

Comparison of Amiodarone with Combined Doses of Magnesium Sulphate and Lidocaine for Prevention of Ventricular Fibrillation Following Coronary Clamp Release During Coronary Artery Bypass Graft Surgery

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ABSTRACT

Objective: To compare the effects of amiodarone with effects of combined doses of magnesium sulphate and lidocaine for prevention of ventricular fibrillation following coronary clamp release during (coronary artery bypass grafting) CABG.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Army Cardiac Centre, Lahore Pakistan, from Jun 2021 to Dec 2021.

Methodology: One hundred patients who reported at Army Cardiac Centre Lahore, Pakistan for coronary artery bypass grafting surgery, were involved in comparative study. Patients satisfying the inclusion criteria were allocated into the LM (Lidocaine Magnesium) and A (Amiodarone) groups. Following aortic cross clamp release, the incidence of ventricular fibrillation (VF) and other arrhythmias was calculated in first 30 minutes and up to 24 hours later. The inotropic agent used was epinephrine at a rate of 0.05 to 0.1 micrograms/kg/minute. Within 15 minutes of anesthetic induction and 15 minutes after the CPB pump was removed, hemodynamic parameters were assessed and recorded.

Results: Arrhythmias within 30 minutes and up to 24 hours after aortic cross clamp ACC release in A and LM group were compared. The difference between two groups, having arrhythmias and no arrhythmias was statistically insignificant ($p \geq 0.050$) except VF up to 24 hours after ACC release. The highest voltage for defibrillation was used in Group-A $n=20$ (40.0%) and $n=27$ (54.0%) in L.M group, ($p=0.004$). The average electrical defibrillations in group-A was less than that of group L.M, ($p=0.000$). While, the use of inotropic agent was almost equal in both the groups, ($p=0.975$).

Conclusion: Overall, the amiodarone group had a decreased incidence of VF when the ACC was released, while the difference was not statistically significant.

Keywords: Amiodarone, Arrhythmias, Cardiopulmonary bypass, Coronary artery bypass grafting (CABG), Lidocaine, Magnesium sulphate, Ventricular fibrillation (VF).

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INTRODUCTION

Ventricular fibrillation (VF) is a condition in which the heart's ischemic zone is reperfused which results in the oxygen free radicals and ion formation and which in turn can lead to an increase in oxygen consumption of myocardium¹. This also leads to cardiac stress, acidosis, and myocardial reperfusion injury.² In patients undergoing coronary artery bypass graft (CABG), the frequency of VF following aortic cross clamp (ACC) release was found to be 74 percent to 96 percent and 70 percent to 93 percent^{1,2}

Ventricular fibrillation and atrial fibrillation can be treated with a defibrillator using electric shock and several drugs.¹⁻³ Intensive defibrillation treatment of arrhythmias, on the other hand, might cause myocardial dysfunction after resuscitation.⁴ It may be beneficial to

utilize intravenous medications to reduce the risk of fibrillation. Lidocaine is an antiarrhythmic class Ib drug. It blocks sodium channel currents entirely, thus results in a reduction in depolarization and increase in the action potentials in diastolic phase in Purkinje fibers⁵ In several investigations, lidocaine has shown to reduce the frequency of ventricular fibrillation by 50 percent to 80 percent.^{1,2}

Magnesium sulphate is a Class-V anti-arrhythmic drug and is used at a dose of 30mg/kg to prevent reperfusion-induced ventricular fibrillation during coronary artery revascularization.² It has been demonstrated to be beneficial in decreasing the frequency of ventricular fibrillation in several researches. Although a research found that magnesium sulphate has no role in prevention of atrial fibrillation,^{6,7} it has been observed to be useful in preventing AF in another study.⁸

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Amiodarone is Class-III anti-arrhythmia medication that works by inhibiting potassium channels in cardiac muscle to lengthen the action potential. Amiodarone has been shown to be useful in avoiding ventricular fibrillation after the removal of an aortic cross-clamp in earlier investigations,^{1,6} however, amiodarone was shown to be less efficacious than metoprolol in preventing AF in another investigation.⁹ In addition, the combination of lidocaine and magnesium sulphate has been proven to be useful in avoiding ventricular fibrillation.¹⁰

Our hypothesis is that giving amiodarone before aortic cross clamp release is better than combination of lidocaine and magnesium sulphate in preventing arrhythmias after release of cross clamp.

In this study the effectiveness of amiodarone and a combination of magnesium sulphate+lidocaine will be compared in these patients, based on the results of previous studies and the significance of preventing arrhythmias especially VF following the release of the ACC during CABG.

