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Research Article

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

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Abstract

Background: The prevalence of ventricular fibrillation after removal of the aortic cross - clamp in patients undergoing coronary artery bypass surgery is about 74% - 96%. Defibrillation shock and different types of agents are used to treat ventricular fibrillation (VF).

Objectives: This study was aimed to compare the effects of combining Lidocaine + Magnesium Sulfate with Amiodarone + Magnesium Sulfate in the prevention of reperfusion - induced ventricular fibrillation.

Methods: This randomized, double- blinded clinical study included 74 ASA class II and III patients undergoing coronary artery bypass grafting (CABG) in a university - affiliated hospital, Bandar Abbas, Iran, in the years 2015 - 2016. Patients were divided into two groups based on a random sample table of the lock. Both groups received Magnesium Sulfate through the cardiopulmonary bypass pump. Lidocaine 2% (100 mg) and Amiodarone (300 mg) were injected respectively to group Lidocaine + Magnesium Sulfate (LM) and group Amiodarone + Magnesium Sulfate (AM) patients before aortic cross - clamp release. The incidences of arrhythmias were recorded within 30 minutes after release of the aortic cross - clamp (ACC). Additionally, the defibrillation shocks (frequency and level of Joules delivered), amount of inotrope agent, and the hemodynamic and arterial blood gas parameters were recorded up to 24 hours postoperatively.

Results: There was no significant difference between the two groups in terms of demographic characteristics, ejection fraction, and ASA class. The prevalence of ventricular fibrillation (VF) and atrial fibrillation (Af) 30 minutes after ACC release were 46.7% and 53.3% ($P = 0.240$) vs. 33.3% and 66.7% ($P > 0.999$); while, up to 24 hours post - operatively were 60% and 20.0% vs. 0.0% and 0.0% in groups LM and AM respectively. The number of defibrillations in the Lidocaine + Magnesium Sulfate group was significantly higher; 57.9% vs. 25% in groups LM and AM respectively ($P = 0.004$).

Conclusions: The use of Amiodarone + Magnesium Sulfate reduces the number of defibrillation following the release of the Aortic cross - clamp compared with Lidocaine + Magnesium Sulfate.

Keywords: Amiodarone, Atrial fibrillation, Lidocaine, Bypass, Coronary Artery, Clamp, Magnesium Sulfate, Ventricular Fibrillation

1. Background

The prevalence of ventricular fibrillation after aortic cross - clamp (ACC) release in patients undergoing coronary artery bypass graft (CABG) was reported to be 74% - 96% (1) and 70% - 93% (2). Ventricular fibrillation (VF) caused by reperfusion of the ischemic region of the heart that leads to the production of oxygen free radicals and ion disorders that can increase myocardial oxygen consumption (2). Additionally, this causes myocardial wall stress, myocardial acidosis, and subsequent myocardial damage (2). To treat ventricular fibrillation and atrial fibrillation a defibrillator with electric shock and multiple medications can be used (1-3). However, more intensive defibrillation therapy can result in post - resuscitation myocardial dysfunction (4). Applying intravenous agents in order to decrease the chance of fibrillation can be useful.

Lidocaine as an antiarrhythmic class Ib agent completely abolishes the currents through the sodium channels thereby decreasing the depolarization and increases the diastolic phase of action potentials in the Purkinje fibers (5). In some studies, Lidocaine resulted in a 50% to 80% reduction in the incidence of ventricular fibrillation (1, 2).

Magnesium Sulfate is an anti - arrhythmic class V drug that is used at a dose of 30 mg/kg for preventing ventricular reperfusion- induced fibrillation after coronary revascularization (2). Some studies have shown that magnesium. Magnesium sulfate has been effective in preventing the atrial fibrillation (6, 7), although a study has shown that Magnesium Sulfate cannot prevent atrial fibrillation (8).

Amiodarone is an anti - arrhythmia class III drug that prolongs the action potential by blocking the potassium channels in cardiac muscle. Some previous studies show that Amiodarone is effective in preventing ventricular fibrillation after aortic cross - clamp removal (1, 6) while in another study Amiodarone was less effective than metoprolol in preventing atrial fibrillation (9). Also, it has been shown that the combination of Lidocaine + Magnesium Sulfate is effective in preventing ventricular fibrillation (10).

2. Objectives

Considering the previous studies and their variable results and also the importance of prevention of ventricular fibrillation and other arrhythmias following the removal of the aortic cross - clamp in cardiac surgery, we decided to conduct a study to compare the effectiveness of combining Lidocaine + Amiodarone and Magnesium Sulfate + Amiodarone in these patients.

3. Methods

3.1. Patients

Seventy - four ASA II-III patients undergoing CABG surgery who referred to Shahid Mohammadi Hospital, (affiliated to Hormozgan University of Medical Sciences), Bandar Abbas, Iran, were enrolled in a randomized, double - blinded clinical study from the year 2015 to 2016. The study approved by the thesis committee of Medical School and the ethics committee of vice - chancellor of research of the University (HUMS-REC-1394-65) and Iranian clinical trials registry (IRCT2015081723660N1).

