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PREOPERATIVE AMIODARONE AS PROPHYLAXIS AGAINST ATRIAL FIBRILLATION AFTER HEART SURGERY

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ABSTRACT

Background Atrial fibrillation occurs commonly after open-heart surgery and may delay hospital discharge. The purpose of this study was to assess the use of preoperative amiodarone as prophylaxis against atrial fibrillation after cardiac surgery.

Methods In this double-blind, randomized study, 124 patients were given either oral amiodarone (64 patients) or placebo (60 patients) for a minimum of seven days before elective cardiac surgery. Therapy consisted of 600 mg of amiodarone per day for seven days, then 200 mg per day until the day of discharge from the hospital. The mean (\pm SD) preoperative total dose of amiodarone was 4.8 ± 0.96 g over a period of 13 ± 7 days.

Results Postoperative atrial fibrillation occurred in 16 of the 64 patients in the amiodarone group (25 percent) and 32 of the 60 patients in the placebo group (53 percent) ($P=0.003$). Patients in the amiodarone group were hospitalized for significantly fewer days than were patients in the placebo group (6.5 ± 2.6 vs. 7.9 ± 4.3 days, $P=0.04$). Nonfatal postoperative complications occurred in eight amiodarone-treated patients (12 percent) and in six patients receiving placebo (10 percent, $P=0.78$). Fatal postoperative complications occurred in three patients who received amiodarone (5 percent) and in two who received placebo (3 percent, $P=1.00$). Total hospitalization costs were significantly less for the amiodarone group than for the placebo group ($\$18,375 \pm \$13,863$ vs. $\$26,491 \pm \$23,837$, $P=0.03$).

Conclusions Preoperative oral amiodarone in patients undergoing complex cardiac surgery is well tolerated and significantly reduces the incidence of postoperative atrial fibrillation and the duration and cost of hospitalization. (N Engl J Med 1997;337:1785-91.)

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POSTOPERATIVE atrial fibrillation occurs in 10 to 40 percent of patients undergoing cardiac surgery.¹⁻¹² Although prophylactic therapy with beta-adrenergic blockers reduces the incidence of postoperative atrial fibrillation,^{8,11,13-17} this arrhythmia remains an important cause of increased hospital stays and expenses after heart surgery.¹⁸ Amiodarone is a class III antiarrhythmic drug that is effective for atrial fibrillation¹⁹⁻²⁵ and that can be begun safely on an outpatient basis in patients with structural heart disease.^{26,27} The purpose of this study was to assess the use of oral amiodarone as prophylaxis against atrial fibrillation after heart surgery.

METHODS

Patient Population

From June 1, 1995, to September 30, 1996, 373 patients for whom cardiac surgery was scheduled at least one week in advance were screened in the cardiac-surgery clinics of the University of Michigan Hospital and Harper Hospital for participation in this study. To be included, patients had to give informed consent, be more than 18 years old, be scheduled for elective heart surgery requiring cardiopulmonary bypass, have at least one week before surgery was scheduled, and have normal sinus rhythm. Patients were excluded if they were allergic to amiodarone; had used amiodarone within four months of enrollment; had a history of amiodarone toxicity; had participated in another investigational protocol; required the use of antiarrhythmic therapy other than beta-receptor antagonists, calcium-channel antagonists, or digitalis; had untreated thyroid disease; had serum aspartate aminotransferase or alanine aminotransferase concentrations four times the upper limit of normal; were pregnant; had a resting heart rate of less than 50 beats per minute in the absence of medical therapy

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known to slow the sinus rate; or had uncontrolled heart failure. One hundred forty-five patients (39 percent) were excluded because they had participated in another investigational protocol (77 patients), had chronic atrial fibrillation (33), used antiarrhythmic medication (13), had resting heart rates of less than 50 beats per minute (11), were less than 18 years old (5), had untreated thyroid disease (2), had uncontrolled heart failure (2), or had an elevated aspartate aminotransferase concentration (2). Among the remaining 228 eligible patients, 131 (57 percent) consented. Surgery was canceled for seven patients after randomization, however, and these patients were not included in the study. Therefore, 124 patients (118 at the University of Michigan Hospital and 6 at Harper Hospital) were randomly assigned in a double-blind fashion to either oral amiodarone (64 patients) or placebo (60 patients). The characteristics of the patients are summarized in Table 1. There were no significant differences between the patients who received amiodarone and those who received placebo.