METHODOLOGY

From June 2021 to December 2021, 100 patients with ASA II and III receiving coronary artery bypass grafting surgery at Army Cardiac Centre Lahore Pakistan, were included in a comparative study. The ethical committee (IERB Ltr# 7/5/ACC/2021) of Army Cardiac Centre Lahore Pakistan, gave the approval to conduct the study.

Sample Size: Sample size was calculated using the reference study by Kashani *et al.*¹¹ with prevalence of 6.89% (n=100).

Inclusion criteria: All patients with no history of Digoxin intake, lidocaine, Amiodarone, or magnesium sulphate intake, ejection fraction > 30%, patients with no history of prior cardiopulmonary resuscitation, and with normal sinus rhythm were included in the present study.

Exclusion Criteria: Patients with hypersensitivity or contraindication to lidocaine, amiodarone, or magnesium sulfate, emergency surgeries, cardiac surgeries such as valvular replacement, combined valve plus CABG surgeries, patients with hyper/hypothyroidism, patients with high LFTs, patients serum creatinine levels >2 mg/dL were all excluded.

Patients were divided into two groups. One group was given the lidocaine and magnesium (LM group). The other group received amiodarone (Agroup).

Oral Lorazepam 3mg and intra venous morphine 5mg were given to all of the patients as preoperative sedation. Standard monitoring was started as soon as the patient entered the operating room, and an arterial catheter was placed. After inducing anaesthesia, the central venous catheter was placed. After recording the initial hemodynamic values, all patients were intubated with a conventional endotracheal tube and mechanical ventilation was provided after induction of anaesthesia with Midazolam, morphine, Propofol, and Cis-atracurium. Midazolam, and Atracurium were continuously instilled by syringe pump for the maintenance of anaesthesia. CABG operation was performed following a midline sternotomy and full heparinization done with 300 IU/kg heparin to the point where ACT was obtained in 480 seconds under cardiopulmonary pump. During the heart-lung bypass procedure, the patients were given a pulseless flow and their mean arterial pressure was kept between 60 and 70 mmHg while they were kept at a temperature of 28 to 30 degrees Celsius. Cardioplegic solution was administered antegradely with a minimum temperature of 4°C for myocardial protection. If the heart's electrical activity returned, the cardioplegic solution was repeated every 20 minutes or sooner. Before removing the ACC, the blood gases and potassium levels were recorded and kept within normal limits. The cardiac bypass pump administered magnesium sulphate at a dosage of 30 mg/kg to all patients in group LM. All equipment was calibrated in accordance with the manufacturer's instructions. Two minutes before the ACC removal, 5mL lidocaine 2% was administered to patients of LM group. In group A ten minutes before removing the ACC, 300mg of amiodarone was administered. After removing the aortic cross-clamp, the initial cardiac rhythm was continually monitored until normal sinus rhythm was obtained. Following ACC release, the incidence of arrhythmias especially VF was measured in: first 30 minutes and up to 24 hours later. The inotropic agent used was epinephrine at a rate of 0.05 to 0.1 microgram/kg/minute. Within 15 minutes of anaesthetic induction and up to 15 minutes after the CBP was turned off, hemodynamic parameters were assessed and recorded. The data for this study was gathered by a resident of anesthesiology who was blind to the study groups.

The data was analyzed with SPSS Software version 19.0 (SPSS Inc., Chicago, IL, USA). The dependent variables were compared using a comparison test

and statistical tests such as the Chi-square test and the t-test. Statistical significance was defined as *p*-values less than 0.05. The Wilcoxon and Friedman tests, Mann-Whitney U test and independent t-test were used to develop association between quantitative variables.

RESULTS

One hundred patients of both genders were included in our study. All the study patients were divided into two equal groups as Amiodarone (A) and Lidocaine+Magnesium Sulphate (L.M). The mean age, weight, height, gender and ASA status was almost equal in both the groups, (*p*>0.050) (Table-I).

Table-I: Demographics and Baseline Characteristics of the Study Groups

Variable	Group		<i>p</i> -value
	A n=50	L.M n=50	
Age (years)			
Mean±S.D	61.06±7.76	61.98±9.52	0.598
Weight (kg)			
Mean±S.D	60.98±4.98	61.06±4.01	0.930
Height (cm)			
Mean±S.D	161.20±3.56	161.74±3.36	0.438
EF (%)			
Mean±S.D	54.58±2.23	50.28±3.13	<0.001
Gender			
Male	n=29 (58.0%)	n=38 (76.0%)	0.056
Female	n=21 (42.0%)	n=12 (24.0%)	
ASA Status			
II	n=42 (84.0%)	n=37 (74.0%)	0.220
III	n=8 (16.0%)	n=13 (26.0%)	

The hemodynamic parameters as CVP, arterial blood pressure and heart rate at post induction and post CPB was less in L.M group than Group-A, (*p*<0.050) except post-induction heart rate (*p*=0.186). (Table-II).