3.2. Determining the Sample Size

Sampling was carried out using a purposive sampling method through random - block - division (random allocation software). All patients who met the inclusion criteria were divided into Lidocaine + Magnesium Sulfate or Amiodarone + Magnesium Sulfate groups based on the date of entry into the cardiac surgery operating room according to the scheduled table and the randomized block. This practice continued until achieving the desired sample size was attained. The sample size was determined for the two - sample parallel design hypothesis. Patients recruitment and the assignments to the study are shown in the consort diagram (Figure 1).

In this study, α (type I error rate) = 0.01, 1 - β (test power) = 0.9, Referring to the study of Samantary et al. (11), the sensitivity ratio in the study and control groups were 18% and 65% respectively. The calculated minimum sample size was 35 for each group.

All patients who met inclusion criteria were enrolled in the studied groups. Inclusion criteria included: 1, all patients with ASA II and III who were a candidate for CABG operation due to the coronary artery diseases; 2, lack of a history of taking Digoxin, Amiodarone, Lidocaine or Magnesium Sulfate; 3, lack of a history of previous cardiopulmonary resuscitation; 4, patients with an ejection fraction above 30% and 5, patients who have normal sinus rhythm. Exclusion criteria included: 1, Patients who have a contraindication or hypersensitivity to taking Amiodarone, Lidocaine and Magnesium Sulfate; 2, Associated cardiac surgeries such as cardiac valvular replacement operation; 3, Surgeries that were performed on an emergency basis; 4, Patients with hypo/hyperthyroidism diagnosed on clinical basis by an endocrinologist; 5, Patients with elevated liver enzyme levels; 6, Patients with creatinine levels above 2 mg/dL due to renal impairment.

3.3. Procedure

The processes of the study and the possible side effects were explained to the patients, and a written informed consent was obtained from all patients in accordance with the Helsinki Declaration.

All patients were premedicated with oral Lorazepam and intra - muscular Morphine sulfate. After entering the operating room, standard monitoring was applied, and an arterial catheter was inserted. The central venous catheter was inserted after induction of anesthesia. After recording the initial hemodynamic parameters (SpaceLabs Healthcare®, patient monitoring module, model No: 90 387, USA), all patients were intubated with standard endotracheal tube after induction of anesthesia using Midazolam, Fentanyl, Etomidate, and Cis-atracurium, and the mechanical ventilation was applied (Drager Fabius® Plus, model 8713030G, Germany). Anesthesia was maintained by a continuous infusion of Sufentanil, Midazolam, and Atracurium by the syringe pump (Perfuser® Space, Melsungen AG, 8713030 G, 09112, B BRAUN, Germany). CABG

