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Original Article

Effect of Single Dose of Lidocaine before Removal of Cross-Clamp on Prevention of Ventricular Fibrillation in On-Pump CABG Surgery

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ABSTRACT

Objective: To determine the efficacy of Lidocaine administration before removal of cross-clamp on prevention of Ventricular Fibrillation (VF) in patients who underwent Coronary Artery Bypass Graft (CABG).

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Cardiothoracic Anesthesia, Army Cardiac Center, Lahore Pakistan, from Sep 2021 to Mar 2022.

Methodology: One hundred and sixty-two patients were selected non-randomly via consecutive sampling. Patients were divided into two groups i.e., Control and Lidocaine group. Patients of control group were given intravenous Normal Saline while patients in Lidocaine group were given intravenous 2% Lidocaine in dose of 1mg/kg just before release of aortic cross clamp. Main outcome variable was frequency of Ventricular Fibrillation after removal of cross-clamp whereas bypass time, cross-clamp time, Mean Arterial Pressure (MAP) after cardiopulmonary bypass were noted for comparison purpose. Chi-square and t-test were used to compare frequency and mean differences of study variables among study groups. p-value<0.05 was considered statistically significant.

Results: One hundred and sixty-two patients with mean age 55.92±6.81 years were recruited. Ventricular Fibrillation (VF) was noted in 43(53.1%) in control group and 11(13.5%) in Lidocaine group (p<0.001). The use of intravenous Lidocaine caused reperfusion VF to occur less frequently which in turn reduced the requirement for electric counter-shock defibrillation.

Conclusion: The use of intravenous Lidocaine (1 mg/kg) 2 minutes prior to release of the aortic cross-clamp decreased the frequency of reperfusion Ventricular Fibrillation among subjects who underwent CABG.

Keywords: Coronary Artery Bypass Graft, Cross-clamp, Lidocaine, Reperfusion Ventricular Fibrillation.

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INTRODUCTION

Cardioplegia and myocardial protection have significantly improved the outcome of Coronary Artery Bypass Graft (CABG) surgery using Cardio-pulmonary Bypass (CPB). However, morbidity and death related to CABG are still mostly caused by sub-endocardial damage brought on by ischemic injury. Ventricular Fibrillation (VF) reperfusion rates in patients having heart surgery following the release of the aortic cross-clamp range from 42 to 63%.[1] Involvement of this complication is associated with ischemia induced enhancement of automaticity, reentry and reperfusion injury.[2] Ventricular Fibrillation may increase the myocardial wall tension, myocardial oxygen consumption and intra myocardial acidosis.[3] It can be managed with defibrillation with direct current but counter shocks may cause injury to myocardium.[4] Occurrence of VF as well as its management with defibrillation increases the rate of myocardial injury which may result in patient's surgery-related mortality and morbidity.[5] Aforementioned, it is important to reduce Ventricular Fibrillation, as VF is a significant cause of reperfusion injury in patients undergoing heart surgery.[6] Many antiarrhythmic drugs and other methods are in practice for this purpose.[7]

Lidocaine is recognized as an antiarrhythmic agent and belongs to class I-B that inhibits cation membrane permeability by binding Na+ channels. Lidocaine reduces phase IV depolarization plateau and increases diastolic electrical flow threshold in Purkinje fibers. It increases the threshold for Ventricular Fibrillation; however, this impact is directly proportional to Lidocaine plasma concentrations. As a result, once the aortic cross-clamp is released, Lidocaine is quite helpful in precluding reperfusion Ventricular Fibrillation.[8]

Literature showed that Lidocaine lowers the frequency of Ventricular Fibrillation, the mechanism is still not fully understood. Limited data is available on the effectiveness of Lidocaine on prevention of Ventricular Fibrillation in Asian population. However,

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it has been demonstrated to be effective in the management of ventricular ectopic premature beats.[8,9] Lidocaine has been demonstrated to delay conduction in myocardial ischemia circumstances.[10] Therefore, we conducted the study to find out that either the Lidocaine given according to the body weight of the patient before aortic cross-clamp release helps to prevent Ventricular Fibrillation or not.

