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Original Article

Comparison Between Effects of Amiodarone vs. Nebivolol in Treating Atrial Fibrillation Following Coronary Artery Bypass Grafting

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Abstract

Background: Atrial fibrillation (AF) is the most prevalent type of arrhythmia following cardiac surgery. Several agents are used for managing postoperative AF, but their efficacy is controversial. This study evaluated the effectiveness of amiodarone versus nebivolol in treating postoperative AF.

Methods: This randomized trial was conducted from November 2022 to November 2023 and involved 100 patients who developed postoperative AF after coronary artery bypass grafting. Patients were divided into two groups: Group A (n=50) received amiodarone, and Group B (n=50) received nebivolol.

Results: Compared with Group B, Group A had a significantly longer aortic clamp time [60.9 ± 11.27 vs. 55.6 ± 10.18 min; p value= 0.051]. Moreover, the total cardiopulmonary bypass time did not significantly differ between the two groups [89.62 ± 19.76 vs. 92.44 ± 17.74 min; p value= 0.455]. Compared with Group B, sinus rhythm control in Group A was notably better at 6 hours (16% vs. 2%), 12 hours (44% vs. 12%), 24 hours (62% vs. 16%), 48 hours (83.3% vs. 17%), and 72 hours (100% vs. 25.5%) postintervention ($p < 0.001$). However, no significant difference was observed in the effect of either drug on the rate control at these intervals. Moreover, the morbidity and mortality rates were not significantly different between the two groups.

Conclusion: Amiodarone might be superior to nebivolol in the treatment of postoperative AF following coronary artery bypass grafting. Amiodarone could be the treatment of choice for postoperative AF after CABG.

KEYWORDS

Amiodarone; Nebivolol; Atrial Fibrillation; Coronary Artery Bypass Grafting

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Introduction

Atrial fibrillation (AF) is a frequent arrhythmia after coronary artery bypass grafting (CABG) [1,2]. Postoperative AF prevention can be achieved through the use of beta-blockers as well as antiarrhythmic medications such as amiodarone. Beta-blockers reduce oxygen demand in the heart muscle and, consequently, ischemic events during the postoperative period. This mechanism is achieved by inhibiting both the chronotropic and inotropic effects of catecholamine surges [3]. Both amiodarone and beta-blockers are versatile in their administration in clinical settings, as they can be delivered either orally or intravenously. Nevertheless, prior research on the effectiveness

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of these medications has yielded conflicting results [3,4].

Most modern guidelines advocate amiodarone as the primary choice for preemptive treatment of AF following heart surgery [5]. However, despite the prevalent recommendation of amiodarone, approximately 25% of physicians opt for nebivolol, a β-blocker, as the primary agent for preempting AF following surgery. Given the significant impact of this common arrhythmia on morbidity, mortality, and healthcare costs [6, 7], the current research evaluated the efficacy of nebivolol vs. amiodarone for treating postoperative atrial fibrillation (POAF) following CABG.

Patients and Methods

Design and patients

A prospective randomized, single-blind trial was conducted from November 2022 to November 2023 on patients who underwent CABG with or without ischemic mitral valve repair and developed postoperative AF.

The inclusion criteria were patients aged between 45 and 80 years of both genders. Eligible participants had no prior history of open-heart surgery or preexisting arrhythmias and were not on any antiarrhythmic medications.

The exclusion criteria included patients who developed AF following CABG and had electrical cardioversion, patients with a previous history of arrhythmia, patients who were using antiarrhythmic drugs or emergency surgery, and patients with known hypersensitivity to nebivolol or amiodarone.

Randomization

One hundred patients were randomly allocated into two equal groups utilizing computer-generated numbers, and their allocation codes were securely stored in closed opaque envelopes. Blocking randomization was used to create two equal groups. Group A (n=50) consisted of patients who developed AF postoperatively and promptly received a bolus dose of 300 mg of amiodarone, followed by a bolus dose of 1–3 mg/kg for the first 6 hours and a maintenance dose of 0.5 mg/kg for the subsequent 18 hours. Group B (n=50) comprised patients who developed AF postoperatively and received a single 2.5 mg tablet of nebivolol, providing a sustained effect for 24 hours.

Data and outcomes

Age, sex, body mass index (BMI), ejection fraction (EF), aortic cross clamp data, and ischemic data were collected. The study outcomes were heart rate, rate, and rhythm control. The study outcomes were evaluated up to 72 hours postoperatively. Chest infection, wound infection, renal impairment, pericardial effusion, and stroke were compared between the two groups. Renal impairment was defined as an increase in postoperative creatinine of 1.5 times compared to the preoperative level or the need for dialysis.

