

Original Article

Effect of Intraoperative Loading Dose of Amiodarone for Prophylaxis Against Atrial Fibrillation in Patients with Rheumatic Valvular Heart Disease Undergoing Valve Replacement Surgery

Romena Rahman¹, AM Asif Rahim², AYM Shahidullah³, QM Anisujjaman⁴,
ASM Iftekher Hossain², Md Kamrul Hasan¹, Sanjay Kumar Raha¹

¹National Institute of Cardiovascular Diseases, Dhaka, ²Chattogram Medical College, Chattogram,

³Fortis Escort Heart Institute, Khulna, ⁴Impulse Hospital, Dhaka

Abstract

Key Words :
Amiodarone,
atrial fibrillation,
rheumatic heart
disease.

Background: Atrial Fibrillation (AF) is the most common arrhythmia occurring after cardiac surgery and its peak incidence is between second or third postoperative day. It occurs in 40% to 50% of patients after valve surgery alone or combined valve and CABG surgery respectively. Among all the anti-arrhythmic drugs evaluated for AF, amiodarone has shown the most promising results with successful conversion and maintenance of normal sinus rhythm achieved in 50%–70% of patients.

Methods: Sixty diabetic patients purposively selected who underwent isolated off pump coronary artery bypass procedure in NICVD. Group A – 30 patients receiving loading dose of amiodarone intra-operatively before establishment of CPB during valve replacement surgery and Group B- 30 patients without receiving loading dose of amiodarone intra-operatively during valve replacement surgery. Incidence of atrial fibrillation in postoperative period was evaluated.

Results: Atrial fibrillation was observed in 8 (26.7%) patients in group A and 18 (60%) patients in group B ($p=0.009$). Ventricular tachycardia developed in 6.7% patients in group B and none in group A ($p=0.47$). Mean duration of ICU stay was 2.04 ± 0.30 days in Group A and Group B was 2.98 ± 0.77 days ($p=0.03$). Mean duration of post-operative stay was 7.20 ± 0.66 days in Group A and Group B was 7.85 ± 0.60 days ($p=0.10$).

Conclusion: A single intra operative dose of intravenous amiodarone increases the incidence of conversion of AF to normal sinus rhythm. When AF persisted, use of amiodarone reduces the frequency of need for cardioversion and the energy required for it.

(*Cardiovasc. j.* 2020; 12(2): 102-108)

Introduction:

Atrial Fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function.¹ The prevalence of atrial fibrillation is increasing worldwide. In developed countries a predominant cause of AF is elderly age while in developing countries it is

predominantly attributed to valvular heart disease mitral stenosis (MS) and mitral regurgitation (MR) of rheumatic origin.² AF is the most common arrhythmia occurring after cardiac surgery and its peak incidence is between second or third postoperative day. Specially AF occurs in nearly 30% of patients undergoing coronary bypass grafting (CABG), and in 40% to 50% of patients

Address of Correspondence: Dr. Romena Rahman – Assistant Professor, Department of Cardiac Surgery, NICVD, Dhaka, Bangladesh. Email: drromena@gmail.com

© 2020 authors; licensed and published by International Society of Cardiovascular Ultrasound, Bangladesh Chapter and Bangladesh Society of Geriatric Cardiology. This is an Open Access article distributed under the terms of the CC BY NC 4.0 (<https://creativecommons.org/licenses/by-nc/4.0>).

after valve surgery alone or combined valve and CABG surgery respectively.³ The exact mechanism of AF after valve replacement surgery is not known but the contributing factors can be use of Cardio Pulmonary Bypass (CPB), beta-blocker withdrawal, pericarditis, electrolytes imbalance, exogenous and endogenous catecholamine, atrial injury and inadequate atrial protection. Additional risk factors are advanced age, chronic obstructive pulmonary disease (COPD), prolonged cross clamped periods.⁴ The adverse effects of atrial fibrillation are due to –i) Rapid ventricular response: reduces diastolic filling and reduces cardiac output. Ii) Loss of AV synchrony: atrial contribution to ventricular filling is lost. Iii) Stasis of blood: encourages thrombosis and embolism.⁵ AF remains an important cause of patient discomfort, anxiety, hemodynamic deterioration, stroke, exposure to the risks of tachyarrhythmia treatments, prolongation of hospital stays, and expenses after heart surgery.²

