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Use of Amiodarone to Prevent Atrial Fibrillation After Cardiac Surgery

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In the United States, more than 600 000 patients undergo cardiac surgery annually.¹ Atrial fibrillation is the most common arrhythmia after cardiac surgery and is estimated to occur in 10% to 50% of all cardiac surgery patients, with a higher incidence in elderly patients and patients undergoing valve surgery.²⁻⁵ Postoperative atrial fibrillation is often well tolerated and usually resolves on its

own within 6 to 8 weeks after surgery, but it does increase the risk for various complications, including thromboembolic events and ventricular arrhythmias that can compromise hemodynamic status or cause acute congestive heart failure.⁶ Atrial fibrillation may also precipitate postoperative myocardial ischemia and necessitate placement of a permanent pacemaker.⁷ Furthermore, patients who experience atrial fibrillation after cardiac surgery have longer hospital stays and higher healthcare costs than do patients who do not have this arrhythmia.^{7,9} These differences are due in part to the time required to treat atrial fibrillation and the resources needed to manage the complications associated with the arrhythmia.⁷

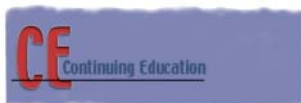
Investigators have examined the use of several pharmacological agents,

including digoxin, β -adrenergic blockers, calcium channel blockers, and class I and class III antiarrhythmic agents, to prevent postoperative atrial fibrillation.⁷ The results of clinical trials have indicated that digoxin and verapamil are no more effective than placebo; however, β -blockers and antiarrhythmic agents are effective in reducing the likelihood of postoperative atrial fibrillation.³ Most recently, researchers have investigated amiodarone, a class III antiarrhythmic agent that can block α - and β -adrenergic receptors and sodium, calcium, and potassium channels.¹ Treatment with amiodarone can reduce the occurrence of postoperative atrial fibrillation by 50%.⁹ This discovery has promising implications for patients who undergo cardiac surgery and provides a unique opportunity to develop standard prophylactic therapy to prevent postoperative atrial fibrillation.

The purpose of this article is to review studies on the use of amiodarone to prevent atrial fibrillation after cardiac surgery and discuss the various regimens for administration of amiodarone.

Atrial Fibrillation After Cardiac Surgery

Atrial fibrillation in the general population is attributed to multiple reentry wavelets of excitation that circulate throughout the atria and are triggered by premature atrial contractions.⁷ These wavelets vary in their rates of conduction and refractory periods.⁷ Slowed conduction with short refractory periods provides



* This article has been designated for CE credit. A closed-book, multiple-choice examination follows this article, which tests your knowledge of the following objectives:

1. Discuss the indications for use of amiodarone for the prevention of atrial fibrillation after cardiac surgery
2. Identify the mechanisms of action of amiodarone
3. Summarize study findings related to the use of amiodarone for atrial fibrillation
4. Describe the nursing implications related to use of amiodarone after cardiac surgery for the prevention of atrial fibrillation

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Table 1 Multivariate predictors of postoperative atrial arrhythmias in patients undergoing myocardial revascularization surgery

Advanced age
Male gender
Peripheral arterial disease
Chronic lung disease
Valvular heart disease
Left atrial enlargement
Previous cardiac surgery
Discontinuation of β -blocker medication
Preoperative atrial tachyarrhythmias
Pericarditis
Elevated postoperative adrenergic tone

Reprinted from Creswell et al.¹⁰ with permission from Society of Thoracic Surgeons.

numerous areas of excitable and depolarized tissue, thus facilitating the onset of atrial fibrillation.⁷

Atrial fibrillation after cardiac surgery is thought to be influenced by several factors (Table 1), but the exact mechanism is still not known. Advanced age has consistently been a predictor of postoperative atrial fibrillation.^{3,11} The reason for this finding most likely is chronic degenerative changes such as atrial fibrosis, muscle atrophy, decreased conductivity of tissue, and atrial dilatation.⁶ These degenerative changes prolong atrial conduction and lower the threshold for arrhythmia, thus precipitating the development of atrial fibrillation.^{3,11} As the age of patients who have cardiac surgery continues to increase, so will the incidence of postoperative atrial fibrillation.¹²

Several intraoperative factors may also influence the frequency of postoperative atrial fibrillation, including prolonged aortic cross-clamp times, atrial incisions, placement of venous cannulas, and pulmonary vein vent-

ing.⁶ Surgical trauma to the atrium, via dilation and stretching, can initiate a local inflammatory process, thus increasing the risk for premature atrial contractions and atrial fibrillation.³ Simply opening the pericardium and manipulating the heart during surgery can also activate this inflammatory process.³

Postoperative respiratory complications including pneumonia and prolonged ventilation, as well as congestive heart failure, are also associated with an increased incidence of atrial fibrillation.⁶ These complications cause an increase in pressures in the right side of the heart, usually leading to volume overload and right atrial dilatation and stretching, thus precipitating atrial fibrillation.⁶ Finally, the increase in endogenous catecholamines, which intensifies sympathetic tone, and the administration of exogenous catecholamines and inotropic agents are thought to stimulate premature atrial contractions and therefore atrial arrhythmias.³