Study Protocol

The study protocol was approved by the University of Michigan and Harper Hospital human-research committees. The patients were interviewed on the day of their initial evaluations in the cardiac-surgery outpatient clinic. The patients who consented were randomly assigned in a double-blind fashion to begin oral therapy on the same day. Patients were enrolled a mean (\pm SD) of 13 ± 7 days before surgery. Amiodarone (Cordarone, Wyeth-Ayerst Laboratories, Philadelphia) was prescribed at a dosage of one tablet (200 mg) three times a day for seven days, then one tablet each day while the patient was hospitalized. Amiodarone was discontinued on the day of hospital discharge. The placebo tablets were identical in appearance to the amiodarone tablets. For the patients being treated with digitalis or warfarin, the doses of these drugs were halved, and the prothrombin time was measured one week later. Other medical therapy was unchanged. Outpatient compliance was monitored by pill count and was 96 percent. To screen for outpatient complications, a telephone interview was conducted with each patient one week after enrollment.

The patients were hospitalized on the day of surgery. All patients were placed on cardiopulmonary bypass. Coronary-artery bypass graft surgery was performed in 52 patients (42 percent), valvular surgery in 41 (33 percent), both coronary-artery bypass and valvular surgery in 22 (18 percent), and other surgical procedures in 9 (7 percent). Myocardial protection was provided by cold cardioplegia in 116 patients and retrograde perfusion in 8 patients.

After surgery, each patient was admitted to an intensive care unit and was subsequently transferred to a monitored unit. An investigator evaluated the patients daily. Three-lead telemetric monitoring (Marquette Series 7500, Milwaukee) was performed continuously for a mean of 7.2 ± 3.6 days after surgery. The electrocardiographic data were stored for 24 hours and reviewed on a daily basis. An episode of atrial fibrillation was counted if it persisted for more than five minutes. Management of atrial fibrillation was directed by the cardiac-surgery team.

The study agent was discontinued on the day of hospital discharge. A home-nurse evaluation was performed 7 ± 2 days after the patients were discharged and included measurements of vital signs in all the patients and single-lead electrocardiography in 84 patients (68 percent). At the routine postdischarge evaluation in the cardiac-surgery clinic, a 12-lead electrocardiogram was recorded, and patients were queried about intercurrent hospitalizations or emergency-room evaluations. These medical records were reviewed by an investigator.

Cost Data

Data on hospitalization costs for the study population were provided through the use of a commercially available decision-support information software system (Model 204, Transition Systems, Boston), operated by the University of Michigan Budget

TABLE 1. CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	AMIODARONE (N=64)	PLACEBO (N=60)
Age (yr)	57 \pm 14	61 \pm 13
Male sex (no.)	44	40
Left ventricular ejection fraction	0.48 \pm 0.12	0.48 \pm 0.13
NYHA functional class	2.4 \pm 0.9	2.5 \pm 1.0
History of congestive heart failure (no.)	38	32
Presence of mitral regurgitation (no.)	35	31
Presence of left ventricular aneurysm (no.)	14	11
Previous myocardial infarction (no.)	20	18
History of paroxysmal atrial arrhythmias (no.)	5	4
Preoperative use of beta-blockers (no.)	26	18
Preoperative use of digitalis (no.)	10	11
Systemic hypertension (no.)	32	30
Chronic obstructive pulmonary disease (no.)	7	7
Current tobacco use (no.)	20	14
Diabetes mellitus (no.)	10	8
Chronic renal insufficiency or dialysis (no.)†	2	2
Type of heart surgery (no.)		
CABG	28	24
Valvular	22	19
Mitral valve	20	13
Concomitant CABG and valvular	9	13
Other	5	4
Bypass-pump time (min)	155 \pm 56	147 \pm 52
Aorta cross-clamp time (min)	103 \pm 41	98 \pm 41
Myocardial protection by cold cardioplegia (no.)	59	57
Saphenous-vein grafting (no./patient)	2.8 \pm 1.1	2.4 \pm 1.1
Internal-thoracic-artery grafts (no./patient)	0.9 \pm 0.5	0.8 \pm 0.5

*NYHA denotes New York Heart Association, and CABG coronary-artery bypass grafting.

†Chronic renal insufficiency was defined as a creatinine concentration ≥ 2.5 mg per deciliter (220 μ mol per liter).

