

Comparison of Rosuvastatin versus Atorvastatin for Preventing Postoperative Atrial Fibrillation

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ABSTRACT

Background: Postoperative atrial fibrillation (AF) following cardiac surgery is associated with an increased risk of stroke, prolonged hospitalization, and increased costs. Statin therapy is associated with a lower incidence of postoperative AF. We aimed to compare the preventive effects of rosuvastatin and atorvastatin on postoperative AF.

Methods: This study included 168 patients undergoing elective cardiac surgery with cardiopulmonary bypass. Patients were divided into 2 groups according to treatment of statin. Group 1 (n = 96) was patients receiving atorvastatin, and group 2 (n = 72) was patients receiving rosuvastatin. Postoperative electrocardiographs (ECGs) and telemetry strips were examined for AF within postoperative period during hospitalization.

Results: The incidences of postoperative AF were 17.9% (n = 17) in group 1 and 22.2% (n = 16) in group 2 (P = .48). Left ventricular end-diastolic diameter (LVEDD) and ejection fraction (EF) were not different between groups. Incidence of diabetes, hypertension, hyperlipidemia, smoking, myocardial infarction in past medical history, family history of atherosclerosis, male sex, drug use, and perioperative features were similar between groups.

Conclusions: The present study revealed that preoperative rosuvastatin or atorvastatin treatment did not have a different effect in preventing postoperative AF.

INTRODUCTION

Postoperative atrial fibrillation (AF) is a frequent complication after cardiac surgery, occurring in 20% to 30% of patients [Frost 1992], and is associated with increased mortality, significant morbidity, and increased length of hospital stay and costs [Almassi 1997; Mathew 2004]. Although the exact pathophysiologic mechanism causing AF after cardiac surgery is not well defined, a number of clinical and perioperative factors have been shown to be associated with this arrhythmia [Aranki 1996; Almassi 1997]. Recent studies found that atrial fibrillation after cardiac surgery may be associated with

inflammatory response, and statins have been shown to inhibit such inflammatory response and reduce the incidence of AF after cardiac surgery [Young-Xu 2003; Boos 2006]. Rosuvastatin is a new generation statin with a highly effective lipid lowering and antiatherosclerotic activity. Its pharmacologic action has been shown at lower doses, but only few data are available about its advantageous anti-inflammatory properties [Resch 2006]. Previous studies have suggested that preoperative atorvastatin treatment significantly reduces postoperative AF [Patti 2006; Song 2008]. The aim of the present study was to compare the effects of 2 widely used statins—atorvastatin and rosuvastatin—on prevention of postoperative AF.

METHODS

Patients

Between December 2009 and January 2011, we retrospectively enrolled 578 consecutive patients undergoing isolated coronary artery bypass graft surgery (CABG) at our institute. Patients with history of AF, previous CABG, moderate-severe heart valve disease, previous treatment with statins (>1 week), elevated liver enzymes, chronic renal failure, history of liver or muscle disease, and inflammatory diseases that required therapy with steroids or nonsteroidal anti-inflammatory drugs were excluded. In all, 168 patients with normal sinus rhythm were included in the study. In our institute, preoperative beta blocker and statin therapy are given routinely to all patients for prevention of postoperative AF and ischemic heart disease without contraindications to these drugs. Patients were divided into 2 groups according to preoperative statin use. Group 1 (n = 96) was patients receiving atorvastatin, and group 2 (n = 72) was patients receiving rosuvastatin. Statin treatment was continued after extubation on postoperative first day. Patients were given the same statin as started in the preoperative period. Information on demographics, established cardiovascular risk factors, medical history, perioperative features, and transthoracic echocardiograms were recorded for each patient. All operations were performed using standard sternotomy approaches by experienced cardiac surgeons.