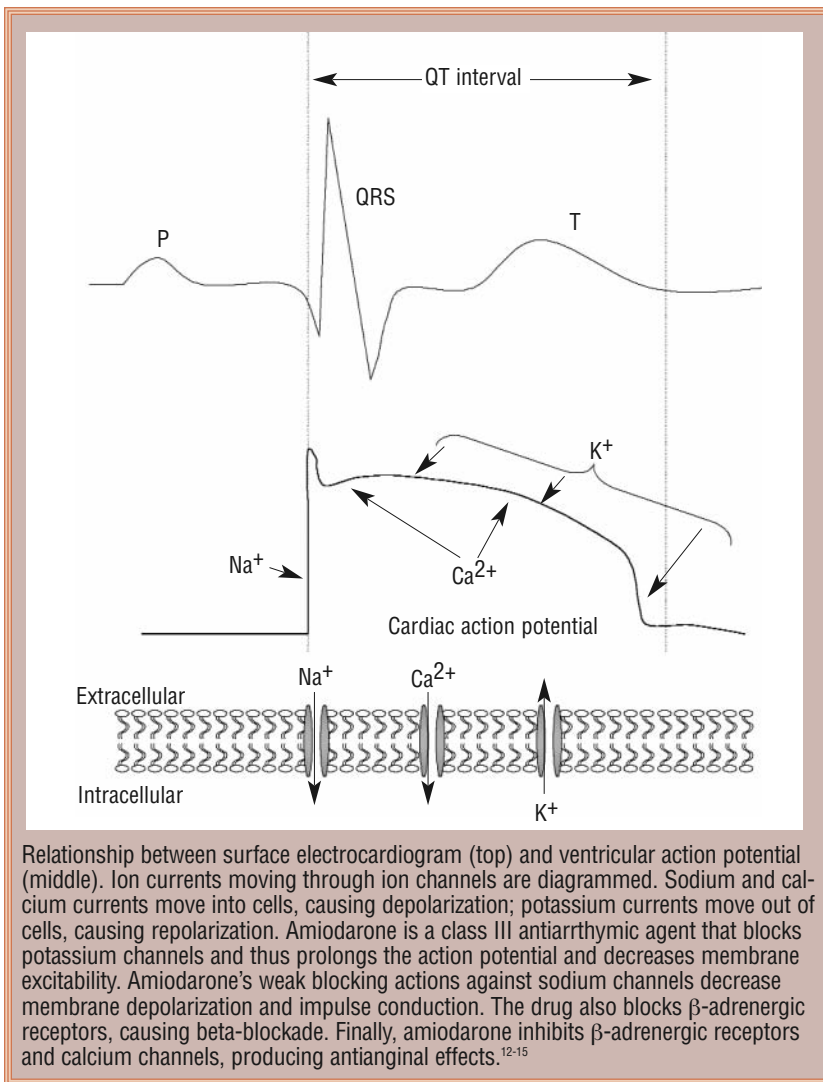
Atrial fibrillation after cardiac surgery generally occurs 2 to 3 days postoperatively but can develop any time within the first month.³ This delay is thought to be due to an exaggerated inflammatory process that is initiated by atrial trauma during venous cannulation.³ Another possible explanation for the delay in onset could be postoperative mobilization of interstitial fluid, which can lead to increased intravascular volume and increased atrial stretching.³

Mechanism of Action of Amiodarone

Amiodarone is a unique drug with a combination of pharmacological properties that are effective in treating a variety of arrhythmias^{6,12-15} (see Fig-

ure). This medication is a class III antiarrhythmic that blocks potassium channels and thus prolongs the action potential and refractory period in myocardial cells, thereby decreasing membrane excitability.¹³ Unlike other class III antiarrhythmic agents, amiodarone maintains this prolonged myocardial action potential despite faster heart rates, a characteristic that explains its effectiveness in treating tachycardias.¹³ Amiodarone also acts as a weak sodium channel blocker, causing a decline in the rate of membrane depolarization and impulse conduction.¹⁴ It directly decreases the sinus rate and slows atrioventricular conduction.¹⁴ In addition, amiodarone acts as a noncompetitive β -blocker by inhibiting β -adrenergic receptors.¹⁴ Finally, it inhibits α -adrenergic effects and calcium channels, giving it antianginal effects. These properties cause smooth muscle relaxation as indicated by dilatation of coronary and peripheral arteries, thereby increasing coronary blood flow and reducing systemic blood pressure and afterload.^{13,16}

Amiodarone can be administered orally or intravenously. With intravenous administration, although the onset of action is variable, maximal effects can occur within minutes to several hours.¹⁷ With oral administration, the onset of action can range from 2 to 21 days because of the slow and variable absorption of the drug in the gastrointestinal mucosa.¹⁷ The half-life of amiodarone is long and unpredictable, from 16 to 180 days.¹⁴ Because it is predominantly protein and lipid bound, amiodarone has a large volume of distribution throughout the body.¹⁴ This large volume of distribution and prolonged half-life necessitate a long loading period (2-4 weeks). The beneficial and adverse effects of amiodarone can



occur for several weeks after the drug is discontinued.^{13,14} Amiodarone is predominantly metabolized by the liver to a single primary metabolite, desethyl-amiodarone, which has antiarrhythmic properties comparable to those of amiodarone, thus adding to the prolonged effects that occur after administration of the drug has been discontinued.¹⁴

Literature Review

A literature search of MEDLINE, via PubMed, and CINAHL, via OVID, with key terms “amiodarone” and “postoperative atrial fibrillation” produced 13 relevant studies. Of the

13, 2 were nonrandomized studies,^{18,19} and 1 was a randomized prospective study²⁰ that included only elderly patients more than 60 years old.

