Treatment of Postoperative Atrial Fibrillation After Coronary Artery Bypass Grafting with Amiodarone

KORONER ARTER BYPASS GREFTLEME AMELİYATLARINDAN SONRA OLUŞAN ATRİAL FİBRİLASYONUN AMİODARON İLE TEDAVİSİ

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Summary

Objective: Atrial fibrillation (AF) is a common complication encountered after coronary artery bypass grafting (CABG) operations. It is seen as much as 20-50% postoperatively and may cause morbidity and mortality. Pre-, per- and postoperative predictors of AF after CABG and outcome of amiodarone treatment were evaluated retrospectively.

Material and Methods: 82 consecutive patients underwent CABG operation. AF was seen in 24 (29.3%) patients and intravenous amiodarone; firstly a loading dose, then continuous infusion were given and then continued orally. Preoperative risk factors, peroperative and postoperative variables for new onset of AF were analyzed to investigate the reasons of AF.

Results: Two (2.4%) of the patients died. All patients experiencing atrial fibrillation were restored into sinus rhythm. Amiodarone was discontinued in one patient (1.25%) due to nodal rhythm and changed in another one (1.25%) with another drug due to recurrence of AF. Statistical analysis revealed advanced age, upper age group, multi-vessel disease, preoperative myocardial infarction, right coronary artery bypass grafting, increased number of grafts, use of intra-aortic balloon pump, lengthened ventilatory support and longer hospital stay to be correlated significantly with AF (P=0.017, P=0.04, P=0.01, P=0.018, P=0.024, P=0.038, P=0.005, P=0.002, and P<0.0001 respectively). Overall predictors of AF were advanced age, upper age group and longer hospital stay in logistic regression analysis (P<0.0001, P=0.001, and P<0.0001).

Conclusion: Amiodarone is an effective drug in reversion of AF after CABG with no serious side effects. Prophylactic use of amiodaron for prevention of AF after CABG in patients carrying the predicted risk factors must also be investigated.

Key Words: Atrial fibrillation, Coronary bypass, Amiodarone

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Özet

Amaç: Atrial fibrilasyon (AF) koroner arter bypass greftleme (KABG) ameliyatlarından sonra görülebilen bir komplikasyondur. Postoperatif dönemde %20-50 oranında görülür ve morbidite – mortaliteye neden olur. Bu çalışmada KABG sonrasında ortaya çıkan AF' un preoperatif peroperatif ve postoperatif ön belirleyicileri ve amiodaron ile tedavide elde edilen bulgular retrospektif olarak incelenmiştir.

Gereç ve Yöntemler: KABG operasyonuna alınan ardışık 82 hasta çalışmaya dahil edildi. 24 hastada (%29.3) postoperatif AF gelişti. İntravenöz olarak önce yükleme daha sonra idame dozunda amiodaron verildi ve müteakiben oral amiodaron ile devam edildi. Yeni oluşan AF' un nedenlerini ortaya koymak amacıyla preoperatif peroperatif ve postoperatif risk faktörleri incelendi.

Bulgular: Hastaların 2 tanesi (%2.4) ex oldu. AF' a giren hastaların tümü sinüs ritmine geri döndü. Bir hastada (%1.25) amiodaron infüzyonu hastanın nodal ritme girmesi nedeniyle sonlandırıldı. Başka bir hastada ise (%1.25) infüzyon sırasında AF' un nüks etmesi üzerine amiodaron başka bir ilaç ile değiştirildi. İstatistiksel analiz sonucunda ileri yaş, ileri yaş üst gruplarında olmak çok damar hastalığı, preoperatif miyokard enfarktüsü varlığı, sağ koroner artere bypass greftleme, artmış greft sayısı, intra aortik balon pompası kullanımı, uzamış ventilatör tedavisi olması ve uzamış hastane yatışının AF ile doğrudan ilgisi olduğuna dair veriler elde edilmiştir (P=0.017, P=0.04, P=0.01, P=0.018, P=0.024, P=0.038 P=0.005, P=0.002, and P<0.0001). Lojistik regresyon analizi uygulamasından sonra ise AF' un en önemli ön belirleyicileri olarak ilerlemiş yaş, üst yaş grubunda olmak ve uzamış hastane yatışı anlamlı bulunmuştur (P<0.0001, P=0.001, and P<0.0001).

Sonuç: Amiodaron, KABG ameliyatlarından sonra görülen AF' un tedavisinde ciddi yan etkiler olmadan kullanılabilecek emniyetli bir ilaçtır. Amiodaronun postoperatif AF gelişmesinde ön belirleyici kriterleri tanımlanmış olan hastalarda profilaktik kullanımının anlamlı olup olmadığı yönünde daha kapsamlı çalışmalara gereksinim vardır.

