Intraoperative loading dose of amiodarone for prophylaxis against atrial fibrillation after valvular heart surgery

Yasser Mohamed Amr, Elsayed M. Elmistekawy, Abd-Almohsen M. Hammad

Departments of Anesthesia and Cardiothoracic Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding author: Dr. Yasser Mohamed Amr, Department of Anesthesia, Faculty of Medicine, Tanta University, Tanta - 31527, Egypt.
E-mail: yasser.amr@gmail.com

Anesth Essays Res 2010, 4: 96-101

Abstract

**Objective:** Benefit of amiodarone in restoring sinus rhythm (SR) after cardiac surgery was concluded in previous studies that used different protocols for giving amiodarone. The purpose of this study was to assess the use of single parenteral intraoperative loading dose of amiodarone without maintenance as prophylaxis against atrial fibrillation (AF) after valvular heart surgery.

**Materials and Methods:** This was a prospective, randomized, double-blind controlled study on 94 patients listed for valvular heart surgery. The patients received either amiodarone, 3 mg/kg diluted in 100 ml of normal saline and started prior to making skin incision and administered through venous line over a period of 30 minutes, or the same volume of normal saline infused in a similar fashion. The incidence of AF during the first 5 days after surgery was the main outcome measured.

**Results:** There was significant difference in favor of the amiodarone group regarding restoration of sinus rhythm after aortic cross-clamp removal, number of patients requiring cardioversion, incidence of AF and the time elapsed before incidence of it postoperatively (P values=0.02, 0.04, 0.02, 0.02, respectively). There was no difference in hospital mortality, major postoperative morbidity, intensive care unit (ICU) stay or hospital stay.

**Conclusions:** Amiodarone prophylaxis in a single intraoperative dose was significantly effective in prevention of new-onset postoperative AF after valvular heart surgery. This amiodarone dose is well tolerated and not associated with postoperative complications.

**Key words:** Amiodarone, atrial fibrillation, valvular heart surgery

INTRODUCTION

Postoperative atrial fibrillation (AF) is recognized as a common complication of cardiac surgery, occurring in up to 43.7% of the patients.[1] AF remains an important cause of patient discomfort, anxiety, hemodynamic deterioration, stroke, exposure to the risks of tachyarrhythmia treatments, prolongation of hospital
stay, and expenses after heart surgery. AF is facilitated by atrial manipulation, epicardial inflammation, hypoxia, acidosis, electrolyte disturbances, and electrophysiological changes that accompany sympathetic nervous system discharge. These factors are common in valvular surgery.

Amiodarone is a class III antiarrhythmic drug that is effective for the treatment of AF and can be given safely in patients with structural heart disease.

Several studies had evaluated the effects of perioperative oral amiodarone on AF after cardiac surgery. Oral amiodarone in addition to delayed onset of action needs either admission or frequent outpatient visits to monitor the patient. Taking into consideration the rapid onset of action of intravenous amiodarone, we postulated that a loading dose of IV amiodarone in the operative room may reduce the risk of development of postoperative AF. The purpose of this study was to assess the use of parenteral intraoperative loading dose of amiodarone as prophylaxis against AF after valvular heart surgery.

MATERIALS AND METHODS

This study included adult patients of either gender with sinus rhythm (SR), scheduled for elective isolated valve surgery with cardiopulmonary bypass (CPB). The protocol was approved by the institutional ethical committee, and informed consent was signed by all the patients. All the patients had their baseline electrocardiogram (ECG) evaluated. Patients were excluded if they were allergic to amiodarone, had used amiodarone within 4 months of enrollment or had a history of amiodarone toxicity. Patients receiving class I, III or IV antiarrhythmic therapy, patients with untreated thyroid disease, elevation of liver enzyme concentrations to four times the upper limit of normal, pregnant patients, patients with resting heart rate <50 beats/minute, uncontrolled heart failure or in NYHA (New York Heart Association functional classification system) class VI were also excluded from the study.

