

Evaluation of amiodarone versus metoprolol in treating atrial fibrillation after coronary artery bypass grafting

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(Received: January 19, 2017; Accepted: February 9, 2017)

Abstract: *Introduction:* Atrial fibrillation (AF) is the most common arrhythmia affecting patients in open heart ICU after coronary artery bypass grafting (CABG). Most cardiac surgery textbooks recommend beta blockers as the drug of choice for treating such a condition while many experienced physicians and a number of anesthesiology references offer amiodarone as the drug of choice. Therefore, because of insufficient evidence and the aforementioned controversy, we decided to conduct a study evaluating these two antiarrhythmic medicines. *Methods:* This is a double-blind, randomized, clinical trial performed on patients admitted for CABG at Amir al Momenin hospital in Arak province, Iran, who developed new onset AF after surgery. Based on the type of medication used, these patients were randomly divided into two groups: amiodarone (A) group and metoprolol (M) group. Each group consisted of 73 cases. All data were analyzed via SPSS 19. *Results:* Among the results achieved in this study, amiodarone was successful in treating AF in 55 patients (73%), while metoprolol achieved normal rhythm in treating AF in 69 patients (92%). With a *p*-value of 0.04, it seems that metoprolol is more effective in treating AF. *Conclusion:* Metoprolol seems to be a most efficacious medication for post-CABG AF (*p*-value = 0.004).

Keywords: atrial fibrillation, coronary, grafting, amiodarone, metoprolol

Introduction

Atrial fibrillation (AF) is a very common arrhythmia following open heart surgery [1, 2]. AF takes place when irregular simulation is observed in atriums with no specific direction. In other words, the muscular cells of atrium are simulated irregularly [3, 4]. This pulse has a normal rate of 6 per second. In AF, there is no regular atrial contraction, which means that atrium will have no appropriate time for contraction and remain practically stationary. As a result, atrium fails to completely evacuate blood to ventricles and the cardiac output of the heart will decrease [5, 6]. At the same time, ventricular beats that follow the pattern of atrium will also become partially unworkable and irregular. Finally, this blood immovability in atria (stasis) will result in intra-atrial thrombus and embolism of this thrombus and problems associated with it [6, 7].

In recent times, more cases of postoperative atrial fibrillation (POAF) are observed because of higher number of heart operations performed (which have various causes such as an increase in the number of elderly people) [8]. With the increase in the elderly people population size, cases of AF also increase [9]. The number of POAF cases following revascularization and aortic valve replacement varies significantly, and different studies have reported a frequency of 3%–90%. However, the majority of these researches have reported a frequency of 20%–40% as a result of various factors and causes such as the age of population, methodology and length of research, how cares were given for the arrhythmia, and different types of medicines taken [10, 11].

Although POAF is temporary and causes no complications, cases of severe complications include high risk of renal failure caused by pulmonary artery embolism, lack

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of hemodynamic stability, heart failure, brain stoppage (6%–24% of ischemic strokes are caused by AF), mesenteric embolism, organ failure, and even death [12]. Furthermore, as the results indicate, AF is associated with lower levels of mental functioning and delirium [13]. In addition to the aforementioned cases of morbidity, prolonged hospitalization not only imposes high costs on patients but also occupies hospital beds and puts extra burden on the healthcare system of the country. As a result, there remains no doubt that preventing and treating this common arrhythmia is of significant importance.

The majority of current guidelines introduce β -blockers as the first line of preemptive treatment for AF following heart surgery [14]. However, 19% of doctors use amiodarone as the first line of AF preemption following operation [15]. Considering the morbidity, mortality, and costs caused by this common arrhythmia, we decided to study the effectiveness of metoprolol and amiodarone (which are commonly used to prevent POAF) in treating POAF.

Materials and Methods

This is a double-blind, randomized, clinical trial conducted on the patients who were admitted for coronary artery bypass grafting (CABG) resorting to Amir al Momenin hospital in Arak.

The patients admitted for CABG and meeting the inclusion criteria of this study were randomly divided into amiodarone and metoral groups.