The 2 nonrandomized studies^{18,19} examined the use of oral amiodarone given postoperatively to a treatment group and a historical control group. Both studies had considerably larger sample sizes than did the randomized studies on amiodarone.^{9,15,21-28} In both studies,^{18,19} patients treated with amiodarone had significantly less postoperative atrial fibrillation than did patients in the control groups. Unfortunately, the lack of randomization and blinding strategies poten-

tially introduced bias. Therefore, to find the most effective dosing regimen, we analyzed the remaining prospective, randomized, double-blind studies in which postoperative dosing, combined preoperative and postoperative dosing, or combined intraoperative and postoperative dosing was examined.

Combined Intraoperative and Postoperative Dosing Studies

In 2 prospective, randomized, double-blinded trials,^{21,22} intravenous amiodarone prophylaxis was started during the intraoperative period. In the study by Dorge et al,²² postoperative amiodarone was given intravenously, whereas in the study by Butler et al,²¹ it was given both intravenously and orally (Table 2).

Although positive trends were evident in both studies, a statistically significant decrease in the incidence of atrial fibrillation among patients treated with amiodarone did not occur in either study. Furthermore, the studies varied widely in the percentage of patients in whom atrial fibrillation developed postoperatively. In the study by Dorge et al,²² atrial fibrillation developed in 24% and 28% of patients in the 2 treatment groups (groups differed in dosage). In comparison, in the study by Butler et al,²¹ in which therapy with intravenous administration of amiodarone intraoperatively was followed by oral administration postoperatively, the incidence of supraventricular tachycardia in the treatment group was only 8%. This dissimilarity could be the result of the variations in sample characteristics, amiodarone dosing, and postoperative cardiac monitoring procedures.

Table 2 Combined intraoperative and postoperative treatment with amiodarone to prevent atrial fibrillation after cardiac surgery

Study	Sample size (N)	Sample characteristics	Definition of an episode of atrial fibrillation	Amiodarone dosing	Length of continuous observation	Outcomes*
Butler et al, ²¹ 1993	120	CABG patients who required CPB Excluded patients with a history of atrial fibrillation	Any episode lasting >5 minutes with a pulse rate >100/min and not sinus tachycardia was considered clinically significant and was treated Any episode longer than 1 minute detected by Holter monitoring was considered significant	Initially, 15 mg/kg to a maximum of 1500 mg infused intravenously over 24 hours Then, 200 mg given orally 3 times a day for 5 days	Continuous bedside cardiac monitoring for 48 hours ECG) Holter monitoring starting immediately after surgery for 6 days 12 lead ECG monitoring before surgery and on postoperative days 1, 3, and 5 and when clinical findings suggestive of atrial fibrillation occurred	Atrial fibrillation in 8% of the treatment group and 20% of the control group <i>P</i> = .07
Dorge et al, ²² 2000	150	CABG patients who required CPB Excluded patients with a history of chronic or intermittent atrial fibrillation	Any episode lasting >5 minutes was considered significant	Group 1: 300 mg intravenous bolus followed by continuous infusion of 20 mg/kg per day for 3 days Group 2: 150 mg intravenous bolus followed by continuous infusion of 10 mg/kg per day for 3 days	Continuous ECG monitoring for 10 days after surgery	Atrial fibrillation in 24% of group 1, 28% of group 2, and 34% of control group <i>P</i> = not significant

Abbreviations: CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; ECG, electrocardiogram.

*None of the differences were statistically significant.

The sample characteristics were similar in the 2 studies except for the use of β -blockers preoperatively. In the investigation by Butler et al,²¹ 78% of the treatment group and 80% of the control group were taking β -blockers preoperatively; Dorge et al²² did not address the preoperative use of β -blockers. Because β -blockers themselves may prevent atrial fibrillation after surgery, differences in their use could explain the lower incidence of atrial fibrillation in the study by Butler et al.

The doses of amiodarone in the 2 studies^{21,22} were similar in amount but differed in duration of administration. Dorge et al²² stopped the infusion on postoperative day 3, whereas Butler et al²¹ stopped treatment on postoperative day 5. The prolonged administration of

amiodarone might have resulted in a decreased occurrence of atrial fibrillation after cardiac surgery. Dorge et al,²² however, did continuous cardiac monitoring for 10 days postoperatively, a procedure that could account for the observed increase in the incidence of atrial fibrillation. Butler et al²¹ stopped continuous monitoring on postoperative day 6, just 1 day after treatment with amiodarone was discontinued. Because the onset of atrial fibrillation is delayed when amiodarone is used, the lack of monitoring after the discontinuation of the drug might have resulted in missed episodes of atrial fibrillation.