Table-II: Hemodynamic Parameters of the Study Groups

Variable	Group		<i>p</i> -value
	A n=50	L.M n=50	
CVP			
Post-induction	7.24±1.98	6.35±1.28	0.009
Post-CPB	6.53±1.25	5.25±1.26	0.000
Arterial Blood Pressure			
Post-induction	95.23±5.79	88.11±6.47	0.000
Post-CPB	72.92±4.58	62.06±6.45	0.000
Heart Rate			
Post-induction	70.77±4.80	72.13±5.35	0.186
Post-CPB	72.12±3.68	51.92±4.77	0.000

In First 30 minutes after ACC release, 20 patients of group A had arrhythmias while 27 patients of L.M group showed arrhythmias (*p*=0.545, Table-III). However upto 24hrs of ACC removal, the patients of group A had less number of arrhythmias than patients of group L.M (*p*=0.161) (Table-III), which was not statistically significant. The highest voltage used for defibrillation in group A n=20 (40.0%) and n=27 (54.0%) in L.M group, (*p*=0.004).

Table-III: Comparison of Arrhythmias in Both Groups

Variable	Group		<i>p</i> -value	
	A n=50	L.M n=50		
Arrhythmias within first 30 Minutes after ACC Release				
Normal	30 (60.0%)	23 (46.0%)	0.545	
No. of Arrhythmias	20 (40.0%)	27 (54.0%)		
Types of Arrhythmias	VF	10 (50.0%)	20 (74.1%)	0.424
	AF	10 (50.0%)	7 (25.9%)	
	PVC	0 (0%)	0 (0%)	
Arrhythmias up to 24 hours after ACC Release				
Normal	45 (90.0%)	35 (70.0%)	0.161	
No. of Arrhythmias	5 (10.0%)	15 (30.0%)		
VF	5 (100.0%)	10 (100.0%)	<0.001	

ACC=Aortic Cross Clamp; VF=Ventricular Fibrillation; AF=Atrial Fibrillation; PVC=Premature Ventricular Contractions

The average electrical defibrillations in Group-A was less than that of group L.M, (*p*=0.000). While, the use of inotropic agent was almost equal in both the groups, (*p*=0.975) (Table-IV).

Table-IV: Comparison of Defibrillation and Inotrope Among Study Groups

Variable	Group		<i>p</i> -value
	A n=50	L.M n=50	
Highest Voltage Used for Defibrillation			
Yes	n=20 (40.0%)	n=27 (54.0%)	0.004
No	n=30 (60.0%)	n=23 (46.0%)	
Electrical defibrillations (Mean±SD)	0.5±0.25	1.32±1.23	<0.0001
Inotropic agent used	n=3 (6.0)	n=2 (4.0)	0.975
AF	n=0 (0%)	n=5 (50.0%)	
PVC	n=0 (0%)	n=0 (0%)	

DISCUSSION

Ventricular arrhythmias, such as ventricular tachycardia and VF, are caused by multiple causes, one of them is myocardial reperfusion injury after coronary artery bypass grafting. The efficacy of sodium channel blockers to reduce reperfusion-induced arrhythmias has been demonstrated^{2, 10,12,13}

The impact of lidocaine+magnesium sulphate in combination with amiodarone in the prevention of arrhythmias especially VF was studied in this study. According to the findings, the frequency of normal sinus rhythm was greater in the amiodarone group. However, the lidocaine+magnesium sulphate group had a higher rate of VF, AF, and PVC arrhythmias; none of these changes were statistically significant. In our search of the scientific literature, we were unable to locate any study that specifically compared the effects of lidocaine+magnesium sulphate with amiodarone. As a consequence, we compared the findings to trials that utilised either one of the medicines alone or both of them in combination. The findings of our investigation are similar to those of previous studies,^{14,15} who found that administering the amiodarone or lidocaine alone had no effect on the frequency of ventricular fibrillation following the removal of ACC.