Table 1: Comparison of preoperative and operative data between patients who received amiodarone (Group A) and those who received nebivolol (Group B) for treating atrial fibrillation after coronary artery bypass grafting. The data are presented as the means (SDs) or numbers and percentages

	Group A (n= 50)	Group B (n= 50)	p value
Age (years)	61.6 ± 10	64.42 ± 9.05	0.142
Male	32 (64%)	35 (70%)	0.523
Weight (kg)	82.68 ± 9.98	79.3 ± 11.12	0.113
BMI (kg/m2)	29.06 ± 3.66	27.58 ± 4.08	0.058
Ejection fraction (%)	50.86 ± 6.42	51.56 ± 4.96	0.602
Aortic-cross clamp time (min)	60.9 ± 11.27	55.6 ± 10.18	0.015
CPB time (min)	89.62 ± 19.76	92.44 ± 17.74	0.455

BMI: body mass index; CPB: cardiopulmonary bypass

Table 2: Comparison of heart rate, rate, and rhythm control between patients who received amiodarone (Group A) and those who received nebivolol (Group B) for treating atrial fibrillation after coronary artery bypass grafting

	Group A (n= 50)	Group B (n= 50)	p value
Heart rate			
At admission	151.08±18.95	156.86±16.57	0.108
6 hours	133.88±18.45	138.92±15.83	0.146
12 hours	122.3±14.12	124.16±14.76	0.521
24 hours	106.64±8.71	108.06±10.78	0.471
48 hours	96.13±4.95	98.15±6.13	0.083
72 hours	77.62±4.44	79.68±7.47	0.148
Rhythm control			
6 hours	8 (16%)	1 (2%)	0.031
12 hours	22 (44%)	6 (12%)	<0.001
48 hours	40/48 (83.3%)	8/47 (17%)	<0.001
72 hours	48/48 (100%)	12/47 (25.5%)	<0.001
Rate control			
6 hours	133.88±18.45	138.92±15.83	0.146
12 hours	122.3±14.12	124.16±14.76	0.521
24 hours	106.64±8.71	108.06±10.78	0.471
48 hours	96.13±4.95	98.15±6.13	0.083
72 hours	77.62±4.44	79.68±7.47	0.148

Statistical analysis

Data management and statistical analysis were performed using SPSS version 28 (IBM, Armonk, New York, United States). The normality of the quantitative data was assessed using the Shapiro–Wilk test and histograms. According to normality, quantitative data are summarized as the means and standard deviations or medians and ranges. Categorical data are summarized as numbers and percentages. Quantitative data were compared between the studied groups using the independent t test or Mann–Whitney U test for normally and nonnormally distributed quantitative variables, respectively. Categorical data were compared using the chi-squared test or Fisher's exact test. A two-tailed p value of less than 0.05 was considered significant.

Results

Preoperative and operative data

There were no significant differences in age, sex, weight, BMI, or EF between the two groups. The duration of aortic clamping was substantially greater in Group A than in Group B (p value = 0.015). There was no significant difference in cardiopulmonary bypass time between the two groups (Table 1).

Operative outcome

The two groups had no significant differences in heart rate (HR) at 0, 6, 12, 24, 48, or 72 hours. The effect of both drugs on sinus rhythm control was significantly lower at 6, 12, 24, 48, and 72 hours in Group B than in Group A. The effects of both drugs on rate control were not significantly different at 6, 12, 24, 48, and 72 hours between the two groups (Table 2).

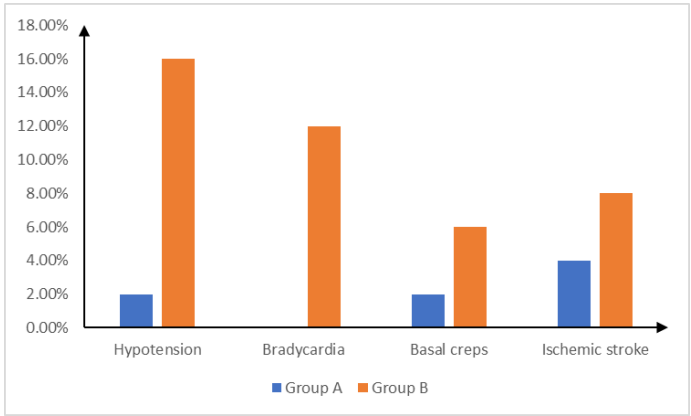

Figure 1: Comparison of complications between patients who received amiodarone (Group A) and those who received nebivolol (Group B) for treating atrial fibrillation after coronary artery bypass grafting

There was a significant increase in hypotension and bradycardia in Group B compared to Group A. The basal CRP levels were not significantly

Table 3: Comparison of postoperative morbidity and mortality between patients who received amiodarone (Group A) and those who received nebivolol (Group B) for treating atrial fibrillation after coronary artery bypass grafting. Data are presented as numbers and percentages

	Group A (n= 50)	Group B (n= 50)	p value
Chest infection	0	1 (2%)	>0.99
Wound infection	1 (2%)	1 (2%)	>0.99
Renal impairment	2 (4%)	3 (6%)	>0.99
Pericardial effusion	1 (2%)	2 (4%)	>0.99
Hospital mortality	2 (4%)	3 (6%)	>0.99

different between the two groups (Figure 1). In Group A, 2 (4%) patients died, while in Group B, 3 (6%) patients died. The differences in postoperative morbidity and mortality between the two groups were not statistically significant (Table 3).

