

# INTRA-OPERATIVE ADMINISTRATION OF AMIODARONE AGAINST POST-OPERATIVE ATRIAL FIBRILLATION IN PATIENTS UNDERGOING ELECTIVE CARDIAC SURGERY

# KHAN AK<sup>\*1</sup>, PANNU FY<sup>2</sup>, AMIN M<sup>3</sup>, IQBAL S<sup>4</sup>, MUQEET S<sup>4</sup>

<sup>1</sup>Department of Cardiac Surgery, Punjab Institute of Cardiology Lahore, Pakistan <sup>2</sup>Department of Cardiology, Mayo Hospital Lahore, Pakistan <sup>3</sup>Department of Cardiology, Pakistan Kidney & Liver Institute & Research Lahore, Pakistan <sup>4</sup>Department of Cardiology, Rahbar Medical and Dental College Lahore, Pakistan \*Corresponding author`s email address: <u>drakkhan\_kemu@yahoo.com</u>

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**Abstract:** Postoperative atrial fibrillation (*AF*) is a common complication following cardiac surgery, associated with increased morbidity, prolonged hospital stays, and higher healthcare costs. Amiodarone is frequently used as a prophylactic measure to reduce the incidence of *AF*, but its efficacy and safety in this context remain controversial. **Objective:** To assess the outcome of peri-operative amiodarone administration for the prevention of atrial fibrillation in patients undergoing elective cardiac surgery. **Methods:** A prospective study was conducted in the Cardiac Surgery Department of Punjab Institute of Cardiology, Lahore from November 2023 to November 2024. A total of 150 patients undergoing elective cardiac surgery at high risk of developing postoperative atrial fibrillation were selected. The cases group included 75 patients who were administered 400 mg amiodarone twice daily for 5 days before surgery and 5 days after surgery once a day. The control group included 75 patients who were administered placebo treatment. Cardiac surgeries were performed as per usual procedure without any changes. **Results:** Atrial fibrillation occurred in 30 (40%) patients in the control group and 27 (36%) patients in the cases group, however, this difference was insignificant. None of the patients died in both groups as reported after 6 weeks follow-up. 6 (8%) patients in the cases group experienced bleeding complications and 3 (4%) patients in the cases groups. **Conclusion:** No difference in clinical outcomes was observed by administration of amiodarone for prevention of post-op atrial fibrillation.

Keywords: Atrial Fibrillation, Arrhythmia, Cardiac Surgery, Heart

#### Introduction

Atrial fibrillation, characterized by abnormal heart rhythm, is a common condition after heart surgery occurring in 25-50% of patients (1). Older patients, patients with dysfunctional hearts, and those undergoing valve procedures are predisposed to develop this condition postoperatively (2). AF increases the risk of morbidity and mortality as it is a risk factor for strokes, acute limb ischemia, hemodynamic instability, and ischemia colitis (3). Anticoagulation medication is administered for the prevention of these complications; however, these lead to bleeding complications.

AF is treated with various medications including digoxin, beta-receptor blockers, and calcium channel blockers which show variable degrees of success(4). In addition, antiarrhythmic drugs such as Amiodarone and sotalol have been proven successful in restoring normal rhythm (5, 6). Some patients still stay resistant to these treatments and require anticoagulation.

This study was conducted to assess the outcome of perioperative amiodarone administration for the prevention of atrial fibrillation in patients undergoing elective cardiac surgery.

#### Methodology

A prospective study was conducted in the Cardiac Surgery Department of Punjab Institute of Cardiology, Lahore from November 2023 to November 2024. A total of 150 patients undergoing elective cardiac surgery (valve or combined valve surgery) at high risk of postoperative AF (elderly and patients with ejection fraction less than 40%) were selected. Patients with a pulse of less than 60, systolic blood pressure less than 100mmHg, baseline long QTc interval less than 500 ms, heart blocks, history of thyroid disease, interstitial lung disease, amiodarone allergy, patients on class I or III antiarrhythmics, two chronotropic agents or amiodarone two months before the study were excluded. All patient provided their consent for inclusion in the study. The ethical board of the hospital approved the study. Patients were divided into two groups.