Office. These data represent the sum of variable direct costs, fixed direct costs, and indirect costs. Professional-service fees were not included in these costs. Cost data were collected for 114 patients (58 given placebo and 56 given amiodarone) who underwent surgery at the University of Michigan and were hospitalized no more than 21 days from the day of surgery. The cost of amiodarone therapy was estimated at \$2.61 per tablet.²⁸

Statistical Analysis

Data were analyzed on the basis of the intention-to-treat principle. Continuous variables were expressed as means \pm SD. Continuous variables were compared by means of Student's *t*-test, and categorical variables were compared by Fisher's exact test. Kaplan-Meier analysis with the log-rank test was used to compare the probability of atrial fibrillation in the amiodarone and placebo groups. After an episode of atrial fibrillation or after the postdischarge clinic evaluation, the patient was withdrawn from further analysis. A *P* value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Outpatient Therapy and Surgical Data

The mean number of preoperative days of therapy was significantly greater for the patients randomly assigned to receive placebo (15.0 ± 8.7) than for

those randomly assigned to receive amiodarone (12.0 ± 5.0 , $P=0.02$). The mean total outpatient amiodarone dose was 4.8 ± 0.96 g (median, 5.0; range, 0.6 to 7.0). Except for two patients who elected to stop outpatient therapy because of minor gastrointestinal side effects (one receiving placebo and one receiving amiodarone, $P=1.00$), no patients had side effects or adverse reactions during outpatient therapy. There was no significant change in the serum concentration of aspartate aminotransferase or alanine aminotransferase on the day of surgery as compared with the day of enrollment in either group (Table 2).

Other than fewer defibrillations per patient to restore sinus rhythm after release of the aortic cross-clamp in the amiodarone group, there were no significant differences in surgical data between the amiodarone and placebo groups (Table 2).

Postoperative Atrial Fibrillation

The percentages of patients remaining free of atrial fibrillation in the amiodarone and placebo groups are shown in Figure 1. When episodes of atrial fibrillation that occurred during and after hospitalization are considered, the incidence of atrial fibrillation was 25 percent (16 of 64 patients) in the amiodarone group and 53 percent (32 of 60 patients) in the placebo group ($P=0.003$).

The prevalence of atrial fibrillation occurring during hospitalization in the amiodarone group was 23 percent (15 of 64 patients), as compared with 42 percent (25 of 60 patients) in the placebo group ($P=0.03$). Atrial fibrillation occurred a mean of 2.5 ± 1.7 days after surgery in the patients assigned to amiodarone and 2.7 ± 1.6 days after surgery in the patients assigned to placebo ($P=0.79$). The maximal ventricular rate during atrial fibrillation was significantly lower in the amiodarone group than in the placebo group (112 ± 21 vs. 135 ± 31 beats per minute, $P=0.03$); however, there was no significant difference between the groups in the duration of atrial fibrillation (13.8 ± 13.4 vs. 9.3 ± 10.3 hours, $P=0.27$ by Student's t-test) (Table 3).

Symptoms attributable to atrial fibrillation were reported by 13 of 15 patients (87 percent) in the amiodarone group and 21 of 25 patients (84 percent) in the placebo group ($P=1.00$). Atrial fibrillation was initially managed by an antiarrhythmic medication in 10 patients (67 percent) assigned to amiodarone and in 14 patients (56 percent) assigned to placebo ($P=0.74$). Spontaneous conversion without antiarrhythmic medication occurred in five patients receiving amiodarone (33 percent) and in nine receiving placebo (36 percent, $P=1.00$). Electrical cardioversion was performed on no patients in the amiodarone group and two in the placebo group (13 percent, $P=0.52$).

Patients were evaluated 7 ± 2 days after hospital dis-

TABLE 2. SURGICAL AND POSTOPERATIVE CLINICAL DATA.

VARIABLE*	AMIODARONE (N=64)	PLACEBO (N=60)	P VALUE
AST concentration — IU per liter			
On day of study enrollment	25 ± 4†	26 ± 6‡	0.21
On day of surgery	25 ± 6	27 ± 4	0.15
ALT concentration — IU per liter			
On day of study enrollment	26 ± 4§	26 ± 5¶	0.57
On day of surgery	25 ± 5	26 ± 5	0.63
Epicardial defibrillation to restore sinus rhythm			
No. of patients requiring	39	39	0.85
No. per patient	1.5 ± 1.0	2.6 ± 1.6	0.001
Postoperative day of extubation	2.1 ± 5.5	1.9 ± 4.4	0.80
Intubation for >3 days — no. of patients	2	3	0.67
Temporary epicardial pacing required for >3 days — no. of patients	3	2	0.69
Postoperative continuation of beta-blockers — no./total (%)	24/26 (92)	17/18 (94)	0.98

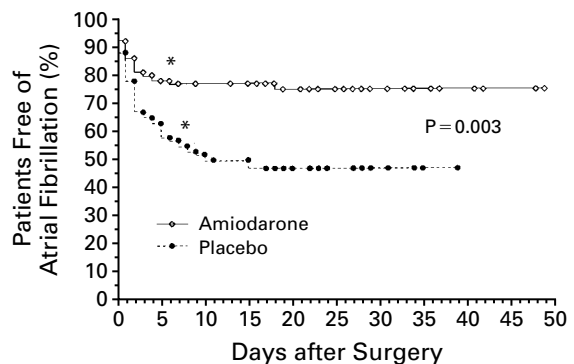
*AST denotes aspartate aminotransferase, and ALT alanine aminotransferase.

† $P=0.81$ for the comparison with the concentration on the day of surgery.

‡ $P=0.65$ for the comparison with the concentration on the day of surgery.

§ $P=0.36$ for the comparison with the concentration on the day of surgery.

¶ $P=0.34$ for the comparison with the concentration on the day of surgery.



NO. OF PATIENTS AT RISK

Amiodarone group	64	48	44	41	31	18	10	6	4	2	1
Placebo group	60	37	28	26	13	10	4	2	1		

Figure 1. Kaplan-Meier Analysis of the Percentages of Patients Remaining Free of Atrial Fibrillation after Surgery in the Amiodarone and Placebo Groups.

The asterisks indicate the mean days of hospital discharge.

charge by a home nurse and at 24 ± 9 days in the cardiac-surgery outpatient clinic. Sinus rhythm was present in each patient at the home-nurse visit and the outpatient-clinic visit. After discharge from the hospital, 7 patients who had received amiodarone (14 percent) and 11 who had received placebo (31 percent) were evaluated for acute symptoms by their physicians ($P=0.10$). Atrial fibrillation was diagnosed in one patient who had received amiodarone (2 percent) and seven patients who had received placebo (12 percent, $P=0.03$) a mean of 12 ± 5 days after discharge. The medical therapy at the time of these episodes of atrial fibrillation is summarized in Table 4.

The use of beta-blockers did not influence the prevalence of atrial fibrillation in either study group. In the placebo group, the incidence of atrial fibrillation was 61 percent (11 of 18 patients) among the patients receiving beta-blockers and 33 percent (14 of 42 patients) among those not receiving beta-blockers ($P=0.09$). The incidence of atrial fibrillation among the amiodarone-treated patients receiving beta-blockers (27 percent [7 of 26]) was not significantly different from that among the amiodarone-treated patients not receiving beta-blockers (21 percent [8 of 38], $P=0.76$).

The incidence of atrial fibrillation was significantly higher among patients who had valvular surgery (46 percent [33 of 71]) than among patients who underwent only coronary-artery bypass surgery (29 percent [15 of 52], $P=0.04$).

Length of Hospital Stay and Total Costs

The patients in the amiodarone group were hospitalized for significantly fewer days than those in the placebo group (6.5 ± 2.6 vs. 7.9 ± 4.3 days, $P=0.04$). In the amiodarone group, the mean length of stay was 7.9 ± 4.6 days for the patients with atrial fibrillation and 6.1 ± 1.3 days for those without atrial fibrillation ($P=0.02$). In the placebo group, the patients with episodes of atrial fibrillation were also hospitalized for significantly more days (9.4 ± 3.6 vs. 6.8 ± 4.5 days, $P=0.02$). The mean total cost of hospitalization for the amiodarone group was $\$18,375 \pm \$13,863$, as compared with $\$26,491 \pm \$23,837$ for the placebo group ($P=0.03$).

Morbidity and Mortality in the Hospital

There was no significant difference in the incidence of intraoperative complications between the amiodarone and placebo groups ($P=0.12$) (Table 5). Postoperative complications occurred in 19 patients (8 in the placebo group and 11 in the amiodarone group, $P=0.62$). Six patients in the placebo group and eight in the amiodarone group had major morbidity ($P=0.78$) (Table 6). Death occurred in two patients assigned to placebo (3 percent) and in three patients assigned to amiodarone (5 percent, $P=1.00$) (Table 6).