Definition of Atrial Fibrillation

Postoperative electrocardiographs (ECGs) and telemetry strips were examined for AF within the postoperative period during hospitalization. This study included patients who were monitored continuously with ECG telemetry equipment, and 12-lead ECGs were obtained daily until discharge. AF was

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Table 1. Clinical and Demographic Parameters*

	Group 1 (n = 96)	Group 2 (n = 72)	P
Age, y	60.7 ± 10.4	61.6 ± 8.5	.55
Male sex	71 (74.0%)	62 (86.1%)	.06
Diabetes	34 (35.4%)	28 (38.9%)	.64
Hypertension	60 (37.5%)	38 (47.2%)	.20
Hypercholesterolemia	46 (47.9%)	40 (55.6%)	.32
Smoking	56 (41.7%)	50 (30.6%)	.14
Body mass index, kg/m ²	27.2 ± 3.8	26.3 ± 2.9	.10
Previous myocardial infarction	27 (28.1%)	14 (19.4%)	.34
Congestive heart failure	12 (12.8%)	10 (13.9%)	.46
Chronic obstructive pulmonary disease	5 (5.2%)	2 (2.8%)	.43
Left ventricular ejection fraction	50 ± 9.2	53.8 ± 8.9	.01
Left ventricle hypertrophy	20 (20.8%)	19 (26.4%)	.39
Left atrium diameter, cm	3.71 ± 0.5	3.76 ± 0.4	.49
Left ventricle diameter, cm	5.0 ± 0.5	5.0 ± 0.5	.73
Multivessel coronary artery disease	89 (92.7%)	64 (88.9%)	.39
Serum creatinine, mg/dL	0.98 ± 0.1	1.0 ± 0.2	.41
Serum CRP levels, mg/dL	12.7 ± 23.05	10.1 ± 9.25	.36
Statin dose, mg†	40	20	
Digoxin	8 (8.3%)	5 (6.9%)	.73
Beta blockers	60 (62.5%)	48 (66.7%)	.68
ACE inhibitors	56 (58.3%)	38 (52.8%)	.70
Postoperative AF	17 (17.9%)	16 (22.2%)	.48

*Data are presented as n (percentage) or n ± standard deviation. CRP indicates C-reactive protein; ACE, angiotensin converting enzyme; AF, atrial fibrillation.
†Median.

defined as absent P wave before the QRS complex together with irregular ventricular rhythm on the ECG.

Statistical Analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) for Windows version 12 (Chicago, Illinois, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were displayed in numbers and percentages. Continuous variables were compared among the groups of patients with independent Student's t-test for normally distributed data. Group comparisons of categorical variables were performed using the Chi-square or Fisher's Exact test, as appropriate. Multiple logistic regression analysis was utilized to identify factors related to postoperative AF. Values of $P < .05$ were considered significant in all analyses.

RESULTS

Of the 168 patients enrolled in the study, 96 were in group 1 (atorvastatin) and 72 were in group 2 (rosuvastatin). Postoperative AF occurred in 17 (17.9%) of 96 patients in group 1 versus 16 (22.2%) of 72 patients in group 2. Peak incidence of postoperative AF was on day 2. Postoperative AF was restored by

amiodarone infusion in all patients. Sinus rhythm maintained in all patients until discharge. The baseline clinical characteristics of the study population are presented in Table 1. No significant differences existed in age, gender, incidence of diabetes, hypertension, hyperlipidemia, congestive heart failure, chronic obstructive pulmonary disease, and smoking and drug use between the 2 groups. Left ventricular end-diastolic diameter (LVEDD), left atrium diameter, and left ventricle hypertrophy were not different between groups. Left ventricular ejection fraction (EF) was significantly higher in group 2 ($P = .01$). Postoperative C-reactive protein (CRP) levels were similar between groups (12.7 ± 23.05 versus 10.1 ± 9.25 , $P = .36$). Perioperative variables of the study group are given in Table 2. Perioperative features were similar between groups. Multivariate logistic regression analysis was performed to determine the independent predictors of postoperative AF including age, hypertension, diabetes mellitus, EF, left atrial size, beta blocker usage, and statin group. In this analysis, hypertension was the only predictor of postoperative AF.

