greatest in Group L (84.87), but the difference was not statistically significant ($p > 0.05$). The mean HR at medication administration was 83.87 in Group L, which was the highest, although the difference was not statistically significant ($p > 0.05$) [Table 3].

The difference in mean baseline and medication administration time SBP was statistically significant ($p<0.05$) in group L (125.57 and 124.57). Group L also had higher baseline and drug administration time DBP and MAP levels. Statistical significance was observed among baseline DBP and DBP as well as MAP values at the time of drug administration ($p<0.05$) [Table 3].

Hemodynamic parameters were measured at 1 min post-drug administration, at the time of extubation, and post-extubation at minutes 1 to 5. While group N displayed higher HR values, group D was observed to have with lowest HR values throughout the time post-drug administration and post-extubation with a highly significant statistical significance ($p<0.05$) (Table 4). About SBP, only the values taken 1 min post-drug administration were higher in groups N and D. However, the values were not statistically significant ($p>0.05$). At other measurement times, group D displayed the lowest SBP values ($p<0.005$) [Table 4]. A similar trend was also observed with the values of both DBP and MAP [Table 4].

Table 1: Patient categorisation

Group	Drug Administered
D	Diltiazem 0.2mg/kg IV 2 minutes prior to extubation
L	2% Lignocaine (preservative free) 1mg/kg 2 minutes prior to extubation
N	Normal saline 5ml IV 2 minutes prior to extubation

Table 2: Demographic data of patients under study

Parameter	Drug group			P value
	Group D	Group L	Group N	
Age (years)	42.03 ± 14.29	38.57 ± 11.18	37.97 ± 13.17	0.426
Gender				
Males	14 (46.66%)	13 (43.33%)	6 (20%)	0.066
Females	16 (53.33%)	17 (56.66%)	24 (80%)	

Table 3: Hemodynamic parameters at baseline and at the time of drug administration

Parameter	Drug group	Mean	Std. Deviation	P value
Heart Rate				
Baseline at the end of surgery	Group D	84.47	5.26	0.334
	Group L	84.87	9.22	
	Group N	81.70	11.32	
At administration of a drug	Group D	83.47	5.26	0.334
	Group L	83.87	9.22	
	Group N	80.70	11.32	
SBP				
Baseline at the end of surgery	Group D	119.47	7.49	0.045
	Group L	125.57	10.08	
	Group N	122.10	10.17	
At administration of a drug	Group D	118.47	7.49	0.042
	Group L	124.57	10.08	
	Group N	121.23	9.88	
DBP				
Baseline at the end of surgery	Group D	78.90	6.97	0.010
	Group L	83.87	5.73	
	Group N	80.43	6.25	
At administration of a drug	Group D	77.93	6.94	0.004
	Group L	83.37	5.56	
	Group N	79.43	6.25	

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MAP				
Baseline at the end of surgery	Group D	92.57	6.18	0.014
	Group L	97.57	6.42	
	Group N	94.33	7.07	
At administration of a drug	Group D	91.47	6.12	0.004
	Group L	97.03	6.27	
	Group N	93.37	6.96	

Table 4: Hemodynamic parameters post-drug administration

Group	Time of measurement (minutes)						
	1 min post-drug delivery	Extubation	Post extubation				
		0	1	2	3	4	5
HR							
D	65.77 ±4.02	76.07± 4.36	75.50± 4.53	74.27± 5.13	72.60±5.67	71.33± 3.99	70.83± 2.82
L	75.17± 8.96	97.20± 10.82	96.17±10.82	91.47±10.88	86.90± 8.97	84.23± 6.65	81.5± 6.49
N	79.90± 9.03	115.03 ±13.31	113.73± 13.69	107.37± 11.35	100.7± 10.37	92.5± 9.67	87.57± 8.31
P value	0.001	0.001	0.001	0.001	0.001	0.001	0.001
SBP							
D	119.13±7.9	119.07± 6.35	119.07± 6.35	117.2± 7.34	115.23± 6.88	113.1± 6.91	112.53 6.52
L	115.9 8.51	132.27± 11.16	132.27± 11.16	128.93± 9.96	126.2± 9.59	122.57± 8.05	121.27± 6.79
N	120.07 8.75	154.73± 10.37	154.73± 10.37	146.7± 9.51	140.1± 7.35	132.93± 7.41	126.97± 6.90
P value	0.001	0.001	0.001	0.001	0.001	0.001	0.001
DBP							
D	77.07± 8.35	79.60± 5.53	119.07± 6.35	117.20± 7.34	115.23 ±6.88	113.10± 6.91	112.53± 6.52
L	78.83± 6.13	89.73± 6.34	132.27± 11.16	128.93± 9.96	126.20± 9.59	122.57± 8.05	121.27± 6.79
N	79.47± 5.57	107.50± 9.33	154.73 ±10.37	146.70± 9.51	140.10± 7.35	132.93± 7.41	126.97± 6.90
P value	0.370	0.001	0.001	0.001	0.001	0.001	0.001
MAP							
D	77.07± 8.35	79.60 ± 5.53	79.60± 5.53	75.97± 4.97	73.97± 4.43	73.50 ± 3.45	73.60 ± 3.35
L	78.83± 6.13	89.73± 6.34	89.73± 6.34	87.93± 7.05	85.83± 6.36	81.10 ± 4.42	81.13± 4.83
N	79.47± 5.57	107.50± 9.33	107.50± 9.33	100.90± 7.08	95.53± 6.86	89.50± 7.05	83.27± 6.64
P value	0.370	0.001	0.001	0.001	0.001	0.001	0.001

