

Effect of Pre-operative Amiodarone on Atrial Fibrillation after Off-Pump Coronary Artery Bypass Surgery

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Abstract:

Background: Atrial Fibrillation (AF) is common in early recovery period after cardio-thoracic surgery. There have been several pharmacological and non-pharmacological strategies suggested for prevention against AF after coronary artery bypass grafting. The purpose of this study was to evaluate the effect of oral amiodarone in the prevention of atrial fibrillation in patients who underwent off pump coronary artery bypass graft (OPCAB).

Methods: This interventional study was conducted from February 2017 to January 2018 in the department of cardiac surgery, National Institute of Cardiovascular Disease (NICVD) Dhaka, Bangladesh. By purposive sampling a total of 100 patients having sinus rhythm who will undergo OPCAB were selected for the study. Among them 50 patients (Group-A) got amiodarone (600mg/day started 3 days prior to surgery) and 50 patients (Group-B) did not get amiodarone. Two (2) patients of group-A were excluded from the study due to conversion to on pump from off pump during operation. So, finally group A had 48 patients and group-B had 50 patients. Preoperative electrocardiography (ECG), serum electrolytes (e.g. potassium & magnesium), thyroid function test, liver function test and echocardiogram were done in all patients under study. Per-operative occurrence of AF was assessed

on operation theatre monitor. Each patient was evaluated by continuous ECG up to 5th post-operative day (POD). Serum potassium & magnesium were measured in every alternative day up to 5th POD. ECG with long lead tracing was done for all patients on the day of hospital discharge & was recorded. Data were analyzed by SPSS 24.0 (Statistical Package for the Social Sciences) and tested by student T-test and Chi-square test. $P < 0.05$ was considered significant.

Results: Pre-operative baseline characteristics were similar in both groups. Per-operative and post-operative AF occurred more frequently in group B than group A. Those were 10(20.83%) and 32(64.0%) per-operative, 9(18.75%) and 31(36.0%) immediate post-operative period respectively in group A and group B. The result was statistically significant (P value $< .05$). Post-operative amiodarone used in all patients who developed AF irrespective of groups. This also decreased AF significantly. There were statistically no significant difference found in postoperative serum electrolytes and use of inotropes, anti-arrhythmic drugs. All patients recovered well.

Conclusion: This study concluded that preoperative oral administration of amiodarone can prevent the occurrence of atrial fibrillation in patients undergone Off Pump Coronary Artery Bypass (OPCAB).

Key words: Amiodarone, Postoperative atrial fibrillation,

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Introduction:

Atrial tachyarrhythmias are common during early recovery after cardiothoracic surgery, occurring with a frequency

ranging from 10% to 30%^{1, 2}. Atrial fibrillation (AF) often occurs in patients after both conventional and off-pump

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Coronary Artery Bypass Graft (OPCAB)^{3,2}. AF after OPCAB most often develops between the second and fifth postoperative day with a peak incidence in the 2nd to 3rd postoperative days¹

The incidence is mainly dependent on the type of operation as well as on patient characteristics. As the population is aging and number of cardiac surgical operations is increasing, incidence of AF has gradually increased recently. Moreover, AF brings about several problems, including hemodynamic derangement, thromboembolic complications, longer time of hospital stay, and higher costs.³

There have been several pharmacological and non-pharmacological strategies suggested for prevention against AF after coronary artery bypass grafting (CABG). The mechanism of atrial fibrillation involves two processes, focal triggers of enhanced automaticity and multiple wavelets of macro-reentry activation migrating across the atria⁴. Risk factors for developing atrial fibrillation include inflammation, oxidative stress, and atrial morphology Also β -blockers withdrawal, right coronary artery occlusion, reduced left ventricular function & left ventricular hypertrophy are risk factors as well⁵. However the aging is a constant independent predictor for the incidence of AF after OPCAB¹. Although AF in the early postoperative period is often sudden and self-limiting but can be continued for weeks and leads to increased morbidity, cardiac loss, embolic complications and the need for pacemaker⁶

Amiodarone acts as anti-arrhythmic drug mainly by blocking potassium (K⁺) channel and increasing the refractory period. It can be given both in oral & intravenous form. Usual dosage varies from 600-1200 mg/day as loading and 200-600 mg/day as maintenance. It can cause bradycardia, QT prolongation, hypotension, AV conduction disturbances, peripheral vasodilation, hypo or hyperthyroidism, chemical pneumonitis & pulmonary fibrosis, photosensitivity, ocular deposition, peripheral neuropathy etc. Most of these complications are dose dependent & rare in short term low dose use⁷