Postoperative Studies

The use of amiodarone postoperatively to prevent atrial fibrillation

was examined in 4 prospective, randomized, double-blinded trials.²³⁻²⁶ Guarnieri et al²⁴ and Hohnloser et al²³ studied the use of intravenous amiodarone, Yazigi et al²⁵ examined oral administration of amiodarone, and Yagdi et al²⁶ investigated a combination of both oral and intravenous administration (Table 3).

Although a statistically significant decrease in the occurrence of atrial fibrillation in the treatment groups was detected in all 4 studies, the results varied widely. The occurrence of atrial fibrillation ranged from 5% to 35% in the treatment groups and from 21% to 47% in the control groups. These variations could be due to the differences between the studies in sample characteristics, amiodarone dosing, defi-

Table 3 Postoperative treatment with amiodarone to prevent atrial fibrillation after cardiac surgery

Study	Sample size (N)	Sample characteristics	Definition of an episode of atrial fibrillation	Amiodarone dosing	Monitoring	Outcomes
Hohnloser et al, ²³ 1990	77	CABG patients only who required CPB	Any episode that required therapeutic intervention was considered significant	300 mg administered intravenously over 2 hours immediately after surgery 1200 mg given intravenously over 24 hours for the next 2 days 900 mg given intravenously over 24 hours for the next 2 days	Holter monitoring beginning 1 day before surgery and continuing for 48 hours after surgery	Atrial fibrillation in 5% of the treatment group and 21% of the control group <i>P</i> < .05*
Guarnieri et al, ²⁴ 1999	300	Included patients undergoing open heart surgery who required CPB Excluded patients with history of atrial fibrillation	Any episode that required any treatment	1 g infused intravenously over 24 hours for a total of 2 g in 48 hours Infusions were started within 3 hours of arrival in the ICU	Continuous monitoring throughout the hospital stay	Atrial fibrillation in 35% of the treatment group and 47% of the control group <i>P</i> = .01*
Yazigi et al, ²⁵ 2002	200	CABG patients only who required CPB	Any episode lasting >5 minutes	Initially, 15 mg/kg orally administered within 4 hours of arrival in the ICU Then, 7 mg/kg per day orally until discharge from the hospital	Continuous monitoring for 72 hours postoperatively in the ICU ECGs twice daily and if any findings suggestive of atrial fibrillation	Atrial fibrillation in 12% of the treatment group and 25% of the control group <i>P</i> = .02*
Yagdi et al, ²⁶ 2003	157	CABG patients only who required CPB	Any episode that lasted >5 minutes or required treatment because of a compromise in hemodynamic status	10 mg/kg per day intravenously for 48 hours after surgery Then, 600 mg orally 3 times a day for 5 days Then, 400 mg twice a day orally for the next 5 days and 200 mg/d for 20 days	Continuous monitoring until discharge from the hospital and routine daily 12-lead ECGs	Atrial fibrillation in 10.4% of the treatment group and 25% of the control group during hospitalization <i>P</i> = .02*

Abbreviations: CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; ECG, electrocardiogram; ICU, intensive care unit.
*Differences between groups were statistically significant.

nition of episodes of atrial fibrillation, and monitoring.

Hohnloser et al,²³ Yazigi et al,²⁵ and Yagdi et al²⁶ examined use of amiodarone in patients undergoing coronary artery bypass graft (CABG) surgery; Guarnieri et al²⁴ included patients undergoing various types of open heart surgery. The inclusion of patients having surgery other than CABG surgery could explain the higher occurrence of atrial fibrillation observed by Guarnieri et al,²⁴ because

valvular surgery has been associated with an increased risk for postoperative atrial fibrillation.³ In all 4 studies, postoperative administration of amiodarone began within 4 hours after surgery. However, the dosages of amiodarone varied; the total dosages were 4 g in the study by Hohnloser et al,²³ 4.5 g in the investigation by Yazigi et al,²⁵ 2 g in the study by Guarnieri et al,²⁴ and approximately 18 g in the study by Yagdi et al.²⁶ These differences could explain the wide range of

results. The duration of dosing also varied. Guarnieri et al²⁴ administered amiodarone for only 48 hours postoperatively, a practice that could account for the increased incidence of atrial fibrillation in their study, because this arrhythmia often does not occur until 2 to 3 days after surgery.¹ Hohnloser et al²³ and Yazigi et al²⁵ continued administration of amiodarone until patients were discharged, and Yagdi et al²⁶ administered amiodarone for a total of 30

days postoperatively. However, the results in all 4 studies²³⁻²⁶ were based on the occurrence of episodes of atrial fibrillation during hospitalization.

