EFFICACY OF AMIODARONE IN THE TREATMENT OF VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH CORONARY ARTERY DISEASE IN BANGLADESH

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Abstract

Background: *Ventricular arrhythmias (VA) are among the most feared complications of coronary artery disease (CAD) and one of the major contributors of death in CAD patients. Antiarrhythmic drug (AAD) therapy is required for recurrent significant VA in the absence of need for further revascularization. But all AADs do not have the same efficacy against life threatening VA and supraventricular arrhythmias (SVAs).*

Methodology: *All (50) patients admitted in the department of Cardiology, BSMMU with ventricular arrhythmias with CAD fulfilling the inclusion and exclusion criteria were included in the study. Informed written consent was taken from each patient before enrollment. Detailed history was taken and relevant physical examinations were done. Loading dose followed by maintenance dose of amiodarone was given and recorded. Relevant lab investigations were performed and recorded in predesigned semi-structured data collection sheet. Symptomatic improvement was assessed, relevant physical examination was done and lab investigations were performed at 1, 3 and 6 month follow up. After editing data analysis was carried out by using the Statistical Package for Social Science (SPSS) version 23.0 windows software.*

Results: *The mean age was found 57.7±8.0 years with a range of 45 to 78 years. Almost two third (62.0%) patients were male and 19(38.0%) patients were female. Male female ratio was 1.6:1. Almost three fourth (74.0%) patients had chest pain, 15(30.0%) had palpitation and 11(22.0%) had shortness of breath. Two third (66.0%) patients had hypertension, 23(46.0%) had dyslipidemia, 17(34.0%) had smoking and 9(18.0%) had diabetes mellitus. Twenty nine (58.0%) patients had family history of IHD. The difference was statistically significant ($p<0.05$) when compared to baseline. Regarding arrhythmia, 45(90.0%) patients was found to have PVC in baseline and 3(6.4%) at 6th month. The reduction of PVC and VT at six month were statistically significant ($p<0.05$) when compared to baseline. Regarding outcome 2(4.1%) patients died, one patient dropped out due to thyroid dysfunction and 47 were alive.*

Conclusion: *In conclusion it was found that different forms of ventricular arrhythmias like PVCs, VT were significantly reduced gradually with amiodarone therapy at 6th month follow up.*

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Introduction

Ventricular arrhythmias are among the most feared complications of coronary artery disease (CAD). Ventricular fibrillation (VF) accounts for the majority of deaths occurring in the acute phase of an ischemic event,[1] and can be the first manifestation of the disease in more than half of all cases. The incidence of VF complicating an acute myocardial infarction (MI) has been reported to be around 4.7%, and has remained relatively stable over the time in long-term observational studies.[2] It is estimated that 90% of patients with out-of-hospital VF do not reach the hospital alive.[3] Sustained, monomorphic ventricular tachycardia (VT) occurs most frequently in the setting of healed MI, and may appear in the subacute phase or long after the acute ischemic injury.[4] The extent of myocardial necrosis and the degree of left ventricular (LV) dysfunction are important determinants of arrhythmia risk following MI. Sustained, monomorphic VT usually develops in patients with more extensive MI who also have lower LV ejection fraction (LVEF).[4]

Robust evidence for anti-arrhythmic drug (AAD) use in the early dynamic phase of ischaemia and reperfusion within the first 48–72 hours post-MI is lacking in comparison to use in the chronic phase. Despite the availability of early revascularization and beta-blocker use, 6% of patients in this early phase are still affected by sustained VAs.[5] While the immediate treatment for VAs with hemodynamic collapse remains direct current cardio version, recurrent sustained VAs in the absence of need for further revascularization and normal electrolytes usually calls for some form of drug therapy along with implantable cardioverter defibrillator (ICD) in relevant cases. Beta-blockers have been effectively used in patients with acute coronary events, reducing major cardiac events including sudden cardiac death (SCD).[6] In a meta-analysis by Huang et al.[7] use of beta-blockers was associated with reduction of all-cause mortality in patients with acute MI undergoing PCI. The benefit was restricted to those with reduced EF, low use of other secondary prevention drugs or with non STEMI. The association between the use of beta-blockers and improved survival rate was significant only in <1-year follow-up duration. They concluded that there was a lack of evidence to support routine use of beta-blockers in all patients with AMI who underwent PCI. In the carvedilol post-infarct survival control in left ventricular dysfunction study (CAPRICORN) trial, carvedilol was shown to have significant anti-arrhythmic effect after AMI. It suppressed both atrial and ventricular arrhythmias in these patients.[8] There are conflicting reports concerning the class Ib drug lidocaine of either a significant trend towards a lower risk of death in the early post-MI period [9] and less VAs and a survival benefit post-cardiac arrest when used prophylactically to a neutral effect on overall mortality or a trend towards excess mortality.[10] Prophylactic lidocaine use has largely been discouraged although it remains a potential intravenous treatment for recurrent sustained VAs post-MI. The class Ic drugs like flecainide and propafenone cause significant slowing of conduction, which may exacerbate VAs in the post-MI setting and should not be used.[10]