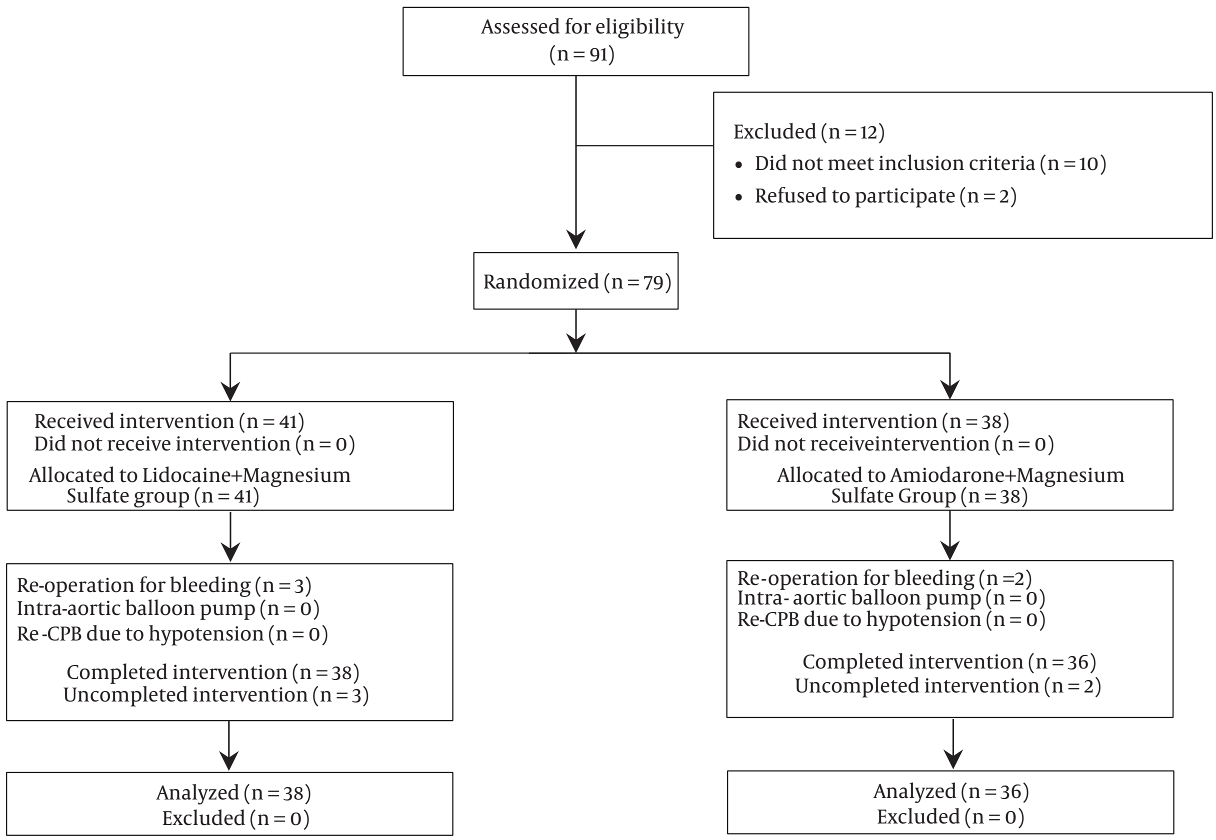

Figure 1. Study flowchart

surgery was carried out after midline sternotomy and complete heparinization with heparin 300 IU/kg to the extent that ACT (Hemochrone® JR signature +, international technidyne corporation, 8 Olsen Avenue, Edison, NJ 08820 USA) over 480 seconds was achieved under cardiopulmonary pump (Stokert® S3, Sorin Group Deutschland GmbH, Lindberghstrasse 25, 80939 Munchen, Germany). A pulseless flow was applied to the patients during the heart - lung bypass period, and the mean arterial pressure was maintained between 50 - 80 mmHg under mild hypothermia of 28 - 30°C. For myocardial protection cardioplegic solution was applied antegradely with a minimum temperature of 4°C. The cardioplegic solution was repeated every 20 minutes or sooner in the case of return of electrical activity of the heart. The blood gases and potassium levels were kept in the normal range before removing the ACC (the blood sample was warmed to at least 34°C). All patients received Magnesium Sulfate (20% vials, Pasteur Institute, Iran) at a dose of 30 mg/kg through the cardiopulmonary bypass pump. All equipment calibrated according to the manufacturer guidelines.

Patients were divided into two groups LM and AM according to the randomization table:

Group LM: Two syringes (A1 and A2) were assigned for intervention. The syringe A1 contains 10 mL Normal Saline that administrated 10 minutes before the aortic cross - clamp removal. Syringe A2 contains 5 mL Lidocaine 2% (100 mg/5mL ampoule of pharmaceutical company of Caspian-Tamin, Rasht, Iran) was injected two minutes before the ACC removal.

Group AM: Two syringes of B1 and B2, which B1 syringe contains 300 mg Amiodarone (SANOFI-AVENTIS, France) that was filled with 10 mL of Normal saline and was injected 10 minutes before the ACC removal. B2 syringe containing 5 mL of saline was injected two minutes before removing the ACC. The patients were removed from the cardiopulmonary bypass pump when the patients, core temperature reached to 34°C, the hemodynamics were stable, and the ABG parameters and electrolytes indices were normal. The first heart rhythm was continuously recorded after removal of the aortic cross - clamp until a normal sinus rhythm was achieved. In patients who developed fibrillation (atrial or ventricular) after discontinuation of the cardiopulmonary pump, synchronized cardioversion shock, and in cases of atrioventricular node (AV node) block, a pacemaker was applied. The incidence of ventricular fibrillation and other arrhythmias were recorded after ACC release defined in two separate time - intervals; during the first 30 - minutes after ACC release and up to 24 hours afterward during ICU stay. The Joule levels and frequencies of the shocks were recorded in all patients (the shock energy level was increased from 10 to 15, and 20 J for first, second and third shocks, respectively). Epinephrine 0.1 to 0.2 μg/kg/minute was used as an inotrope agent. Hemodynamic parameters were measured and recorded within 15 minutes after induction of anesthesia and up to 15 minutes after removal of the cardiopulmonary pump. This study was double - blinded, and the data were collected by an anesthesiology resident unaware of the study groups.

3.4. Data Analysis

Data were analyzed using SPSS Software version19.0 (SPSS Inc., Chicago, IL., USA), and descriptive statistics analysis was carried - out using mean perversion standard - frequency. The dependent variables were compared in the intervention group using comparison test and statistical tests, including Chi-square test and t-test. The P values less than 0.05 were considered statistically significant. The Wilcoxon and the Friedman tests were used to investigate the distribution of quantitative variables, and the non-parametric test of Mann-Whitney U test and the Pillari's trace test (repeated measurement analysis) were used in cases of existing a significant difference. Furthermore, Independent t-test was used in cases that the difference was not significant (normal distribution).

4. Results

4.1. Demographic Findings

Out of 74 participants, 38 and 36 patients were respectively divided into group LM (Lidocaine and Magnesium Sulfate) and group AM (Amiodarone and Magnesium Sulfate). The average age of participants was 58.44 $\pm$ 9.38 years. There were 47 male (63.5%) and 27 female (36.5%) patients in the study. Average weight (kg) and height (cm) of patients were calculated, 61.57 $\pm$ 12.13 and 161.87 $\pm$ 10.25, respectively. Other demographic data are presented in Tables 1 and 2.