This study was carried out on 97 patients. All the patients underwent the routine preoperative workup. The baseline ECG was evaluated for rhythm pattern. A prospective, randomized (sealed envelope indicates the group of assignment), double-blind design was used. An independent anesthesiologist, who did not participate in the study or data collection, read the number contained in the envelope and made group assignments.

Patients were randomized in two groups and received either a loading dose of amiodarone (3 mg/kg) or a similar volume of normal saline as a placebo. Infusion sets were identical, covered, and encoded group I (amiodarone group) or II (placebo group) by blinded anesthetist and a nurse not participating in the study or data collection.

Anesthesia technique

All the patients were premedicated with intramuscular injection of morphine 0.1 mg/kg and promethazine 0.5 mg/kg, 1 hour before induction.

In the operation theater, patients were monitored using ECG, pulse oxymetry and noninvasive blood pressure. After establishing intravenous cannulae and arterial line, anesthesia was provided according to a fixed protocol. General anesthesia was induced with the following drugs intravenously: 2 µg/kg of fentanyl, 0.02 mg/kg of midazolam, 5 mg/kg of thiopentone and tracheal intubation was achieved with 0.1 mg/kg of pancuronium. Anesthesia was maintained with incremental doses of fentanyl, midazolam, isoflurane and pancuronium. The right internal jugular vein was cannulated with double or triple lumen central venous catheter. Ventilation was adjusted to maintain the PaCO₂ between 35 and 40 mmHg. Frequent assessment of the blood gases and electrolyte state of the patient was done.

Operative technique

All operations were performed through median sternotomy. Heparin was administered in a loading dose of 300 units/kg to achieve an activated clotting time (ACT) of 480 seconds or more.

CPB was established in a standard way; the ascending aorta was cannulated for arterial input and venous return was achieved with either a single two-stage venous cannula or bicaval cannulation. Myocardial protection was achieved with intermittent cold crystalloid cardioplegia administered every 20 minutes via antegrade, retrograde or both routes. After release of aortic cross-clamp, the initial rhythm was noted. Internal cardioversion was done using 10–40 J for AF, ventricular fibrillation or ventricular tachycardia. Pacing was used for patients with atrioventricular block. Inotropes (dobutamine±adrenaline) were used to maintain hemodynamic performance if hypotension was encountered. After protamine sulfate, 1 mg/100 units heparin was given to neutralize the effect of heparin and bring ACT to normal range, then aorta was decannulated.

Postoperative management

On return to cardiac surgical intensive care unit (ICU), all the patients were continuously monitored. Mean arterial blood pressure was kept between 60 and 90 mm Hg and the heart rate between 60 and 100 beats/minute. Electrolytes were kept within the normal range. Weaning from mechanical ventilation was started when appropriate.

All the patients had continuous display of the ECG in the ICU and continuous monitoring in the step-down unit up to the 5th postoperative day.
Twelve-lead electrocardiography was done daily starting from the day of operation to the 5th postoperative day, and on demand to document any rhythm disturbance then at discharge. No specific protocol for AF treatment was specified and the treatment was done as directed by the attendant physician.

**Study protocol**

In amiodarone group, 3 mg/kg total dose diluted in 100 ml of normal saline was started prior to making skin incision and administrated through venous line over a period of 30 minutes. In the control group, the same volume of normal saline was infused in a similar fashion. If bradycardia, heart rate <60 beats/minute, or hypotension defined as systolic blood pressure <90 mmHg was noted, the infusion was temporarily discontinued, and preload was optimized to treat hypotension. Inotropic support was initiated if required to achieve hemodynamic stability. When hemodynamic stability was reestablished, reinjection of the drug was completed. The surgical team and anesthesia team were not aware of patients’ allocations to either group.