Preoperative prescription of amiodarone is an interventional method which may reduce the incidence of AF after cardiac surgery⁶. Using low-dose intravenous or oral administration for 3-5 days before and after CABG surgery has reduced the incidence of AF.³

Despite the high frequency of AF encountered during clinical practice, the concept of a proactive preventative measures became very appealing. Therefore the present study investigated the role of preoperative oral amiodarone in prevention of AF following OPCAB.

Materials and methods:

It is an interventional study conducted in department of cardiac surgery, National Institute of Cardiovascular Disease (NICVD), Dhaka, Bangladesh during the period of 1st

February 2017 to 31st January 2018 with the consent of ethical committee of this institute. By purposive sampling a total of 100 patients having sinus rhythm will undergo OPCAB were selected for the study. Among them 50 patients (Group-A) got amiodarone and 50 patients (Group-B) did not get amiodarone. Two (2) patients of group-A were excluded from the study due to conversion to on pump from off pump during operation. So, finally group A had 48 patients and group-B had 50 patients. Patients with sinus bradycardia (Heart rate below 60 beats/min), on other anti-arrhythmic drugs (Except β -blockers), Redo, Urgent or Emergency CABG, patients with thyroid or liver dysfunction were excluded from the study. The objective of this study was to evaluate the effect of pre-operative oral amiodarone in the prevention of atrial fibrillation for patients undergoing OPCAB. Also to evaluate incidence of postoperative AF after OPCAB in both groups and to compare the outcome between two groups. The patients under study were hospitalized at least 7 days before surgery. Preoperative ECG, serum electrolytes (e.g. potassium & magnesium), thyroid function test, liver function test and echocardiogram were done in all patients under study. Amiodarone (Trade name: Pacet) was prescribed at a dosage of one tablet (200 mg) three times daily (600mg/day) 3 days prior to surgery. Other medical therapy was unchanged. Per operative occurrence of AF was assessed on operation theatre monitor. After OPCAB surgery, each patient was transferred to intensive care unit and then at 3rd postoperative day was transferred to a step down or high dependency unit (HDU).

In intensive care unit (ICU) & HDU, patients were evaluated by continuous ECG monitoring. Inotropic supports given to each patient up to 5th postoperative day. Serum potassium & magnesium were measured in every alternative day up to 5th postoperative day. An episode of atrial fibrillation was counted if it persisted for more than five minutes. Electrocardiography (ECG) with long lead tracing was done for all patients on the day of hospital discharge & was recorded. At the end of study, patients' data was analyzed by SPSS software version 24.0. The numerical data obtained from the study was analyzed and significance of difference was estimated by using statistical methods. Continuous variables were expressed as mean values \pm standard deviation and compared using Student's t-test. Categorical variables were expressed as frequencies with percentages and compared using Chi-square test when and where appropriate. $P < 0.05$ was considered significant.

Result:

Total 100 patients were selected for OPCAB. Among them 50 patients (Group A) got amiodarone and 50 patients (Group B) did not get amiodarone. 2 patients of group A were excluded from the study due to conversion to on pump from off pump during operation. So, finally group A had 48 patients and group B had 50 patients. The findings of the study obtained from data analysis are presented below.

Table-I
*Comparison of Preoperative data between
two groups (N=98)*

Preoperative variables	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Age(years)	60.68±7.47	60.06±6.16	-
Sex	40(83.33%)	45(90.0%)	-
Male	8(16.67%)	5(10.0%)	
Female			
Pulse rate			0.646 ^{ns}
Normal	45(93.75%)	48(96.0%)	
Tachycardia	3(6.25%)	2(4.0%)	
Pulse rhythm			-
Regular	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	
ECG			-
Normal	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	
TFT			-
Euthyroid	48(100.0%)	50(100.0%)	
Hypothyroid	0(0.0%)	0(0.0%)	
Hyperthyroid	0(0.0%)	0(0.0%)	
LFT			-
Normal	48(100.0%)	50(100.0%)	
Abnormal	0(0.0%)	0(0.0%)	
LVEF			0.545 ^{ns}
≥ 50%	23(47.92%)	20(40.0%)	
< 50%	25(52.08%)	30(60.0%)	
Coronary artery involved			.565 ns
Single	4(8.33%)	3(6.0%)	
Double vessel	16(31.25%)	17(34.0%)	
Triple vessel	28(60.42%)	30(60.0%)	