The Pharmacological Intervention in Atrial Fibrillation (PIAF) trial suggested that the maintenance of normal sinus rhythm (NSR) in patients with AF leads to symptomatic improvement.⁶ In addition to improving symptoms, the potential benefits of restoring and maintaining sinus rhythm include avoidance of the development of atrial cardio-myopathy from ongoing AF, improvement in heart failure and improved overall quality of life.⁷ Various medications can be used to prevent the post-operative occurrence of AF. This include Magnesium Sulphate, beta blockers, amiodarone either preoperatively orally or preoperatively IV. If the AF does occur, we can use different method to restore and maintain NSR, control the ventricular rate and prevent complications. These include amiodarone, magnesium sulphate, calcium channel blockers, or cardioversion.⁸

Among all the anti-arrhythmic drugs evaluated for AF, amiodarone has shown the most promising results with successful conversion and maintenance of NSR achieved in 50%–70% of patients. Oral amiodarone therapy needs frequent visits to the hospital and intense monitoring for side effects. However, the onset of the anti-arrhythmic effect of intravenous amiodarone is rapid.⁹ Reports regarding the use of intra-

operative intravenous amiodarone in patients with AF of rheumatic origin, undergoing valvular heart surgery seem to be scarce. Prophylactic oral amiodarone was shown to reduce the incidence of new onset AF in patients undergoing open heart surgery.⁹ One study was performed by Parash Pant, et al, in NICVD, showed that the peri-operative use of amiodarone was safe and significantly reduced the incidence of post-operative atrial fibrillation in patient undergoing off pump coronary artery bypass surgery. Prophylactic amiodarone is effective in preventing the genesis of arrhythmias in the presence of a large irritative arrhythmia prone left atrium as observed in rheumatic heart diseases. The low arrhythmogenic and negligible negative inotropic effects of amiodarone make it particularly useful in treating high-risk patients prone to sudden cardiac death. Use of amiodarone reduced the frequency and energy required for cardioversion, recurrence of AF until hospital discharge and fast ventricular rate.¹⁰

In this study we evaluated the effect of IV administration of amiodarone per-operatively in patient with concomitant rheumatic valvular heart disease undergoing valve replacement surgery.

Methods:

This is prospective non randomized clinical study carried out in the Department of Cardiac surgery, National Institute of Cardiovascular Disease (NICVD), Dhaka during the period of July 2013 to December 2014. For the purpose of the study a total 60 (sixty) consecutive patients of valve replacement surgery was enrolled. Group A- 30 patients receiving loading dose of amiodarone intra-operatively before establishment of CPB during valve replacement surgery and Group B - 30 patients without receiving loading dose of amiodarone intra-operatively during valve replacement surgery. Exclusion criteria were: Bradyarrhythmia, Elevated liver enzyme levels, Renal dysfunction (Serum creatinine>1.4 mg/dl), Thyroid disease and Patients allergic to amiodarone.

Amiodarone 150 mg was added with 5%DA in burette so that the volume becomes 100 ml. In Group-A, amiodarone 150 mg in 5% DA was started as intravenous infusion through the central venous

route over a period of 10 -15 minutes prior to institution of CPB. In Group-B, amiodarone was not given. CPB was established in a standard way. Myocardial protection was achieved with intermittent cold blood cardioplegia administered every 20 minutes. The valve replacement was carried out under CPB with mild hypothermia using standard extracorporeal techniques. All the patients were re-warmed to 37°C. Serum potassium level was optimized to 4-4.5 mEq/L throughout surgery to prevent arrhythmia induced by hypo- or hyperkalemia. After surgical closure, the patient was transferred to the postoperative ICU. In the ICU, the patient was followed up for occurrence of any arrhythmia for 24 hours and was treated accordingly.

Preoperative variables: Demographic such as age, sex, weight others were LA size, NYHA class; **Per-operative variables:** types of surgery – MVR/AVR/DVR, CPB time in minute, ACC time in minute, use of other anti-arrhythmic agent or cardioversion or temporary pacing. HR – 5 min after drug infusion, Rhythm after cross clamp release (AF/VT/VF/SR etc.); **Post-operative variables** were Incidence of AF at the end of surgery, recurrence of AF in ICU within 24 hours., treatment of AF on first post-operative day, ICU Stay (days), total post-operative hospital stays (days), number of patients with AF on discharge from hospital. Data were collected, recorded and interpretation was done by using SPSS version(version-16). p value .05 was regarded as significant.