Based on the sample size in each group, 73 patients who applied for CABG, met the inclusion criteria of this study, and suffer from POAF were randomly divided into amiodarone (A) and metoral (M) groups according to the table of randomized numbers. Depending on the type of group, a treatment was chosen, and the final results were compared between groups.

If the patients requested for CABG, they should be exhibited the inclusion criteria of atrial fibrillation rhythm until 4 h after entering intensive care unit (ICU), and also the patients were randomly divided into two groups: amiodarone and metoral group. Patients in the amiodarone group were given a STAT dose of 300 mg of amiodarone (A) followed by a dose of 1–3 mg/kg for every 6 h and 0.5 mg/kg 18 h later. However, patients in the metoral group (M) were given a dose of 1–3 mg/kg/h for 24 h. For each group, antiarrhythmia medicines were prescribed for 24 h. Then, the results of AF treatment following CABG were compared between groups.

Statistical analysis and deduction: Questionnaire information was statistically analyzed using the table of randomized numbers, and the resulting data were further statistically analyzed by t -test and χ^2 test. The results were finally represented in terms of statistical tables and graphs. It is noticeable that questionnaires were used to collect information, so that the evidences can be documented.

Inclusion criteria were as follows:

1. Patients applied for CABG, but reported no valve conflicts and required no further operations.
2. Patients aged 45–80 years old.
3. Patients with no history of open heart surgery.
4. Patients with no history of arrhythmia, particularly AF prior to operation.
5. Patients not taking antiarrhythmia medicines.

Exclusion criteria were as follows:

1. Patients suffering from AF following CABG and not responding to treatments.
2. Patients requiring DC shock to treat arrhythmia.
3. Patients requiring treatments other than CABG.
4. Patients with a history of arrhythmia or using antiarrhythmia medicines.
5. Patients not in the age range of 45–80 years old.
6. All emergency patients candidated for CABG.

Pattern used to calculate the number and volume of the sample: 73 people were included.

$$N = \frac{(Z_1 - \alpha K + Z_1 - \beta)^2 (\delta_1 + \delta_2)^2}{(\mu_1 - \mu_2)^2},$$

where $Z_1 - \alpha/F$: 1/96, $Z_1 - \beta$: 2/33, δ_1 : 18/8, δ_2 : 14.2, μ_1 : 38, and μ_2 : 30. Each group consisted of 73 people.

Results

The results indicate 55 (73%) patients from the amiodarone group and 69 (92%) patients from the metoral group recovered from the disease. The significant difference between these two groups with p -value = 0.004 points to the fact that metoral is more effective in treating AF following CABG. These results are presented in *Table I*.

The frequency of arrhythmia in these two groups is presented in *Table II* and the postoperative death rate in these two groups is presented in *Table III*.

A significant difference was observed between the two groups in terms of staying in open heart ICU, and the groups that had received metoral had shorter stay in ICU. The average length of hospitalization in ICU was 8.5 days for amiodarone group and 5.8 days for metoral group. These results are presented in *Table IV*.

Other types of arrhythmia observed in two groups are presented in *Table V*.

The most frequent type of arrhythmia (except AF) observed in both groups following treatment was sinus tachycardia.

Other differences observed in this research are represented in *Tables VI* and *VII*. *Table VI* represents the

Table I Comparing the therapeutic effects of amiodarone and metoral in treating post-CABG AF

		Drug		<i>p</i> -value
		Amiodarone	Metoral	
Cure	Yes	55	69	0.004
	No	20	6	
Total		75	75	

Table II Comparing the occurrence of other arrhythmia (except AF) after treatment in both groups

		Drug		<i>p</i> -value
		Amiodarone	Metoral	
Arrhythmia	Yes	40	32	0.194
	No	35	43	
Total		75	75	

As $p \geq 0.05$, no significant difference was observed between the two groups in terms of the occurrence of other arrhythmia (except for AF) after treatment