Two different definitions of atrial fibrillation were used in the 4 studies. In the investigations by Hohnloser et al²³ and Guarnieri et al,²⁴ any episode of atrial fibrillation requiring any therapeutic treatment was considered significant. In the studies of Yazigi et al²⁵ and Yagdi et al,²⁶ an episode of atrial fibrillation was considered significant if it persisted longer than 5 minutes. The difference in these definitions does not allow an equal comparison of the occurrence of atrial fibrillation between the studies because the number of episodes that occur that last longer than 5 minutes most likely is greater than the number of episodes that require treatment.

Finally, all 4 studies varied in the length of continuous cardiac monitoring after surgery. Hohnloser et al²³ monitored patients by using Holter monitoring for 48 hours postoperatively. Yazigi et al²⁵ monitored patients continuously for 72 hours and then obtained electrocardiograms in patients whenever findings suggestive of atrial fibrillation occurred and twice daily. The lack of continuous monitoring after postoperative day 2 or 3 might have resulted in missed episodes of atrial fibrillation and therefore could account for the smaller percentages of atrial fibrillation observed in the studies of Hohnloser et al²³ and Yazigi et al²⁵ compared with the percentages in the studies of Guarnieri et al²⁴ and Yagdi et al.²⁶ Similarly, Guarnieri et al²⁴ and Yagdi et al²⁶ continuously monitored patients throughout the patients' hospital stay, thus increas-

ing the potential to detect episodes of atrial fibrillation. This difference in monitoring could explain the higher occurrence of atrial fibrillation in the study by Guarnieri et al²⁴ but contradicts the lower occurrence observed by Yagdi et al.²⁶

The Atrial Fibrillation Suppression Trial II²⁹ was a randomized, prospective study on the use of combination intravenous and oral amiodarone administered postoperatively to prevent atrial fibrillation after cardiac surgery. Although amiodarone reduced the incidence of atrial fibrillation by 43%, the comparison of patients given amiodarone with patients given placebo involved a small subgroup, so this trial is not included in this literature review.

Preoperative and Postoperative Comparison Studies

A combined regimen of preoperative and postoperative dosing of amiodarone to reduce the risk of atrial fibrillation was examined in 4 prospective randomized, double-blind studies.^{9,15,27,28} Daoud et al,⁹ Redle et al,²⁷ and Maras et al¹⁵ examined oral administration of amiodarone, whereas Lee et al²⁸ examined intravenous administration (Table 4).

Overall, the 4 studies had similar results in favor of using preoperative and postoperative amiodarone dosing to prevent atrial fibrillation after cardiac surgery. The decrease in the occurrence of atrial fibrillation ranged from 8% to 64%. Similar to the studies²³⁻²⁶ in which amiodarone was given postoperatively only, this wide variation in outcomes could be due to differences between the studies^{9,15,27,28} in sample characteristics, amiodarone dosing only, definition of episodes of atrial fibrillation, and monitoring.

The diverse sample characteristics may have affected the wide range of results. Of these 4 studies,^{9,15,27,28} only the investigation by Daoud et al⁹ included patients undergoing all types of open heart surgery; the other 3 studies included only patients undergoing CABG surgery. As a result, Daoud et al detected a higher rate of atrial fibrillation than did the other researchers.^{15,27,28} These 4 studies also differed in their exclusion criteria. Maras et al¹⁵ and Lee et al²⁸ excluded patients with any history of atrial fibrillation. Redle et al²⁷ excluded patients who had had atrial fibrillation in the preceding 6 months. Daoud et al⁹ included patients with a history of atrial fibrillation but excluded patients with chronic atrial fibrillation, thus possibly increasing the risk for atrial fibrillation in the patients in that study.

A wide dosing range of amiodarone was used in these studies. The total amount of amiodarone given ranged from 2.8 g to approximately 6.0 g. Preoperative dosing with various doses was started anywhere from 7 days to 1 day before surgery. The duration of postoperative dosing was more consistent; Daoud et al,⁹ Redle et al,²⁷ and Maras et al¹⁵ continued treatment with amiodarone for 7 days or until the patients were discharged. Lee et al²⁸ discontinued treatment with the drug on postoperative day 5.

The greatest variation among the studies was in the definition of episodes of atrial fibrillation. Daoud et al⁹ considered any episode of atrial fibrillation significant if the episode lasted at least 5 minutes, whereas Lee et al²⁸ included only episodes that lasted at least 10 minutes. Redle et al²⁷ considered an episode of atrial

Table 4 Preoperative and postoperative treatment with amiodarone to prevent atrial fibrillation after cardiac surgery

