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Statins' Protective Effect for The Prevention of Atrial Fibrillation Incidence After Coronary Artery Bypass Surgery

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Abstract: Atrial fibrillation (AF) after cardiac surgery is associated with an increased risk of complications, length of stay, and cost of care. Recent studies have demonstrated that statins have pleiotropic effects, including anti-inflammatory effects and preventing atrial fibrillation (AF). The objective of this study was to assess the efficacy of preoperative statin therapy in preventing AF after coronary artery bypass grafting (CABG). 53 patients underwent CABG in our hospital from February to August 2018. Patients were randomized into two groups to examine the effect of statins: those with atorvastatin 20 mg/day during the preoperative period (Atorvastatin group, n = 26) and those with rosuvastatin 10 mg/day (Rosuvastatin group, n = 27). The primary end-point is postoperative AF (POAF), with an overall incidence of postoperative AF of 11.3%. Postoperative AF incidence was insignificantly different between the atorvastatin and rosuvastatin groups (7.7% vs. 14.8%; p = 0,669). Our study indicated that atorvastatin had a similar protective effect to rosuvastatin in terms of post-operative AF prevention.

Keywords: statin, post-operative AF

INTRODUCTION

Atrial fibrillation (AF) is currently the most common heart rhythm disorder, affecting about 1-2% of the general population. About 2.5 million people in the United States experience atrial fibrillation, and this number is increasing in the elderly and with the presence of structural heart disease. [1] Atrial fibrillation is also the most common complication in post-surgical conditions, both cardiac surgery and other surgeries. The incidence of atrial fibrillation varies between 10–60% in the patient population after cardiac surgery.[2,3] In general, atrial fibrillation occurs between 24 hours and 96 hours postoperatively, with a peak incidence on the second and third days after surgery.

Although some cases are transient and well tolerated, post-

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surgical atrial fibrillation can be life-threatening, especially in elderly patients with impaired left ventricular function, and is associated with higher mortality and morbidity. The chronic condition of atrial fibrillation is also considered to be a major contributor to high health costs. Higher morbidity, mortality rates, and costs require the need for effective strategies to reduce the incidence of atrial fibrillation.

The use of anti-inflammatory drugs such as corticosteroids and ketorolac can reduce the incidence of post-surgical atrial fibrillation. However, these types of drugs might delay the wound healing process and increase the risk of bleeding.

METHOD

This study is a prospective cohort study of patients undergoing coronary bypass surgery at Haji Adam Malik Medan General Hospital. The samples in this study were patients diagnosed with coronary heart disease with significant lesions based on the results of coronary angiography who underwent coronary bypass surgery.

The collection of samples for this study was conducted from February 2018 to August 2018. All samples included in this study were randomized into 2 groups using the block randomization method. The patients in the first group were given atorvastatin 20 mg/day. The patients in the second group were given rosuvastatin 10 mg/day. Both statins were administered at least 7 days before surgery and continued for up to 3 days after surgery.

Clinical examination, laboratory results, ECG, and echocardiography are among the data collected. Atrial fibrillation after coronary bypass surgery (POAF) will be observed using an ECG monitor or on 12 lead ECG recordings. A POAF is defined as a documented incident of atrial fibrillation after coronary bypass surgery for more than 5 minutes. The data obtained then will be analyzed with SPSS software.

RESULT

In this study, there were 53 patients as subjects that were divided into 2 groups; 26 patients in the atorvastatin group and 27 patients in the rosuvastatin group. Table 1 shows the baseline characteristics of subjects based on the type of statin used.

Of the 50 patients in this study, 49 were male (94.3%), and 3 other patients were female (5.6%). The mean age of the atorvastatin group was 54.9 years and 58.7 years in the rosuvastatin group ($p = 0.066$). There was no significant difference in mean body mass index between the two groups.