**Primary end point**

The primary end point of this study was occurrence of AF during the first 5 days after surgery. For the purpose of the study, AF was defined as any episode of new onset AF of more than 5 minutes duration, regardless of the effect on the hemodynamic status or the need for medication. ECG was continuously observed using the cardiac monitor and any episode of arrhythmia was recorded with single-lead print out or 12-lead ECG whenever possible.

**Secondary end points**

The number of AF episodes, the duration of the longest episode, and the total duration of AF (number of hours of AF during the first five postoperative days) were recorded. The ventricular response rate on the subsequent postoperative day of occurrence of AF was also recorded. Moreover, the number of patients who had symptoms of AF in the form of palpitation, anxiety or chest discomfort was reported. Finally, morbidity, adverse events potentially attributable to amiodarone, and the length of postoperative hospital stay were also recorded.

**Statistical analysis**

Statistical presentation was conducted using means±SD and student’s t-test for continuous variables. Categorical variables were compared by means of Chi-square test. A P value of <0.05 was considered statistically significant.

**RESULTS**

**Preoperative patients’ characteristics**

The characteristics of the patients are summarized in Table 1.

There was no statistically significant (NS) difference between the two groups in terms of gender, age, ejection fraction, diabetes mellitus, chronic obstructive pulmonary disease, hypertension and preoperative medications.

**Operative characteristics**

There was no significant difference in the surgical data (type of procedure, cross-clamp time, total bypass time) between the two groups. Temporary pacemaker was needed in one patient in the control group.

In the amiodarone group, the initial rhythm after the release of aortic cross-clamp was noted to be AF in 2.2% (n=1) and ventricular tachycardia/fibrillation in 30.4% (n=14); all were converted to normal SR. In the control group, the rhythm after the release of aortic cross-clamp was AF in 14.6% (n=7) and ventricular tachycardia/fibrillation in 39.6% (n=19); all were converted to normal SR.

**Table 1: Preoperative characteristics**

|                     | Amiodarone (n=46) | Placebo (n=48) | P value | NS |
|---------------------|-------------------|----------------|---------|----|
| Age* (years)        | 36.36±10.68       | 37.33±10.79    | 0.66    |    |
| Gender: Male/female | 25/21             | 25/23          | —       |    |
| Body weight* (kg)   | 75.15±12.51       | 77.50±12.83    | 0.37    |    |
| Body surface area* (m²) | 1.82±0.21    | 1.85±0.21      | 0.49    |    |
| Preoperative NYHA class* | 2.21±0.72   | 2.22±0.75      | 0.95    |    |
| Class†              |                   |                |         |    |
| I                   | 8                 | 9              | 0.86    |    |
| II                  | 20                | 19             | 0.70    |    |
| III                 | 18                | 20             | 0.80    |    |
| Preoperative ejection fraction* | 59.93±7.11 | 59.27±7.23    | 0.66    |    |
| Comorbidities†      |                   |                |         |    |
| Hypertension        | 5 (10.86%)        | 9 (18.75%)     | 0.28    |    |
| Diabetes mellitus   | 4 (8.69%)         | 8 (16.66%)     | 0.27    |    |
| Smoking             | 10 (21.37%)       | 11 (22.91%)    | 0.89    |    |
| COPD                | 1 (2.17%)         | 2 (4.61%)      | 0.58    |    |
| Cerebrovascular diseases | 3 (6.52%)       | 2 (4.61%)      | 0.61    |    |
| Preoperative medications† |                 |                |         |    |
| Digitalis           | 33 (71.73%)       | 34 (70.83%)    | 0.92    |    |
| Beta blockers       | 17 (36.95%)       | 19 (39.58%)    | 0.79    |    |
| Diuretics           | 29 (63.04%)       | 30 (62.50%)    | 0.95    |    |
| ACE/ARB             | 9 (19.56%)        | 9 (18.75%)     | 0.92    |    |