Anahtar Kelimeler: Atrial fibrilasyon, Koroner bypass, Amiodaron

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Atrial fibrillation (AF) is one of the most common complications encountered after coronary artery bypass grafting (CABG) operations and may lead to coronary ischemia, congestive heart failure, thromboembolic events, prolonged hospital stay and rise in costs (1). It is seen as much as 20-50% postoperatively after CABG operations (1-4). Pharmacological measures are applied firstly in an attempt to restore the patients into sinus rhythm and to maintain them in this rhythm and/or to control the ventricular rate in AF (3). The most frequently used agents to achieve this goal have been amiodarone, propafenon, sotalol (5-6), quinidine, Verapamil (6), magnesium sulphate (7) and beta blocking agents together with magnesium sulphate (8).

In this study we present our results with amiodarone in the treatment of AF ensuing after CABG and preoperative, peroperative and postoperative parameters that can be held responsible in the development of this clinical entity.

Material and Methods

82 consecutive patients who primarily underwent CABG were examined retrospectively. All of the patients were analyzed together with the purpose of finding which factors were related with new onset of postoperative AF and then differences between AF and no AF patients were investigated. The youngest patient was 28 years old and the oldest patient was 79 years old and the median was found to be 59.4 years. The demographic presentation of the patients is given in Table 1.

All patients received per oral alprazolam 1mg. (Xanax, Eczacıbaşı, Turkey) for sedation on the night before the operation. Following neurolept anesthesia a standard median sternotomy, double stage venous and aortic cannulation and continuous flow cardio-pulmonary bypass (CPB) with moderate hypothermia was used. After cross clamping the aorta cold crystalloid cardioplegic solution (Plegisol, Abbot, USA) was administered at an initial dose of 15cc/kg and blood cardioplegia was given regularly in every 20 minute intervals and all of the patients received warm blood cardioplegia just before the aortic cross clamp removal. The proximal anastomoses were performed with the application of a side clamp. Table 2 outlines operative and postoperative findings.

Table 1. Patients'demogra.phics and preoperative data are shown

	N	%	Mean	Std. Error	Std. Deviation
Age	82	100	57,89	1,23	11,10
Male	61	74,4			
Female	21	25,6			
Smoking	51	62,2			
Hypertension	39	47,6			
Diabetes mellitus	12	14,6			
Beta blocker use	59	72,0			
Preop MI	16	19,5			

(MI: myocardial infarction)

Amiodarone (Cordarone, Sanofi, Turkey) therapy for patients who experienced AF postoperatively was standardized to be a loading dose of 300mg infused in 30 minutes and continued as maintenance infusion of 900mg/24 hours and then oral amiodaron 200mg/24 hours during the rest of their stay in the hospital until the 30^{th} day after discharge.

The patients were followed with continuous electrocardiography (ECG) monitoring for the first 48 hours and then with 12 lead ECG twice a day unless otherwise a rhythm change was established. AF was defined as continuous AF for at least 30 minutes or AF requiring treatment for symptoms of haemodynamic compromise. The amiodarone therapy was followed with the monitoring of QTc in the ECGs of the patients.

Relation of the preoperative, operative and postoperative parameters with new onset of postoperative AF and the predictors of postoperative AF were also investigated. All the parameters (preoperative demographics, peroperative and postoperative factors in AF patients and no AF patients) that thought to be correlated with AF were evaluated by Pearson correlation analysis and a p value <0.05 was considered to be significant. Predictors of atrial fibrillation for preoperative, operative and postoperative parameters, and for all

Table 2. Operative and postoperative data

	N	%	Mean (min-max)	Std. Error	Std. Deviation
Involved vessel number	82		2,38	,0084	,76
Greft number	82		2,71	,12	1,11
Pump time	82		131,99	5,93	53,70
Cross clamp time	82		78,45	3,51	31,82
Associated valve procedure	3	3,7			
LV aneurysmectomy	3	3,7			
Endarterectomy	3	3,7			
IABP use	10	12,2			
Asist device use	1	1,2			
Postop atrial fibrillation	24	29,3			
RCBG	45	54,9			
Intubation time (hours)	82		6,88	1,17	10,63
Hospital stay (days)	82		8,02 (5-16 days)	,29	2,64

(LV: left ventricle, IABP: intra-aortic balloon pump, RCBG: right coronary bypass grafting, min: minimum, max: maximum).

parameters were evaluated with conditional forward stepwise logistic regression analysis. A p value <0.05 was considered to be significant and for each significant parameter exponent B (Exp B) values and 95% confidence interval (95% CI) were calculated to express significance.