METHODOLOGY

This Quasi-experimental study was performed at the Department of Cardiothoracic Anesthesia, Army Cardiac Centre Lahore, from September 2021 to March 2022. After receiving ethical permission from the committee, the study was started at Army Cardiac Centre, Lahore (ERC No: 25/ESTB/ACC dated 25Aug 2021). Patients were selected non-randomly for study via consecutive sampling technique after taking written informed consent from them.

Sample size of 150 was calculated, 75 for each group (Lidocaine and Control group) by using anticipated population proportion for Lidocaine group (p_1=0.20) and for Control group (p_2=0.41) with 80% power of study and 5% margin of error using WHO sample size calculator for comparing two independent samples.[11] However, we collected data from 162 patients, 81 in each group.

Inclusion criteria: Patients of both gender and age range 30-70 years who underwent On Pump CABG.

Exclusion criteria: Patients with history of redo surgery, low ejection fraction <30%, implanted cardiac defibrillator/pacemaker, dilated cardiomyopathy and valvular surgery.

One hundred and sixty two patients were recruited and equally divided into two groups i.e., Control group (n=81) and Lidocaine group (n=81). Patients in Lidocaine group were given 2% Lidocaine in dose of 1mg/kg, 2 minute before release of Aortic Cross-clamp (ACC) and in Control group, equal volume of Normal Saline was given. All preoperative drugs were given as per routine procedure to maintain standardization in between both groups until the completion of surgery except for antiplatelet medicines, diuretics, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers. Morphine 0.15 mg/kg was given as premedication. For invasive blood pressure monitoring, the radial artery was employed. Anesthesia was induced by 0.03 mg/kg Midazolam, 1.5-2 mg/kg Propofol, and 1-1.5 mg/kg Suxamethonium. Endotracheal intubation was done and ventilation was controlled with 100% oxygen saturation. Maintenance of neuromuscular block was done with 0.03mg/kg Cisatracurium. Electrocardiography leads II and V5 were attached to detect arrhythmias/ischemia. Hemodynamic monitoring was continued throughout the conduction of anesthesia and surgery.

By injecting 1200–1500 ml of cold blood cardioplegic solution (4:1) into the proximal aortic root, cardiac arrest was brought on in all patients. Some surgeons also employed topical iced Ringer's solution. At intervals of 20–30 minutes, more cardioplegia doses (200–300 ml) were administered. The same amount of cardioplegia was administered to both groups throughout. The volumes were influenced by the length of operation and the number of grafts.

Routine Cardiopulmonary Bypass (CPB) protocol was followed for establishing the CPB during surgery. Pre-operative patients' age, gender, and Body Surface Area (BSA) were noted. Intraoperative data like CPB time, aortic cross-clamp time, number of grafts, cardioplegia volume, serum electrolytes, and core body temperature were noted at removal of cross-clamp.

After unclamping, cardiac rhythm was monitored until normal sinus rhythm was achieved and compared between two groups. After removal of aortic cross-clamp, if Ventricular Fibrillation was noted, direct current shock was given. Hemodynamic parameters like Heart Rate (HR), Mean Arterial Pressure (MAP) and Central Venous Pressure (CVP) were noted in both the groups after weaning-off the pump and compared with each other.

Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 24:00. Age and hemodynamic data were reported in the form of Mean±SD while gender and number of grafts were presented as frequency and percentages. Chi-square and t-test were used to compare frequency and mean differences of study variables among study groups. p-value ≤0.05 was considered statistically significant.

RESULTS

Our study addressed 162 patients in total. The study population's average age was 55.92±6.81 years. Out of 162, 102(62.9%) were males and 60(37.1%) were females. Demographic and intraoperative characteristics of control and Lidocaine group patients were almost similar and no statistically significant differences were found except for age and number of

grafts (p<0.05). Mean CPB time was comparatively higher in Control group than Lidocaine group (159.6±34.30 minutes vs 104.83±26.97 minutes) respectively but the difference was not statistically significant (p=0.50) as shown in Table-I.