The cases group included 75 patients who were administered 400 mg amiodarone twice daily for 5 days before surgery and 5 days after surgery once a day. The control group included 75 patients who were administered placebo treatment. Cardiac surgeries were performed as per usual procedure without any changes. The primary outcome was the development of atrial fibrillation requiring



treatment post-operatively. Secondary outcomes were the length of hospital stay, AF and anticoagulatory complications, adverse effects of amiodarone, postoperative myocardial infarction, rhythm status at discharge, and rate of mortality. Electrolyte dysfunction on days 0, 1, 2 and 4 after surgery was also recorded. All data was analyzed by SPSS version 23. Continuous variables and dichotomous variables were compared by student t-test and chi-square test, respectively. A p-value less than 0.05 was taken as significant.

#### Results

Table 1 shows patients' baseline characteristics between both groups. There was a significant difference between the control group and cases group concerning preoperative parameters and treatment. Intraoperatively, however, 25%of the cases group required inotropic support as compared to 4% of patients in the control group (p=0.05). There was

a significant difference between cross-clamping time, ventricular tachycardia, bradycardia, and the need for shock or transfusion between both groups during surgery.

Table 2 shows postoperative data and outcomes between both groups. Atrial fibrillation occurred in 30 (40%) patients in the control group and 27 (36%) patients in the cases group, however, this difference was not significant. The mean duration of AF in the control group was 12.5 hours as compared to 15.5 hours in cases, the difference was insignificant. None of the patients died in both groups as reported after 6 weeks follow-up. 6 (8%) patients in the cases group experienced stroke or TIA as compared to none in the control group. 24 (32%) patients in the control group experienced bleeding complications and 3 (4%) patients in the cases groups. The groups did not differ significantly concerning thromboembolic events or bleeding complications. Electrolyte levels were comparable between both groups post-op.

Variables	Control group	Cases group	P value
Mean age	$60.72 \pm 12.0$	$56.69 \pm 11.98$	0.31
Male gender	48 (64%)	37 (49.3%)	0.38
BMI	$27.25 \pm 3.47$	$25.26 \pm 3.48$	0.22
Obese	27 (36%)		0.63
<b>Pre-operative comorbidities</b>			
Myocardial infarction	6 (8%)	3 (4%)	0.59
Diabetes mellitus	3 (4%)	3 (4%)	0.42
Hypertension	36 (48%)	24 (32%)	0.28
Cholesterol	30 (40%)	20 (26.7%)	0.38
Atrial fibrillation	9 (12%)	3 (4%)	0.32
Peripheral vascular disease	-	3 (4%)	0.31
Chronic renal failure	-	3 (4%)	0.32
Transient ischemic attack	3 (4%)	7 (9.4%)	0.50
COPD	9 (12%)		0.1
Left ventricle class I	60 (80%)	57 (76%)	0.95
Left ventricle class II	9 (12%)	9 (12%)	
Left ventricle class III	6 (8%)	9 (12%)	
Preoperative treatments			
Beta-blockers	15 (20%)	14 (18.7%)	0.92
Calcium blockers	12 (16%)	-	0.07
Ace inhibitors	24 (32%)	45 (60%)	0.06
Aspirin	27 (36%)	27 (36%)	1
Plavix	3 (4%)	3 (4%)	0.89
Coumadin	6 (8%)	3 (4%)	0.71
Diuretics	24 (32%)	34 (45.4%)	0.36
Statins	30 (40%)	17 (22.7%)	0.18
Preoperative parameters			
Heart rate	$70.1 \pm 8.16$	$70.29 \pm 10.87$	0.88
Cardiac index	$1.9 \pm 0.39$	$1.9 \pm 0.27$	0.72
Hemoglobin	$140.3 \pm 17.31$	$138.57 \pm 19.75$	0.81
Potassium	$3.97 \pm 0.39$	$3.98 \pm 0.39$	0.39
Creatinine	$79.28 \pm 12.10$	87.15 ± 20.94	0.12
Glucose	$6.04 \pm 1.53$	$5.91 \pm 1.87$	0.81