Table-II
Comparison of per-operative data between two groups (N=98)

Per operative variables	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Occurrence of AF (monitor)			<0.001*
Yes	10(20.83%)	32(64.0%)	
No	38(79.17%)	18(36.0%)	
Grafts given			0.629ns
One	9(18.75%)	6(12.0%)	
Two	14(29.17%)	17(34.0%)	
Three	25(51.08%)	27(54.0%)	

Figures in the parentheses indicate corresponding percentage; ns = not significant, *significant Chi-squared Test was done to analyze the data.

Table-III
Comparison of immediate Postoperative data between two groups (N=98)

Postoperative variables	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Postoperative ECG			
Normal	39(81.25%)	19(38.0%)	<0.001*
AF	9(18.75%)	31(62.0%)	
Postoperative BP			
Low	7(14.6%)	0(0.0%)	<0.001*
Normal	41(85.4%)	36(72.0%)	
High	0(0.0%)	14(28.0%)	
Postoperative use of anti-arrhythmic drug			
Yes	10(20.8%)	32(64.0%)	0.097 ^{ns}
No	38(79.2.0%)	18(36.0%)	

Figures in the parentheses indicate corresponding percentage; ns = not significant, *significant
Chi-squared Test was done to analyze the data.

Table-IV
Postoperative ECG monitoring between two groups (N=98)

Postoperative ECG monitoring	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Continuous ECG (ICU) in 1 st POD			0.006*
Normal	39(81.2%)	27(54.0%)	
AF	9(18.8%)	23(46.0%)	
Continuous ECG (ICU) in 2 nd POD			<0.001*
Normal	38(79.2%)	22(44.0%)	
AF	10(20.8%)	28(56.0%)	
ECG in HDU in 3 rd POD			<0.001*
Normal	48(100.0%)	30(60.0%)	
AF	0(0.0%)	20(40.0%)	
ECG in HDU in 4 th POD			0.063 ^{ns}
Normal	48(100.0%)	45(90.0%)	
AF	0(0.0%)	5(10.0%)	
ECG in HDU in 5 th POD			0.240 ^{ns}
Normal	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	
12 Lead ECG on discharge			0.068 ^{ns}
Normal	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	

In table 1 showed preoperative pulse rhythm, ECG, TFT, LFT were normal in all patients (100%). Pulse rate were normal in 93.75% and 96% of group A and group B respectively, tachycardia in 6.25% and 4% of group A and group B respectively. LVEF was $\geq 50\%$ in 47.92% and 40% of group A and group B respectively and was $< 50\%$ in 52.08% and 60% of group A and group B respectively. Regarding coronary artery involvement, single vessel involvement was 8.33% and 6% in group A and group B respectively; Double vessel involvement was 31.25% and 34% in group A and group B respectively; Triple vessel involvement was 60.42% and 60% of group A and group B respectively. All the results were statistically not significant. ($P > 0.05$).

In table-2, per-operatively one graft was given for 18.75% and 12% in group A and group B respectively; two grafts were given for 29.17% and 34% in group A and group B respectively; three grafts were given for 52.08% and 54% in group A and group B respectively. P value was > 0.05 which is statistically not significant.

Regarding AF occurrence (seen in monitor) per operatively, AF occurred 20.83% in group A and 64% in group B; AF did not occur 79.17% in group A and 36.0% in group B. The result was statistically significant (P value < 0.05).

In table 3, postoperative pulse was normal in 81.25% and 38.0% of group A and group B respectively; was AF in 18.75% and 62.0% of group A and group B respectively. The result was statistically significant (P value < 0.05).

Postoperative BP was low in 14.6% and 0.0% of group A and group B respectively; was normal in 85.4% and 72.0% of group A and group B respectively and was high in 0.0% and 28.0% of group A and group B respectively. The result was statistically significant (P value < 0.05).

Postoperative antiarrhythmic drugs were used in 20.8% and 64.0% of group A and group B respectively and not used in 79.2% and 36.0% of group A and group B respectively. The result was statistically not significant (P value > 0.05).