Table-I: Demographic and Intra-operative characteristics of the study groups (n=162)

Variables		Control Group (n=81) Mean±SD	Lidocaine Group (n=81) Mean±SD	*p*-value
Age (years)		57.44±5.52	54.53±7.68	0.01
Gender Frequency (%)	Male	47 (46.07)	55 (53.90)	0.19
	Female	34 (56.60)	26 (43.30)	
Body Surface Area (BSA) m^2		2.01±1.08	2.00±1.15	0.93
Total Bypass time (minutes)		159.6 ±34.30	104.83 ± 26.97	0.50
Aortic Cross-clamp time (minutes)		46.05±7.77	47.23±6.67	0.36
Total cardioplegia (mL/Kg)		45.68±9.41	45.66±8.33	0.21
Serum Potassium (mmol/L)		4.02±0.58	4.29±0.39	0.50
Blood temperature (°C) at removal of cross clamp		34.55±6.87	33.84±6.54	0.54
Serum Calcium (mmol/L)		1.13±0.40	1.17±0.95	0.62
Number of grafts [Frequency (%)]				
1		1(1.2)	8(9.9)	0.004
2		6(7.4)	17(21.0)	
3		47(58.0)	36(44.4)	
4		27(33.3)	20(24.7)	

Hemodynamic characteristics after induction of anesthesia of both the groups showed that averages of Heart Rate (HR), Mean Arterial Pressure (MAP), and Central Venous Pressure (CVP) were identical and were not statistically significant, (p>0.05) as shown in Table-II.

Table-II: Hemodynamic characteristics of the study participants (n=162)

Variable	Control Group (n=81) Mean±SD	Lidocaine Group (n=81) Mean±SD	*p*-value
HR (beats/min)	67.89±.90	67.83±3.58	0.91
MAP (mmHg)	81.14±2.97	81.64±2.77	0.29
CVP (mmHg)	10.01±0.82	9.98±0.81	0.84

**HR: Heart Rate, MAP: Mean Arterial Pressure, CVP: Central Venous Pressure*

Out of 162, 54(33.3%) patients had Ventricular Fibrillation after cardiac surgery. Considering our main outcome variable, reperfusion Ventricular Fibrillation was noted in 43 patients (53.1%) in control group and in 11 patients (13.5%) in Lidocaine group, (p<0.001) (Table-III).

Table-III: Frequency Distribution of VF in On-pump CABG

Primary Outcome	Control Group (n=81) Frequency(%)	Lidocaine Group (n=81) Frequency(%)	*p*-value
Reperfusion VF	43(53.1%)	11 (13.5%)	<0.001

**VF: Ventricular Fibrillation*

DISCUSSION

Multiple factors have been listed in regards to incidence of Ventricular Fibrillation after removal of aortic cross-clamp namely myocardial ischemia, metabolic alterations, systemic temperature, serum electrolytes (for example potassium) and levels of on board membrane-stabilizing anti-arrhythmic agents like Lidocaine.[12]

According to Kashani S and colleagues, Lidocaine with $MgSO_4$ group experienced VF less frequently after ACC release than the amiodarone and control groups [6 (20.7%), 8 (27.6%) vs 12 (41.4%); (p=0.21)].[11] Comparable outcomes were observed in our investigation, wherein the Lidocaine group experienced much less reperfusion VF than the control group (13.5% vs. 53.1%; p<0.001).

Removal of aortic cross-clamp may end in myocardial ischemia and reperfusion injury although myocardium is protected by cardioplegia solution.[13] In the study titled "Effects of Preoperative Statin on the Frequency of Ventricular Fibrillation and C-Reactive Protein Level in Patients Undergoing Isolated CABG," the administration of 100 mg of Lidocaine two minutes before aortic cross-clamp in the statin-receiving group was associated with a reduced reperfusion rate of Ventricular Fibrillation. Specifically, the Statin+ Lidocaine group demonstrated significantly lower DC Shock counts and a decreased incidence of Ventricular Fibrillation development compared to the control group (p< 0.001).[13] Notably, our study produced similar findings with a significant reduction (p< 0.001) in Defibrillator Cardiac (DC) Shock counts and Ventricular Fibrillation occurrence. However, it is important to highlight that our study utilized a Lidocaine dose of 1 mg/kg body weight, and we did not focus on use of statins.