### Table 2: Post-operative data and complications

Post-operative data	Control group	Case group	P value
Blood transfusion	24 (32%)	14 (18.7%)	0.52
Length of hospital stay	$6.55 \pm 6.51$	$6.76 \pm 7.74$	0.86
ICU stay	$1.52 \pm 0.59$	$2.03 \pm 2.1$	0.08
Pacing	9 (12%)	17 (22.7%)	0.27

Normal sinus rhythm at discharge	72 (96%)	65 (86.7%)	0.19
Potassium level			
Day 0	$4.09 \pm 0.42$	$3.95 \pm 0.42$	0.70
Day 1	$4.31 \pm 0.44$	$4.10 \pm 0.43$	0.65
Day 2	$4.11 \pm 0.41$	$4.07 \pm 0.38$	0.84
Day 4	$3.66 \pm 0.58$	$3.85 \pm 0.50$	0.36
Complications			
Atrial fibrillation	30 (40%)	27 (36%)	Not significant
Stroke/ TIA	-	6 (8%)	Not significant
Bleeding	24 (32%)	3 (4%)	Not significant

# Discussion

This study was conducted to assess the outcomes of amiodarone administration in patients at high risk of developing atrial fibrillation postoperatively. Atrial fibrillation occurred in 30 (40%) patients in the control group and 27 (36%) patients in the cases group. Since the difference was insignificant, it indicated that amiodarone provides no additional preventive benefits against AF.

However, this result was in contrast to other studies that report a significant role of amiodarone in reducing the incidence of postoperative AF (7, 8, 9). This can be explained by the fact that most of the previous studies are conducted in patients undergoing CABG, however, most patients in our study were undergoing valve surgery which is more invasive, resulting in frequent arrhythmias that are drug resistant. The mean duration of AF in the control group was 12.5 hours as compared to 15.5 hours in cases, the difference was insignificant which is contrary to previous studies (10, 11). Parent et al reported a 25% incidence of AF in the amiodarone group as compared to 53% in the placebo group and the duration of AF was also shorter in the former group (12).

There was no difference in the rate of mortality between both groups as no patient died in our study which can be accounted for by a selection of low-risk surgery patients undergoing elective procedures and that mortality due to atrial fibrillation is less common. In addition, the age of patients in our study was 55-60 years which is younger than the age of cardiac surgery patients in other studies (13, 14). Other thromboembolic events and bleeding complications were manageable and were comparable between both groups. Among secondary outcomes, the groups did not differ significantly with respect to length of ICU and hospital stay although previous studies suggest a longer stay in amiodarone patients (15).

#### Conclusion

No difference in clinical outcomes was observed by administration of amiodarone for prevention of post-op atrial fibrillation.

#### Declarations

# Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate Approved by the department Concerned. (IRBEC-NHMMMS-23432/23)

#### Consent for publication Approved Funding Not applicable

#### **Conflict of interest**

The authors declared absence of conflict of interest.

#### Author Contribution

# AHMAD KAMRAN KHAN (SR Cardiac Surgery)

Coordination of collaborative efforts. Study Design, Review of Literature. FUROAN YAOUB PANNU (SR Cardiology) Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript. Conception of Study, Final approval of manuscript. MUZAMIL AMIN (Registrar Cardiology) Manuscript revisions, critical input. Coordination of collaborative efforts. SHAHID IQBAL (Assistant Professor) Data acquisition, analysis. Manuscript drafting. SAKHA MUOEET (SR Cardiology) Data entry and Data analysis, drafting article. Data acquisition, analysis. Coordination of collaborative efforts.

#### References

1. Elliott AD, Middeldorp ME, Van Gelder IC, Albert CM, Sanders P. Epidemiology and modifiable risk factors for atrial fibrillation. Nature Reviews Cardiology. 2023;20(6):404-417.