*Values are expressed as means±standard deviation; †Values are expressed as number; Gender: Male/female is expressed in number; NYHA - New York Heart Association functional classification system; COPD - Chronic obstructive pulmonary disease; ACE - Angiotensin converting enzyme inhibitors; ARB - Angiotensin receptor blockers; NS - Not significant
normal SR. Number of patients requiring cardioversion and amount of required energy for cardioversion was significantly less in amiodarone group ($P$ value 0.04 and 0.001, respectively). There was a statistically significant difference in favor of the amiodarone group regarding spontaneous restoration of SR after aortic cross-clamp removal [amiodarone group (31/46=67.4%) versus placebo group (21/48=43.8%)] ($P$ value 0.02) [Table 2].

**Postoperative atrial fibrillation**

The incidence of AF was 17.4% (8 out of 46 patients) in the amiodarone group and 39% (19 out of 48 patients) in the placebo group; the difference was statistically significant ($P$ value 0.02).

AF occurred at a mean of 3.3±0.9 days after surgery in the amiodarone group and 2.9±0.8 days after surgery in the placebo group ($P=0.02$). The maximal ventricular rate during AF was insignificantly lower in the amiodarone group than in the placebo group (159.2±11.2 versus 162.9±9.8 beats/minute) ($P=0.09$, NS). However, there was no significant difference between the two groups in the total duration of AF (240±193.4 versus 254.7±110.4 minutes) ($P=0.65$, NS).

Symptoms attributable to AF were reported in 3 out of 8 (37.5%) patients who developed AF in the amiodarone group and 11 out of 19 (57.8%) patients who developed AF in the placebo group ($P=0.33$, NS) [Table 3].

AF was initially managed with antiarrhythmic medication in 3 patients (37.5%) assigned to amiodarone group and in 11 patients (57.3%) assigned to placebo ($P=0.33$, NS) group. Spontaneous conversion occurred in five patients receiving amiodarone (62.5%) and in eight patients receiving placebo (42.1%) ($P=0.33$, NS).

In spite of the absence of predesigned standard protocol to manage postoperative AF, we found that all patients who required antiarrhythmic treatment received oral amiodarone either solely (six patients) or after intravenous loading (eight patients).

**Length of hospital stay**

The duration of ICU stay and the total hospital stay were insignificantly shorter in the amiodarone group versus placebo group (2.4±0.5 versus 2.5±0.5 days, respectively) ($P=0.52$, NS) and (10.9±2.5 days versus 11.3±3.0 days, respectively). Also, when considering the patients who developed AF, the mean length of stay was 12.1±2.8 days in the amiodarone group versus 12.4±3.5 days in the placebo group ($P=0.66$, NS) [Table 2].

**Morbidity and mortality in the hospital**

No mortality was recorded in this series of patients. There was no significant difference in the incidence of complications between the amiodarone and placebo groups. Major postoperative complications occurred in 9 patients in the amiodarone group (19.6%) and in 10 patients in the placebo group (20.1%) ($P=0.88$, NS) [Table 3].

None of our patients showed important side effects of amiodarone, e.g., bradycardia, hypotension, hepatotoxicity, pulmonary toxicity or QT interval prolongation during patient hospitalization.

**Table 2: Operative characteristics**

|                      | Amiodarone (n=46) | Placebo (n=48) | $P$ value |
|----------------------|-------------------|----------------|-----------|
| Type of operation†   |                   |                |           |
| MV replacement       | 21 (45.65%)       | 22 (45.83%)    | 0.69 (NS) |
| AV replacement       | 7 (15.21%)        | 7 (15.83%)     | 0.93 (NS) |
| DV replacement       | 8 (17.39)         | 9 (18.75%)     | 0.86 (NS) |
| MV repair            | 5 (10.86%)        | 4 (8.33%)      | 0.68 (NS) |
| MV replacement + TV repair | 3 (6.52%) | 4 (8.33%) | 0.74 (NS) |
| DV replacement + TV repair | 2 (4.43%) | 1 (2.08%) | 0.53 (NS) |
| Cardiopulmonary bypass time (minutes)* | 80.9±24.67 | 81.56±23.81 | 0.89 (NS) |
| Cross-clamp time (minutes)* | 62.1±20.80 | 63.41±19.81 | 0.76 (NS) |