Hemodynamic parameters, including CVP, MAP, and HR were statistically analyzed at various times between the two groups. There was no significant difference between groups regarding the CVP amount 15 minutes after induction of anesthesia (P = 0.229). However, a significant difference was observed 15 minutes after the CPB- pump removal (P = 0.052). On the other hand, there was no significant difference in group LM concerning the amount of CVP at two time - intervals (P = 0.082), while the amount of CVP was significantly different in the two time periods in thegroup AM (P = 0.031). There was a significant difference between the two groups in terms of the MAP value at the targeted times (P = 0.015). Also by through comparing the MAP in the study groups, the only significant difference was noted in the 15 - minutes after -CPB- pump removal (P = 0.003);no significant difference was noted after induction of anesthesia (P = 0.149). There was no significant difference between the two groups in terms of heart rate after induction of anesthesia (P = 0.480). However, there was a significant difference between the two groups regarding the heart rate after completion of the cardiopulmonary pump (P = 0.002). There was no significant difference in group LM in terms of heart rate at two targeted times (P = 0.526). In other words, Lidocaine had no significant effect on heart rate in CABG surgery. Also, there was a significant difference in Group AM concerning heart rate at both time - intervals (P = 0.001). In other words, Amiodarone has been effective on heart rate after cardiopulmonary bypass pump.

4.2. Evaluation and Comparison of the Arterial Blood Gas Parameters at Various Times Between the Two Groups

According to Tables 4 and 5, there was no significant difference between the two groups regarding basic plasma pH, arrest time, and CPB - removal time ($P > 0.05$); However, there was a significant difference between the two groups regarding the warming time (P = 0.036). There was a significant difference between both groups concerning the plasma pH values at various time phases ($P < 0.05$).

The results of investigating and comparing the hematocrit percentage showed a significant difference between the two groups at the warming phase of cardiopulmonary bypass (P = 0.022) (Table 6).

4.3. Evaluation and Comparison of the Cardiac Rhythm at Different Times After Removal of the Aortic Clamp Between the Two Groups

According to the data shown in Table 7 and the numeric level of $P > 0.05$, there is no difference between both groups in terms of the cardiac rhythm. However, the frequency of arrhythmias was lower in the Amiodarone + Magnesium Sulfate group compared to Lidocaine + Magnesium Sulfate group (Table 7 and Figure 2).

According to the data in Tables 8 and 9, there was no significant difference between the two groups in terms of

Table 1. Demographic Information of Studied Quantitative Variables

Quantitative Variable	Groups				P Value[a]
	LM		AM		
	Mean/Median	Standard Deviation (Q1 - Q3)	Mean/Median	Standard Deviation (Q1 - Q3)	
Age, y	56.97	10.24	60.22	8.52	0.141
Weight, kg	61.11	12.14	62.03	12.23	0.746
Height, cm	160.68	10.94	163.06	9.56	0.152
EF, %	55.00	(45.00 - 60.00)	50.00	(40.0 - 55.0)	0.084

Abbreviations: AM, Amiodarone + Magnesium Sulfate; EF, ejection fraction; LM, Lidocaine + Magnesium Sulfate.
[a] P < 0.05 was considered significant.

