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The Effect of Lidocaine and Amiodarone on Prevention of Ventricular Fibrillation in Patients Undergoing Coronary Artery Bypass Grafting

Mehmet Yilmaz, MD,[1] Ufuk Aydin, MD,[2] Zehra Ipek Arslan, MD,[1] Canan Balcı, MD,[1] Cevdet Ugur Kocogullari, MD,[3] Yusuf Ata, MD,[2] Tamer Turk, MD[2]

[1]Departments of Anesthesiology and [3]Cardiovascular Surgery, Kocaeli Derince Education and Research Hospital, Kocaeli; [2]Department of Cardiovascular Surgery, Bursa Yuksek Ihtisas Education and Research Hospital, Bursa, Turkey

ABSTRACT

Objective: Ventricular fibrillation is common after aortic declamping in patients undergoing open heart surgery. This situation has a negative impact on morbidity and mortality. The aim of this prospective study was to compare the effect of administering lidocaine versus amiodarone before aortic declamping during elective coronary bypass grafting, paying close attention to when the initial effect of amiodarone sets in.

Methods: In this double blind, prospective, randomized, controlled study, 86 patients who were candidates for elective coronary artery bypass grafting were recruited into three groups: group lidocaine (group L, n = 29); group amiodarone (group A, n = 27); and group placebo (group P, n = 30). Group L patients received 1.5 mg/kg of lidocaine 2 minutes before aortic declamping and group A patients received 300 mg of amiodarone intravenously 15 minutes before release of the aortic cross clamp. The primary endpoints were the incidence of ventricular fibrillation and the number of shocks required to terminate ventricular fibrillation.

Results: The frequency of ventricular fibrillation occurrence was significantly higher in group P (70%) when compared with group A (37%) and group L (38%) (P = .017). There was no statistically significant difference between the amiodarone and the lidocaine groups regarding ventricular fibrillation. However, when ventricular fibrillation occurred, the percentage of patients requiring electrical defibrillation was significantly higher in both group L and group P when compared with group A (P = .023).

Conclusion: We suggest that during coronary arterial bypass surgery, administration of an amiodarone regime before release of the aortic cross clamp, paying particular attention to the start of the initial effect of amiodarone, is no more effective than lidocaine for prevention from arrhythmia; however, amiodarone reduces the need for electrical defibrillation.

INTRODUCTION

The incidence of ventricular fibrillation due to myocardial reperfusion injury following aortic declamping during cardiovascular surgical procedures is reported as 74-96% [Yamaguchi 2002]. Furthermore, occurrence of ventricular fibrillation and the need for repeated defibrillation increases myocardial injury and has a negative impact on postoperative patient mortality and morbidity [Yamaguchi 2002; Leeuwenburgh 2008]. Therefore, in cardiac surgery, it is important to reduce the risk of ventricular fibrillation in patients, which is regarded as a cause of reperfusion injury. To reduce the occurrence of ventricular fibrillation, prophylactic antiarrhythmic drugs are used, among other methods [Yamaguchi 2002; Baraka 2000; Ayoub 2009; Türkay 2000]. For a long time, lidocaine has been the most widely used class I antiarrhythmic agent to reduce reperfusion ventricular fibrillation in cardiac surgery. Amiodarone is preferred among class III antiarrhythmic agents [Leeuwenburgh 2008; Ayoub 2009; Türkay 2000].

Studies have shown amiodarone to be significantly superior to lidocaine for prevention of ventricular fibrillation [Kudenchuk 1999; Nanas 1995]. In the 2010 resuscitation guidelines, amiodarone was addressed as the drug of first choice on refractory ventricular fibrillation, with a recommended dosage of 300 mg bolus intravenously injected [Nolan 2010]. However, although the prophylactic efficacy of amiodarone is not a matter of discussion, there are various recommendations for the timing of administration. It is suggested that amiodarone be given at a dose of 5 mg/kg in 10 to 30 minutes' time before aortic declamping for the peak effect in myocardium [Nanas 1995; Dorian 2002]. Lidocaine was reported to be even more effective than amiodarone when administered 2 minutes before aortic declamping [Ayoub 2009]. However, there are no reports in the literature in which amiodarone was administered more than 10 minutes before the removal of the aortic cross clamp. Therefore, we studied the efficacy of 1.5 mg/kg of lidocaine administered 2 minutes before aortic cross declamping and 300 mg of amiodarone administered 15 minutes before aortic cross declamping in patients undergoing first-time isolated coronary artery bypass grafting.