Results:

Nearly half (40%) of the patients in group A was in the range of 35 - 39 years, followed by 33.3% in 30-34 years, 13.3% 40-44- and 25-29-years age group. In group B, 25-29 years age category formed main bulk (33.3%), 30-34 years comprised of 26.7%, 20% patients in 35-39 and 40-44 years respectively. The mean age of total study patients was 33.77±4.46 in the range of 26-42 years. The mean age was found 34.53±3.91 years in Group A and 33.00±4.89 years in Group B. The mean age difference was statistically insignificant (p=0.19) between two groups in unpaired t-test. Male and female patients predominated in group A and group B respectively. In group A, 16 (53.3%) patients were male and 14 (46.7%) patients were female. In group B, 22

(73.7%) patients were female and 8 (26.7%) were male (p=0.03). Class of NYHA in study patients and found that 20 (66.7%) patients in group A and 22 (73.3%) patients in group B had NYHA of class II. 10 (33.3%) patients in group A and 8 (26.7%) patients in group B had NYHA of class III (p=0.57). None of the patients in either group were in NYHA class I and IV. MVR was predominantly performed in both groups which was 80% of patients. AVR was done in 6.7% patients in group A and none in group B. DVR was done 13.3% patients in group A and 20% patients in group B (p=0.31). The mean body weight of Group A patient was 52.33±8.27 kg and Group B was 49.33±7.24 kg (p=0.14).

The mean LA size of Group A patient had 52.53±4.34 mm and Group B had 54.13±3.69 mm (p=0.13).

Table I shows the use of anti-arrhythmic treatment in study patients. Lignocaine and temporary pacing were required almost identically in both groups without statistical association (p=0.59, p=0.08). In group B 33.3% patients required cardioversion and 10% patients in group A required cardioversion and the association was statistically significant (p=0.03).

The mean XCT of Group A patient was 48.80±7.36 min and Group B was 50.40±8.05 min (p=0.21). Mean XCT of Group A and group B patient having MVR were (44.17±3.0 vs. 47.58±6.24 min) (p=0.10). AVR cannot be computed because there was no patient having AVR in group B. Mean XCT of Group A and group B patient having DVR were (60.00±0.0 vs. 61.67±2.58 min) (p=0.24). mean ECCT was 79.33±6.85 min in Group A and Group B was 81.27±9.28 min (p=0.32). Mean heart rate 5 minute after drug infusion was observed 84.40±9.20 min in Group A and Group B was 93.07±8.69 min (p=0.24).

Table II shows rhythm on release of aortic clamp in study patients. Sinus rhythm developed 73.3% vs 33.3% in group A and group B respectively with significant association (p=0.001). AF was observed 8 (26.7%) patients in group A and 18 (60%) patients in group B with statistically significant association (p=0.009). VT was developed 6.7% patients in group B and none in group A with statistically insignificant association (p=0.47).

Table III shows the incidence of atrial fibrillation at the end of surgery in study patients and found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B were developed AF. Statistically significant ($p=0.03$) association was found in the incidence of AF at the end of surgery.

Table IV shows the recurrence of atrial fibrillation in ICU within 24 hours in study patients and found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B were developed recurrence of AF. Statistically significant ($p=0.03$) association was found in the recurrence of AF in ICU within 24 hours.

Table V shows the number of patients needed treatment of atrial fibrillation in study patients and found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B were needed

treatment of AF. Statistically significant ($p=0.03$) association was found in the number of patients needed treatment.

Table VI shows the atrial fibrillation on discharge of hospital in study patients and found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B were developed AF. Significant ($p=0.03$) association was found in the development of AF on discharge.

The above table shows that mean duration of ICU stay was 2.04 ± 0.30 days in Group A and Group B was 2.98 ± 0.77 days. The difference was statistically significant ($p=0.001$).

that mean duration of post-operative stay was 7.20 ± 0.66 days in Group A and Group B was 7.85 ± 0.60 days. The difference was statistically insignificant ($p=0.10$).

Table-I

Distribution of patients by use of anti-arrhythmic agent (n=60).

Anti-arrhythmic treatment	Group A (n = 30)		Group B (n = 30)		p value
	Number	%	Number	%	
Lignocaine	10	33.3	12	40.0	0.59 ^{ns}
Cardioversion	3	10.0	10	33.3	0.03 ^s
Temporary pacing	1	3.3	5	16.7	0.08 ^s

P value reached from Pearson's Chi-square test and Fisher's Exact Test.