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Table 1. Baseline Characteristic of Patients

Variable	Atorvastatin (n= 26)	Rosuvastatin (n=27)	P value
Age (years ± SD)	54,9 ± 7,3	58,7 ± 7,3	0,066
Sex (n, %)			0,610
Male	24 (92,3)	26 (96,3)	
BMI (kg/m^2±SD)	27,6± 5,1	26,9± 3,4	0,929
DMT2 (n, %)	8 (30,8)	14 (51,9)	0,166
Dyslipidemia (n, %)	16 (61,5)	17 (63)	0,915
Hypertension (n, %)	21 (80,8)	18 (66,7)	0,244
COPD (n, %)	5 (19,2)	5(18,2)	0,940
Heart failure (n, %)	17 (65,4)	18(66,7)	0,920
Heart rate (bpm ± SD)	70,4±12,1	68,1±10,7	0,466
ECG (ms, min-max)			
P wave duration	8 (6-12)	8 (6-12)	1,000
PR interval	16 (10-20)	18 (12-20)	0,129

Based on the presence of comorbidities, it was found that subjects who had a history of diabetes mellitus were more common in the rosuvastatin group, as many as 14 people (51.9%), compared with the atorvastatin group of 8 people (30.8%). However, the difference is not statistically significant (P = 0.166). There were also no significant differences in other comorbidities, such as hypertension, dyslipidemia, and chronic obstructive pulmonary disease, between the two groups.

In the atorvastatin group, 17 patients (65.4%) had heart failure, while in the rosuvastatin group, 18 people (66.7%). The mean heart rate in both groups was also not statistically different (70.4 bpm vs. 68.1 bpm).

From electrocardiographic examination, there were no significant differences between the duration of the P wave and the PR interval in the two groups.

Table 2 shows the characteristics of echocardiographic parameters in this study. Based on the results of echocardiography, the mean left ventricular ejection fraction (LVEF) in the atorvastatin group was 50.4%, whereas in the rosuvastatin group it was 53%. The mean left atrial diameter in the atorvastatin group was 35.3 mm, while the rosuvastatin group was 35.7 mm. Left ventricular dimensions assessed by LVEDD were 49.1 mm in the atorvastatin group and 47 mm in the rosuvastatin group. Of the three echocardiographic parameters, there were no significant differences in both groups.

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Table 2. Perioperative Characteristic of Patients

Variable	Atorvastatin (n=26)	Rosuvastatin (n=27)	P value
On pump (n, %)	23 (88,5)	22 (81,5)	0,704
CPB time (minutes ± SD)	129±18,3	137,8±40,9	0,355
Operating time (hrs ± SD)	4,8±0,7	4,9±1	0,384

Based on perioperative characteristics, most subjects underwent coronary bypass surgery using cardiopulmonary bypass (CPB) machines, 23 people (88.5%) in the atorvastatin group and 22 people (81.5%) in the rosuvastatin group. The CPB machine use time in the two groups was not significantly different. The mean duration of surgery was 4.8 hours in the atorvastatin group and 4.9 hours in the rosuvastatin group, and there were also no significant differences.

A Fisher's test was performed to assess the relationship between the use of atorvastatin and rosuvastatin on the incidence of atrial fibrillation. The results of the statistical tests are shown in table 4. Of the total 53 subjects, 6 (11.3%) had atrial fibrillation after coronary bypass surgery. Of the 6 subjects who experienced the POAF, 4 (66.7%) were given rosuvastatin, while 2 other patients (33.3%) were given atorvastatin. Whereas in the group that did not experience POAF, there were 24 patients (51.1%) from the atorvastatin group and 23 patients (48.9%) from the rosuvastatin group. Fisher's test results showed that in this study there were no significant differences between the types of statins used and the incidence of atrial fibrillation after coronary bypass surgery with a *P* value = 0.669.

Table 3. Relationship of Statin's Type and POAF Incidence Using Fisher's Test

	POAF		
	Yes	No	P value
Statin (n,%)			0,669
Atorvastatin	2 (33,3)	24 (51,1)	
Rosuvastatin	4 (66,7)	23 (48,9)	
Total	6 (11,3)	47 (88,7)	

The relationship between statin uses and the incidence of atrial fibrillation after coronary bypass surgery is also shown in the Kaplan-Meier curve in Figure 1. It shows the free POAF rate during the hospital stay was higher in the atorvastatin group compared to rosuvastatin, but the difference was not statistically significant with a p value of 0.408. The decrease in survival rate mainly occurs on the first day until the second day after surgery.

