

# Prophylactic Use of Amiodarone in Coronary Artery Bypass Graft Patients with Less Ejection Fraction

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## ABSTRACT

**Background:** Dysrhythmias like atrial fibrillation are most common in post-CABG patients, with an incidence of around 40%. Prophylactic amiodarone treatment decreases the occurrence of dysrhythmias in low ejection fraction patients. Some studies have reported that the benefit of giving amiodarone is more in high-risk patients such as those having older age, higher angina class, diabetes, and severe coronary artery disease (CAD). This study aims to determine the role of amiodarone prophylaxis in the prevention of dysrhythmias following CABG in patients with low ejection fractions.

**Methodology:** In this non-randomized study, we included 150 patients who underwent CABG at Multan Institute of Cardiology from Jan-2019 to Aug-2019, having EF  $\leq$ 35%. In the amiodarone group (N=75), 3 mg/Kg of amiodarone was given through CPB machine after removal of the X-clamp and before weaning from cardiopulmonary bypass. While in the remaining 75 patients, no anti-arrhythmic drug treatment was given during the peri-operative period. The occurrence of postoperative arrhythmia during the primary hospital stay after surgery was a primary study endpoint.

**Results:** There was no significant difference between patients' mean age, gender, BMI, and the number of grafts in the amiodarone group  $3.9 \pm 0.53$  and control group  $3.04 \pm 0.50$  (p-value 0.20). The frequency of Post operative Atrial fibrillation (POAF) was significantly different in both groups. In the amiodarone group, 13 (17.3%) patients developed POAF, and in the control group, POAF occurred in 25 (33.3%) patients (p-value 0.024).

**Conclusion:** Amiodarone prophylaxis significantly lowers the incidence of POAF after CABG in low EF patients.

**Keywords:** Amiodarone prophylaxis, Coronary artery bypass grafting (CABG), Post-operative atrial fibrillation (POAF).

### Authors' Contribution:

<sup>1</sup>Conception; Literature research; manuscript design and drafting; <sup>2</sup>Critical analysis and manuscript review; <sup>3</sup>Data analysis; Manuscript Editing.

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## Introduction

Dysrhythmias like atrial fibrillation (AF) and atrial flutter are most common in post coronary artery bypass graft (CABG). The incidence rate is around 40% to 60%,<sup>1,2</sup> the incidence of AF is increasing in cardiac surgery gradually as compared to the past. These arrhythmias usually occur on the 3rd to 5th postoperative day.<sup>3</sup> Atrial fibrillation and atrial flutter may cause post-operative stroke, heart

failure, myocardial infarction, re-intubation and increase the length of hospital stay.<sup>4</sup> Dysrhythmias are independent risk factors of deterioration in the post-cardiac surgery period and cause long term morbidity and mortality.<sup>5,6,7</sup>

There have been some pharmacological and non-pharmacological techniques recommended for post operative atrial fibrillation (POAF) after CABG.<sup>8,9</sup>

Amiodarone is categorized as a class III agent (Vaughn-Williams classification), which combines anti-beta-adrenergic effects with sodium, potassium, and calcium channel blocking properties<sup>10,11,12</sup>. Amiodarone prolongs the AV nodal refraction and conduction time due to calcium-channel blockade. At a constant dose, bradycardia could happen. At a low dose, amiodarone blocks the sodium channel. It may also reduce automaticity by diminishing voltage-dependent inward current, it decreases the phase-4 slopes of an action potential. Long-term therapy prolongs the refractory periods of the atrium and ventricles.<sup>13</sup>

Patients with low ejection fraction are more prone to dysrhythmias in comparison to normal ejection fraction patients. The occurrence of dysrhythmias is a significant contributor to morbidity and mortality in these patients. Therefore, in the present study, we investigated the role of amiodarone as a prophylactic drug in the prevention of dysrhythmias following CABG in patients with low EF.

## Methodology

In this non-randomized comparative study, we included patients who underwent CABG at Multan Institute of Cardiology for 07 months from Jan-2019 to July-2019. Patients planned for elective isolated CABG were included in this analysis. Patients who were diagnosed with having any arrhythmia on admission such as atrial fibrillation or flutter, or any ventricular arrhythmia, those having a previous history of use of anti-arrhythmic drugs, or the patients who have received amiodarone before going on bypass were excluded. Patients having severe pulmonary dysfunction requiring hospital admission were also excluded. All patients signed a written consent before being included in this study. We also took approval from the hospital Institutional Review Board before starting the recruitment of patients.

One day before surgery, data regarding baseline demographics such as age, gender, BMI, presence of co-morbid diseases, and severity of CAD was taken.

The sample size for this study was calculated using the results of a study by Tokmakoglu ET al.<sup>14</sup> They reported POAF in 8.3% of patients who received amiodarone prophylaxis versus in 33.6% of patients in the place group, taking  $(1-\beta)$  80% and  $(\alpha)$  5.0%, the sample size was 47 patients in each group. We took 75 patients in each group making a total number of 150 patients being included in the study. In group I, peri-operative amiodarone was given to 75 patients, while in the remaining 75 patients no anti-arrhythmic treatment was given during the peri-operative period.

**In the intervention(amiodarone) group**, 3 mg/Kg of amiodarone was given through CPB machine, after removal of the X-clamp and before weaning from cardiopulmonary bypass.

The occurrence of postoperative arrhythmia (POAF and bradycardia) during the primary hospital stay after surgery was the primary study objective.

