Intravenous Propafenone: Efficacy in the Conversion to Sinus Rhythm of Recent Onset Atrial Fibrillation—A Single-Blind Placebo-Controlled Study

Francesco Bellandi,1 Roberto Piero Dabizzi,2 Fabrizio Cantini,1 Massimo Di Natale,3 Laura Niccoli
1Second and 3First Divisione di Medicina, Ospedale Misericordia e Dolce, Prato, Italy; 2Clinica Medica I°, University of Florence, Italy

Summary. The effectiveness of intravenous propafenone for conversion to sinus rhythm (SR) of paroxysmal atrial fibrillation (AF), lasting less than 7 days, was evaluated with a single-blind, randomized, placebo-controlled study, given the possible spontaneous conversion of this arrhythmia. Group 1 (98 patients) received intravenous propafenone (2 mg/kg iv over 10 minutes followed by 0.007 mg/kg/min); and group 2 (84 patients) received intravenous placebo (0.9% saline solution). The infusion was continued until restoration of SR but no longer than 24 hours. Eight-nine patients (90.8%) received propafenone and 27 patients (32%) receiving placebo were converted to SR (p < 0.005). The mean conversion time was 2.46 ± 2.59 hours in group 1 and 17.15 ± 5.78 hours in group 2 (p < 0.005). In patients treated with propafenone, conversion of SR mostly occurred in the first 4 hours (86.5%), considered to be the optimal infusion time in our experience. In both groups, the left atrial size was significantly larger in nonconverted than in converted patients. Similarly, the duration of the arrhythmia was significantly longer in nonconverted patients. In nonconverted patients, the mean ventricular rate decreased from 143 ± 16 beats/min to 101 ± 18 beats/min after propafenone and from 135 ± 19 beats/min to 119 ± 16 beats/min after placebo (group 1 vs. group 2: p < 0.005). Two episodes of sinus standstill (3.4 and 3.8 seconds, respectively) occurred at SR restoration obtained with propafenone. Intravenous propafenone is an effective, safe, and usually rapid drug for AF treatment. Moreover, it produces a real and significant reduction in the mean ventricular rate in nonconverted patients.


Key Words. atrial fibrillation, antiarrhythmic agents, propafenone

Atrial fibrillation (AF) is a common cardiac arrhythmia, especially in elderly subjects. Control of the ventricular rate and prevention of embolic complications are the main objectives of chronic AF therapy. In paroxysmal AF, therapy is primarily directed at restoring sinus rhythm (SR) and preventing recurrences. Restoration of SR can be obtained by direct-current cardioversion or by antiarrhythmic drugs [1]. Direct-current cardioversion is the treatment of choice in patients with hemodynamic instability. In subjects without left ventricular failure or angina, the use of antiarrhythmic drugs is directed to restore SR and control ventricular rate during AF. We performed a single-blind, placebo-controlled study to test the effectiveness of intravenous propafenone for conversion to SR in patients with paroxysmal AF lasting more than 30 minutes but less than 7 days before treatment.

Methods

We performed a single-blind randomized study on 182 patients with paroxysmal AF lasting less than 7 days, including 94 men and 88 women, with a mean age of 61.2 years (range 19–76 years). Ninety-eight patients (group 1) received intravenous rapid (10 minutes) propafenone at a dose of 2 mg/kg, followed by slow infusion (0.007 mg/kg/min). Eight-four patients (group 2) received placebo (saline solution 0.9%, 500 ml/24 hr). In both groups, the treatment was prolonged until restoration of SR but no longer than 24 hours. Informed consent was obtained from all patients before randomization. The study was approved by our ethics committee.

The beginning of the arrhythmia was identified by the onset of symptoms (especially palpitations) still present when the patients were enrolled in the study and when AF was proved by an electrocardiogram (ECG) exam. Sodium and potassium levels were assessed in all patients before randomization. They were then submitted to clinical examination, echocardiogram...
phy, and chest x-ray in order to verify the hemodynamic stability of the arrhythmia. Thyroid hormones (free T3 and free T4) and thyrotropin (TSH) were normal in all subjects.