DISCUSSION

The purpose of this study was to compare the effects of 2 different statins with atorvastatin or rosuvastatin on

Table 2. Perioperative Variables*

	Group 1 (n = 96)	Group 2 (n = 72)	P
On-pump surgery, %	100	100	1
Cross-clamp duration, min	82.4 ± 30.9	84.1 ± 44.7	.78
CPB duration, min	148.0 ± 52.1	144.3 ± 61.3	.67
Blood cardioplegia, %	100	100	1
Ventricular pacing	—	—	1
Postoperative myocardial infarction	1 (1.04%)	2 (2.8%)	.40
Postoperative use of inotropic agent	36 (37.5%)	35 (48.6%)	.14
Postpericardiotomy syndrome	—	—	1
Bicaval cannulation	1 (1.04%)	2 (2.8%)	.40

*Data are presented as n (percentage) or n ± standard deviation. CPB indicates cardiopulmonary bypass.

postoperative AF after CABG. The present study revealed that the efficacy of preoperative rosuvastatin or atorvastatin treatment was not different in preventing postoperative AF.

The pathophysiology of postoperative AF is multifactorial, but there is increasing evidence that inflammation and fibrosis play an important role in pathogenesis of AF [Gaudino 2003; Fontes 2005]. The statin's anti-inflammatory effects and protective activity against tissue injury were largely associated with a significant reduction in the risk of AF onset after coronary surgery [Lertsburapa 2008]. The benefits of treatment with statin in reducing the risk of AF among patients with cardiovascular disease may be related to anti-inflammatory and antioxidant actions, improvement of lipid metabolism, prevention of process of atherosclerosis, and reduction of endothelial dysfunction and neurohormonal activation, altered membrane fluidity, and ion channel conductance [Suzumura 1999; Martínez-González 2001; Pound 2001; Plenge 2002].

Several retrospective and observational studies have shown that statin treatment may lower the incidence of AF in postoperative CABG patients [Dotani 2000; Marín 2006; Saveleva 2010]. The ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) study [Patti 2006] was the first randomized, controlled trial that investigated the effects of atorvastatin on postoperative AF in patients undergoing CABG. Two hundred patients undergoing elective CABG, without previous statin treatment or history of AF, were included. Atorvastatin significantly reduced the incidence of AF versus placebo (35% versus 57%, $P = .003$). Also, length of hospital stay was longer in the placebo compared to atorvastatin group (6.9 ± 1.4 days versus 6.3 ± 1.2 days, $P = .001$).

Previous studies have explored an association between the inflammatory markers (interleukin-6 [IL-6] and CRP) and AF [Aviles 2003; Psychari 2005]. Cardiac surgery causes an inflammatory response throughout the postoperative period. Various studies have established that both IL-6 and

CRP were independent predictors of postoperative AF after cardiac surgery [Gaudino 2003; Lo 2005]. Young Joon Hong et al [Hong 2011] have recently demonstrated that rosuvastatin 20 mg versus atorvastatin 40 mg had similar efficacy in low-density lipoprotein cholesterol and high-sensitivity CRP reduction also have similar effects on plaque regression at follow-up. Likewise in our study we found that postoperative CRP levels were similar between the atorvastatin and rosuvastatin groups. The Ongoing Study of Coronary Atheroma by InTravascular Ultrasound: effect of Rosuvastatin versus Atorvastatin (SATURN) trial will compare the effects of rosuvastatin versus atorvastatin on plasma lipids and inflammatory markers and the incidence of clinical cardiovascular events.

Several risk factors for developing postoperative AF have been established, including advanced age, history of supraventricular arrhythmias, male sex, low left ventricular EF, left atrial enlargement, mitral valve surgery, chronic renal failure, chronic obstructive pulmonary disease, diabetes mellitus, increasing aortic cross-clamp time, preoperative use of digoxin, postoperative withdrawal of β -blockers or angiotensin converting enzyme (ACE) inhibitors, and obesity [Creswell 1993; Almassi 1997; Banach 2006; Echahidi 2007]. According to our results, hypertension was the only predictor of postoperative AF.

Although the above mentioned studies have demonstrated the preventive effects of statins on postoperative AF after cardiac surgery, comparison of different statin therapies have not been established. This is the first study comparing the preventive effects of rosuvastatin versus atorvastatin on postoperative AF. We have found that rosuvastatin and atorvastatin had similar effects to prevent postoperative AF. Future randomized, controlled clinical trials are needed to clarify this finding.

Study Limitations

There are several limitations of this study. First, this study is a single-center, retrospective study with a small number of patients that may lead to patient selection bias. Second, comparison anti-inflammatory markers such as IL-6 and preoperative CRP between groups are lacking. Third, long-term follow-up of patients was not performed.

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