TABLE 3. DURATION OF ATRIAL FIBRILLATION.*

DURATION	AMIODARONE (N=15)	PLACEBO (N=25)
	no. of patients	
5–15 minutes	0	2
15–60 minutes	2	2
1–8 hours	2	5
More than 8 hours	11	16

*There was no significant difference in the duration of atrial fibrillation between the patients assigned to amiodarone therapy and those assigned to placebo ($P=0.61$ by chi-square analysis). These data summarize the duration of only the episodes of atrial

TABLE 4. MEDICAL THERAPY WHEN EPISODES OF ATRIAL FIBRILLATION OCCURRED AFTER HOSPITAL DISCHARGE.*

THERAPY	AMIODARONE†	PLACEBO
	no. of patients	
Beta-blocker	0	2
Calcium-channel blocker	0	2
Class I or class III antiarrhythmic agent	0	0
Digitalis	1	4
Diuretic	1	4
ACE inhibitor‡	1	2
Nitrate	0	0

*One patient in the amiodarone group (2 percent) and seven patients in the placebo group (12 percent) were receiving medical therapy when episodes of atrial fibrillation occurred after discharge.

† $P=0.03$ for the comparison with placebo.

‡ACE denotes angiotensin-converting enzyme.

TABLE 5. INTRAOPERATIVE COMPLICATIONS.

COMPLICATION	AMIODARONE*	PLACEBO
	no. (%)	
Excessive suture-line bleeding	2	2
Ventricular tachycardia or fibrillation	1	3
Persistent atrial tachycardia	0	2
Marked hypotension requiring brief CPR†	0	1
Total	3 (5)	8 (13)

* $P=0.12$ for the comparison with placebo.

†CPR denotes cardiopulmonary resuscitation.

TABLE 6. POSTOPERATIVE MAJOR MORBIDITY AND MORTALITY.

VARIABLE	AMIODARONE	PLACEBO
	no. (%)	
Major morbidity*		
Marked increase in prothrombin time after initiation of warfarin	2	1
Myoclonus	1	0
Pneumonitis	1	1
Seizure of unknown cause	1	0
Sternal-wound infection or dehiscence	2	1
Implantation of permanent pacemaker	1	1
Ventricular fibrillation with anoxic encephalopathy	0	1
Acute psychosis	0	1
Total	8 (12)	6 (10)
Mortality†		
Cerebrovascular accident	1	0
Proximal pulmonary-artery embolus	1	0
Right ventricular infarction and sepsis	1	0
Small-bowel infarction and sepsis	0	1
Ventricular flutter	0	1
Total	3 (5)	2 (3)

*P=0.78 for the comparison between amiodarone and placebo.

†P=1.00 for the comparison between amiodarone and placebo.

When both intraoperative and postoperative events were considered, malignant ventricular arrhythmias occurred in five patients in the placebo group (8 percent) and one in the amiodarone group (2 percent, P=0.11).

DISCUSSION

Main Findings

The use of prophylactic oral amiodarone for at least one week before elective heart surgery reduced the incidence of postoperative atrial fibrillation by approximately 50 percent, significantly reduced the length and total cost of hospitalization, and reduced the number of symptomatic episodes of atrial fibrillation occurring after discharge. Amiodarone was well tolerated and did not increase the risk of intraoperative or postoperative complications. Amiodarone therapy was not associated with proarrhythmia or serious adverse reactions, even among patients with severe coronary and valvular heart disease. Among the patients who did have atrial fibrillation, amiodarone reduced the ventricular rate more significantly than did placebo.

In this study, unlike previous ones that included only patients undergoing coronary-artery bypass graft surgery, 57 percent of the population had valvular surgery. Valvular surgery was associated with a

higher incidence of atrial fibrillation, which probably explains the high incidence of atrial fibrillation in the placebo group. This study's heterogeneous population highlights the efficacy of amiodarone for patients undergoing not only bypass but also valvular surgery.

Complications of Outpatient and Inpatient Therapy

Noncardiac toxic effects of amiodarone include dose-related and non-dose-related effects.^{29,30} The low-dose amiodarone regimen used in this study did not result in important side effects, and there were no complications related to outpatient adjustment of digitalis or warfarin dosages. Also, in this study, unlike previous ones,³¹⁻³³ there were no acute pulmonary toxic effects after surgery in the patients randomly assigned to amiodarone.