Rhythm after cross-clamp removal†

|                      | Amiodarone (n=46) | Placebo (n=48) | $P$ value |
|----------------------|-------------------|----------------|-----------|
| VT/VF                | 14 (30.43%)       | 19 (39.58%)    | 0.33 (NS) |
| AF                   | 1 (2.17%)         | 7 (14.85%)     | 0.03      |
| SR                   | 31 (67.39%)       | 21 (43.75%)    | 0.02      |
| JR                   | 0                 | 1 (2.08%)      | –         |
| Number of patients requiring cardioversion† | 15 (32.60%) | 26 (54.13%) | 0.04 |
| Amount of required energy for cardioversion (Joules)* | 20.31±12.56 | 29.23±12.93 | 0.001 |
| Number of patients requiring inotropic support† | 15 (32.60%) | 16 (33.33%) | 0.94 (NS) |

|                      |                   |                |           |

*Values are expressed as mean±standard deviation; †Values are expressed as number and percentage; MV - Mitral valve; AV - Aortic valve; DV - Double valve (mitral and aorta); TV - Tricuspid valve; VT/VF - Ventricular tachycardia/fibrillation; AF - Atrial fibrillation; JR - Junctional rhythm; SR - Sinus rhythm; NS - Not significant.
DISCUSSION

There are many studies reporting on the use of prophylactic measures for the prevention of post cardiac surgery AF. These studies tried to solve three important issues: postoperative AF prevention, safety of prophylactic therapy, and effect of prevention of postoperative AF on adverse outcomes associated with it.9

This study represents another trial aiming at finding out if a single perioperative (pre-CPB) loading dose of amiodarone could decrease the incidence of postoperative new-onset AF, in a group of patients undergoing valvular surgery with non-compromised cardiac function. Our findings confirm the same. This easy regime allowed more patients to be treated; on the contrary, other studies had appreciable numbers of drug discontinuation.

Benefit of amiodarone in restoring SR was concluded in previous studies on Coronary Artery Bypass Grafting (CABG) patients, which used more or less different protocols for giving amiodarone. Lee et al.10 used loading dose of 150 mg and maintenance dose of 0.4 mg/kg/hour for 3 days before and 5 days after operation. Roshanali et al.11 used 800 mg of oral amiodarone, 1 day before surgery and then amiodarone was administered intraoperatively in a 500-mg bolus for 1 hour. Thereafter, the administration of amiodarone was continued as a total maintenance dose of 20 mg/kg weight over 24 hours on the first postoperative day, which was followed from day 2 through day 5 with 800 mg oral dose daily. Zebis et al.12 used 300 mg amiodarone administered intravenously over 20 minutes followed by 600 mg amiodarone orally twice a day for the first five postoperative days. Hohnloser et al.13 used amiodarone after surgery in a loading bolus of 300 mg for 2 hours followed by 1200 mg every 24 hours for 2 days and 900 mg every 24 hours for the next 2 days.

Contrary to these results, a recently published study by Beaulieu et al.14 using intravenous loading dose of 300 mg of amiodarone in the operating room, followed by infusion of 15 mg/kg/24 hours for 2 days did not reduce the burden of post valvular surgery AF. There was a trend in reduction of AF incidence during medication but this trend was reversed after infusion stoppage, and amiodarone group showed higher incidence of AF. However, this is not unexpected for small trials, and the readers cannot be convinced unless greater precision is provided from a much larger trial, or at least a meta-analysis of all relevant trials to date.

