Efficacy of Dronedarone Versus Propafenone in the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation After Electrical Cardioversion

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ABSTRACT

Purpose: Our objective was to compare the efficacy of dronedarone and propafenone in maintaining sinus rhythm in patients with atrial fibrillation (AF) after electrical cardioversion.

Methods: In this single-center, open-label, randomized trial, we randomly assigned patients with AF after electrical cardioversion to receive dronedarone 400 mg BID or propafenone 150 mg TID. Follow-up clinical evaluations were conducted at 1, 2, 3, and 6 months of treatment. The primary end point was the time to the first recurrence of AF.

Findings: A total of 98 patients were enrolled (79 men; mean age, 59.2 years; n = 49 per group). The median times to first recurrence of AF were 31 days in the dronedarone group and 32 days in the propafenone group (P = 0.715). The median (interquartile range) ventricular rates at first recurrence of AF were 76.5 (67.3–86.5) beats/min in the dronedarone group and 83.0 (71.0–96.0) beats/min in the propafenone group (P = 0.059).

Implications: Dronedarone and propafenone had similar efficacies in maintaining sinus rhythm in patients with AF after electrical cardioversion. The ventricular rate at the first recurrence of AF was numerically but not statistically significantly lower in the dronedarone group than in the propafenone group. ClinicalTrials.gov identifier: NCT01991119. (*Clin Ther*. 2014;36:1169–1175)

Key words: atrial fibrillation, dronedarone, electrical cardioversion, propafenone.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia requiring medical therapy.[1–4] The prevalence of AF was 0.95% in persons aged 20 years or older (4). Prevalence increased from 0.1% among adults younger than 55 years to 9.0% in persons aged 80 years or older (4). There are 2 treatment options for the management of AF. One is rhythm control and the other is rate control, but the optimal strategy remains unclear.[5,6] Because the maintenance of sinus rhythm is often associated with an improvement in health-related quality of life and exercise capacity, the restoration and maintenance of sinus rhythm remain the major goals in patients with AF.[7] But the optimal long-term drug strategy is controversial.

Dronedarone is a benzofuran derivative with an electropharmacologic profile closely resembling that of amiodarone, but with structural differences intended to eliminate the adverse effects of amiodarone on thyroid and pulmonary function.[8,9] Propafenone, a class IC antiarrhythmic drug, has been widely used for the prevention of AF recurrence.[10] However, based on a literature search, there are no studies available that have compared the efficacy of dronedarone and propafenone in maintaining sinus rhythm. Our objective was to compare the efficacy of dronedarone and propafenone in maintaining sinus rhythm in patients with AF after electrical cardioversion.

PATIENTS AND METHODS

This single-center, open-label, randomized trial was conducted in men and women who were aged ≥18 years and who had persistent AF nonresponsive to chemical cardioversion. The patients were admitted

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and underwent electrical cardioversion. After conversion to sinus rhythm, eligible patients were randomly assigned to receive dronedarone or propafenone.

Exclusion criteria were an acute myocardial infarction within the 3 months before screening, New York Heart Association functional class IV heart failure, New York Heart Association functional class II or III decompensated heart failure requiring hospitalization, echocardiographic ejection fraction $<35\%$, previous treatment with amiodarone, bradycardia at <50 beat/min, second- or third-degree atrioventricular block or sick sinus syndrome without a permanent pacemaker, severe hepatic dysfunction, pregnancy, QT prolongation of ≥ 500 msec or PR interval >280 msec, and/or hypersensitivity to the study drugs.

Patients were enrolled Between May 2011 and April 2013. The dronedarone regimen was 400 mg BID, and the propafenone regimen was 150 mg TID. If AF recur during follow-up period, the patients were prescribed another antiarrhythmic drug, for example, amiodarone or conducted radiofrequency catheter ablation.

Follow-up visits were scheduled at 1, 2, 3, and 6 months of treatment and included a clinical evaluation and 12-lead ECG. If symptoms that suggested recurrence of AF were noted, additional visits were scheduled and evaluations performed. All patients were followed up for 6 months after randomization.

The primary end point was the time to first recurrence of AF after sinus rhythm had been restored. The secondary end point was the ventricular rate at first recurrence and the risk factors for the recurrence of AF.

All patients provided informed consent for inclusion in the study. The protocol was approved by the institutional review board at Samsung Medical Center, Seoul, South Korea.

Statistical Analysis

The hypothesis for determining the number of patients needed for the study was derived from data from efficacy trials of antiarrhythmic drugs for the maintenance of sinus rhythm in patients with AF.[11,12] On the basis of these studies, the estimated rates of sustained sinus rhythm at 6 months were 75% in the dronedarone group and 45% in propafenone group. To obtain a statistical power of 80% at the 5% level of significance, a sample size of 100 patients (50 in the dronedarone group and 50 in the propafenone group) was needed, assuming a 20% dropout rate and 6-month follow-up period. All reported P values are 2-sided, and P values of <0.05 were considered to indicate statistical significance.

Continuous data are expressed as means (SD) or medians (interquartile range [IQR]). Categorical data are expressed as frequencies and percentages. To evaluate the difference between the study groups, we used the unpaired t test for normally distributed data and the Mann-Whitney U test for skewed data. Categorical data were analyzed with the χ^2 test or the Fisher exact test. The Kaplan-Meier method and log-rank test were used to compare the probability of remaining in sinus rhythm between the 2 study groups.

RESULTS

A total of 100 patients were enrolled; data from 1 patient were omitted due to a protocol violation, and another patient withdrew informed consent, leaving 49 patients randomly assigned to receive dronedarone and 49 to receive propafenone. Table I presents the baseline characteristics of the patients in the 2 study groups. The mean age was 58.6 years and 81.6% were male in the dronedarone group, and the mean age was 59.8 years and 79.6% were male in the propafenone group. The prevalences of hypertension, diabetes, dyslipidemia, and a history of congestive heart failure did not differ significantly between the 2 study groups. The mean left ventricular ejection fraction was 58.86%, and the mean left atrial diameter by transthoracic echocardiography was 44.8 mm in the dronedarone group; corresponding values were 59.12% and 42.9 mm, respectively, in the propafenone group.

The mean (SD) duration of follow-up in the non–end point patients was 172.4 (39.6) days; the median was 177.0 days.

At 6 months, 73.5% of the patients in the dronedarone group and 75.5% of the patients in the propafenone group had a recurrence of AF (hazard ratio in the dronedarone group, 0.898 [95% CI, 0.362–2.229) ($P = 0.817$). The median times to the first documented recurrence of AF were 31 days in the dronedarone group and 32 days in propafenone group ($P = 0.715$) (Table II). The median (IQR) ventricular rates at the first documented recurrence of AF were 76.5 (67.3–86.5) beats/min in the dronedarone group and 83.0 (71.0–96.0) beats/min in the propafenone group ($P = 0.059$).

The Figure shows the Kaplan-Meier estimates of the probability of remaining in sinus rhythm. The