Table-II

Distribution of patients by rhythm at aortic clamp release (n=60).

Rhythm	Group A (n = 30)		Group B (n = 30)		p value
	Number	%	Number	%	
Sinus rhythm (SR)	22	73.3	10	33.3	0.001 ^s
Atrial fibrillation (AF)	8	26.7	18	60.0	0.009 ^s
Ventricular tachycardia (VT)	0	0.0	2	6.7	0.47 ^{ns}

p value reached from Pearson's Chi-square test and Fisher's Exact Test.

Table-III

Incidence of AF at the end of surgery between two groups (n=60).

Incidence of AF at the end of surgery	Group A (n = 30)		Group B (n = 30)		P value
	Number	%	Number	%	
Yes	8	26.7	16	53.3	0.03 ^s
No	22	73.3	14	46.7	

P value reached from Pearson's Chi-square test.

Table-IV
Recurrence of AF in ICU within 24 hrs. between two groups (n=60).

Recurrence of AF in ICU within 24 hrs.	Group A (n = 30)		Group B (n = 30)		p value
	Number	%	Number	%	
Yes	8	26.7	16	53.3	0.03 ^s
No	22	73.3	14	46.7	

p value reached from Pearson's Chi-square test.

Table-V
Treatment of AF on first post-operative day between two groups (n=60).

Needed treatment of AF	Group A (n = 30)		Group B (n = 30)		p value
	Number	%	Number	%	
Yes	8	26.7	16	53.3	0.03 ^s
No	22	73.3	14	46.7	

p value reached from Pearson's Chi-square test.

Table-VI
Atrial fibrillation on discharge of hospital between two groups (n=60).

AF	Group A (n = 30)		Group B (n = 30)		p value
	Number	%	Number	%	
Present	8	26.7	16	53.3	0.03 ^s
Absent	22	73.3	14	46.7	

p value reached from Pearson's Chi-square test.

Table-VII
Comparison of duration of ICU stay between two groups (n=60).

Duration of ICU stay in days	Group A (n = 30)		Group B (n = 30)		p value
	Number	%	Number	%	
2	20	66.7	12	40.0	
3	10	33.3	18	60.0	
Mean ± SD Range (min-max)	2.04±0.30(2 – 3)		2.98±0.77(2 – 4)		0.001 ^s

p value reached from unpaired t-test

Discussion:

Atrial Fibrillation is the most common arrhythmia after cardiac operations occurring in up to 18-53% in which CPB is used. In our study MVR was predominantly performed in both groups which was 80% of patients. AVR was done in 6.7% patients in group A and none in group B. DVR was done 13.3% patients in group A and 20% patients in group B (Table IV). No statistically significant association was found in types of heart surgery in the above table. Our study is consistent with the study done by Selvaraj et al.⁹

In our study Lignocaine was required 33.3% and 40% ingroup A and group B respectively with nonsignificant association. Cardioversion were required 10% and 33.3% ingroup A and group B respectively with significant association. 3.3% patients in the group A required temporary pacemaker and 16.7% patients in group B required temporary pacemaker and the association was statistically not significant. Our study is consistent with the study done by Selvaraj et al.⁹

In a study of Selvaraj et al. the mean heart rate 5 minute after drug infusion was observed

85.50±21.49 min in Group A and Group B was 91.3±23.29 min. In our study the mean heart rate 5 minute after drug infusion was observed 84.40±9.20 min in Group A and Group B was 93.07±8.69 min. The difference was statistically not significant.⁹

AF was observed in 8 (26.7%) patients in group A and 18 (60%) patients in group B, which is significant. VT developed in no patients in group A and 6.7% in group B with statistically insignificant association. Our study is consistent with other studies.^{9,10}

In a study of Selvaraj et al the incidence of atrial fibrillation at the end of surgery was 9.5% in amiodarone group and 32.5% in control group. In our study the incidence of atrial fibrillation at the end of surgery in study patients and found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B. Our study is consistent with the above study.⁹

In our study the recurrence of atrial fibrillation in ICU within 24 hours was found in 8 (26.7%) patients in group A and in 16 (53.3%) patients in group B. Our study is consistent with the study done by Selvaraj et al.⁹

In our study the number of patients needed treatment of atrial fibrillation found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B needed treatment of AF. Statistically significant association was found in the number of patients needed treatment. Our study is consistent with the study done by Selvaraj et al.⁹

In a study of Selvaraj et al.⁹ the incidence of atrial fibrillation on discharge from hospital was 26.2% in amiodarone group and 67.5% in control group. In our study the incidence of atrial fibrillation on discharge from hospital in study patients and found that 8 (26.7%) patients in group A and 16 (53.3%) patients in group B.