Amiodarone, a class III antiarrhythmic drug which acts by potassium channel blockade remains the most commonly used AAD in post-MI period and is particularly useful in presence of severe structural disease. Its use following out-of-hospital cardiac arrest in patients with shock refractory VF was associated with a survival benefit in comparison with lidocaine. In patients who survived more than 3 hours after MI, use of amiodarone was associated with increased short (30 days) and long-term (6 months) mortality compared with lidocaine for use in the ACS setting.[11]

European Society of Cardiology (ESC) position paper on anti-arrhythmic drugs on 2018 stated that prevention of SCD in patients with ACS is based on revascularization and beta-blockade. Amiodarone may have the most balanced efficacy-to-risk profile, and should be considered only if episodes of VT or VF are frequent, and can no longer be controlled by successive electrical cardioversion or defibrillation.[12,13] A recent meta-analysis confirmed that amiodarone decreases the SCD risk and represent a viable alternative in patients who are not eligible for, or who do not have access to ICD therapy.[14] The combined

analysis of European Myocardial Infarct Amiodarone Trial (EMIAT) and Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT)[15] confirmed the positive antiarrhythmic interaction between amiodarone and beta-blockers in preventing SCD. Lidocaine may reduce the incidence of ventricular arrhythmias related to myocardial ischaemia, although no beneficial effect on early mortality has been demonstrated.[16] When compared to amiodarone for the treatment of ventricular arrhythmias complicating ACS, lidocaine may have a more favourable safety profile.[17]

Till date these guidelines are based on old trial & evidences done before the latest interventional management era, for example- EMIAT, CAMIAT 2009.[11] If the efficacy of amiodarone could be proved this drug might be advocated in VAs in large population who are not able or eligible for ICD implantation. During this modern intervention era short term use of amiodarone may reduce VAs related mortality effectively.

So, our study was intended to document the efficacy of amiodaone in Bangladeshi patients with CAD in the absence of need for further revascularization and with normal biochemical profile.

Methodology

The quasi experimental study was conducted in the Department of Cardiology in Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka during April, 2019 to March, 2020. Patients got admitted in the Department of Cardiology, BSMMU with chronic ischemic heart disease with reduced ejection fraction having significant ventricular arrhyhthmia treated with amiodarone were included in this study. Patients with baseline pronged QT interval, having structural and valvular heart diseases other than ischemic heart disease and patients who were unwilling to give informed written consent were excluded from the study. All patients got guideline directed therapy including revascularization. Loading dose followed by maintenance dose of amiodarone was given and recorded. Baseline demographics, ECG (significant number of PVC, multifocal in origin, R on T phenomenon, couplets, triplets, short run), Echo, 24 hours Holter ECG (significant number of PVC, multifocal in origin, R on T phenomenon, couplets, triplets, short run, non sustained VT) or cardiac monitoring record, serum electrolytes, creatinine, thyroid profile reports, eye findings were recorded. Patients were followed up at end of first, third & sixth month. Occurrence of symptoms of arrythmia, hospitalization form arrhythmia and cardiac death were noted. Focused clinical examination of eye, skin, nervous system, thyroid status, cardiovascular, respiratory system was done and 12 lead ECG was taken in each visit. If any adverse effect of amiodarone arises, then the patient was treated according to standard guideline and amiodarone was discontinued in relevant cases. 24 hours Holter ECG to look for correction of index arrhythmia or appearance of newer arrhythmia, thyroid function test, X-ray of chest, liver function tests were done after 6 months in asymptomatic cases, and early in clinically relevant cases. Data were recorded in preformed data sheets. Treatment outcome and complications were analyzed. Statistical analyses were carried out by using the Statistical Package for Social Sciences (SPSS) version 23.0 for Windows Software. Continuous data were expressed as mean ± standard deviation (SD) and categorical data were expressed as frequency and percentages. Mean and standard deviation were computed for quantitative variables and were analyzed by paired t-test. Chi square test was used for categorical variables. P values <0.05 was considered as statistically significant.