The following patients were excluded from our study: (a) subjects with angina or clinical signs of heart failure, presenting with resting dyspnea, pulmonary congestion, or systolic blood pressure <90 mmHg; (b) patients with a slow spontaneous ventricular rate (<70 beats/min); (c) patients already being treated with digoxin, calcium antagonists, or other antiarrhythmic drugs. One hundred and twenty-one patients (66.4%), 67 (68.3%) in group 1 and 54 (64.3%) in group 2 had previously experienced at least one paroxysmal AF episode, documented by ECG (mean 1.67, range 1–4 episodes), with no statistically significant difference between the two groups. Seventy-three episodes of paroxysmal AF (60%) occurred in the last year, without differences in both groups.

In 137 patients, AF was associated with coronary artery disease, hypertensive heart disease, valvular heart disease, dilated cardiomyopathy, and cor pulmonale. In 45 patients, there was no evidence of cardiac pathology (Table 1). The two groups were homogeneous for age, arrhythmia duration, left atrial size, mean heart rate, and systolic blood pressure. Diastolic blood pressure was significantly higher in group 1 patients (Table 2). Electrocardiographic oscilloscopic monitoring was maintained during drug infusion. A 12-lead electrocardiogram was recorded every 10 minutes for an hour; thereafter every 30 minutes for 3 hours, and then every 60 minutes until the end of infusion and immediately after conversion to SR. Blood pressure was measured every 2 minutes during the first 30 minutes, and then every 30 minutes. We evaluated (a) conversion to SR and time of conversion; (b) changes from baseline data of QRS and QTc duration, or appearance of conduction defects at the end of infusion; (c) side effects, including hypotension, symptoms or signs of low cardiac output, and pulmonary congestion; and (d) mean ventricular rate, calculated at the end of the infusion over a 10-second period in patients not converted to SR. The analysis of QRS and QTc (derived from Bazett's formula [2]) was expressed as the mean of three consecutive cardiac cycles of the ECG strips. M-mode echocardiography was performed in all patients in order to determine left atrial size. Results were analyzed by Student's t-test and chi-square analysis. A p value <0.05 was considered significant. Results were expressed as the mean ± standard deviation (SD).

### Results

The treatment with propafenone was generally well tolerated; in no case was the dose reduced or the treatment interrupted. In six patients (6%) of group 1, we noticed bradycardia (<40 beats/min) immediately after conversion to SR, rapidly returning to normal in 1–3 minutes. Two patients (2%) treated with propafenone experienced one episode of sinus standstill, lasting 3.4 and 3.8 seconds, respectively, a few minutes after the end of the infusion. No therapy was necessary, however. In 16 patients (16.3%) treated with propafenone, restoration of SR was preceded by atrial flutter, lasting 3–18 minutes, with atrioventricular conduction varying from 2:1 to 4:1, and ventricular rate ranging from 146 to 78 beats/min.

In group 1, minor digestive side effects (especially nausea), dizziness, and headache were observed in 11, 7, 6 patients, respectively. No significant modification of blood pressure and of other hemodynamic parameters occurred after drug infusion, both in converted and nonconverted patients.

Conversion to SR was obtain in 89 patients (90.8%) of group 1 and in 27 (32%) of group 2 (p < 0.005). The percentage rates of conversion to SR with respect to the time of infusion are shown in Figure 1. The mean conversion time was 2.46 ± 2.59 hours (range 0.10–13 hours) in group 1 and 17.15 ± 5.78 hours (range 4.80–23.30 hours) in group 2 (p < 0.005). In group 1,

### Table 1. Associated cardiac pathologies in patients treated with propafenone (group 1) and with placebo (group 2)

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Group 1 no. pts (%)</th>
<th>Group 2 no. pts (%)</th>
<th>Overall no. pts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic AF</td>
<td>24 (24.4%)</td>
<td>21 (25%)</td>
<td>45 (24.7%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>24 (24.4%)</td>
<td>19 (22.6%)</td>
<td>43 (23.6%)</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>19 (19.3%)</td>
<td>19 (22.6%)</td>
<td>38 (20.8%)</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>20 (20.4%)</td>
<td>17 (20.2%)</td>
<td>37 (20.3%)</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>6 (6%)</td>
<td>5 (5.9%)</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td>5 (5%)</td>
<td>3 (3.5%)</td>
<td>8 (4.3%)</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation.