ORIGINAL ARTICLE

Amiodarone vs digoxin in the treatment of atrial fibrillation in postoperative rheumatic cardiac valvular patients

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Abstract

Objective: To compare the efficacy of amiodarone and digoxin for patients who underwent valve-related cardiac surgery and had atrial fibrillation in the first 72 hours post-operatively.

Methods: The observational/descriptive study was conducted at the Punjab Institute of Cardiology, Lahore, Pakistan, from January to December 2011. Patients with associated cardiac problems were excluded. Those selected were followed up for 3 days in intensive care unit after undergoing operation on cardiac valves. They were divided into three groups: those who had new onset atrial fibrillation, chronic atrial fibrillation or no atrial fibrillation. The diagnosis was established on the basis of electrocardiogram. The surgeon, the attending doctor in intensive care and the patient were all unaware of the study. The decision to use either digoxin or amiodarone was left to the duty doctor in intensive care unit. The first two groups were further subdivided into Group A that had those who received amiodarone while Group B patients received digoxin. SPSS 19 was used for data analysis.

Results: Out of the 176 patients operated, 93(52.9%) had atrial fibrillation post-operatively. Of them, 65(69.9%) were men and 28 were women. Group A had 29(31.2%) patients and Group B had 64(68.9%). Overall, 49(52.7%) patients developed new onset atrial fibrillation, while 44(47.3%) had chronic atrial fibrillation when received in the intensive care unit. Atrial fibrillation was not reverted in 12(41.4%) patients from Group A and 32(50%) from Group B, whereas no symptom improvement was found in 2(6.9%)patients of Group A and 7(10.9%)of Group B. The two groups had the same effect in the treatment of atrial fibrillation in post-operative patients for cardiac rheumatic valve disease (P-value=0.441).

Conclusion: Amiodarone was found to be as effective as digoxin in reverting atrial fibrillation and improving symptoms and none of the two drugs had greater benefit than the other.

Keywords: Amiodarone, Digoxin, Arrhythmias, Valvular heart disease. (JPMA 66: 1098; 2016)

Introduction

Postoperative atrial fibrillation (AF) is rather common and occurs in 20%-40% of preoperative patients undergoing open-heart surgery and 16-46% postoperatively, especially between second to fifth postoperative day.[1,2] It is associated with a higher incidence of mortality, stroke and coronary events compared to those in sinus rhythm. AF with a rapid ventricular rate (VR) may cause a tachycardia-related cardiomyopathy.[1-3] Numerous pharmacological and electrical therapies have been used as a prophylaxis to prevent this dysrhythmia.[2] The goals of AF management are to alleviate patient symptoms, improve patient quality of life and minimise the morbidity associated with AF. Arrhythmia management usually commences with drugs to slow VR. In old patients many cardiologists prefer warfarin with VR control rather than anti-arrhythmic drugs. The addition of class I or class III anti-arrhythmic drugs for restoration or maintenance of sinus rhythm is largely determined by patient symptoms and preferences. For rate control, treatment of persistent or permanent AF, aim should be for a resting heart rate (HR) of <100 beats per minute. Digoxin and amiodarone may be used in combination with other agents to optimise rate control.[4,5]

Both digoxin and amiodarone are used to control the arrhythmias. Little work is done to find out which among them is better for the control of dysrhythmias in valvular patients, especially in our part of the world, as our population is different from the well-studied Caucasians. The current study was planned to evaluate which is the comparatively better drug between amiodarone and digoxin for patients who undergo valve-related cardiac surgery and have AF in first the 72 hours of operation.

Patients and Methods

This observational/descriptive study was conducted at the Punjab Institute of Cardiology, Lahore, Pakistan, from January to December 2011. Patients undergoing mitral valve replacement (MVR), aortic valve replacement (AVR), double valve replacement (DVR) involving both MVR and AVR, DVR with tricuspid valve repair (TVr) or MVR+TVr were included. Non-probability consecutive sampling

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technique was used in which all the patients who fulfilled the criteria were included till the sample size was achieved.

They all had rheumatic heart disease (RHD). Patients with clot in left atrium, concomitant ischaemic heart disease (IHD), and those undergoing only mitral valve repair were excluded. The surgeon, the attending doctor in intensive care unit (ICU) and the patient were not aware of the study. These patients were followed up for 3 days in ICU after undergoing operation on cardiac valves. Later on, the patients were divided into three groups on the basis of whether they had new onset AF, chronic AF or no AF, respectively. The diagnosis of AF was established based on 12-lead electrocardiogram (ECG) criteria (absence of p waves, presence of irregular atrial electrical activity and irregular RR intervals). The decision to use either digoxin or amiodarone was left entirely to the duty doctor in ICU. The first two groups were further subdivided, and evaluated as to whether patients receiving amiodarone who were in Group A, or digoxin in Group B had better rhythm control. Patient's weight was measured to allow dose calculations of anti-arrhythmic drugs per kilogram of weight. Amiodarone was given as loading dose {weight(kg) x 5(mg)} and then maintenance dose {weight(kg) x 15(mg)}) over a 24-hour period. If normal sinus rhythm (NSR) was established within 24 hours, the intravenous (IV) infusion was continued for another 24 hours with concomitant oral amiodarone overlap. Digoxin was loaded intravenously (the number of doses was calculated by formula 0.9 x BSA / 0.125, and then IV dose of 0.125 mg was given keeping K+ level above 4 mEq/L. Dose was not given if HR reached <80 beats per minute and then converted into the oral form (0.25mg per day). The primary end point was sustained VR control (<90 bpm) within 24 hours; the secondary end points included AF symptom. Conversion to NSR was verified by 24-hour monitoring. Moreover, 12-lead ECGs were recorded before drug ingestion and once either the AF reverted or symptoms improved. The results of therapy were assessed after the drug intake. To evidence any possible side effects from the drug intake, patients' complaints were carefully searched for and recorded.

SPSS 19 was used for data analysis. Qualitative variables were presented as frequency/ percentages. Quantitative variables were presented as mean and standard deviation. Chi-squared test and Fisher's exact test (if cell frequency was less than 5) was applied to observe the association of qualitative variables with amiodarone and digoxin group, while for quantitative variables independent sample t-test was applied. $P \leq 0.05$ was considered significant.

Results

Out of the 176 patients, only 93(52.9%) had AF postoperatively. Of them, 65(69.9%) were men and 28(30.1%) women (Figure-1). Moreover, Group A had 29(31.2%) patients and Group B had 64(68.9%). The patients' age ranged from 20 to 45 years.

Furthermore, 32(34.4%) patients underwent MVR; 15(16.1%) AVR, 13(14%) MVR+TVr, 18(19.3%) DVR, whereas 15(16.1%) underwent DVR+TVr (Figure-2). Cross-clamp

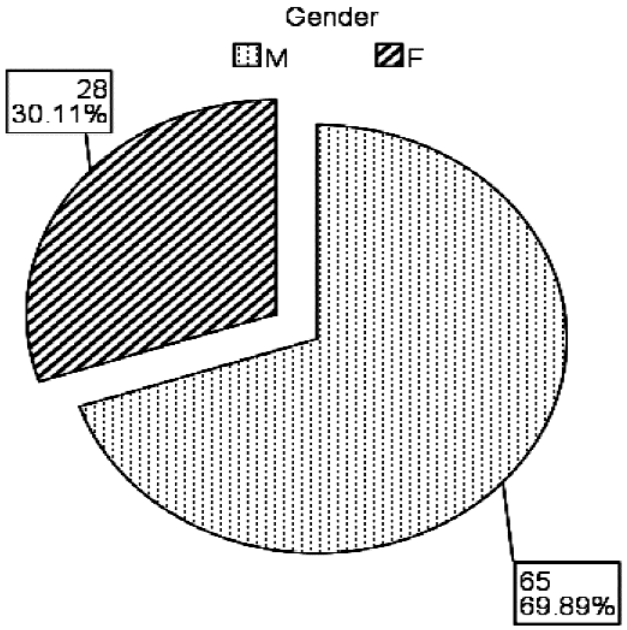
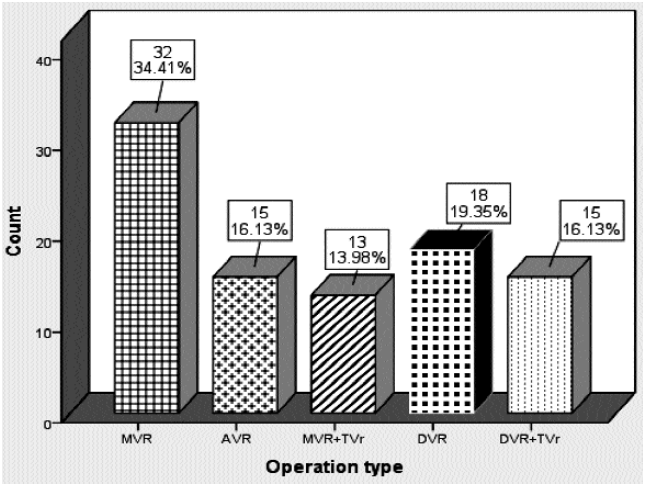


Figure-1: Graphical distribution with respect to gender.



MVR: Mitral Valve Replacement. AVR: Aortic Valve Replacement. TVR: Tricuspid Valve Replacement. DVR: Double Valve Replacement.

Figure-2: Valvular patient's distribution according to the operation type.

Table: Distribution of the demographical and clinical characteristics in treatment groups.

		GROUPS		p-value
		Amiodarone	Digoxin	
Sex	Male	19 (65.5%)	46(71.9%)	0.536
	Female	10(34.5%)	18(28.1%)	
Age	MEAN±SD	39.00±12	30.11±6.4	0.001
Ejection Fraction ≤ 40		8(27.6%)	6(9.4%)	0.023
Operation	MVR	10(34.5%)	22(34.4%)	0.076
	AVR	9(31.0%)	6(9.4%)	
	MVR+TVr	4(13.8%)	9(14.1%)	
	DVR	3(10.3%)	15(23.4%)	
	DVR+TVr	3(10.3%)	12(18.8%)	
Cardiopulmonary Bypass time >60 min		27.0(93.2%)	50.0(78.1%)	0.135
Cross Clamp time <60 min		27(93.1%)	52(81.2%)	0.212
Time on Ventilator <8 hours		26(89.65%)	48(75%)	0.086
ICU stay > 2days		6(20.7%)	11(17.2%)	0.826
Inotopes	Dopamine	16(55.2%)	7(10.9%)	0.000
	Adrenaline	5(17.2%)	32(50.0%)	
	Noradrenaline	8(27.6%)	25(39.1%)	
Mortality		1(3.4%)	1(1.6%)	0.529
Atrial fibrillation reverted		17(58.6%)	32(50%)	0.441
Symptoms improved		27(93.1%)	57(89.1%)	0.541

MVR: Mitral valve replacement. AVR: Aortic valve replacement. TVr: Tricuspid valve repair. DVR: Double valve replacement. ICU: Intensive care unit. SD: Standard deviation.

time was >60 minutes in 14(15%) patients whereas cardiopulmonary bypass time was >60 minutes in 77(82.8%) patients. The time of ICU stay was upto 48 hours in 76(81.7%) patients. Time on ventilator was 8 hours or less in 74(79.6%) patients. During the study period, 2(2.15%) patients died, 1(3.45%) in Group A and 1(1.56%) in Group B. Of all, 49(52.7%) patients developed new onset AF, while 44(47.3%) had chronic AF when received in ICU. AF was not reverted in 12(41.4%) patients from Group A, and 32(50%) patients from Group B. No symptom improvement was found in 2(6.9%)patients of Group A and 7(10.9%)of Group B. Group A and Group B had the same effect in the treatment of AF (P-value=0.441) (Table).