2. Sagris M, Vardas EP, Theofilis P, Antonopoulos AS, Oikonomou E, Tousoulis D. Atrial fibrillation: pathogenesis, predisposing factors, and genetics. International journal of molecular sciences. 2021;23(1):6.

3. Bizhanov KA, Abzaliyev KB, Baimbetov AK, Sarsenbayeva AB, Lyan E. Atrial fibrillation: Epidemiology, pathophysiology, and clinical complications (literature review). Journal of Cardiovascular Electrophysiology. 2023;34(1):153-165.

4. Jost N, Christ T, Magyar J. New strategies for the treatment of atrial fibrillation. Pharmaceuticals. 2021;14(9):926.

5. Lenhoff H, Järnbert-Petersson H, Darpo B, Tornvall P, Frick M. Mortality and ventricular arrhythmias in patients on d, l-sotalol for rhythm control of atrial

fibrillation: A nationwide cohort study. Heart Rhythm. 2023;20(11):1473-1480.

6. Mujović N, Dobrev D, Marinković M, Russo V, Potpara TS. The role of amiodarone in contemporary management of complex cardiac arrhythmias. Pharmacological Research. 2020;151:104521.

7. Polintan ET, Monsalve R, Menghrajani RH, Sirilan KY, Nayak SS, Abdelmaseeh P, et al. Combination prophylactic amiodarone with beta-blockers versus betablockers in atrial fibrillation after cardiac surgery: A systematic-review and meta-analysis. Heart & Lung. 2023;62:256-263.

8. Ray WA, Chung CP, Stein CM, Smalley W, Zimmerman E, Dupont WD, et al. Risk for bleeding-related hospitalizations during use of amiodarone with apixaban or rivaroxaban in patients with atrial fibrillation: a retrospective cohort study. Annals of internal medicine. 2023;176(6):769-778.

9. Shurrab M, Jackevicius CA, Austin PC, Tu K, Qiu F, Singh SM, et al. Association between concurrent use of amiodarone and DOACs and risk of bleeding in patients with atrial fibrillation. The American Journal of Cardiology. 2023;186:58-65.

10. Lin S-Y, Liu Y-B, Ho L-T, Peng Y-F, Kuo C-H, Tang S-C, et al. Impact of amiodarone on plasma concentration of direct oral anticoagulant in patients with atrial fibrillation. Journal of the Formosan Medical Association. 2023;122(8):776-784.

11. Rasmussen PV, Dalgaard F, Gislason GH, Torp-Pedersen C, Piccini J, D'Souza M, et al. Amiodarone treatment in atrial fibrillation and the risk of incident cancers: a nationwide observational study. Heart Rhythm. 2020;17(4):560-566.

12. Parent S, Amant JS, Remortel SV, Kahn S, Vaka R, Courtman D, et al. Atrial Fibrosis and Inflammation in Postoperative Atrial Fibrillation: Comparative Effects of Amiodarone, Colchicine, or Exosomes. Clinical Electrophysiology. 2024;10(6):1037-1049.

13. Taha HS, Youssef G, Omar RM, El Din AMK, El Din AAS, Meshaal MS. Efficacy and speed of conversion of recent onset atrial fibrillation using oral propafenone versus parenteral amiodarone: a randomized controlled comparative study. Indian Heart Journal. 2022;74(3):212-217.

14. Caspersen E, Guinot P-G, Rozec B, Oilleau J-F, Fellahi J-L, Gaudard P, et al. Comparison of landiolol and amiodarone for the treatment of new-onset atrial fibrillation after cardiac surgery (FAAC) trial: study protocol for a randomized controlled trial. Trials. 2023;24(1):353.

15. Tsioufis P, Tsiachris D, Doundoulakis I, Kordalis A, Antoniou C-K, Vlachakis PK, et al. Rationale and Design of a Randomized Controlled Clinical Trial on the Safety and Efficacy of Flecainide versus Amiodarone in the Cardioversion of Atrial Fibrillation at the Emergency Department in Patients with Coronary Artery Disease (FLECA-ED). Journal of clinical medicine. 2023;12(12):3961.



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