MATERIALS AND METHODS

In prospective, randomized, and controlled study, we evaluated patients undergoing first-time isolated coronary artery bypass surgery (CABG) who had no preoperative cardiac rhythm problems. Complete approval of the institutional and ethical committee was obtained and every patient gave

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Correspondence: Prof. Dr. Tezok, Caddesi No: 1 Bursa Yüksek İhtisas Eğitim ve Arastırma Hastanesi, Yıldırım, Bursa, Turkey; +90224-360-50-50; fax: +90224-360-50-55 (e-mail: tturkon@yahoo.com).

an informed consent. Patients who were on antiarrhythmic drugs; had moderate to severe cardiac valvular disease; functional thyroid or hepatic deficiency; moderate to severe obstructive or restrictive pulmonary disease; an ejection fraction lower than 30%; serum creatinin over 2.5 mg/dL; any known hypersensitivity to amiodarone; or were undergoing an emergent surgery were not included in the study.

Computerized randomization was done for all patients to be placed in group L (lidocaine, n = 29), group A (amiodarone, n = 27), and group P (placebo, n = 30) in the operating room. Patient baseline characteristics including age, sex, body weight, height, medical history, preoperative medications, electrocardiogram, and transthoracic echocardiography were recorded.

Standard anesthetic induction with intravenous propofol, fentanyl, and rocuronium bromide following standard monitorization (ECG, arterial catheterization, sPO2) was performed in all patients. The anesthetic management was made using inhalation of 60% oxygen and 6% desflurane. All of the patients were operated on with median sternotomy using cardiopulmonary bypass (CPB). CPB was obtained by cannulation of the ascending aorta and right atrium (double-stage single cannula) under moderate hemodilution (hematocrit of 22-25%) and moderate systemic hypothermia (32 C°). Myocardial protection was achieved by topical hypothermia and by an initial antegrade infusion of the St Thomas' crystalloid cardioplegia, and then continued with intermittent antegrade and retrograde cold blood cardioplegia. Distal and proximal anastomoses were constructed during one period of aortic cross-clamping. All patients were given warm blood cardioplegia (36 C°, 5 ml·kg^{-1} blood, 10 mEq $NaHCO_3$ and 1500 mg $MgSO_4$) before aortic declamping, and the aortic cross clamp was removed as soon as the patient's body temperature reached 34 C° (transvesical). Reversal of heparin was achieved with protamine.

Group L patients received 1.5 mg/kg of intravenous lidocaine 2 minutes before aortic declamping, whereas Group A patients received 300 mg of intravenous amiodarone mean 15 (12-21) minutes before the removal of the aortic cross clamp. The timing of amiodarone administration was planned in consideration of the beginning of the last distal coronary anastomosis, which lasted approximately 15 minutes. Patients did not receive extra magnesium sulphate during the study period, other than cardioplegia because of potential confounding effects of potential arrhythmias. Surgeons were blinded to the type of drugs used during this study.

All of the patients were monitored for 15 minutes after aortic cross declamping and any abnormal electrical rhythm (including ventricular fibrillation) was recorded; if prolonged ventricular fibrillation (more than 2 minutes) or repeated ventricular fibrillation was encountered, electrical defibrillation was performed.

The primary endpoints compared among the 3 study groups were: (1) the incidence of ventricular fibrillation after aortic declamping and (2) the number of defibrillations required to terminate ventricular fibrillation.

In cases of recurrent ventricular fibrillation after aortic declamping, defibrillation was performed with 20 joules in the first three attempts, 30 joules in the fourth attempt, and 50 joules in the fifth attempt.

Peripheral oxygen saturation; arterial blood gas analysis values; duration of aortic cross clamping; whole blood hematocrit and electrolyte levels; transvesical body temperature at the time of aortic declamping; duration of CPB; the number of coronary artery anastomoses; cardiac rhythm; need for a pacemaker; need for inotropic agents; and length of ICU and hospital stay of the patients were recorded.

Statistical Analysis

All data were analyzed using Statistical Package for Social Sciences 16 (SPSS Inc, Chicago, IL, USA). The χ^2 test was used for categorical data, the one-way ANOVA test for numeric data matching normal distribution, and the

Table 1. Demographic Characteristics*

	Lidocaine (n = 29)	Amiodarone (n = 27)	Placebo (n = 30)	*P*
Age, y	61.6 ± 8.6	57.2 ± 7.9	59.7 ± 9.8	.18
Female sex, n (%)	7 (24%)	5 (19%)	6 (20%)	.86
Weight, kg	77.6 ± 12.6	77.8 ± 15.9	77.4 ± 15.2	.99
Height, cm	168.9 ± 8.2	169 ± 5.4	169.2 ± 8.1	.99
Left atrial diameter, cm	3.8 ± 0.4	3.8 ± 0.4	3.8 ± 0.4	.99
Ejection fraction	52.8 ± 9	53.2 ± 10.3	52.5 ± 9	.7
Diabetes mellitus	10 (34%)	12 (44%)	11 (36%)	.73
Systemic hypertension	20 (68%)	15 (55%)	20 (66%)	.67
Calcium-channel blocker use	3 (10%)	3 (11%)	2 (6%)	.83
Beta-blocker use	18 (62%)	15 (55%)	17 (56%)	.87
ACEI/ARB	9 (31%)	8 (30%)	10 (33%)	.96