Several meta-analyses have shown amiodarone to be effective in reducing the incidence of AF and its complications after CABG alone or after combined CABG and valvular surgery.15,16

Beta blockers are strong negative risk factors for the development of postoperative AF, especially when patients take beta blockers prior to surgery. Beta blockers were continued in both groups and did not affect the accuracy of the results because of no significant difference in the drug usage between groups.

Selveraj et al.17 evaluated the effect of intraoperative single-dose intravenous amiodarone to convert AF into SR in patients undergoing valvular heart surgery. 75% of the patients in the amiodarone group and 47.4% in the control group reverted to SR after cardioversion. However, in our study, we examined amiodarone prophylactic effect in prevention of new-onset postoperative AF.

Intravenous amiodarone was found to be well tolerated and did not increase the risk of postoperative

**Table 3: Postoperative data**

|                                | Amiodarone (n=46) | Placebo (n=48) | P value |
|--------------------------------|-------------------|----------------|---------|
| Number of patients who had AF† | 8 (17.39%)        | 19 (39.58%)    | 0.02    |
| Number of patients who needed treatment for AF† | 3 (37.5%)        | 11 (57.89%)    | 0.33 (NS) |
| Number of episodes of AF/patient* | 1.72±0.78        | 1.78±0.63      | 0.68 (NS) |
| Duration of AF/patient* (minutes) | 240±193.38       | 254.73±110.37  | 0.65 (NS) |
| Ventricular rate/minute*       | 159.23±11.24     | 162.89±7.95    | 0.09 (NS) |
| Ventilator time* (hours)       | 7.69±2.70        | 7.60±2.20      | 0.86 (NS) |
| ICU stay* (days)               | 2.43±0.54        | 2.50±0.50      | 0.52 (NS) |
| Hospital length of stay* (days)| 10.93±2.55       | 11.27±3.00     | 0.56 (NS) |
| Major complications (total)†   | 9 (19.56%)       | 10 (20.08%)    | 0.88 (NS) |
| Bleeding                       | 2                | 3              |         |
| Wound infection                | 2                | 3              |         |
| Stroke                         | 1                | 1              |         |
| Ventricular tachycardia        | 1                | 1              |         |
| Prolonged ventilation          | 1                | 1              |         |
| Chest infection                | 2                | 1              |         |

*Values are expressed as mean±standard deviation; †Values are expressed as number and percentage; ICU - Intensive care unit; NS - Not significant
complications. This finding was confirmed by the present study as well.

Despite having different mechanisms, magnesium administration and statin therapy are also important in prevention of postoperative AF. However, none of our patients used these drugs.

The small size of the study population, non measurement of amiodarone level in the blood and lack of holter monitoring are the limitations of this study. Due to the absence of standardized protocol for management of postoperative AF, data which depend upon AF response to treatment (length of stay, duration of AF, etc.) contain an undefined amount of noise. Also, with the small sample size, it may be difficult to statistically account for a multivariate analysis of other risk factors of postoperative AF.

CONCLUSIONS

Amiodarone prophylaxis in a single intraoperative dose was significantly effective in prevention of new-onset postoperative AF after valvular heart surgery. This amiodarone dose is well tolerated and not associated with postoperative complications. Future research is still required to develop evidence-based practice standards for the most effective regimen of amiodarone for prevention of postoperative AF.