Table III Comparing the post-CABG death rate in both groups

		Drug		<i>p</i> -value
		Amiodarone	Metoral	
Expire	Yes	10	6	0.293
	No	65	69	
Total		75	75	

According to this table and as $p \geq 0.05$, no significant difference was observed between the two groups in terms of death rate

Table IV Comparing the length of staying in open heart ICU in both groups

		Drug		<i>p</i> -value
		Amiodarone	Metoral	
Admit	3 nights	0	13	0.001
	4 nights	10	14	
	5 nights	5	6	
	6 nights	0	18	
	7 nights	10	6	
	8 nights	10	6	
	9 nights	10	6	
	10 nights	15	6	
	More than 10 nights	15	0	
	Total		75	

Table V Type of arrhythmia observed in each group

		Drug		Total
		Amiodarone	Metoral	
Arrhythmia type	PVC	10	13	23
	Sinus tachycardia	15	13	28
	Bradycardia	0	6	6
	Fluther + PVC	5	0	5
	PAC + PVC	5	0	5
	PVC + sinus tachycardia	5	0	5
	Total		40	32

Table VI Gender in each group

		Drug		Total
		Amiodarone	Metoral	
Gender	Male	42	37	79
	Female	33	38	71
Total		75	75	150

As $p \geq 0.05$, no statistically significant difference was observed between the two groups

Table VII The length of using medicine in each group

		Drug		Total
		Amiodarone	Metoral	
Cure time	1	15	26	41
	2	0	25	25
	3	20	0	20
	4	15	18	33
	5	5	0	5
Total		55	69	124

gender of participants and *Table VII* presents the length of using metoral and amiodarone to improve AF rhythm.

Discussion

Post-CABG AF is the most common complication observed in such patients. This complication will lead to significant increase of side effects, thus delaying patients' discharge that results in extra costs. In average, patients with AF stay 13 h in general unit and 2 days in ICU [16]. If POAF is not treated properly, during hospitalization may continue for several weeks, and it may increase the possible death, heart stroke, and

embolism [17]. Factors such as growing older, high blood pressure, decreased performance of left ventricle, and heart failure may contribute to high possibilities of AF [18]. Thus, any measure that can reduce the frequency and occurrence of POAF is economically affordable.

The results obtained from previous researches are nearly in line with those of our research. Dörge et al. [18] showed that amiodarone (a daily dose of 400 mg for 1–3 days before operation and up to 7 days after operation) is not able to reduce the occurrence of POAF. But another research found that amiodarone is effective in reducing AF, but it should not be taken routinely [19]. The suggested another research to compare the role of beta blockers with amiodarone. In another research, Lamb et al. [20] studied the effect of atenolol on preventing supraventricular arrhythmias following CABG for the first time. He analyzed the report of 60 patients who had undergone CABG and concluded that using atenolol for 72 h prior to operation for patients with appropriate left ventricle functioning is really effective in reducing the frequency of supraventricular arrhythmias.

In another research by Halonen et al. [21], AF was observed among 23.9% of patients who had received metoprolol and 28% of patients who had received amiodarone. No statistically significant difference was observed between these two groups (p -value = 0.85). However, a significant difference was observed in terms of AF between these two groups (p -value = 0.004).

In another research by Johnson and Brophy [22], the group who had taken sotalol exhibited fewer cases of AF and other associated diseases. This research showed that the mortality risk in the group that had taken sotalol was significantly less than the group that had taken amiodarone, and this was also in line with the results of our research. In another research conducted by Esmail et al. [23], it was concluded that using amiodarone even less than the dose prescribed in various sources has preemptive effects on occurrence of post-CABG AF.