*Data are presented as the mean ± SD where indicated. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table 2. Perioperative Data*

	Lidocaine (n = 29)	Amiodarone (n = 27)	Placebo (n = 30)	*P*
Duration of CPB, min	113.6 ± 27.8	104.1 ± 31.3	114.4 ± 27.6	.33
Duration of aortic cross clamp, min	64.1 ± 18.9	67.6 ± 19.7	63.2 .8	.89
No. of grafts	2.8 ± 0.7	2.7 ± 0.6	2.9 ± 0.6	.36
Pacemaker wire +/-	3 (10%)	4 (14%)	4 (13%)	.89
Hematocrit, %	34.0 ± 5.92	33.1 ± 6.14	34.5 ± 6.09	.87
Potassium (during cross clamp)	4.8 ± 0.61	5 ± 0.63	4.4 ± 0.89	.83
Lactic acid (during cross clamp)	2.8 ± 1.39	2.8 ± 9.31	2.9 ± 8.32	.48
pH (during cross clamp)	7.5 ± 0.51	7.4 ± 0.04	7.4 ± .06	.82
Transvesical temperature, C°	34.3 ± 1.7	34.1 ± 2.3	34.3 ± 2.0	.89
VF (after cross clamp removal)	11 (38%)	10 (37%)	21 (70%)	.017†
No. of electrical defibrillations	1.2 ± 1.7	0.6 ± 0.9	1.7 ± 1.5	.023†
Perioperative myocardial infarction	0 (0%)	0 (0%)	1 (3%)	.39
Inotropic agent (after cross clamp removal)	3 (10%)	4 (15%)	8 (26%)	.29
ICU stay	1.7 ± 0.43	1.8 ± 0.42	2.1 ± 1.6	.39
Duration of hospital stay, d	7 ± 0.8	7 ± 0.9	7.1 ± 1	.89
Operative mortality	0 (0%)	0 (0%)	1 (3%)	.39

*Data are presented as the mean ± SD where indicated. CPB indicates cardiopulmonary bypass; VF, ventricular fibrillation.
†$P < .05$.

Kruskal-Wallis H test for numeric data unmatching normal distribution. A *P* value of less than .05 was accepted as statistically significant.

RESULTS

The preoperative demographic variables of the patients were similar (Table 1). Perioperative data were similar among the groups except for incidence of ventricular fibrillation after aortic declamping and number of electrical defibrillations needed (Table 2). There were no pulmonary complications related to amiodarone.

The frequency of occurrence of ventricular fibrillation was significantly higher in group P (70%) when compared with group A (37%) and group L (38%) ($P = .017$) (Figure 1). There was no statistically significant difference between the amiodarone and the lidocaine groups regarding ventricular fibrillation. However, when ventricular fibrillation occurred, the percentage of patients requiring defibrillation counter shocks was significantly higher in both group L and group P when compared with group A (1.2 ± 1.7; 1.7 ± 1.5 versus 0.6 ± 0.9, respectively) ($P = .023$) (Figure 2).

DISCUSSION

Ventricular arrhythmias following aortic declamping are very common in cardiac surgery. It is necessary to treat ventricular fibrillation, regarded as one of the rhythms of cardiac arrest, emergently. Although it is treated, it negatively affects mortality and morbidity in the postoperative period as a result of duration of fibrillation and myocardial hazard from the number of defibrillation attempts [Yamaguchi 2002; Leeuwenburgh 2008]. Therefore, it is very important to prevent the heart from ventricular fibrillation after aortic declamping. Antiarrhythmic drugs are used to prevent ventricular fibrillation, with lidocaine and amiodarone among the most common. Baraka et al showed that administration of 100 mg bolus lidocaine 2 minutes before aortic declamping reduces ventricular fibrillation rates from 70% to 11% with respect to the control group [Baraka 2000]. Ayoub et al divided 120 patients undergoing CABG into three groups, placebo, amiodarone and lidocaine, and administered 150 mg amiodarone and 100 mg lidocaine 2 minutes before the removal of the aortic cross clamp, disregarding the initial time required for each drug to take effect. They reported a higher incidence of ventricular fibrillation and more need for defibrillation in groups amiodarone and placebo [Ayoub 2009]. We believe that this result was due to disregarding the amount of time amiodarone needs to show its peak effect after administration. Because the time needed for amiodarone to start taking effect is longer than that of lidocaine, amiodarone should be administered before lidocaine to show its antiarrhythmic effect. Apart from the other studies, we administered 300 mg intravenous amiodarone 15 minutes before the removal of the aortic cross clamp and 1.5 mg/kg intravenous lidocaine 2 minutes before the removal of the aortic cross clamp. As a