REFERENCES

1. Banach M, Goich A, Misztal M, Rysz J, Jasiewski R, Goich JH. Predictors of paroxysmal atrial fibrillation in patients undergoing aortic valve replacement. J Thorac Cardiovasc Surg 2007;134:1569-76.
2. Echahidi N, Pibarot P, O’Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. J Am Coll Cardiol 2008;51:793-801.
3. Shantsila E, Watson T, Lip GY. Atrial fibrillation post-cardiac surgery: Changing perspectives. Curr Med Res Opin 2006;22:1437-41.
4. Aasbo JD, Lawrence AT, Krishnan K, Kim MH, Trohman RG. Amiodarone prophylaxis reduces major cardiovascular morbidity. Length of stay after cardiac surgery: A meta-analysis. Ann Intern Med 2005;143:327-36.
5. Gu S, Su PK, Liu Y, Yan J, Zhang XT, Wang TY. Low-dose amiodarone for the prevention of atrial fibrillation after coronary artery bypass grafting in patients older than 70 years. Chin Med J (Engl) 2009;122:2928-32.
6. Redlie JD, Khurana S, Marzan R, McCullough PA, Stewart JR, Westveer DC, et al. Prophylactic oral amiodarone compared with placebo for prevention of atrial fibrillation after coronary artery bypass surgery. Am Heart J 1999;138:144-50.
7. Maras D, Boskovic SD, Popovic Z, Neskovic AN, Kovacevic S, Otasevic P, et al. Single-day loading dose of oral amiodarone for the prevention of new-onset atrial fibrillation after coronary artery bypass surgery. Am Heart J 2001;141:E8.
8. 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 2009;27:253-8.
9. Shrivastava R, Smith B, Caskey D, Reddy P. Atrial fibrillation after cardiac surgery: Does prophylactic therapy decrease adverse outcomes associated with atrial fibrillation. J Intensive Care Med 2009;24:18-25.
10. Lee SH, Chang CM, Lu MJ, Lee RJ, Cheng JJ, Hung CR, et al. Intravenous amiodarone for prevention of atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 2000;70:157-61.
11. Roshanali F, Mandegar M, Yousefjia M, Afaedini F, Saidi B. Prevention of atrial fibrillation after coronary artery bypass grafting via atrial electromechanical interval and use of amiodarone prophylaxis. Interact Cardiovasc Thorac Surg 2009;8:421-5.
12. Zebis LR, Christensen TD, Kristiansen IS, Hjortdal VE. Amiodarone cost effectiveness in preventing atrial fibrillation after coronary artery bypass graft surgery. Ann Thorac Surg 2008;85:28-32.
13. Hohnloser SH, Meinerz T, Dannmbacher T, Steiert K, Jahnchen E, Zehender M, et al. Electrocardiographic and antiarrhythmic effects of intravenous amiodarone: Results of a prospective, placebo-controlled study. Am J Cardiol 1991;61:89-95.
14. Beaulieu Y, Denaout AY, Couture P, Roy D, Talajic M, O’Meara E, et al. Perioperative intravenous amiodarone does not reduce the burden of atrial fibrillation in patients undergoing cardiac valvular surgery. Anesthesiology 2010;112:128-37.
15. Bagshaw SM, Galbraith PD, Mitchell LB, Sauve R, Exner DV, Ghali WA. Prophylactic amiodarone for prevention of atrial fibrillation after cardiac surgery: A meta-analysis. Annu Thorac Surg 2006;82:1927-37.
16. Perkerson KA, Gillespie EL, White CM, Kluger J, Takata H, Kardas M, et al. Impact of prophylactic amiodarone on length of hospital stay, stroke, and atrial fibrillation after cardiothoracic surgery. Pharmacotherapy 2005;25:320-4.
17. Selevaraj T, Kiram U, Das S, Chauhan S, Sahu B, Gharde P. Effects of single intraoperative dose of amiodarone in patients with rheumatic valvular heart disease and atrial fibrillation undergoing valve replacement surgery. Ann Card Anaesth 2009;12:10-6.
18. Tiriyakio glu O, Demircas S, Ari H, Tiriyakio glu S, Huysal K, Selimoglu O, et al. Magnesium sulphate and amiodarone prophylaxis for prevention of postoperative arrhythmia in coronary by-pass operations. J Cardiothorac Surg 2009;4:68.
19. Saos S, Vecht J, Rao C, Protopapas A, Ashrafian H, Leff D, et al. Statin therapy may influence the incidence of postoperative atrial fibrillation: What is the evidence? Tex Heart Inst J 2009;36:521-9.

Source of Support: Nil, Conflict of Interest: None declared.