Trials in which medicines like Lidocaine, magnesium, and amiodarone were given alone or in combination, the frequency of VF and AF was varied. According to Abdel Bakey Elnakera *et al.* the frequency of VF and other arrhythmias in the lidocaine+magnesium group was 22.5 percent and 7.5 percent 10 respectively. In the trial done by Vaziri *et al.*¹⁸ the frequency of VF was 9.26 percent in the lidocaine group and 12 percent in the magnesium sulphate group, respectively. Furthermore, Cagli *et al.*¹⁹ found that the amiodarone and amiodarone+magnesium sulphate groups had AF frequency of 31% and 9%, respectively

The current study's findings on AF rhythm are conflicting with some of the previous studies^{6,12,16,17}, all of whom found that magnesium sulfate is helpful in lowering the frequency of atrial fibrillation and other arrhythmias. The contradiction identified between the current study and above studies can be related to the timing of medication administration, drug dose, the number of patients, age, and other demographic variables as well as eliminating patients with poor EF. For example, in our trial, 300mg amiodarone was given ten minutes before ACC release, but in Alizadeh-Ghavidel *et al.* study, 150 mg amiodarone was given three minutes before ACC release.¹⁵

In our study, we experienced that the frequency of VF rhythm in the first 30 minutes was n=20 in the lidocaine+magnesium Sulfate group and n=10 in the amiodarone group. However, in the lidocaine +

magnesium sulphate and amiodarone groups, the frequency of AF was n=7 and n=10, respectively, with no statistically significant difference between the two groups. The frequency of VF and AF varied statistically significantly among the two groups when compared upto 24hrs with 5 patients of Group-A having VF as compared to 10 in L.M group and none of the Group-A patients had AF while 5 of L.M group patients had AF.

LIMITATIONS OF STUDY

The main limitation of this study, that could influence the results obtained was small sample size. The results of the current study on AF rhythm are in limitation with some of the findings of earlier studies, all of which revealed that magnesium sulphate is effective in reducing the frequency of atrial fibrillation and other arrhythmias. The timing of medicine delivery, drug dosage, the number of patients, age, and other demographic factors, as well as the exclusion of patients with low EF, can all contribute to the discrepancy between the results of the current study and the studies mentioned above.

CONCLUSION

Overall, the amiodarone group had a decreased incidence of ventricular fibrillation when the aortic cross-clamp was released, while the difference was statistically significant when compared upto 24 hours.

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Author,s Contribution

Following authors have made substantial contributions to the manuscript as under:

MAA: Concept, Study design, Manuscript drafting, Data collection

MN: Statistical analysis, study design & interpretation

FF: Critical review, review articles, reference setting

HK: Statistical analysis and interpretation

NA: Critical review, Final approval, study design

IAC: Critical review, Final approval, proof reading

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.