Results

During the postoperative period all of the patients were followed intubated and the shortest and longest intubation times were 2 and 72 hours respectively. Table 2 demonstrates operative findings and the additional interventions performed to the patients. All the patients who did not have any problems were discharged from the intensive care unit at the end of 24 hours and by the end of 48 hours the chest tubes were removed and continuous ECG monitoring was stopped. One patient (1.2%) who had had a peroperative myocardial infarction was lost by the end of 72nd hours postoperatively due to low cardiac output and another patient who had severe rheumatoid arthritis died due to cerebro-vascular accident post discharge from the hospital (Table 3).

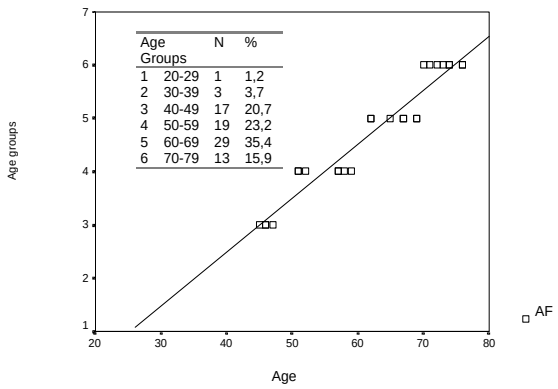
In 24 patients (29.3%) AF ensued between 18 and 55 hours postoperatively with high ventricular rates. All of these patients returned to normal sinus rhythm after the initiation of amiodarone protocol between 6-17 hours but among these, one of the patients (1.2%) experienced recurrent AF while under amiodarone infusion, so his therapy was continued with another drug and another patient (1.2%) developed nodal bradicardia on the 16th hour after the initiation of the infusion therapy and hence the amiodaron infusion was stopped. This latter patient returned to normal sinus rhythm 8 hours after the cessation of the infusion spontaneously. No recurrent AF was established during controls. Since at the end of 30 days after discharge all patients were found to be in sinus rhythm the drug was ceased in all.

Table 3. Postoperative mortality

	N	%
No exitus	80	97,6
Exitus	2	2,4
Cardiac exitus	1	1,2
Non-cardiac exitus	1	1,2
Total	82	100,0

(N: Number of patients)

Factors that might have been responsible for the postoperative AF were analyzed with Pearson Correlation test parametrically and age, right coronary artery bypass, preoperative myocardial infarction, prolonged intubation period, number of attacked coronary vessels and number of coronary bypass grafts were found to be statistically significant (p<0,05, p<0,05, p<0,05, p<0,01, p<0,05 and



(N: Number of patients)

Figure 1. Prevalence of atrial fibrillation increased with age. AF increased after 60 years of age and was seen much more in upper age group (70-79).

p<0,05 respectively). Patients were divided into age groups and it was found that 74,5 % of patients was over age of 50 and as age increased incidence of AF increased too (Figure 1).

The preoperative, peroperative, both pre and peroperative and finally overall predictors of AF were analyzed with forward stepwise logistic regression analysis. The results are demonstrated in Table 4. In our study, preoperative beta-blocker usage, diabetes mellitus and sex were not found to be significant as predictors of new AF formation after CABG.

Discussion

AF is one of the most important complications encountered after CABG operations that can lead to morbidity and/or mortality (1). It can lead to morbidities such as coronary ischemia, congestive heart failure, thrombo-embolic events, prolonged ventilator times and may give rise to lengthened hospital stays and increased hospital costs (1). In an effort to prevent the onset of postoperative AF and/or control the ventricular rate and for medical cardioversion numerous studies with different drugs have been performed but it seems amiodarone is one of the most effective among them (1). Kochiadakis et al (5) have compared sotalol, propafenon and amiodarone and found out that propafenon and amiodarone are superior to sotalol in restoring patients to sinus rhythm postoperatively. Although it was not statistically significant they have indicated that amiodaron seemed superior to propafenon in both restoring the patients to sinus rhythm and in maintaining them in this condition. In another study Jensen et al (9) have administered $MgSO_4$ four days in advance from the operation but found out that this application did not prevent new onset of AF but reduced the duration. Solomon et al (8) forwarded that the use of propranolol

Table 4. Preoperative, peroperative, pre and peroperative and overall predictors of postoperative atrial fibrillation