In a similar research by Onk et al. [24], it was observed that 14 patients out of the whole 122 patients who had received amiodarone (one week prior to CABG and up to a certain period after operation) suffered from AF. On the other hand, 16 patients out of the whole 129 patients who had received metoprolol (one week prior to CABG and up to a certain period after operation) suffered from AF. These assessments were carried out from 3 days to 4 weeks after operation. No significant difference was observed between these two groups; thus, it was concluded that there was no difference between using amiodarone and metoprolol in reducing the risk of AF. These results are not in accordance with the results achieved in this research, and this may be attributed to the difference between metoral and metoprolol. Kojuri et al. [25] studied the effect of amiodarone and propranolol when taken separately and when taken in

combination. Post-CABG AF was observed among 13 patients (16.3%) of those who had taken propranolol, 5 patients (6.3%) of those who had taken amiodarone, and 4 patients (5%) of those who had taken them both in combination. Amiodarone in combination with propranolol had greater protective effects compared with the time when propranolol was taken separately. The results of these two researches are not in line with this study, and this is probably because of the difference between metoprolol and propranolol with metoral. Another research by Sleilaty et al. [26] compared the effects of amiodarone and bisoprolol in reducing the occurrence frequency of post-CABG AF, showing a frequency of 15.3% for AF among those who had taken amiodarone, while a frequency of 12.7% among those who had received bisoprolol. In statistical terms and in a p -value level less than 0.05, this difference was not statistically significant. All these researches point to the need of a similar study with different populations in different centers. This study also tried to compare the frequency of occurrence of AF among patients undergoing CABG who had received amiodarone and metoral.

Conclusion

According to the results of this study, a significant difference was observed in terms of length of treatment and hospitalization between the two groups who had received amiodarone and metoral. According to these results, treatment with metoral seems to be a most effective alternative.

Less sample size and poor cooperation from the patient's side were the limitations of this research. Overcoming these limitations would help us to achieve more useful results. It is also recommended to replicate this research in other centers, with larger sample size and with less limitations, so that more assertive results can be achieved.

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Funding sources: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' contribution: AK and MS performed and designed experiments, prepared figures, and drafted and revised the manuscript. AS and EM performed and designed experiments and revised the manuscript. All authors read and approved the final manuscript.

Conflict of interest: None.

Acknowledgements: The authors would like to thank the Research and Technology Deputy of Medical Sciences University for their aid in approving the proposal and supporting us throughout the research. We would also like to express our gratitude to the personnel of open heart ICU and open heart surgery units who cooperated with us to carry out this research.