Results:

This Quasi experimental study was carried out in the Department of Cardiology, University Cardiac Center, Bangabandhu Sheikh Mujib Medical University, Dhaka from April, 2019 to March, 2020. A total of 50 patients with ventricular arrhythmias in the background of ischemic heart disease were enrolled in the study. This study was to find out the efficacy of amiodarone in the treatment of ventricular arrhythmias in patients with coronary artery disease in Bangladesh.

Table 1
Baseline characteristics of the study patients (n=50)

	Frequency	Percentage
Age (years)		
≤50	11	22.0
51-60	20	40.0
61-70	18	36.0
>70	01	02.0
Mean±SD	57.7	±8.0
Range (min-max)	45.0	-78.0
Sex		
Male	31	62.0
Female	19	38.0
BMI (kg/m^2)		
18.5-22.9 (Normal)	14	28.0
23.0-24.9 (Over weight)	25	50.0
≥25.0 (Obese)	11	22.0
Symptoms		
Chest pain	37	74.0
Palpitation	15	30.0
Shortness of breath	11	22.0
Risk factors		
Hypertension	33	66.0
Dyslipidemia	23	46.0
Smoking	17	34.0
Diabetes mellitus	9	18.0
Family history of IHD	29	58.0

Table 1 shows that majority (40.0%) of the patients belonged to age of 51-60 years. The mean age was found to be 57.7±8.0 years ranging from 45 to 78 years. Almost two third (62.0%) patients were male, 25(50.0%) had BMI of 23.0-24.9 kg/m^2 (over weight), 37(74.0%) had chest pain, 15(30.0%) had palpitation, 11(22.0%) had shortness of breath, 33(66.0%) had hypertension, 23(46.0%) had dyslipidemia, 17(34.0%) had smoking, 9(18.0%) had diabetes mellitus and 29(58.0%) patients had family history of IHD.

In the ECG variables, 45(90.0%) patients had PVCs in the baseline ECG and 3(6.4%) had the same at 6th month. In 24 hours Holter ECG, 44(97.8%) patients had significant number of PVCs in baseline and 2(4.4%) at 6th month. In 1(2.2%) patient baseline VT was found, but with treatment VT was not found in 24 hours Holter ECG at 6th month of follow up. The difference was statistically significant ($p<0.05$) when compared to baseline with that of at 6th month follow up.

Table-II
ECG and 24 hours Holter ECG variables in different follow up

Variables	Baseline (n=50) n (%)	1st month (n=50) n (%)	3rd month (n=50) n (%)	*6th month (n=47) n (%)	P value (baseline vs 6th month)
ECG					
PVC	45 (90.0)	23 (46.0)	10 (20.0)	3 (6.4)	
VT	5 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Normal	0 (0.0)	27 (54.0)	38 (76.0)	41 (87.2)	0.001^s
Bradyarrhythmia	0 (0.0)	0 (0.0)	2 (4.0)	3 (6.4)	
24H Holter ECG					
Significant No. of PVC	44 (97.8)	16 (69.6)	4 (40.0)	2 (66.7)	
VT	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	
Normal	0 (0.0)	7 (30.4)	6 (60.0)	1 (33.3)	0.001^s
Brady arrhythmia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

* At 6 month, 1 patient dropped out due to hypothyroidism and 2 patients died

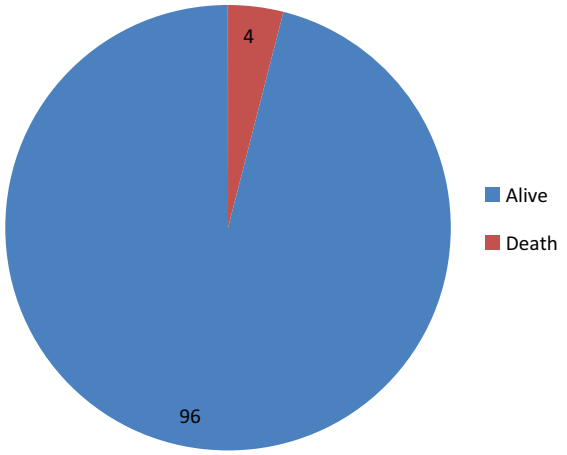

Figure 1: *Pie chart showing outcome of the study patients (n=49)**

*One patient dropped out due to hypothyroidism

Figure 1 shows that 2(4.1%) patients had death and 47 remained alive.