Lidocaine has been used as a prophylactic agent against VF in myocardial infarction patients. A study suggested prophylactic Lidocaine use reduces VF but increases mortality rates after acute Myocardial infarction. But its prophylactic use was reduced after the advent of Streptokinase. This study was done on 50 patients who underwent revasculrization.[14] In our study, we also used Lidocaine as a prophylactic agent and which was found to be effective in reducing Ventricular Fibrillation. (p<0.001)

Schnittger *et al*.[15] in their study compared Lidocaine with Tocainide and concluded that Lidocaine and Tocainide were associated with increase in threshold of Ventricular Fibrillation (68%vs. 61% p<0.001) but Lidocaine was more effective. Lidocaine is useful alternate of any other drug that is in practice for reduction of Ventricular Fibrillation and our study also gave similar results as compared to control group (13.5% vs. 53.1%; p<0.001).

In another study conducted by Gianelly *et al*.[16] also reported that Lidocaine is more effective as compared to tocainide in increase of Ventricular Fibrillation threshold. Although in our study we did not compare Lidocaine with other drugs however our study showed similar results.

A study conducted by Ayoub *et al*.[17] a comparison was made among the effects of Lidocaine (100 mg), Amiodarone (150 mg), and a placebo in patients undergoing CABG surgery. These drugs were administered 2 minutes prior to the release of the cross clamp. The findings revealed that Lidocaine 8(20%) cases was associated with a lower incidence of Ventricular Fibrillation compared to amiodarone 19(48%) and the placebo 18(45%) although the difference was not statistically significant (p> 0.05). In contrast we did not use the fixed dose of Lidocaine but our results were quite similar to them.

Similarly, in a separate study by Samantaray *et al*.[18] consistent results were reported, emphasizing Lidocaine's effectiveness in reducing Ventricular Fibrillation following CABG. Our study corroborates these findings, indicating a significant reduction in Ventricular Fibrillation incidence with Lidocaine (13.5%) compared to Control group (53.1%) (p<0.001).

In the study conducted by Mauermann *et al*.[19] conflicting results emerged as they reported that both Lidocaine and Amiodarone were ineffective in preventing Ventricular Fibrillation. However, there was a notable observation of reduced need for defibrillation in the amiodarone group. Additionally, Yilmaz *et al*.[20] found that Ventricular Fibrillation occurred in 38% of patients in the Lidocaine group, 37% in the Amiodarone group, and 70% in the placebo group. While a significant difference was noted between the placebo and Lidocaine groups, no significant difference was observed between the Amiodarone and Lidocaine groups in preventing Ventricular Fibrillation. In contrast, our investigation revealed a distinct outcome, with the Lidocaine group experiencing a four-fold reduction in Ventricular Fibrillation 11(13.5%) compared to the control group 43(53.1%).

A research by Barak *et al*.[21] found that (70%) of patients in the Control group and (11%) of patients in the group receiving 100 mg of Lidocaine prior to ACC removal experienced VF (p<0.0005).Ventricular Fibrillation incidence rate was significantly lower in the Amiodarone than in the Lidocaine group 20.6% Vs. 50%.[22] In our study, patients in the Lidocaine group received intravenous 2% Lidocaine at a variable dose depending on the body weight (1 mg/kg) , and it was found to be helpful in reducing the frequency of Ventricular Fibrillation than control group (p<0.001)

Our study sought to highlight Lidocaine's efficacy in treating Ventricular Fibrillation, diverging from a minority of studies that suggested ineffectiveness. The majority of evidence, including our findings, underscores Lidocaine's effectiveness in preventing Ventricular Fibrillation in On-pump CABG surgeries.

LIMITATIONS OF STUDY

Considering the involvement of an Intervention, Randomized Control Trial would have been a better study design and the sample size in the current study was small due to refusal of patients to participate in the intervention group.

CONCLUSION

Administration of intravenous 1 mg/kg of Lidocaine, 2 minutes before release of aortic cross-clamp can reduce the frequency of reperfusion Ventricular Fibrillation in patients of On-Pump Coronary Artery Bypass Graft Surgery.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript:

RNI & FF: Study design, Drafting the manuscript, Data interpretation, Critical review, Approval of the final version to be published.

RS & MN: Data acquisition, Data analysis, Approval of the final version to be published.

HK& AA: Critical review, Study concept, Drafting the manuscript, Approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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