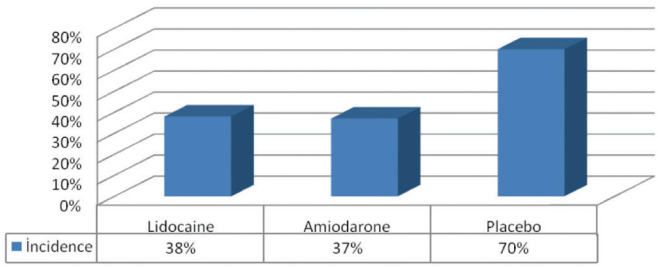

Figure 1. Ventricular fibrillation after cross-clamp removal.

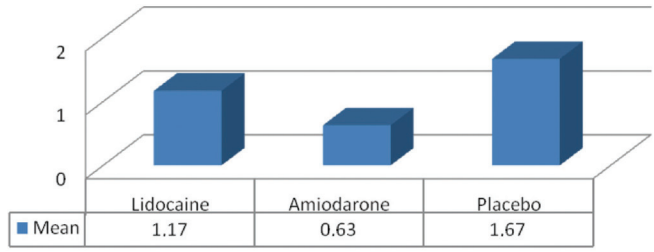

Figure 2. Number of electromechanical defibrillations.

result, although there was no statistically significant difference in ventricular fibrillation rates, we detected less of a need for additional defibrillation in the amiodarone group.

Superiority of lidocaine and amiodarone with respect to placebo has been shown in various studies [Baraka 2000; Ayoub 2009; Samantaray 2010]. Samantaray et al, who compared a group of CABG patients given 150 mg amiodarone 3 minutes before the removal of the aortic cross clamp with a control group, reported lower ventricular fibrillation rates, and less need for defibrillation and inotropic agents in the amiodarone group [Samantaray 2010]. This result is similar to our findings.

It has been controversial for a long time as to whether amiodarone is much more effective than lidocaine in prevention of ventricular fibrillation. There are three cases regarding this issue reported by Tempe et al, Morita et al, and Suzuki et al [Tempe 2007; Morita 2010; Suzuki 2010].

The way in which amiodarone should be administered in order to prevent ventricular fibrillation is also a matter of controversy. Kerstein et al gave oral amiodarone 48 hours before the operation and also continued in this same way postoperatively. In their study, in comparison with the control group, they reported less frequent arrhythmia rates, lower duration of hospital stay, and therefore lower hospital costs in the group in which the patients were given amiodarone orally [Kerstein 2004]. However, intravenous administration was used in our study for amiodarone and no statistically significant difference was detected between the amiodarone and lidocaine groups regarding duration of hospital stay.

In another study by Kar et al, arrhythmia rates and the need for defibrillation were lower among patients given amiodarone when undergoing elective cardiac valve replacement. There was a higher need for a pacemaker in the amiodarone group, although there was no difference between the groups regarding the need for inotropic agents [Kar 2011]. In our study, the patient groups consisted solely of patients operated on with coronary arterial bypass, and amiodarone was administered with a single prophylactic dose. No difference was detected between the patient groups regarding the need for a pacemaker.

In a study among patients undergoing open cardiac surgery by Mauermann et al, amiodarone and lidocaine were found ineffective in prevention of ventricular fibrillation, however, less need for defibrillation was detected in the amiodarone group compared with the lidocaine group [Mauermann 2012]. In our study, need for defibrillation was less likely to occur in the amiodarone group. Although the markers of myocardial injury were not sought in our study, it is previously reported that the need for recurrent defibrillations increases myocardial injury and impairs postoperative patient mortality and morbidity [Yamaguchi 2002; Leeuwenburgh 2008]. Therefore, amiodarone may result in an improvement in patient mortality and morbidity, lowering the need for recurrent defibrillations.

We did not come across any pulmonary complications. We assume in this way that a single dose of amiodarone administered prophylactically is safe.

According to the data resulting from our study, we detected that there is no superiority between lidocaine administered before removal of the aortic clamp and amiodarone administered by paying attention to the duration of its initial effect after conventional CABG with cardioplegic arrest and CPB; however, application of amiodarone lowered the need for additional defibrillation. As a result, we suggest that administration of amiodarone before removal of the aortic cross clamp has a positive impact on perioperative ventricular arrhythmias and can be used safely.

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