For data interpretation and analysis, we used SPSS v23 software. For comparison of continuous variables, sample t-test statistics were used. While for comparison of qualitative variables, the chi-square test was used. P-value  $\leq 0.05$  was taken as statistically significant.

## Results

There were 75 patients in each group. There was no significant difference between the mean age and gender of patients in the two groups. The mean Body mass index (BMI) was not different between the two groups of patients. There was also no significant difference in pre-surgery Canadian Cardiovascular Society (CCS) class and EF between the groups. Detailed information is given in Table I.

Regarding per-operative data, there was no significant difference in the number of grafts in the amiodarone group  $3.9 \pm 0.53$  and the control group  $3.04 \pm 0.50$  (p-value 0.20). Cardiopulmonary bypass

(CPB) time and cross-clamp (X-clamp) time in both groups were also almost the same. Intra-aortic balloon pump (IABP) was insertion was done in 10 (13.3%) patients in the amiodarone group and in 08 (10.7%) patients in the control group (p-value 0.80) (Table-II).

The frequency of POAF-was significantly different in both groups. In the amiodarone group, 13 (17.3%) patients developed POAF and in the control group, POAF occurred in 25 (33.3%) patients (p-value 0.024) (Table-III).

**Table-I: Baseline Characteristics of patients.**

Characteristics	Amiodarone group	Control group	p-value
Number,(n)	75	75	
Age (years)	55.44+_10.78	57.90+_9.6	0.14
Gender (Male/Female)	58(77.3%)/17(22.7%)	59(78.7%)/16(21.3%)	0.84
BMI(kg/m <sup>2</sup> )	26.76±4.94	26.57	0.81
<b>Canadian Cardiovascular Society Class (CCSC), n (%)</b>			
I	10 (13.5%)	9(12.7%)	0.73
II	1 (1.3%)	2 (2.7%)	
III	60 (80.0%)	57 (76%)	
IV	4 (5.3%)	7 (9.3%)	
Ejection fraction (%)	33.13±2.82	32.44±3.2	0.16
<b>Major additional diseases</b>			
Hypertension, n (%)	40(55.6%)	32(44.4%)	0.14
Diabetes mellitus, n (%)	35(54.7%)	29(45.3%)	0.40

**Table-II: Operative values of patients**

	Amiodarone	Control	p-value
Number (n)	75	75	
Number of grafts	3.9 ± 0.53	3.04±0.50	0.20
CPB time (min)	117 ± 29.9	116±29.6	0.91
X-Clamp time	66 ± 21.85	66.56±18.0	0.98
IABP, n (%)	10 (13.3%)	08 (10.7%)	0.80

**Table-III. Comparison of Study Endpoints.**

	Amiodarone	Control	p-value
AF after surgery, n (%)	13 (17.3 %)	25 (33.3%)	0.024*
Symptomatic bradycardia after surgery	07(9.3%)	04 (5.3%)	0.34

**P<0.05 \***

## Discussion

Prophylactic amiodarone treatment decreased the occurrence of dysrhythmias (AF) in low ejection fraction patients.<sup>15,16</sup> Some studies have reported that the benefit of giving amiodarone is more in high-risk patients such as those having older age, higher angina class, diabetes, and severe CAD.<sup>17,18</sup> In the present study, we included only high-risk patients; those having low EF (≤35%). Moreover, different regimens have been described in the literature, in the present study we gave amiodarone through a cardiopulmonary bypass circuit after removing the X-clamp.

Studies have also reported variability in outcomes using peri-op IV administration followed by oral administration of Amiodarone.<sup>19</sup> A study by Moroi et al. compared the IV amiodarone administration followed by 5 days of oral amiodarone with a

placebo drug after CABG surgery, the authors reported supraventricular arrhythmias in 8.0% of patients in amiodarone versus in 20% of patients in the placebo group. While ventricular arrhythmias occurred in 15.0% of patients in amiodarone versus 33.0% of patients in the placebo group.<sup>18</sup>

A study by Thanavaro et al. compared the prophylactic amiodarone administration with the control group. The authors reported a significantly lower incidence of postop AF, 17.0% in the amiodarone group versus 25.9% in patients who did not receive amiodarone.<sup>20</sup> Another study by Esmail et al. also reported similar results. In their study, POAF occurred in 16.1% of patients in whom amiodarone was given versus in 33.9% of patients in whom it was not given.<sup>21</sup> The major difference between these studies and the present study is that these authors included all patients planned for CABG and we only included patients with low EF.

In the present study, AF occurred in 17.3% of patients in the amiodarone prophylaxis group versus in 33.3% of patients without prophylactic amiodarone. In our comparative study, the amiodarone treatment was well tolerated and it reduced the significant occurrence of post-operative AF. Amiodarone treated group patients had a low number of side effects without a significant difference compared with the control group patients, a more prophylactically effective amiodarone concentration among all low ejection fraction patients should reduce the onset of AF after CABG.

Amiodarone didn't build the operative complications. The prophylactic amiodarone treatment of high-risk patients was not associated with pro-arrhythmia or reduced EF.

There are limitations of this study, the sample size of this study was small and we only took patients who underwent on-pump CABG. The role of amiodarone for patients undergoing off-pump CABG, and those undergoing valvular heart surgeries need to be evaluated further.

## Conclusion

Amiodarone prophylaxis significantly lowered the incidence of POAF after CABG in patients with low EF. Amiodarone is easy to administer and is a valuable adjuvant for the prevention of postoperative dysrhythmias.

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**Conflict of Interest: None**

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