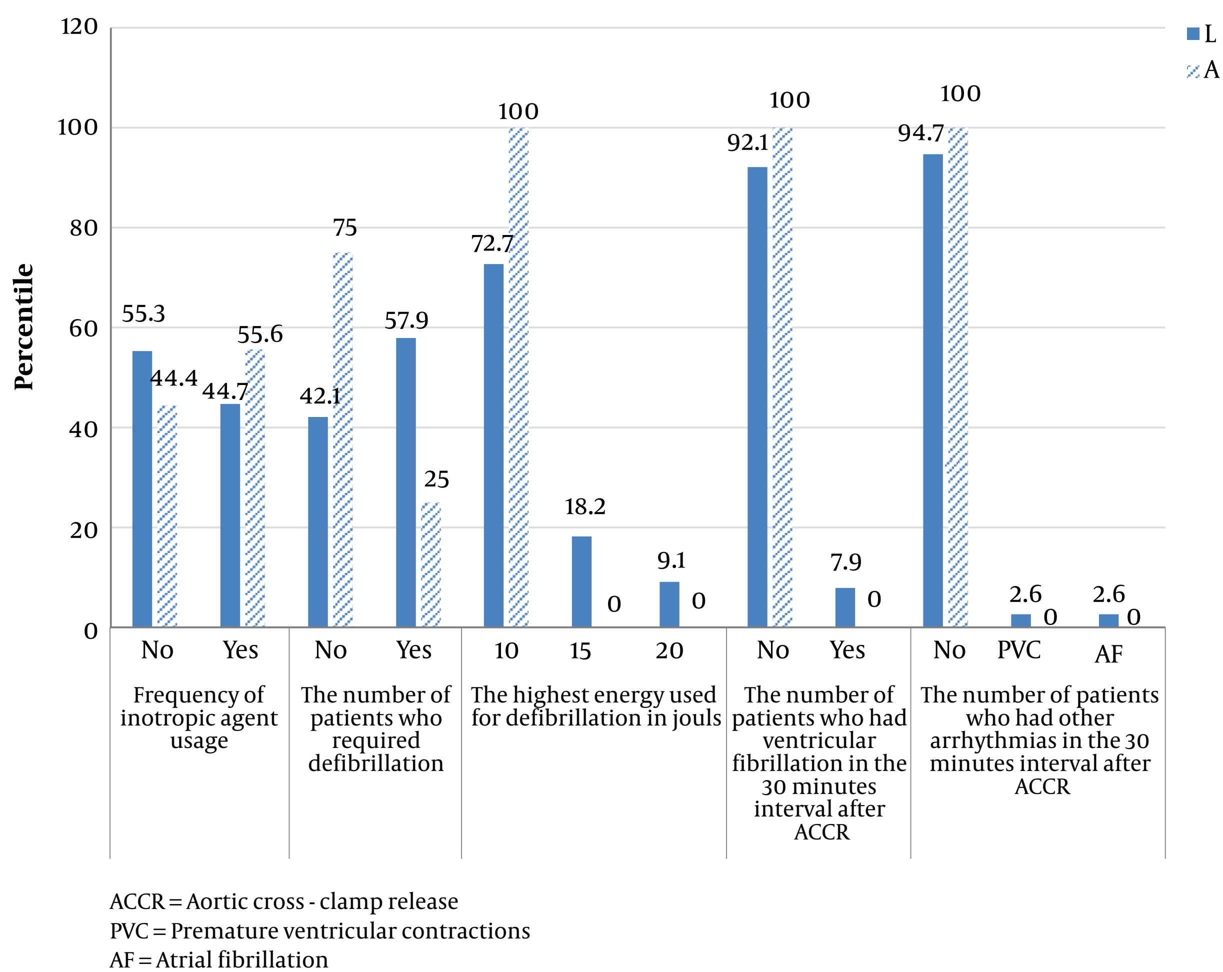

Figure 2. The plot for the frequency of patients who needed inotropic agents or defibrillation, highest energy used for defibrillation. The number of patients who had ventricular fibrillation (VF), atrial fibrillation (AF) and premature ventricular fibrillation (PVC).

the need for inotrope and the highest used energy level (P > 0.05), however, the need for defibrillation was significantly higher in group LM (P = 0.004). Additionally, the amount of energy (Joules) needed for defibrillation was not significantly different between the two groups (Table 8 and Figure 2). The number of patients who needed an inotropic

Table 2. Demographic Information of Studied Qualitative Variables[a]

Qualitative Variable	Groups		P Value[b]
	LM	AM	
Gender			0.019
Male	22 (57)	25 (69.4)	
Female	16 (42.1)	11 (30.6)	
ASA class			0.717
II	31 (81.5)	28 (77.8)	
III	7 (18.4)	8 (22.2)	
MR severity in echocardiography			0.834
Mild	11 (91.7)	8 (88.9)	
Average	1 (8.3)	1 (11.1)	
Severe	0 (0)	0 (0)	
AR severity in echocardiogram			0.083
Mild	1 (50)	6 (100)	
Average	1 (50)	0 (0)	
Severe	0 (0)	0 (0)	
VD rating in angiography			0.639
One	0 (0)	0 (0)	
Two	3 (8.1)	5 (13.5)	
Three	34 (91.9)	32 (86.5)	

Abbreviations: AR, aortic regurgitation; AM, Amiodarone + Magnesium Sulfate; ASA, American society of anesthesiologists; LM, Lidocaine + Magnesium Sulfate; MR, mitral regurgitation; VD, vessel disease.
[a]Values are expressed as the number of frequency (%).
[b]$P < 0.05$ was considered significant.

agent in the post- CPB period was more in the AM group; however, it did not reach a significant level (Table 8 and Figure 2).

There was no significant difference between the two groups in terms of heart-lung pumping time, time need for aortic clamp placement and removal, clamp release time until the removal of the patient from the pump, used cardioplegic volume, hemofiltration volume, and the temperature at aortic cross - clamp release time.

5. Discussion

Post-myocardial-ischemia reperfusion causes ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation. It has been shown that sodium channel blockers have the ability to prevent reperfusion-induced arrhythmias (2, 10, 12, 13).

The present study investigated the effect of Lidocaine + Magnesium Sulfate with Amiodarone + Magnesium Sulfate in the prevention of VF and other arrhythmias. Results of the study revealed that the prevalence of normal sinus rhythm was higher in Amiodarone + Magnesium Sulfate group. However, the VF, AF, and PVC arrhythmias were more incident in the Lidocaine + Magnesium Sulfate group; none of these differences were statistically significant. We could not find any study that was precisely comparing the effect of Lidocaine + Magnesium Sulfate combination with Amiodarone + Magnesium Sulfate in the scientific literature resources. Therefore, we compared the results with studies that had used each of the drugs individually or one of these two agents in combination. The results of our study are consistent with the results of the study conducted by Mauermann et al. (14) and Alizadeh-Ghavidel et al. (15) who showed that the administration of Lidocaine or Amiodarone alone did not affect the incidence of VF following the release of aortic cross- clamp. The results of the present study are also inconsistent with the results of the study conducted by Vaziri et al. (1) who showed the effectiveness of Magnesium Sulfate in preventing VF compared to Lidocaine.