In our study the mean duration of ICU stay was 2.11±0.30 days in Group A and Group B was 2.79±0.77 days. The difference was statistically significant. Our study is consistent with the study done by Selvaraj et al.⁹ But in our study the mean duration of post-operative stay was 7.20±0.66 days in Group A and Group B was 7.45±0.60 days. The difference was statistically insignificant. This is consistent with the study done by Selvaraj et al.⁹

So, from above finding it may be concluded that Intraoperative prophylactic single loading dose of amiodarone reduces incidence of atrial fibrillation and improve outcome in patients with rheumatic valvular heart disease undergoing valve replacement surgery.

Conclusion:

From our study it may be concluded that A single intra operative dose of intravenous amiodarone increases the incidence of conversion of atrial fibrillation to normal sinus rhythm. When AF persisted, use of amiodarone reduces the frequency of need for cardioversion and the energy required for it. Recurrence of AF until hospital discharge and occurrence of fast ventricular rate is also reduced.

Limitation of the study:

We have got some limitations of this study. It was not a randomized control trial, Study was conducted in a single center, sample size was small and we followed the patients for only hospital stay period.

Recommendation:

We recommend future study involving a prospective randomized multi-center trial with larger sample size and long term follow up to confirm our finding and clarify whether intraoperative prophylactic single loading dose of amiodarone reduces incidence of atrial fibrillation in patients with rheumatic valvular heart disease undergoing valve replacement surgery.

Conflict of Interest - None.

References:

1. Fuster V, Ryden LE, Gibbson RJ, Antman EM, Klein WW. ACC/AHA/ESC Guideline for the management of patient with atrial fibrillation. *J Am Coll Cardiol* 2001; 38: 1260-1261.
2. Yasser MA, Elmistekawy EM, Hammad AM. Intraoperative loading dose of amiodarone for prophylaxis against atrial fibrillation after valvular heart surgery. *Anesth Essays Res* 2010; 4 : 96-101.
3. Koniari L, Apostolakis E, Rogkakou C, Baikoussis NG, Dougenis D. Pharmacologic prophylaxis for atrial fibrillation following cardiac surgery: a systematic review. *J Cardiothorac Surg* 2010; 5: 121-126.
4. Redle JD, Khurana S, Marzan R, Mccullough PA, Stewart JR, Westveer DC, et al. Prophylactic oral amiodarone compared with placebo for prevention atrial

- fibrillation after valvular surgery. *Am Heart J* 1999; 138 : 144-150.
5. Julian DG, Cowan JC, McLenachan JM. *Disorders of rate rhythm and conduction, in Cardiology*. 8th edition. UK: Elsevier Saunders, 2005 ; 159-202.
 6. Hohnloser SH, Kuck KH, Lilienthal J, for the PIAF Investigators. Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial. *Lancet* 2000; 356 (9244): 1789- 1794.
 7. Cantillon DJ, Saliba WI, Wazni OM, Kanj M, Starling RC, Tang WH1, et al. Low cardiac output associated with ventricular tachyarrhythmias in continuous-flow LVAD recipients with a concomitant ICD (LoCo VT Study). *J Heart Lung Transplant* 2014 Mar; 33(3): 318-20.
 8. Bojar RM. Cardiovascular Management. In: *Manual of Perioperative Care in Adult Cardiac Surgery*. 4th edition. Massachusetts. Blackwell publishing, 2005; 250-251.
 9. Selvaraj T, Kiran U, Das S, Chauhan S, Sahu B, Gharde P. Effect of single intraoperative dose of amiodarone in patients with rheumatic valvular heart disease and atrial fibrillation undergoing valve replacement surgery. *Ann Card Anaesth* 2009; 12 : 10-16.
 10. Kar SK, Dasgupta CS, Goswami A. Effect of prophylactic amiodarone in patients with rheumatic valve disease undergoing valve replacement surgery. *Ann Card Anaesth* 2011; 14 :176-182.