Discussion

AF after cardiac surgery occurs in approximately one-third of patients and is associated with an increase in adverse events in all measurable outcomes of care. This increases the use of hospital resources and the cost of care. Strategies to reduce the incidence of AF after cardiac surgery should favourably affect surgical outcomes and reduce utilisation of resources and thus lower cost of care.[1-5]

NSR is difficult to achieve and maintain in patients with RHD.[6] The loss of atrial systole and rapid VR may cause haemodynamics deterioration in these patients.[7] In addition, the issue of rate control versus rhythm control has not been critically evaluated in patients with RHD.[7-9]

A study found intravenous amiodarone to be well tolerated and it did not increase the risk of post-operative complications.[10] Although digoxin has been widely used in patients with AF, its efficacy for the control of VR and rhythm irregularity is unsatisfactory.[11] Digoxin and low-dose amiodarone had similar efficacy in the control of VR during ambulatory activity and exercise. However, both were less effective during exercise and did not significantly affect rhythm irregularity, exercise capacity, quality of life and AF symptomatology in patients with chronic AF.[11] Our study observed only the efficacy of both digoxin and amiodarone to control of VR while the patient was in ICU and started to get mobilised. Moreover, both were found to have similar efficacy as far as the rate control and symptoms improvement are concerned.

Galve Eet al.[12] suggested that intravenous amiodarone, at the doses used in their study, produces a modest but not significant benefit in converting acute AF to sinus rhythm.In our study, follow-up was shorter, therefore, comparable results could not be defined. HouZY[13] described that the digoxin group had fewer dramatic alterations in heart rates, compared to the amiodarone group, in the first 8 hours ($p<0.05$). Maximum reduction was reached only after 8 hours. The amiodarone infusion was prematurely aborted in two patients due to severe bradycardia and death after conversion to sinus rhythm in one patient and aggravation of heart failure in the other.

In our study, none of the patients treated with amiodarone developed hypotension or bradycardia.

Study by Hashemzadeh K[14] et al (2013) reported that only 14.54% (180/1254) undergo valve related cardiac surgery patients treated with Amiodarone from 2007 to 2011 (four year time period) while present study conducted from (Jan 2011 to Dec 2011) one year time period, 29/176patients 16.47% received the treatment Amiodarone. Kar KS[15] et al (2011) established in their randomized control trial that out of 56 patients with rheumatic valve disease undergoing valve replacement surgery, 28 patients were treated with Amiodarone and 28 with Digoxin. In the randomized control trial Simopoulos V[16] et al out of 41 patients 21 were treated with Amiodarone at one year.

Present results are purely recorded on the basis of observation; observer did not intervene in this work. Randomized double blind technique was used for this purpose. The surgeon did not know if patients received amiodarone or digoxin. As digoxin is the primary treatment for valvular patients so surgeons prefer digoxin over Amio treatment.

Our study confirms the findings of Doyle JF[17] that amiodarone, as part of a strategy to achieve and maintain sinus rhythm, appears to be safe and effective in AF.

The current study has some limitations as well. For instance, as there was no follow-up after hospital discharge, the impact of both amiodarone and digoxin on the AF in the long term is unknown. Secondly, the sample size was small and thus a larger randomised controlled study is needed to assess the impact of restoration of sinus rhythm and its persistence later on.

Conclusion

Amiodarone was found to be as effective as digoxin in reverting AF and improving symptoms, and no drug had greater benefit than the other. Both can be used in patients who had or develop AF after a procedure on rheumatic valve.

Disclaimer: None.

Conflict of Interest: None.

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