The findings related to AF rhythm obtained in the present study are inconsistent with the results of the study conducted by Naito et al. (6), Toraman et al. (12), Tabari et al. (16) and Taksaudom et al. (17) who showed that magnesium is effective in reducing the occurrence of AF arrhythmias. The inconsistency observed between the present study and above studies can be attributed to the time of drug administration, drug dose, the number of patients, age, and other demographic characteristics as well as excluding patients with low EF. For example, in our study, 300 mg Amiodarone was administered ten minutes before ACC release while 150 mg Amiodarone was administrated three minutes before the ACC release in Alizadeh-Ghavidel et al.'s study (15). In our study, the prevalence of VF rhythm in the first 30 minutes was 18.5% and 8.3% in Lidocaine + Magnesium Sulfate and Amiodarone + Magnesium Sulfate groups, respectively. Also, the prevalence of AF was 21% and 16.7% in Lidocaine + Magnesium Sulfate and Amiodarone + Magnesium Sulfate groups, respectively, which did not have any statistically significant difference between the two groups. Perhaps we cannot make any judgment on the effect of these drug combinations on the prevalence of VF and AF considering lack of similar studies as well as lack of control groups. However, overal, the incidence of VF and AF was variable in several studies, in which drugs such as Lidocaine, magnesium and Amiodarone have been used alone or in combination. Abdel Bakey Elnakera et al. reported that the prevalence of VF and other arrhythmias was 22.5% and 7.5% (10) in the Lidocaine + Magnesium group, respectively. Also, the prevalence of VF, in the study conducted by Vaziri et al. (1) was 9.26% and 12% in the Lidocaine and Magnesium Sulfate groups, respectively. Moreover, Cagli et al. (7) reported AF prevalence rate of 31% and 9% in the Amiodarone and Amiodarone + Magnesium Sulfate groups, respectively. In our study, there was no significant difference between patients in the two groups in terms of the need to inotrope and the amount of energy used to shock. How-

Table 3. Values of Hemodynamic Parameters (Central Venous Blood Pressure, Blood Pressure, and Heart Rate) Recorded Within 15 Minutes After Induction of Anesthesia and up to 15 Minutes After Removal of Cardiopulmonary Pump in the Study Groups[a,b]

Hemodynamic Parameters	Group		Test Statistics	Degrees of Freedom	P Value[c]
	LM	AM			
CVP					
Post - induction	7.24 ± 6.50	6.50 ± 2.89	-1.202	-	0.229
Post - CPB	6.32 ± 2.59	5.19 ± 2.27	1.980	71	0.052
Arterial blood pressure					
Post - induction	91.62 ± 14.34	86.44 ± 15.92	1.41	71	0.149
Post -CPB	69.37 ± 13.41	61.36 ± 8.34	3.031	69	*0.003
Heart rate					
Post - induction	67.63 ± 15.20	70.25 ± 16.53	-0.710	72	0.480
Post - CPB	70.20 ± 22.05	53.56 ± 22.23	-3.158	-	*0.002

Abbreviations: AM, Amiodarone + Magnesium Sulfate; CVP, central venous pressure; LM, Lidocaine + Magnesium Sulfate; SD, standard deviation.
[a]Values are expressed as mean ± SD.
[b]Post- induction, 15 minutes after induction of anesthesia; Post- CPB, 15 minutes after cardiopulmonary bypass pump.
[c]$P < 0.05$ was considered significant.

Table 4. Arterial Blood Gas and Electrolytes Parameters at Time Phases (Baseline, Cardiac Arrest, Warming Phase, Cardiopulmonary Bypass- Pump Removal) Throughout the Coronary Artery Bypass Graft Operation

Parameter	Baseline		Cardiac Arrest		Warming Phase		CPB - Pump Removal		Test Statistics	P Value[a]
	Mean/Median	SD/ (Q1 - Q3)	Mean/Median	SD/ (Q1 - Q3)	Mean/Median	SD/ (Q1 - Q3)	Mean/Median	SD/ (Q1 - Q3)		
LM Group										
pH	7.44	(7.42 - 7.48)	7.44	(7.43 - 7.48)	7.44	(7.37 - 7.49)	7.36	(7.32 - 7.41)	23.902	< 0.001
CO_2	36.38	5.29	37.00	(32.90 - 39.00)	34.84	4.77	39.00	(37.00 - 41.00)	15.602	< 0.001
O_2	455.50	(416.00 - 506.00)	397.00	(367.00 - 433.00)	317.29	81.74	358.64	120.97	44.766	< 0.001
HCO_3	24.33	2.45	24.50	2.95	22.62	2.63	22.35	3.78	1.039	0.312
BE	0.68	2.30	0.58	2.64	- 0.97	3.21	- 2.96	4.39	1.946	0.167
Na	139.00	(137.00 - 141.00)	137.00	(135.00 - 139.00)	137.76	4.26	142.00	(139.00 - 145.00)	35.667	0.001
K	3.40	(3.17 - 3.70)	4.55	0.94	5.09	(4.50 - 5.98)	4.00	0.81	31.288	< 0.001
Glu	104.05	(85.20 - 140.00)	143.5	49.4	185.3	42.4	197.4	62.6	69.357	< 0.001
AM Group										
pH	7.44	(7.41 - 7.45)	7.43	(7.39 - 7.46)	7.40	(7.35 - 7.45)	7.34	(7.29 - 7.37)	46.405	< 0.001
CO_2	36.35	4.23	37.00	(35.00 - 39.5)	37.05	4.25	40.00	(37.45 - 42.00)	67.23	< 0.001
O_2	457.00	(375.00 - 498.00)	397.50	(357.5 - 433.00)	37.05	4.25	40.14	3.55	41.072	< 0.001
HCO_3	24.14	2.16	24.24	2.75	22.98	2.80	20.84	2.44	1.039	0.312
BE	0.28	1.87	0.11	2.48	-1.42	3.34	- 4.31	3.56	1.946	0.167
Na	138.00	(136.50 - 139.00)	137.00	(134.00 - 138.50)	138.09	4.48	140.00	(137.00 - 144.00)	21.674	< 0.001
K	3.35	(3.30 - 3.55)	4.10	0.71	4.50	(4.06 - 5.50)	3.85	0.59.21	56.301	< 0.001
Glu	107.15	(98.55 - 121.90)	145.6	29.1	193.7	48.4	201.7	42.2	80.633	< 0.001

