Clinical Course of Recent-Onset Atrial Fibrillation Treated With Oral Propafenone*

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Atrial fibrillation (AF) is one of the most common cardiac arrhythmias in the adult population. Propafenone is a class 1c antiarrhythmic agent that has an electrophysiologic profile suggesting that it might be potentially effective in recent-onset AF. The present study was undertaken, therefore, to examine the time course as well as the frequency of successful conversion in patients with recent-onset AF treated with propafenone administered orally. Fifty patients with recent-onset AF were recruited into 2 groups: 25 patients were given propafenone, 150 mg every 4 h, and 25 patients served as a control group and received verapamil (a drug known to slow the ventricular response but not to restore sinus rhythm) 40 mg, every 4 h and up to 48 h or until conversion to sinus rhythm occurred. Of the 50 patients, 2 refused to continue the study and another 2 were excluded because of lost heart failure. Conversion to sinus rhythm occurred in 21 of 24 patients (87 percent) in the propafenone group as compared with 9 of 22 (41 percent) in the verapamil group (p<0.001). In 10 patients in the propafenone group, conversion occurred within 12 h, within 24 h in another 9 patients, and between 24 and 48 h in the remaining 2 patients. There was no correlation between the duration of AF prior to entry into the study and the subsequent incidence of and time to conversion with propafenone. With respect to cause of AF, all groups showed a high incidence of conversion. Two patients developed heart failure during treatment and one patient (in the verapamil group) developed embolic stroke while still having atrial fibrillation. We conclude that in patients with AF, the prognosis for conversion to sinus rhythm within 48 h, with propafenone, is excellent (87 percent) and safe.

AF=atrial fibrillation

METHODS

Patients

Fifty patients (mean age, 67.3±5.0 years) who were first seen in the hospital emergency department after having come on their own initiative or on referral from their family physician, with AF, were selected for the study. Patients were accepted when the clinical history and previous medical records clearly indicated that the arrhythmia was not chronic and in all likelihood was of no more than 2 weeks' duration. Patients with congestive heart failure were excluded from this study. The patients' symptoms are summarized in Table 1.

Duration of AF

Determination of the exact duration of AF prior to inclusion in the study was accomplished with varying degrees of certainty. Estimation of duration was based on symptoms and thus involved a degree of imprecision. Nineteen patients reported to the emergency department within 8 h of the acute onset of symptoms; in 10 patients the attack had lasted between 8 and 24 h, and in the final group of 13 patients, the AF was of longer duration, and in 8 cases the exact time of onset was not clear, but was less than 2 weeks.

Protocol

Once entered into the study, the patients were admitted to the department of medicine for continuous ECG monitoring and were recruited into two groups in randomized manner: 25 patients were given propafenone (group p), 150 mg every 4 h, and 25 patients served as a control group and received verapamil (group v), a drug known to slow the ventricular response but not to restore sinus rhythm,46,17 40 mg every 4 h, up to 48 h or until conversion to sinus rhythm occurred. Rhythm strips were re-
Table 1—Patients' Symptoms Caused by AF

<table>
<thead>
<tr>
<th>Group</th>
<th>Pulitations, No. (%)</th>
<th>Dyspnea, No. (%)</th>
<th>Chest Pain, No. (%)</th>
<th>Weakness, No. (%)</th>
<th>Sweat, No. (%)</th>
<th>Other No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verapamil</td>
<td>18 (82)</td>
<td>4 (18)</td>
<td>5 (23)</td>
<td>4 (18)</td>
<td>2 (9)</td>
<td>4 (18)</td>
</tr>
<tr>
<td>Propafenone</td>
<td>23 (96)</td>
<td>7 (20)</td>
<td>6 (25)</td>
<td>4 (17)</td>
<td>3 (13)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Overall</td>
<td>41 (89)</td>
<td>11 (24)</td>
<td>11 (24)</td>
<td>8 (17)</td>
<td>5 (11)</td>
<td>8 (17)</td>
</tr>
</tbody>
</table>

The rate of conversion to normal sinus rhythm in each group and between groups were carried out using the two-way repeated measures analysis of variance (ANOVA).