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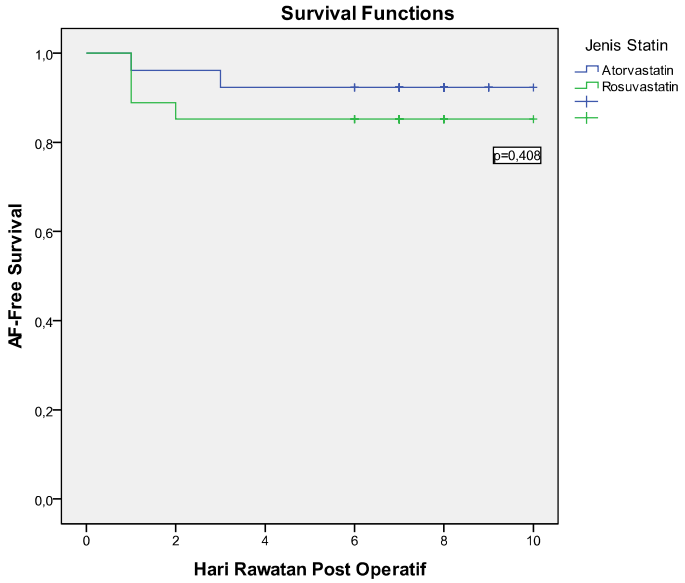

Figure 1. Kaplan-Meier Curve for POAF Free Incidence and Type of Statin

DISCUSSION

This study is a prospective cohort study aimed at comparing the protective effects of atorvastatin and rosuvastatin on the incidence of atrial fibrillation after coronary bypass surgery. The impact of atrial fibrillation on higher morbidity, mortality, and maintenance costs is one of the important aspects of the background of this study.

Based on the characteristics of the study subjects, it was found that most of the samples were men, as many as 50 people (94.3%), although not significantly different between the atorvastatin and rosuvastatin groups.

Male gender is known as one of the risk factors for cardiovascular disease. This can be caused by unhealthy lifestyles such as smoking, consumption of fatty foods, and the habit of drinking alcoholic beverages. This result is consistent with previous studies, where the majority of subjects were men. In a meta-analysis of 12 studies, the percentage of male subjects was 78–80%. [4]

This study showed six (11.3%) patients had experienced POAF, of which 2 patients were given atorvastatin and the other four patients were given rosuvastatin. The incidence of POAF in this study was lower compared to previous studies, with the incidence of POAF ranging from 17–33%. [5,6,7] This may be influenced by the fact that the mean age of patients in this study is 56.8 years, which is relatively younger than the patients in the previous study, who were between 65 and 67 years old. [7,8]

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Older patients have a higher risk of developing atrial fibrillation.

To assess the protective effect of each type of statin on the incidence of POAF, Fisher's test was performed with the result of no significant differences between the two groups of statins with p = 0.669. These results indicate that the use of rosuvastatin 10 mg/day was not superior to atorvastatin 20 mg/day in preventing the occurrence of atrial fibrillation after coronary bypass surgery. Previous studies using several types of statins in 213 patients who underwent coronary bypass surgery showed similar results, in which statin type was not associated with the incidence of POAF. [8]

However, when compared with placebo or standard treatment, there was a decreased risk of POAF in the group given perioperative statins with OR values between 0.33 and 0.74.[5,9,10,11] Previous data showed the incidence of POAF in patients undergoing coronary bypass surgery at Haji Adam Malik General Hospital for 1 year at 24.7%, with the type of statin used being simvastatin with a dose range of 10–20 mg. 12. The incidence of POAF is 2 times higher than the results of this study, which is only 11.3%. The decrease in the incidence of POAF in this study may be related to the use of different types of statins.

Statin's protective mechanism against the incidence of POAF is not fully understood. Several studies have shown that statins have a variety of pleiotropic effects, including anti-inflammatory and antioxidant effects, modifying extracellular matrix remodeling, myocardial protection from ischemia, indirect anti-arrhythmic effects via autonomic system modulation, and direct anti-arrhythmic effects via ion stabilization effects on transmembrane canals. [13,14] The role of inflammation in the POAF mechanism was proven by CRP levels as one of the inflammatory markers experiencing a significant increase in the group experiencing POAF.14 This study showed the post-surgical leukocyte value was higher in the group of patients who experienced POAF, 20,035/µl in the atorvastatin group and 22,190/µl in the rosuvastatin group (P = 0,032). This also supports the hypothesis that the inflammatory process plays an important role in the occurrence of POAF.

CONCLUSION

The use of atorvastatin at 20 mg/day showed a protective effect that is equivalent to rosuvastatin at 10 mg/day in preventing the occurrence of atrial fibrillation after coronary bypass surgery. Routine use of statins for perioperative management is a feasible and safe strategy to prevent POAF.

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