Study	Sample size (N)	Sample characteristics	Definition of an episode of atrial fibrillation	Amiodarone dosing	Monitoring	Outcomes
Daoud et al, ⁹ 1997	124	Patients undergoing open heart surgery who required CPB Included patients with a history of atrial fibrillation Excluded patients with chronic atrial fibrillation	Any episode lasting >5 minutes was considered significant	200 mg orally 3 times a day for at least 7 days before surgery 200 mg/d orally postoperatively until discharge from the hospital	Continuous monitoring throughout hospitalization	Atrial fibrillation in 25% of the treatment group and 53% of the control group <i>P</i> = .003*
Redle et al, ²⁷ 1998	143	CABG patients who required CPB	Any episode that lasted for at least 30 minutes or that required treatment for symptoms or a compromise in hemodynamic status was considered significant	2 g orally in a graduated dosing schedule over a maximum of 4 days preoperatively 400 mg/d orally for 7 days starting on postoperative day 1	Continuous monitoring for 96 hours after surgery	Atrial fibrillation in 24.7% of the treatment group and 32.8% of the control group <i>P</i> = .30
Maras et al, ¹⁵ 2001	315	CABG patients who required CPB	Any episode that lasted >1 hour or was associated with a compromise in hemodynamic status	1200 mg orally 1 day before surgery 200 mg/d orally for 7 days after surgery	For at least 24 hours postoperatively	Atrial fibrillation in 19.5% of the treatment group vs 21.2% of the control group In elderly patients, atrial fibrillation in 27% of the treatment group vs 43% of the control group <i>P</i> = .78
Lee et al, ²⁸ 2000	150	CABG patients who required CPB	Any episode lasting >10 minutes was considered significant	150 mg intravenous loading dose and then 0.4 mg/kg per hour intravenously for 3 days preoperatively and 5 days postoperatively	Continuous monitoring throughout the hospital stay	Atrial fibrillation in 12% of the treatment group and 34% of the control group <i>P</i> < .01*

Abbreviations: CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass.
* Differences between groups were statistically significant.

fibrillation significant if it lasted at least 30 minutes or required immediate treatment. Finally, Maras et al¹⁵ only examined episodes associated with compromise in hemodynamic status or episodes that lasted longer than 1 hour. The shorter duration required for an episode of atrial fibrillation to be considered significant could increase the num-

ber of episodes observed in the studies by Daoud et al⁹ and Lee et al²⁸ and could account for the higher rate of occurrence of atrial fibrillation observed in their studies. These differences in definition can also explain why Redle et al²⁷ and Maras et al¹⁵ detected fewer episodes than did Daoud et al⁹ and Lee et al.²⁸ The longer duration of episodes of atrial

fibrillation considered significant also accounts for the lack of statistical significance in the studies by Redle et al²⁷ and Maras et al.¹⁵

Finally, the diverse methods of cardiac monitoring postoperatively may have influenced the wide range of outcomes. Daoud et al⁹ and Lee et al²⁸ used continuous cardiac monitoring throughout patients' hospi-

talization. Redle et al²⁷ monitored patients continuously for 96 hours postoperatively. Maras et al¹⁵ monitored patients continuously for 24 hours after surgery and then obtained electrocardiographs twice daily and periodically monitored pulse rates to detect palpitations. The lack of prolonged continuous monitoring in the studies by Redle et al²⁷ and Maras et al¹⁵ could have influenced the reported incidence of atrial fibrillation, because episodes that occurred after the period of continuous monitoring might have been missed, a situation that might explain the lack of statistical significance in these 2 studies.

Summary of Study Findings

Statistically significant results in 6 of the studies reviewed^{19,23-26,28} support the use of amiodarone. In the remaining 4 studies,^{15,21,22,27} the researchers detected favorable trends toward a significant decrease in atrial fibrillation in the general population; Butler et al²¹ found a significant reduction in atrial fibrillation in elderly patients treated with amiodarone, and Redle et al²⁷ reported a statistically significant decrease in the need for treatment of either supraventricular or ventricular arrhythmias in patients treated with the drug. Unfortunately, because of the variability between all the studies in terms of dosing regimens, exclusion criteria, patients' characteristics, and definitions of episodes of atrial fibrillation, it is not possible to decipher which regimen is the most effective for guiding evidence-based practice.

The majority of the studies involved patients undergoing CABG surgery; only 2 of the studies included patients undergoing all types of cardiac surgery. Of interest, no studies have examined the benefits of amio-

darone prophylaxis in patients undergoing valve surgery only, which has a higher incidence of postoperative atrial fibrillation. In studies that did include patients undergoing valve surgery, the occurrence of atrial fibrillation was not given for each surgical group; thus, the impact of each group of patients on the overall results cannot be determined.

The characteristics of the patients also differed between studies. The mean age of the patients in the samples differed; therefore, studies in which the mean age of the patients was higher could have had higher incidences of atrial fibrillation, making it difficult to compare results. The percentages of patients taking β -blockers, calcium channel blockers, and digoxin before surgery also varied between studies, and these variables were not controlled. Thus, the studies in which higher percentages of patients were taking these medications preoperatively might have had lower rates of postoperative atrial fibrillation because all of these pharmacological agents are associated with decreases in the incidence of atrial fibrillation after surgery. Furthermore, none of the researchers addressed the use of these medications postoperatively, neglecting the possibility of β -blocker withdrawal on the impact of postoperative atrial fibrillation.