In table 4 postoperative ECG in 1st POD was normal in 81.2% and 54.0% of group A and group B respectively and AF was present in 18.8% and 46.0% of group A and group B respectively. Postoperative ECG in 2nd POD was normal in 79.2% and 44.0% of group A and group B respectively and AF was present in 20.8% and 56.0% of group A and group B respectively. Postoperative ECG in 3rd POD was normal in 100.0% and 60.0% of group A and group B respectively and AF was present in 0.0% and 40.0% of group A and group B respectively. On 3rd and 4th POD, ECG was normal in all patients of group A with no AF. But in group B, AF was present in 40% and 10% patient respectively. The

results were statistically significant up to 3rd POD (P value < 0.05).

Regarding 12 lead ECG on discharge, ECG was normal in all patients of both groups. The results were not statistically significant (P value ≥ 0.05).

Discussion:

Ever since the establishment in 1981, National Institute of Cardiovascular Diseases (NICVD), Dhaka is performing a major role in cardiac surgery. This study was carried out in the department of cardiac surgery during the period of February, 2017 to January, 2018. As NICVD plays the central role in the field of cardiac surgery and off pump coronary artery bypass (OPCAB) in Bangladesh, study population was chosen from the institute. On average, around 300 CABG (both on pump and off pump) cases are performed at NICVD in every year⁸. Total 100 patients were selected for this study, divided into two groups. Out of them 50 patients (Group A) was intended to receive oral amiodarone before surgery and 50 patients (Group B) did not receive any amiodarone. But two cases were excluded from group A due to conversion from off pump to on pump CABG. Finally total 98 cases were included under study (48 for Group A and 50 for Group B). The aim of this study was to determine whether preoperative oral amiodarone have any effect in the prevention of atrial fibrillation in patients undergone OPCAB.

The mean age of group A patients were 60.68 ± 7.47 years and group B patients were 60.06 ± 6.16 years both ranging from 40 to 70 years. Analysis revealed that no statistically significant mean age difference was found between group A and group B patients ($p > 0.05$). Homogenously both group had highest percentage (54.17% for group A and 50.0% for group B) of age group from 61-70 years.

In the study, majority of the patients were male in both groups. In group A and group B, 83.33% and 90.0% were male and the rest 16.67% and 10.0% were female respectively. Homogenous distribution of sex was also present in both groups.

Preoperative pulse rhythm, ECG, TFT, LFT were normal in all patients (100%). In group A and group B, pulse rate were normal in 93.75% and 96% and tachycardia in 6.25% and 4% respectively. Several studies also found preoperative normal heart rate, normal BP and normal liver function test^{8,9,11}

In echocardiography, LVEF was $\geq 50\%$ in 47.92% and 40% of group A and group B respectively and was $< 50\%$ in 52.08% and 60% of group A and group B respectively. Results were statistically not significant

Regarding coronary artery involvement, triple vessels involvements were found in majority of the patients. Statistically, single vessel involvement was 8.33% and 6% in group A and group B respectively; Double vessel involvement was 31.25% and 34% in group A and group B respectively; Triple vessel involvement was 60.42% and 60% of group A and group B respectively. All the results were statistically not significant. Several studies also found majority of patient with triple vessels involvement followed by double vessels and single vessel²

Three grafts or more were given in majority of the patients. Per operatively, one graft was given for 18.75% and 12% in group A and group B respectively; two grafts were given for 29.17% and 34% in group A and group B respectively; three grafts were given for 52.08% and 54% in group A and group B respectively. P value was >0.05 which is statistically not significant. Onk and colleagues also found majority of patients (60%) requiring three grafts^{5,12}

Per operatively, AF occurred more frequently in group B than group A. AF occurred 20.83% in group A and 64% in group B; AF did not occur 79.17% in group A and 36.0% in group B. The result was statistically significant (P value <0.05).

Postoperative pulse was within normal limit in majority of the patients in both groups (81.25% and 38.0% in group A and group B respectively. Postoperative AF was high in group B in comparison to group A (18.75% and 36.0% in group A and group B respectively). The result was statistically significant (P value <0.05).