Discussion

This Quasi experimental study was carried out in the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka from April, 2019 to March, 2020. A total of 50 patients with ventricular arrhythmias in the background of ischemic heart disease were enrolled in the study. This study was intended to find out the efficacy of amiodarone in the treatment of ventricular arrhythmia in patients with coronary artery disease in Bangladesh. The present study findings were discussed and compared with previously published relevant studies.

We observed that majority (40.0%) patients belonged to age 51-60 years. The mean age was found to be 57.7±8.0 years ranging from 45 to 78 years. Almost two third (62.0%) patients were male and 19(38.0%) patients were female. Male female ratio was 1.6:1. The mean age was found 64±11 years and 67±8 years by Connolly et al.[18] and Kowey et al.[19] respectively. Dong et al.[20] reported seventy nine consecutive patients (48 males and 31 females; mean age, 64.6±11.2 years; range, 40-80 years). Boutitie et al.[15] showed in their study that the mean age was 60.7±10.7 years and 84.4% were male. Piccini et al.[9] reported mean age as 67.8±9.8 years and 70.0% were male.

Half (50.0%) of the patients had BMI of 23.0-24.9 kg/m^2, 14(28.0%) had 18.5-22.9 kg/m^2 and 11(22.0%) had e”25.0 kg/m^2. Essebag et al.[21] reported that mean BMI was 28.9±6.6 kg/m^2 in their study.

In this study it was observed that two third (66.0%) patients had hypertension, 23(46.0%) had dyslipidemia, 17(34.0%) had smoking 9(18.0%) had diabetes mellitus. Dong et al.[20] observed that 61.12% patients had hypertension and 6.24% had diabetes. Piccini et al.[9] observed that 22% patients had DM and 58% had hypertension. Boutitie et al.[15] reported that 40.8% patients were smoker, 27.0% had previous MI, 39.3% had hypertension and 11.6% had DM.

It was observed that 29(58.0%) patients had family history of IHD. Dong et al.[20] reported that 47.11% patients had coronary artery disease.

In this study we observed that 2(4.1%) patients died and 47 were alive. Previous systematic reviews published more than a decade ago[22,23] have shown that amiodarone is associated with lower death rate due to arrhythmia, however, they did not incorporate more contemporary large-scale trials of amiodarone, including the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) and the Optimal Pharmacological Therapy in Implantable Cardioverter Defibrillator Patients (OPTIC) trial.[24]

Amiodarone suppresses ventricular premature depolarizations (VPDs) and episodes of nonsustained VT.[25-27] This is clearly demonstrated in several of the primary prevention trials of amiodarone in post–myocardial infarction and congestive heart failure (CHF) patients in whom baseline and follow-up 24-hour ambulatory ECGs were performed. In the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT) pilot study[28] which enrolled patients with frequent or repetitive asymptomatic VPDs, 86% of amiodarone patients were observed to have almost complete suppression of VPDs and nonsustained VT compared with 50% of placebo patients. In the Veterans Affairs Congestive Heart Failure Amiodarone Study,[29] after 2

weeks of therapy, 33% of patients on amiodarone had VT events on Holter ECGs compared with 76% of placebo patients (P 0.001). In our study we observed that in 24 hours Holter ECG, 44(97.8%) patients had significant number of PVCs in baseline and 2(4.4%) at 6th month. In baseline, VT was found in 1(2.2%) patient but after treatment, VT was not found in 24 hours Holter ECG at 6th month of follow up. The difference was statistically significant ($p<0.05$) when compared to the baseline findings.

Conclusion

In conclusion it was found that 44(97.8%) patients had significant number of PVCs in baseline and 2(4.4%) at 6th month. In baseline, VT was found 1(2.2%) patient but after treatment with amiodarone VT was not found in 24H Holter ECG at 6th month of follow up, which was statistically significant. The efficacy of amiodarone was found during the course of treatment.

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