Abbreviations: AM, Amiodarone + Magnesium Sulfate; LM, Lidocaine + Magnesium Sulfate; Q1 - Q3, first quartile - third quartile; SD, standard deviation.
[a]$P < 0.05$ was considered significant.

ever, the patients in the LM group compared with the AM group, more often needed defibrillation, which is consistent with the results obtained by Mauermann, et al. (14). However, they did not use magnesium in their study and only compared Amiodarone with Lidocaine.

In another study by Atallah et al. (18), similar effects of magnesium sulfate and Lidocaine was observed in the terms of ventricular fibrillation prevention. This effect may effect be due to the different methodological approach of drugs and the timing of drugs injection, as they administered the drugs 3 - 5 minutes before ACC release. We considered a peak time effect of two minutes for Lidocaine anti-arrhythmic effect, a policy not considered in the other researches. A 5-minute interval may accompany a diluting and less effect of Lidocaine administration. Besides as we have shown in our results Lidocaine and magnesium sulfate are the less effective agents in the terms of ventricular fibrillation. There is no evidence that magnesium could be useful for arrhythmias except for atrial fibrillation (19).

Ventricular fibrillation and intraoperative arrhythmias may be secondary to a history of heart or valvular disease, the use of drugs, type, and volume of the Cardioplegia solution, CPB-pump duration, and the aortic cross-clamp time. In this regard, patients in both groups were nearly

Table 5. The Arterial Blood Gas and Electrolytes Parameters Level of Significance at Time Phases (Baseline, Cardiac Arrest, Warming Phase, Cardiopulmonary Bypass Pump Removal) Throughout the Coronary Artery Bypass Graft Operation[a]

Parameters	Test Statistics	Degrees of Freedom	P Value[b]
pH			
Baseline	-0.809	-	0.418
Cardiac arrest	-1.679	-	0.093
Warming phase	-2.094	-	0.036*
CPB removal	-1.703	-	0.089
CO_2			
Baseline	0.031	75	0.967
Cardiac arrest	-0.889	–	0.374
Warming phase	-2.084	71	0.041*
CPB removal	-1.001	-	0.317
O_2			
Baseline	-0.611	-	0.541
Cardiac arrest	-0.362	-	0.717
Warming phase	1.923	63.704	0.059
CPB removal	-0.399	70	0.691
HCO_3			
Baseline	0.343	72	0.733
Cardiac arrest	0.408	72	0.684
Warming phase	-0.569	71	0.571
CPB removal	2.017	59.867	0.048*
BE			
Baseline	0.832	72	0.408
Cardiac arrest	0.740	72	0.462
Warming phase	0.578	71	0.565
CPB removal	1.425	70	0.159
Na			
Baseline	-1.388	–	0.165
Cardiac arrest	-0.697	–	0.486
Warming phase	-0.328	72	0.744
CPB removal	-2.003	–	0.045*
K			
Baseline	-0.635	–	0.525
Cardiac arrest	2.362	72	0.021*
Warming phase	-1.742	–	0.081
CPB removal	0.935	71	0.353
Glu			
Baseline	0.502	-	-0.671
Cardiac arrest	0.821	60.513	-0.227
Warming phase	0.428	72	-0.797
CPB removal	0.733	63.292	-0.343

Abbreviation: BE, base excess.
[a] PH, potential of hydrogen; CO_2, Carbon dioxide; O_2, oxygen; HCO_3, Bicarbonate; Na, sodium; K, potassium; Glu, glucose.
[b] *$P < 0.05$ was considered significant.

consistent in terms of intraoperative parameters such as duration of CPB and aortic clamping time and the volume of cardioplegia and hemofiltration volume and temperature at the ACC release time. We also compared the hemodynamic parameters between the two groups within 15 minutes after induction of anesthesia and after the aortic cross-clamp release and concluded that there was no significant difference between the two groups after induction; However, the arterial blood pressure and heart rate in the Amiodarone group was significantly lower than LM after the release. Amiodarone prolongs the action potential by blocking the potassium channels in cardiac muscle. This mechanism could also cause bradycardia (1, 2, 13). Contrary, the incidence of bradycardia was higher in the LM group than the control group in the study conducted by Abdel Bakey Elnakera et al. (10) who did not have Amio-

Table 6. Investigating and Comparing the Hematocrit Percentage Between the Two Groups at Time Phases (Baseline, Cardiac Arrest, Warming Phase, Cardiopulmonary Bypass Pump Removal) Throughout the Coronary Artery Bypass Graft Operation

Variables	LM		AM		Test Statistics	P Value[a]
	Mean/Median	SD/(Q1 - Q3)	Mean/Median	SD/(Q1 - Q3)		
Baseline phase	35.4	10.5	5.5	5.5	0.048	0.962
Cardiac arrest phase	23.3	4.6	4.7	4.7	-1.248	0.216
Warming phase	25.3	3.8	3.5	3.5	-2.349	*0.022
CPBP- removal phase	28.00	(26.00 - 31.00)	(26.00 - 31.00)	(26.00 - 31.00)	-0.889	0.376
Test statistics	55.483		33.649			
P value[a]	< 0.001		< 0.001			

Abbreviations: AM, Amiodarone + Magnesium Sulfate; LM, Lidocaine + Magnesium Sulfate; Q1 - Q3, first quartile - third quartile; SD, standard deviation.
[a] $P < 0.05$ was considered significant.