Cardiac toxicity due to amiodarone is uncommon.¹⁹⁻²⁵ The incidence of amiodarone-induced ventricular proarrhythmia is low,²⁵ even in the setting of structural heart disease.³⁴ Furthermore, amiodarone has little or no negative inotropic effect, rarely exacerbates heart failure, and can reduce congestive symptoms.³⁵ In this study, the low complication rate in the amiodarone group confirms the results of other studies that have demonstrated safe initiation of amiodarone treatment in outpatients with coronary artery disease and congestive heart failure.^{26,27}

Complications Occurring after Hospitalization

Although the assigned medical therapy was discontinued on the day of discharge, the incidence of atrial fibrillation was significantly lower in the amiodarone group than in the placebo group during the period immediately following discharge. The half-life of amiodarone is 13 to 103 days.³⁶ It is likely that the lower incidence of atrial fibrillation after discharge in the amiodarone group is attributable to a persistent antiarrhythmic effect.

Hospitalization Costs

Unlike previous trials of prophylaxis against postoperative atrial fibrillation, this study demonstrated a reduction in the total cost of hospitalization for the patients assigned to amiodarone therapy. These data probably underestimate the cost savings attributable to amiodarone therapy, because professional fees were not included in the cost analysis and cost data for only the initial hospitalization were examined. Atrial fibrillation after discharge was more frequent in the placebo group, and hospitalization costs related to the management of these episodes of atrial fibrillation were not analyzed.

Previous Studies

Hohnloser et al. performed a placebo-controlled study of intravenous amiodarone as prophylaxis against atrial fibrillation occurring after heart sur-

gery in 77 patients.³⁷ The total intravenous dose — 4.5 g — was similar to the total outpatient dose of amiodarone in our study. The amiodarone infusion began after the completion of the surgical procedure and significantly reduced the incidence of atrial fibrillation. However, electrocardiographic monitoring was performed only during the first 48 hours after surgery, and amiodarone was discontinued in 18 percent of patients because of side effects.

Some clinical trials using beta-adrenergic antagonists have demonstrated prophylactic benefit against postoperative atrial fibrillation^{8,11,13-17}; other studies, however, came to conflicting conclusions.³⁸⁻⁴⁰ A possible reason for this difference may be that in some studies, patients randomly assigned to placebo were treated with beta-adrenergic blockers until the time of surgery.⁴¹ Therefore, these patients may have experienced beta-blocker withdrawal, which is associated with an increase in the incidence of postoperative atrial fibrillation.^{11,42,43} A second drawback of the studies investigating prophylactic beta-blocker therapy is the exclusion criteria. In most trials, the factors calling for exclusion have included a history of asthma, chronic obstructive lung disease, or diabetes mellitus requiring medical therapy; the presence of a left ventricular aneurysm; the fact that concomitant or primary valvular surgery was to be performed; and the presence of congestive heart failure. These characteristics requiring exclusion are common among patients undergoing cardiac surgery and limit the clinical utility of prophylaxis with beta-blockers.^{11,18}

Prophylactic oral amiodarone circumvents some of the limitations of intravenous amiodarone and beta-adrenergic antagonists. Short-term low-dose oral amiodarone is not associated with the complications of intravenous administration. Also, because it is well tolerated in patients with poor left ventricular function and unlikely to exacerbate preexisting medical conditions, prophylactic low-dose oral amiodarone can be used for patients who are not candidates for beta-blockade.

Limitations of the Study

A limitation of this study is that Holter monitoring was not performed to screen for postoperative atrial fibrillation or other arrhythmias during outpatient therapy. The primary goal of the study, however, was to address the clinical utility of prophylactic oral amiodarone. Failure to detect brief, asymptomatic episodes of atrial fibrillation or asymptomatic arrhythmias was unlikely to influence patient care or affect it adversely and does not detract from the clinical implications of this study.

A second limitation is that the management of atrial fibrillation was directed by the attending cardiac surgeon. It is possible that a uniform protocol of atrial-fibrillation management might have reduced

the length of hospital stay; however, since randomization was blinded, it is improbable that the longer average hospital stay in the placebo group was attributable to a more protracted treatment regimen for atrial fibrillation.

Clinical Implications

Prophylactic low-dose oral amiodarone used in patients undergoing open-heart surgery was well tolerated and significantly reduced the incidence of postoperative atrial fibrillation, as well as the length and cost of hospitalization. Furthermore, unlike class I or other class III antiarrhythmic agents, oral amiodarone was not associated with an increased risk of adverse events, particularly ventricular proarrhythmia. A primary limitation to the widespread use of oral amiodarone prophylaxis, however, is the requirement of a seven-day preoperative treatment period. Whether an accelerated loading regimen of amiodarone over a period of one to two days before surgery might be effective and safe in preventing postoperative atrial fibrillation remains to be determined.

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