DISCUSSION

In reaction to tracheal extubation, a significant rise in HR, SBP, DBP, MAP, cardiac index, and systemic vascular resistance persists during recovery. Extubation irritates the airways, prompting coughing or effort, which raises both BP and HR. In healthy people, the consequences of these hemodynamic alterations may be minor to severe, but they can be deadly in patients with hypertension and coronary artery disease. During tracheal extubation, individuals with cardiovascular disease or those at risk of coronary artery disease have increased myocardial oxygen demand. Following extubation, lignocaine reduces the frequency and intensity of coughing, holding one's breath, and bronchospasm. Diltiazem is a benzodiazepine derivative of a slow calcium channel blocker. Calcium channel blockers slow heart rate (HR), reduce myocardial contractility, slow the speed at which cardiac impulses are transmitted through the atrioventricular node, and relax vascular smooth muscle.

Thirty (33.33%) subjects were divided into Group D, receiving Diltiazem 0.2 mg/kg iv two minutes before extubation. Group L received 2% Lignocaine 71 (preservative free) 1 mg/kg iv two minutes before extubation, and Group N received normal saline 5 mg iv two minutes before extubation. Group L had a mean age of 38.57 years, followed by Group N, with a mean age of 37.97. Group D had a mean age of 42.03 years. In research by Thanvi et al., the mean age was 40.4 years in Group D, 41.57 years in Group L, and 40.1 years in the Normal Saline group.[12]

Compared to Group L, which had 43.33% men and 56.66% women, Group D had 46.66% men and 53.33% women, while Group N had 20% men and 80% women. According to research by Thanvi et al., the normal saline and diltiazem groups had 76.7% and 80% female participants, respectively, whereas the lignocaine group had 80% female participants. According to our research, the mean HR was statistically significantly lower in the Diltiazem group than the Lignocaine group at 1 minute after drug administration, at the time of extubation, 1 minute after extubation, 2 minutes after extubation, 3 minutes after extubation, and 5 minutes after extubation ($p<0.05$). Similar results were reported by Swamy et al. in their study. They also reported no statistical significance among dosage differences of Diltiazem.[13]

In the Diltiazem group compared to the Lignocaine group, the mean SBP, DBP, and MABP were lower at the moment of extubation, 1 minute after extubation, 2 minutes after extubation, 3 minutes after extubation, and 5 minutes after extubation. ($p< 0.05$). According to another study, lignocaine 1 mg/kg is more effective than lignocaine 0.5 mg/kg at reducing the hemodynamic reactions after tracheal extubation. Cough suppression (100%) lignocaine 1 mg/kg was good for post-extubation, and this matched up with our analysis of the values between the L and N groups as well.[13]

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Additionally, lignocaine (1.0 mg/kg) and Diltiazem (0.2 mg/kg) were reported by Thanvi et al. to reduce these increases effectively. Diltiazem had a larger suppressing effect than lignocaine. Farooq et al. discovered that the Diltiazem group saw a substantially smaller change in HR, SBP, and DBP than the Lidocaine group.[14] According to Jain and Khan, during intubation and extubation, the rise in pulse rate (PR) and mean arterial pressure (MAP) was less in the lignocaine group compared to the saline group ($P<0.05$), and the lignocaine infusion significantly lengthens the mean post-operative pain-free period.[15]

According to Nishina et al., the combined impact of PGE1 and lidocaine on BP increase was comparable to that of lidocaine alone, and the combination's suppressive effect on HR increase was also comparable to that of lidocaine alone. In patients undergoing extubation, Nishina et al. showed that the attenuation level by diltiazem 0.1 mg/kg was comparable to that of lidocaine. In contrast, the inhibitory impact on cardiovascular responses was highest with 0.2 mg/kg diltiazem.[16,17]

Verapamil, at 0.1 mg/kg, had a greater inhibitory impact on an increased hemodynamic response than Diltiazem, according to Mikawa et al. Verapamil's 0.05 mg/kg dose had a less effective analgesic effect than Diltiazem's 0.2 mg/kg dose.[17] According to Savitha et al., there was a significant increase in HR, SBP, and MAP in the saline group throughout the study, and the incidence of moderate and severe cough was 43.3% and 30%, respectively. Lignocaine 1 mg/kg was found to be superior at lowering both diastolic blood pressure and mean arterial pressure.[18]

CONCLUSION

In conclusion, our research reveals that Diltiazem group demonstrated significantly lower mean Heart Rate (HR) compared to Lignocaine group at various post-drug administration time points. Additionally, Diltiazem group exhibited markedly reduced mean Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) during and after extubation, indicating stronger cardiovascular reactivity control. Diltiazem's efficacy surpassed Lignocaine in mitigating cardiovascular response fluctuations, highlighting its potential as a superior choice for this purpose.

Limitations and Recommendations

Confounding variables such as pain, negative impacts, and co-morbidities were not investigated. A smaller sample size reduced the study's capacity to be generalised. Further research with larger sample sizes matched for confounding factors in different contexts, such as primary and secondary care, will reveal the actual nature of the findings.

Diltiazem and lignocaine's advantage, beneficial effects, and adverse effects must also be studied to attenuate the hemodynamic changes associated with extubation in patients with coronary artery disease and cerebrovascular disease.

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