REFERENCES

- 1- Kashani S, Jarineshin H, Fekrat F, Shahdadi MM, Shahabadi NS. Comparing the Effect of Lidocaine-Magnesium Sulfate Combination with Amiodarone-Magnesium Sulfate Combination in Preventing Ventricular Fibrillation After Aortic Artery Cross-clamp Removal During Coronary Artery Bypass Graft Surgery. *Iranian Red Crescent Medical Journal*. 2018 May 1;20(5).
- 2- Zheng Y, Gu Q, Chen HW, Peng HM, Jia DY, Zhou Y, Xiang MX. Efficacy of amiodarone and lidocaine for preventing ventricular fibrillation after aortic cross-clamp release in open heart surgery: a meta-analysis of randomized controlled trials. *Journal of Zhejiang University-SCIENCE B*. 2017 Dec;18(12):1113-22.
- 3- Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's Anesthesia*. Eighth ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 19103-2899.
- 4- Nakagawa Y, Amino M, Inokuchi S, Hayashi S, Wakabayashi T, Noda T. Novel CPR system that predicts return of spontaneous circulation from amplitude spectral area before electric shock in ventricular fibrillation. *Resuscitation*. 2017;113:8-12.
- 5- Gheini A, Pourya A, Pooria A. Atrial fibrillation and ventricular tachyarrhythmias: advancements for better outcomes. *Cardiovascular & Haematological Disorders-Drug Targets (Formerly Current Drug Targets-Cardiovascular & Hematological Disorders)*. 2020 Dec 1;20(4):249-59.
- 6- Chaudhary R, Garg J, Turagam M, Chaudhary R, Gupta R, Nazir T, Bozorgnia B, Albert C, Lakkireddy D. Role of Prophylactic Magnesium Supplementation in Prevention of Postoperative Atrial Fibrillation in Patients Undergoing Coronary Artery Bypass Grafting: a Systematic Review and Meta-Analysis of 20 Randomized Controlled Trials. *Journal of atrial fibrillation*. 2019 Jun;12(1).
- 7- Sharma S, Angral R, Saini H. Effect of prophylaxis of amiodarone and magnesium to prevent atrial fibrillation in patients with rheumatic valve disease undergoing mitral valve replacement surgery. *Anesthesia, Essays and Researches*. 2020 Apr;14(2):189.
- 8- Osawa EA, Cutuli SL, Cioccarelli L, Bitker L, Peck L, Young H, Hessels L, Yanase F, Fukushima JT, Hajjar LA, Seevanayagam S. Continuous Magnesium Infusion to Prevent Atrial Fibrillation After Cardiac Surgery: A Sequential Matched Case-Controlled Pilot Study. *Journal of cardiothoracic and vascular anesthesia*. 2020 Nov 1;34(11):2940-7.
- 9- Kamali A, Sanatkar A, Sharifi M. Evaluation of amiodarone versus metoprolol in treating atrial fibrillation after coronary artery bypass grafting. *Inter Med App Sci* 2017; 9(2): 51-55.
- 10- Abdel Baky Elnakera AM, Alawady TSM. Continuous infusion of magnesium-lidocaine mixture for prevention of ventricular arrhythmias during on-pump coronary artery bypass grafting surgery. *Egypt J Anaesth*. 2013;29(4):419-25.
- 11- Kashani S, Jarineshin H, Fekrat F, Shahdadi MM, Shahabadi NS. Comparing the Effect of Lidocaine-Magnesium Sulfate Combination with Amiodarone-Magnesium Sulfate Combination in Preventing Ventricular Fibrillation After Aortic Artery Cross-clamp Removal During Coronary Artery Bypass Graft Surgery. *Iranian Red Crescent Medical Journal*. 2018 May 1;20(5).
- 12- Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S. Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg*. 2001;72(4):1256-61. discussion 1261-2. doi: 10.1016/S0003-4975(01)02898-3. [PubMed: 11603446].
- 13- Joukar S, Zarisfi Z, Sepehri G, Bashiri A. Efficacy of Melissa officinalis in suppressing ventricular arrhythmias following ischemiareperfusion of the heart: a comparison with amiodarone. *Med Princ Pract*. 2014;23(4):340-5.
- 14- Mauermann WJ, Pulido JN, Barbara DW, Abel MD, Li Z, Meade LA, et al. Amiodarone versus lidocaine and placebo for the prevention of ventricular fibrillation after aortic crossclamping: a randomized, double-blind, placebo-controlled trial. *J Thorac Cardiovasc Surg* 2012; 144(5): 1229-34.
- 15- Alizadeh-Ghavidel A, Nabavi S, Haghjoo M, Toutonchi Z, Mirmesdagh Y, Javadikasgari H. Amiodarone versus lidocaine for the prevention of reperfusion ventricular fibrillation: A randomized clinical trial. *ARYA Atheroscler*. 2013;9(6):343-9.
- 16- Tabari M, Soltani G, Zirak N, Goshayeshi L. [Effect of magnesium sulfate on cardiac arrhythmias after open heart surgery]. *Sci J Kurdistan Univ Med Sci*. 2009;14(1). Persian.
- 17- Taksaudom N, Cheewinmethasiri J, Chittawatananat K, Nawarawong W, Ko-iam W, Sudthiviseschai P. Magnesium Sulfate Reduces Incidence of Atrial Fibrillation after Coronary Arterial Bypass Surgery: What Is the Proper Dose? A Randomized Trial. *J Med Assoc Thai*. 2016;99(7):794-801.
- 18- Vaziri MM, Jouibar R, Akhlagh S. The effect of lidocaine and magnesium sulfate on prevention of ventricular fibrillation in coronary artery bypass grafting surgery. *Iran Red Crescent Med J*. 2010;12(3):298-301.
- 19- Cagli K, Ozeke O, Ergun K, Budak B, Demirtas E, Birincioglu CL, et al. Effect of low-dose amiodarone and magnesium combination on atrial fibrillation after coronary artery surgery. *J Card Surg* 2006; 21(5): 458-64.
- 20- He LM, Zhang A, Xiong B. Effectiveness of Amiodarone in Preventing the Occurrence of Reperfusion Ventricular Fibrillation After the Release of Aortic Cross-Clamp in Open-Heart Surgery Patients: A Meta-Analysis. *Front Cardiovasc Med*. 2022 Feb 4;9:821938. doi: 10.3389/fcvm.2022.821938. PMID: 35187132; PMCID: PMC8854653.