Table 7. Evaluation and Comparison of the Cardiac Rhythms at Different Times After Removal of the Aortic Clamp Between the Two Groups[a]

Rhythm	LM	AM	P Value
First 30 minutes after ACC release			
Normal	23 (60.5)	27 (75.0)	0.184
Total number of arrhythmias	15 (39.5)	9 (25.0)	
VF	7 (46.7)	3 (33.3)	0.678
AF	8 (53.3)	6 (66.7)	
PVC	0 (0.0)	0 (0.0)	
Up to 24 hours after ACC release			
Normal	33 (86.8)	36 (100.0)	0.055
Total number of arrhythmias	5 (13.2)	0 (0.0)	
VF	3 (60.0)	0 (0.0)	-
AF	1 (20.0)	0 (0.0)	
PVC	1 (20.0)	0 (0.0)	

Abbreviations; ACC, aortic cross - clamp; AF, atrial fibrillation; AM, Amiodarone + Magnesium Sulfate; LM, Lidocaine + Magnesium Sulfate; PVC, premature ventricular contraction; VF, ventricular fibrillation.
[a] Values are expressed as number of frequency (%).

darone group. However, Amiodarone caused a higher risk of bradycardia than LM in our study.

The incidence of VF was lower in the Amiodarone group indicating a potential preventing effect; however, the arterial blood pressure and heart rate were lower which necessitated a higher amount of inotropic agent usage at the same time though it did not reach a significant level. This finding was in contrast to the findings of Samantaray et al. (11) who had a lower incidence of patients in their Amiodarone group requiring inotropic support. This difference may be due to the different settings of the studies or other factors that need further extensive investigations.

Several factors may affect the incidence of VF; including pre and post-operative acidosis, hypoxia and plasma potassium level. That is why these factors were recorded at four different time points for all patients, in this study (baseline, time of arrest, warm time and clamp removal time).

The acidosis after reperfusion is an issue of investigation, as some studies have shown its adverse effects (20). However, clinical challenges have been made to identify strategies to protect the heart through ischemic conditioning with brief episodes of ischemia that cause acidosis (21). In our study, there was a significant difference between the two groups in terms of pH and CO_2 at the warming time so that pH values were 7.40 and 7.47 in the AM and LM groups, respectively and CO_2 values were 37.05 and 34.84 in AM and LM groups, respectively.

In the present study, whether the Amiodarone + Magnesium had caused ischemic conditioning by producing a mild acidotic state and thereby providing a more protective condition is a matter of debate which needs more detailed investigation with specific markers which we had not used.

5.1. Summary and Final Conclusions

The present study showed a lower incidence of ventricular fibrillation after the release of aortic cross- clamp in the Amiodarone + Magnesium Sulfate group than the Lidocaine + Magnesium sulfate, though was not statistically significant.

5.2. Limitations

The present study also had some limitations. First, the mean ejection fraction (EF) of patients were in the normal range, so it is unclear whether the results of the present study are generalizable to patients with ventricular dysfunction. Secondly, the absence of a control group makes it impossible to compare the effects of the drugs with the

Table 8. Evaluation and Comparison of Other Qualitative Findings Between the Two Groups

	LM	AM	P Value
Frequency of inotropic agent usage, No. (%)			0.352
Yes	17 (44.7)	20 (55.6)	
No	21 (55.3)	16 (44.4)	
The highest energy used for defibrillation, No. (%)			0.239
10 Joules	16 (72.7)	9 (100)	
15 Joules	4 (18.2)	0 (0)	
20 Joules	2 (9.1)	0 (0)	
The need for defibrillation, No. (%)			0.004*
Yes	22 (57.9)	9 (25)	
No	16 (42.1)	27 (75)	
Highest energy, Joules			
Median rank	17.32	13.00	
Mean ± SD	11.82 ± 3.29	0.00 ± 0.088	

Abbreviations: AM, Amiodarone + Magnesium Sulfate; LM, Lidocaine + Magnesium Sulfate; No, number of frequency; SD, standard deviation.

Table 9. The Overall Mean Value of the Highest Energy (Joules) Used for Defibrillation in Both Groups

	Groups[a]				Test Statistics	P Value
	LM		AM			
	Median	Mean ± SD	Median	Mean ± SD		
Highest energy, Joules	17.32	11.82 ± 3.29	13.00	10.00 ± 0.00	-1.707	0.088

[a]LM, Lidocaine and Magnesium Sulfate; AM, Amiodarone and Magnesium Sulfate.

control cases. However, selection of the control group may not be morally good. We suggest additional future studies to verify the results of this study. Also, considering patients with lower ejection fraction levels could be another area of investigation for assessing the effectiveness of these types of preventive interventions.

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