Finally, the most important difference between the studies is the wide range of definitions provided for episodes of atrial fibrillation. These definitions extend from any episode of atrial fibrillation requiring treatment to any episode lasting longer than 1 hour. In all of the studies, any episode resulting in a compromise in hemodynamic status was considered

significant regardless of the duration of the episode; however, hemodynamic compromise is uncommon in patients with postoperative atrial fibrillation.² The variations in the definitions make it almost impossible to compare the findings in each study because the requirement for longer lasting episodes results in fewer occurrences of "significant" atrial fibrillation than does the requirement for shorter lasting episodes.

Nursing Implications

The nursing considerations for patients receiving amiodarone to prevent atrial fibrillation after cardiac surgery include identification of patients at greater risk for atrial fibrillation; the administration, potential side effects, and drug interactions of amiodarone; and monitoring for postoperative atrial fibrillation. Patients at greater risk for postoperative atrial fibrillation include those who are elderly, are men, have a history of atrial fibrillation, are undergoing valve surgery, and have comorbid conditions such as chronic lung disease, hypertension, and congestive heart failure.⁷

The toxic effects of amiodarone have been associated with a variety of complications that occur with early and chronic use. However, toxic effects are mostly related to the duration of administration, and therefore amiodarone is better tolerated in low-dose short-term therapy.³

With initial intravenous administration, cardiac monitoring is necessary because of potential bradycardia and hypotension. Amiodarone also prolongs the QT interval and QRS duration, thus increasing the risk for ventricular arrhythmias, although these arrhythmias rarely

occur.¹³ Pulmonary toxic effects are the most serious noncardiac side effect and if left untreated can result in respiratory failure.¹⁴ Routine chest radiography or chest radiography at the time of the onset of symptoms (cough, shortness of breath, low-grade fever) is the best screening method.¹⁴ Heart failure, thyroid dysfunction, and hepatic toxic effects are also complications associated with long-term amiodarone therapy; therefore, thyroid function tests and liver enzyme assays should be used to monitor for any indications of these effects. Because of the long half-life of amiodarone, the toxic effects may persist long after use of the drug is discontinued.¹⁴

Amiodarone interacts with several medications. It can intensify the effects of anticoagulants, especially warfarin, and so, coagulation times should be monitored.¹³ Monitoring coagulation times is especially important in patients after valve surgery because these patients often require anticoagulants postoperatively. The risk for myopathy and rhabdomyolysis can be increased when amiodarone is given in conjunction with simvastatin.³⁰ Because of the wide range of pharmacological properties of amiodarone, administration of amiodarone in conjunction with β -blockers, calcium channel blockers, and other antiarrhythmic agents can exacerbate the effects of these other medications and lead to worsening bradycardia, hypotension, and arrhythmias.³⁰ Amiodarone may also increase serum levels of digoxin and theophylline, and therefore, routine monitoring is necessary.³⁰

The dosage of amiodarone used depends on whether the patient has any organ dysfunction and the

arrhythmia being treated. Suggested guidelines¹⁴ for treatment of supraventricular arrhythmias include an initial oral loading dose of 600 to 800 mg/d for 4 weeks.¹⁴ The daily dosage can be divided into smaller doses given 2 or 3 times a day; smaller doses given at intervals are usually better tolerated by the gastrointestinal tract than a single large dose is.³⁰ After this initial loading period is completed, the dosage can be decreased to 400 mg/d for 2 to 4 weeks and then to a maintenance dose of 200 mg/d.¹⁴ Daily doses of amiodarone are adequate because of the long half-life of the drug.¹³ Oral amiodarone administered with food has a higher rate of absorption than does amiodarone taken when the stomach is empty; therefore, the drug should be taken with meals.³⁰ Patients taking oral amiodarone should avoid grapefruit juice, which prevents metabolism of the drug and therefore increases the serum levels of amiodarone.³⁰ Finally, the most common side effect of oral administration of amiodarone is nausea and vomiting.³⁰

The only conditions for which intravenous amiodarone is approved by the Food and Drug Administration are recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia.³¹ The manufacturer of amiodarone does not provide dosing guidelines for treatment of supraventricular tachycardia because approval from the Food and Drug Administration for this use has not been obtained.

Institutions vary in the infusion rate and loading dose of intravenous amiodarone used to treat atrial fibrillation. Intravenous administration is often started at 150 to 300 mg or

5 mg/kg given over 30 minutes and then 1 to 1.2 g or 15 mg/kg given over the first 24 hours.^{13,17} Because of amiodarone's long half-life, loading doses are given to decrease the amount of time required for the drug to reach a steady-state serum concentration.³¹ These doses are given slowly to prevent hypotensive episodes.³¹ Intravenous amiodarone is reconstituted in 5% dextrose in water.³¹ Intravenous administration of amiodarone through a central catheter or large-bore intravenous catheter with an in-line filter avoids irritation and potential venous thrombosis.¹⁷ Patients should not be given intravenous amiodarone for longer than 3 weeks, and a change to oral amiodarone at that time should be considered.³¹ Finally, although amiodarone can decrease the occurrence of postoperative atrial fibrillation, it may not prevent the arrhythmia, and therefore monitoring for several days postoperatively is necessary.