		B	S.E.	Wald	df	Sig.	Exp(B)	95,0% C.I.for EXP(B) Lower	Upper
All factors	Age	-,545	,139	15,472	1	,000	,580	,442	,761
	Hospital stay	1,262	,287	19,396	1	,000	3,534	2,015	6,198
	Advanced age group	4,703	1,380	11,611	1	,001	110,244	7,373	1648,468
Preop factors	Age	-,016	,005	11,061	1	,001	,984	,975	,994
	Preop MI	1,214	,583	4,339	1	,037	3,366	1,074	10,548
Preop and Perop factors	Age	-,019	,005	13,749	1	,000	,981	,971	,991
	Preop MI	1,163	,604	3,713	1	,054	3,200	,980	10,448
	IABP usage	1,635	,750	4,752	1	,029	5,130	1,179	22,318
Perop factors	IABP usage	2,163	,797	7,369	1	,007	8,696	1,824	41,449
	Increased cross clamp time	-,012	,003	11,876	1	,001	,988	,982	,995

B: Value of the logistic regression analysis S.E.: Standard error Df: Degrees of freedom Sig: Significance
Exp (B): Exponent value of the B. CI: Confidence interval.

together with $MgSO_4$ did not bring an advantage in the prevention of postoperative new AF onset. Taking these results into account with this study we demonstrated that no matter how much prophylaxis is planned or applied AF is still a problem after CABG and postoperative management is effective with amiodarone.

Amiodarone is basically a class III anti arrhythmic drug which also has the properties of class I and II anti arrhythmic drugs (1, 10-11). Amiodarone is a lipid soluble agent and can be stored widely in numerous tissues, especially in liver and lungs and as for the elimination from the body it has a half-life of 8-110 days (4, 10-11). When amiodarone is administered intravenously, the possibility of side effects to become true increases (11). Among these side effects pulmonary toxicity, thyroid dysfunction, ocular symptoms, neurological disorders, torsades de pointes and other cardiac disorders, photosensitivity and other skin disorders, gastrointestinal and hepatic disorders can be taken into account (1, 10-11). Some of these, especially the cardiac complications may cause serious threats for the patients due to the long half-life of the drug. In our study nodal rhythm ensued in one patient but this clinical situation happened to be of short duration and healed spontaneously simply by the cessation of the drug. Amiodaron cannot be eliminated by hemodialysis (11) therefore it is imperial both for the dose to be titrated and to select the correct patients.

Doud et al (4) mentioned about a 50% reduction in the development of new AF postoperatively by administrating amiodarone orally one week before the operation. Similarly Katariya et al (12) administered oral amiodarone to the patients as soon as they came to the intensive care unit until they were discharged from the hospital and demonstrated similar results. After these oral applications of amiodaron intravenous applications have grown to be more popular and Dorge et al (13) have applied different intravenous amiodarone protocols for the prophylaxis of AF postoperatively but failed to demonstrate the prevention of new onset. In clinical application we preferred to use this drug intra-venously watching very closely for its side effects. Apart from a nodal rhythm no other serious side effect has been seen. For either prevention or treatment of AF with amiodarone these potential risks can be avoided by using low dose schemes. This study points out success of low dose regimen with almost no serious side effects. On the other hand we would like to notify that when considering the potential side effects of especially the intravenous administration of amiodarone we think in favor of using it in patients in whom independent risk factors have been identified. Albeit it is less frequent, AF is also encountered in patients who undergo CABG without the use of CPB (14). This leads us to consider other factors of postoperative AF apart from CPB. On account of this we believe that putting forward the most responsible preoperative, perioperative and postoperative parameters in the development of this clinical situation and applying prophylactic therapy with amiodarone pre or postoperatively to the patient groups having increased risk would be a more meaningful treatment. We found advanced age (age over 50 and more significantly over 60 years) and preoperative MI as preoperative risk factors, and need for IABP for weaning from CPB during operation was related with significantly increased risk for the development of new onset of atrial fibrillation. When all parameters were taken into account, then the predictors were changed to advanced age, upper age group and longer hospital stay, but it is not easy to say that longer hospital stay results in atrial fibrillation and hence it will be more reliable to say that atrial fibrillation results in longer hospital stay in reality.

Conclusion

Amiodarone is an anti arrhythmic agent that can safely be used in low dose schemes for the treatment of postoperative AF seen after CABG. We believe that the studies that will be carried out with the patient populations carrying the risk factors will give us more valuable results in understanding whether prophylactic treatment has or has not any significant value and we suggest the researches to be carried out regarding this point of view in larger patient groups.

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