Group A showed hypotension more in comparison to group B postoperatively (14.58% and 0.0% of group A and group B respectively). Postoperative BP was normal in 85.42% and 72.0% of group A and group B respectively and was high in 0.0% and 28.0% of group A and group B respectively. The result was statistically significant (P value <0.05). Esmail with his colleagues found systolic BP 125±15 mm(Hg) and diastolic BP 76±10 mm(Hg) which were also within normal limit.^{1, 13}

Dopamine was used in 93.8% and 100% of group A and group B respectively. In few patients (6.0% and 18.0% of group A and group B respectively) dobutamine was used in exchange of dopamine after 1st postoperative day. But majority of the patient in both groups did not require dobutamine (94.0% and 82.0% of group A and group B respectively). Some patients required adrenaline (14.0% and 28.0% of group A and group B respectively) along with either dopamine or dobutamine. Noradrenaline was also used in 10.0% and 24.0% of group A and group B respectively with dopamine or dobutamine. No inotropic drugs were used in

high dose. All the results were statistically not significant (P value >0.05).

Postoperative AF was found in both groups in different proportions. Amiodarone (trade name: Pacet) was given in some patients of group A (18.8%) up to 1st POD. But amiodarone was required up to 3rd POD in Group B (46.0%). Postoperative ECG in 1st POD was normal in 81.2% and 54.0% of group A and group B respectively. Postoperative ECG in 2nd POD was normal in 79.2% and 44.0% of group A and group B respectively and AF was present in 20.8% and 56.0% of group A and group B respectively. Postoperative ECG in 3rd POD was normal in 100.0% and 60.0% of group A and group B respectively and AF was present in 0.0% and 40.0% of group A and group B respectively. On 3rd and 4th POD, ECG was normal in all patients of group A with no AF. But in group B, AF was present in 40% and 10% patient respectively. The results were statistically significant up to 3rd POD (P value <0.05).

Both preoperative serum potassium and magnesium was normal in both group. Postoperatively, normal serum potassium and magnesium were found in majority of the patient. Mild hypokalemia and hypomagnesaemia was found more in group A than group B. This electrolyte imbalance may be due to excessive diuretics use and fluid and salt restriction. Though amiodarone itself can cause hypokalemia and hypomagnesaemia, but it is rare in low dose and short term use¹⁴.

In 1st POD, serum potassium was normal in 92.0% and 96.0% of group A and group B respectively; was low in 8.0% and 4.0% of group A and group B respectively. Electrolyte imbalances were corrected accordingly. In 3rd POD potassium was normal in 90.0% and 94.0% of group A and group B respectively; was low in 10.0% and 6.0% of group A and group B respectively. In 5th POD potassium was normal in 90.0% and 96.0% of group A and group B respectively; was low in 10.0% and 4.0% of group A and group B respectively. All the results were statistically not significant (P value >0.05). Regarding serum magnesium, in 1st POD magnesium was normal in 94.0% and 98.0% of group A and group B respectively; was low in 6.0% and 2.0% of group A and group B respectively. In 3rd POD magnesium was normal in 92.0% and 96.0% of group A and group B respectively; was low in 8.0% and 4.0% of group A and group B respectively. In 5th POD magnesium was normal in 88.0% and 92.0% of group A and group B respectively; was low in 12.0% and 8.0% of group A and group B respectively. All the results were statistically not significant (P value >0.05).

Postoperative pulse and BP were normal in majority of the groups. Few members of group A showed bradycardia and hypotension. But they were self-limiting and reverted to

normal in short duration. Postoperatively, Pulse was low in 10.0% and 0.0% of group A and group B respectively; was normal in 62.0% and 64.0% of group A and group B respectively; was high in 28.0% and 36.0% of group A and group B respectively. Blood pressure was low in 6.0% and 0.0% of group A and group B respectively; was normal in 74.0% and 70.0% of group A and group B respectively; was high in 20.0% and 30.0% of group A and group B respectively. All the results were statistically not significant (P value >0.05). This observations were similar to the study of William H, et al.¹⁵

There was no incidence of death in the study population

Conclusion:

In conclusion, our study results suggest that amiodarone administered according to this scheme reduces the onset of post-operative AF in a safe and well-tolerated manner. Thus, prophylactic treatment can be considered effective and should be used routinely for patients undergoing CABG in order to prevent AF thereby reduce the duration of hospital stay and costs.

Conflict of interest: We have no conflicts of interests to disclose.

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