References

- Creswell LL, Schuessler RB, Rosenbloom M, Cox JL: Hazards of postoperative atrial arrhythmias. *Ann Thorac Surg* 56, 539–549 (1993)
- Almassi GH, Schowalter T, Nicolosi AC, Aggarwal A, Moritz TE, Henderson WG, Tarazi R, Shroyer AL, Sethi GK, Grover FL, Hammermeister KE: Atrial fibrillation after cardiac surgery: A major morbid event? *Ann Surg* 226, 501 (1997)
- Waldo AL: Mechanisms of atrial fibrillation. *J Cardiovasc Electro-physio* 14, S267–S274 (2003)
- Schotten U, Verheule S, Kirchhof P, Goette A: Pathophysiological mechanisms of atrial fibrillation: A translational appraisal. *Physiol Rev* 91, 265–325 (2011)
- Daoud EG, Weiss R, Bahu M, Knight BP, Bogun F, Goyal R, Harvey M, Strickberger SA, Man KC, Morady F: Effect of an irregular ventricular rhythm on cardiac output. *Am J Cardiol* 78, 1433–1436 (1996)
- Maisel WH, Stevenson LW: Atrial fibrillation in heart failure: Epidemiology, pathophysiology, and rationale for therapy. *Am J Cardiol* 91, 2–8 (2003)
- Wolf PA, Abbott RD, Kannel WB: Atrial fibrillation as an independent risk factor for stroke: The Framingham study. *Stroke* 22, 983–988 (1991)
- Nair SG: Atrial fibrillation after cardiac surgery. *Ann Card Anaesth* 13, 196 (2010)
- Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, Barash PG, Hsu PH, Mangano DT: A multicenter risk index for atrial fibrillation after cardiac surgery. *Jama* 291, 1720–1729 (2004)
- Crystal E, Connolly SJ, Sleik K, Ginger TJ, Yusuf S: Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery a meta-analysis. *Circulation* 106, 75–80 (2002)
- Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, Collins JJ, Cohn LH, Burstin HR: Predictors of atrial fibrillation after coronary artery surgery current trends and impact on hospital resources. *Circulation* 94, 390–397 (1996)
- Burgess DC, Kilborn MJ, Keech AC: Interventions for prevention of post-operative atrial fibrillation and its complications after cardiac surgery: A meta-analysis. *Eur Heart J* 27, 2846–2857 (2006)
- Chang Y-L, Tsai Y-F, Lin P-J, Chen M-C, Liu C-Y: Prevalence and risk factors for postoperative delirium in a cardiovascular intensive care unit. *Am J Crit Care* 17, 567–575 (2008)
- Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H: Guidelines for the management of atrial fibrillation: The task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 31, 2369–2429 (2010)
- Daoud EG, Strickberger SA, Man KC, Goyal R, Deeb GM, Bolling SF, Pagani FD, Bitar C, Meissner MD, Morady F: Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. *N Engl J Med* 337, 1785–1791 (1997)
- Cundiff D: Coronary artery bypass grafting (CABG): Reassessing efficacy, safety, and cost. *MedGenMed* 4, 7 (2002)
- Cioffi G, Cemin C, Russo TE, Pellegrini A, Terrasi F, Ferrario G: Post-discharge recurrences of new-onset atrial fibrillation following cardiac surgery: Impact of low-dose amiodarone and beta-blocker prophylaxis. *Ital Heart J* 1, 691–697 (2000)
- Dörge H, Schoendube FA, Schoberer M, Stellbrink C, Voss M, Messmer BJ: Intraoperative amiodarone as prophylaxis against atrial fibrillation after coronary operations. *Ann Thorac Surg* 69, 1358–1362 (2000)
- Aasbo JD, Lawrence AT, Krishnan K, Kim MH, Trohman RG: Amiodarone prophylaxis reduces major cardiovascular morbidity and length of stay after cardiac surgery: A meta-analysis. *Ann Intern Med* 143, 327–336 (2005)
- Lamb R, Prabhakar G, Thorpe J, Smith S, Norton R, Dyde J: The use of atenolol in the prevention of supraventricular arrhythmias following coronary artery surgery. *Eur Heart J* 9, 32–36 (1988)
- Halonen J, Lopenon P, Järvinen O, Karjalainen J, Parviainen I, Halonen P, Magga J, Turpeinen A, Hippeläinen M, Hartikainen J, Hakala T: Metoprolol versus amiodarone in the prevention of atrial fibrillation after cardiac surgery: A randomized trial. *Ann Intern Med* 153, 703–709 (2010)
- Johnson SM, Brophy JM: Mortality risk of sotalol and amiodarone for post-CABG atrial fibrillation. *Int J Cardiol* 214, 502–507 (2016)
- Esmail M, Nilufar D, Majid G-E, Reza T-NM, Abolfazl M: Prophylactic effect of amiodarone in atrial fibrillation after coronary artery bypass surgery; a double-blind randomized controlled clinical trial. *J Cardiovasc Dis Res* 6, 12–17 (2015)
- Onk OA, Erkut B: Is the preoperative administration of amiodarone or metoprolol more effective in reducing atrial fibrillation: After coronary bypass surgery? *Medicine* 94, e1576 (2015)
- Kojuri J, Mahmoodi Y, Jannati M, Shafa M, Ghazinoor M, Sharifkazemi MB: Ability of amiodarone and propranolol alone or in combination to prevent post coronary bypass atrial fibrillation. *Cardiovasc Ther* 27, 253–258 (2009)
- Sleilaty G, Madi-Jebara S, Yazigi A, Haddad F, Hayeck G, El Rassi I, Ashoush R, Jebara V: Postoperative oral amiodarone versus oral bisoprolol as prophylaxis against atrial fibrillation after coronary artery bypass graft surgery: A prospective randomized trial. *Int J Cardiol* 137, 116–122 (2009)