Discussion

POAF is a common arrhythmia in 25% of patients following isolated CABG. Although POAF is frequently temporary and benign in nature, it can lead to increased postoperative morbidity and mortality [8-10]. The aforementioned encompasses a multitude of potential adverse events, encompassing but not limited to ventricular dysrhythmias, myocardial ischemia, cardiac decompensation, acute renal injury, cerebrovascular accidents, neurocognitive deficits, and increased susceptibility to infectious pathologies [11]. POAF serves as a standalone indicator for various negative consequences [8]. These patients have a significantly elevated risk, ranging from a two- to fourfold increase in cerebrovascular events, necessitating reoperation due to hemorrhagic complications, infectious processes, renal or respiratory insufficiency, cardiac arrest, and cerebral abnormalities, and the necessity for permanent pacemaker placement. Additionally, POAF is linked to a twofold increase in overall mortality rates at both 30 days and six months postoperatively [12, 13].

Our study revealed that the aortic clamp time was significantly greater in the amiodarone group than in the nebivolol group (p value = 0.015). However, there was no significant difference in bypass time between the two groups. The observation that aortic clamp time was notably longer in patients administered amiodarone than in those given nebivolol during arterial filtration surgeries likely stems from the distinct mechanisms of action of these medications on the cardiovascular system. Amiodarone, classified as a class III antiarrhythmic drug, primarily operates by extending phase III of the cardiac action potential, thereby elongating the refractory period of the heart's conducting tissue. While it has various effects on the heart, including antiarrhythmic properties and vasodilatory effects, it may also induce negative inotropic effects. This intricate action can influence hemodynamics and myocardial function in diverse ways, conceivably resulting in a lengthened aortic clamp time attributable to its impact on cardiac function and rhythm regulation during surgery [14].

Rhythm measurements were notably lower at 6, 12, 24, 48, and 72 hours in the nebivolol group than in the amiodarone group. POAF typically manifests within the temporal window spanning the second to fourth postoperative days, exhibiting a peak incidence on the second day following surgical intervention. In approximately 70% of cases, the onset of POAF precedes the fourth postoperative day, while in 94% of cases, POAF transpires prior to the sixth postoperative day [15].

In our investigation, we found that the efficacy of both medications in controlling sinus rhythm was significantly lower at 6, 12, 24, 48, and 72 hours in the nebivolol group than in the amiodarone group. Amiodarone exhibits a multifaceted mechanism of action encompassing β-adrenergic blockade, calcium channel inhibition, and class III antiarrhythmic properties. Notably, in patients who present with acute-onset AF and compromised left ventricular function,

amiodarone or digoxin is frequently recommended due to its minimal negative inotropic impact. Numerous studies have demonstrated the efficacy of amiodarone in achieving and maintaining sinus rhythm, with reported success rates ranging from 50% to 70% in patients afflicted with persistent AF [16,17].

In this research, the two groups had no statistically significant differences in morbidity or mortality. The therapeutic armamentarium for managing postoperative AF has extensively encompassed both amiodarone and beta-adrenergic antagonists, with contemporary evidence suggesting comparable efficacy outcomes between these pharmacological agents [15]. While β-blockers are employed as a component of the rate control strategy in treating AF, amiodarone plays a dual role, serving as a therapeutic modality for both rate control and rhythm control approaches [18].

The seminal rate control efficacy in the permanent AF (RACE) II trial demonstrated that patients who adhered to a more stringent heart rate target (<80 beats per minute) did not exhibit a reduced incidence of morbidity, mortality, or hospitalization compared to their counterparts in the more permissive heart rate group (<110 bpm). Similarly, in the postoperative AF milieu, both rate control and rhythm control therapeutic paradigms have yielded comparable rates of complications and equivalent durations of hospitalization [21]. Consistent with our findings, Kamali and associates reported no significant differences in morbidity or mortality between amiodarone and metoprolol [20]. Furthermore, our study revealed a significantly greater incidence of recurrent AF within 30 days in the nebivolol group than in the amiodarone group (p value = 0.01), while the frequency of returning to the hospital to the intensive care unit (ICU) due to symptomatic AF did not differ significantly between the groups. In support of our results, Ardaya and coworkers demonstrated no difference in the mean length of hospital stay between the amiodarone and β-blocker groups [17]. Additionally, in agreement with our results, Kamali and associates noted no statistically significant difference in ICU readmission between the amiodarone and metoprolol groups. They also observed that the rate of recurrent AF did not significantly differ between the amiodarone and metoprolol groups [20].

Limitations of the study

This study has several limitations. These included single-center experience, and we included patients who underwent CABG only; therefore, the results may not apply to other types of cardiac surgery. The short-term follow-up also limited the study, and the long-term effects of the medications were not evaluated. Furthermore, patients with an ejection fraction less than 40% were excluded, and the efficacy of both medications in this subset of patients was not assessed.

Conclusion

The cohort receiving nebivolol demonstrated a significantly greater incidence of irregular rhythmic patterns than did the amiodarone group, indicating the superior antiarrhythmic efficacy of amiodarone over the β-adrenergic antagonist nebivolol in the management of postoperative AF following CABG. Patients who received nebivolol exhibited a greater propensity for complications such as hypotensive episodes and bradycardia than those receiving amiodarone therapy.

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