Future Studies

Because of the wide variability among the studies reviewed, future research is still required to develop evidence-based practice standards for the most effective regimen of amiodarone for prevention of postoperative atrial fibrillation. Overall, the sample sizes in the studies^{9,15,21-28} were small; the total number of patients from all the studies was 1279. Future multisite studies with larger sample sizes are necessary to determine the ideal regimen for amiodarone. Additionally, studies including more women and stratifications for sex and age would be of value.²

Future researchers should consider restricting the use of other pharmacological agents preoperatively, in

an effort to eliminate the possible influences of the preoperative agents on the prevention of atrial fibrillation.² However, investigating the effects of combination therapy of amiodarone plus β -blockers, calcium channel blockers, and, possibly, atrial pacing would also be beneficial.² Finally, a comparison of the cost of amiodarone prophylaxis with the cost of complications from postoperative atrial fibrillation would be useful.²

Conclusion

Current guidelines³² for the management of patients with atrial fibrillation recommend the use of β -blockers as the class I therapy for the prevention of atrial fibrillation in patients undergoing cardiac surgery. The use of amiodarone as a prophylactic therapy in this population of patients is a class IIa recommendation based on a lower level of evidence.³² Atrioventricular nodal blocking agents are still the initial therapy recommended for treatment of atrial fibrillation in patients after cardiac surgery.³¹

Although β -blockers are currently the recommended prophylaxis for atrial fibrillation after cardiac surgery, not all patients tolerate β -blockers. Therefore, the finding that both oral and intravenous amiodarone given postoperatively with or without preoperative dosing reduce atrial fibrillation after cardiac surgery is important, and each variation may have a role in preventing atrial fibrillation. When cardiac surgery cannot be scheduled in advance in order to begin preoperative treatment with amiodarone, postoperative treatment with the drug would be appropriate. Some patients may be unable to take an oral medication; for these patients, intravenous administration would

be appropriate. Currently, amiodarone appears to be a promising option for preventing atrial fibrillation after cardiac surgery; however, further studies are required to determine the role of amiodarone relative to other preventive strategies and to define the most appropriate dosing regimen.

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CE Test Test ID C0612: Use of Amiodarone to Prevent Atrial Fibrillation After Cardiac Surgery

Learning objectives: 1. Discuss the indications for use of amiodarone for the prevention of atrial fibrillation after cardiac surgery 2. Identify the mechanisms of action of amiodarone 3. Summarize study findings related to the use of amiodarone for atrial fibrillation 4. Describe the nursing implications related to use of amiodarone after cardiac surgery for the prevention of atrial fibrillation

1. How many cardiac surgery procedures are performed annually in patients in the United States?
 - a. 100 000
 - b. 200 000
 - c. 400 000
 - d. 600 000
2. What is the incidence of atrial fibrillation after cardiac surgery?
 - a. 1% to 5%
 - b. 5% to 20%
 - c. 10% to 50%
 - d. 20% to 70%
3. The incidence of postoperative atrial fibrillation is highest in which of the following cardiac procedures?
 - a. Cardiac vessel stenting
 - b. Coronary artery bypass surgery
 - c. Percutaneous transluminal coronary angioplasty
 - d. Valve surgery
4. Treatment with amiodarone can reduce the occurrence of postoperative atrial fibrillation by what percentage?
 - a. 10%
 - b. 25%
 - c. 50%
 - d. 75%
5. Which of the following intraoperative factors has not been demonstrated to influence the frequency of postoperative atrial fibrillation?
 - a. Cross-clamp times
 - b. Atrial incisions
 - c. Placement of venous cannulas
 - d. Pulmonary artery venting
6. Amiodarone is classified as what type of antiarrhythmic agent?
 - a. Class I
 - b. Class II
 - c. Class III
 - d. Class IV
7. What is the range of onset of action with oral administration of amiodarone?
 - a. 2 to 12 days
 - b. 2 to 21 days
 - c. 2 to 30 days
 - d. 2 to 45 days
8. What is the half-life of amiodarone?
 - a. 5 to 10 days
 - b. 2 to 21 days
 - c. 16 to 180 days
 - d. 21 to 200 days
9. In studies conducted on the use of amiodarone for postoperative atrial fibrillation prevention, what factor had the greatest variation?
 - a. Frequency of daily dosing
 - b. Total duration of dosing
 - c. Definition of episodes of atrial fibrillation
 - d. Methods of postoperative cardiac monitoring
10. How many studies have been conducted on the benefits of amiodarone prophylaxis in patients undergoing valve surgery?
 - a. None
 - b. Two
 - c. Five
 - d. Ten
11. The toxic effects of amiodarone are mostly related to which of the following?
 - a. Total dose
 - b. Duration of administration
 - c. Method of administration
 - d. Concurrent medication use
12. Oral administration of amiodarone has a higher rate of absorption with which of the following?
 - a. Concurrent administration of calcium channel blockers
 - b. Once a day dosing
 - c. Use of an initial oral loading dose
 - d. Concurrent administration with food
13. Amiodarone should not be given intravenously for longer than what time frame?
 - a. 24 hours
 - b. 3 days
 - c. 1 week
 - d. 3 weeks

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

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