RESULTS

Of the 50 patients, 2 refused to continue the study (1 from each group) and another 2 (from the verapamil group) were excluded from the study because they developed left heart failure after entering the study.

Conversion to Sinus Rhythm

Conversion to sinus rhythm occurred in 21 of 24 patients (87 percent) in the propafenone group as compared with 9 of 22 (41 percent) in the verapamil group (p<0.001) (Fig 1). In 10 patients in the propafenone group, and in 3 in the verapamil group, conversion occurred within 12 h, within 24 h in another 9, and 3 patients and between 24 and 48 h in the remaining 2 and 3 patients, respectively.

Conversion With Respect to Cause

Table 2 shows the incidence of conversion to sinus rhythm according to the cause of the AF. Although the numbers are too small to draw statistically significant conclusions, it can be noted that all groups showed a high incidence of conversion in the propafenone group.

Conversion With Respect to Duration of Attack Prior to Therapy

The relationship between the duration of AF prior to entry into the study and the subsequent incidence of conversion with propafenone and verapamil are detailed in Table 3. Of note is the finding that despite the differences among the patients in the duration of the attack prior to hospitalization, conversion to sinus rhythm with propafenone occurred in most of the patients, while in the control group of patients with duration of the attack prior to hospitalization longer than 24 h, the conversion rate was very low.

Conversion With Respect to Left Atrial Size

The mean ± SEM of left atrial anteroposterior

![Diagram](24x12 to 588x780)

Figure 1. Time course and the rate of conversion to sinus rhythm with propafenone and verapamil.

* p<0.001
Table 2—Incidence of Conversion to Sinus Rhythm According to Cause

<table>
<thead>
<tr>
<th>Cause</th>
<th>Verapamil</th>
<th></th>
<th>Propafenone</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conversion</td>
<td>No Conversion</td>
<td>Conversion</td>
<td>No Conversion</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>2</td>
<td>7</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>4</td>
<td>3</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td>Acute infarction</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Hypertension</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Overall</td>
<td>9</td>
<td>13</td>
<td>21</td>
<td>3</td>
</tr>
</tbody>
</table>

dimension was 4.4±1.0 cm (3.2 to 6.8 cm). Although there was no statistically significant correlation between left atrial size and failure to respond to propafenone, a trend for increased left atrial dimension was noted in the patients who failed to convert to sinus rhythm (5.0±1.2 cm vs 4.2±0.9 cm).

Complications

Two patients developed heart failure during treatment and one patient (all in the verapamil group) developed embolic stroke while still having AF.

Propafenone did not significantly alter ECG intervals. The mean PR interval increased from 0.17±0.03 s to 0.18±0.02 s, the QRS duration increased from 0.11±0.03 s to 0.13±0.02 s, and the corrected QTc intervals from 0.39±0.05 s to 0.40±0.05 s, following treatment (differences not significant). There were no episodes of proarrhythmia associated with propafenone.

Discussion

Our results indicate that oral propafenone is an effective and safe agent for the treatment of recent-onset AF in patients with no cardiovascular decompensation. Of the 24 patients with recent-onset AF who were referred for evaluation, 21 were converted to sinus rhythm within 48 h, with oral propafenone, with almost no unfavorable reaction to the therapy.

Atrial fibrillation should be treated, and conversion to normal sinus rhythm is desired because of (1) the hemodynamic impairment, (2) the disconcerting palpitation, and (3) the increased risk for systemic emboli that are associated with this arrhythmia.18

If the sudden onset of AF with a rapid ventricular rate results in acute cardiovascular decompensation, electrical cardioversion is the treatment of choice. If it is not poorly tolerated, the arrhythmia may be treated with digitalis at doses sufficient to keep the ventricular response rate at 70 to 90/min. This therapy may restore sinus rhythm but conversion to sinus rhythm often requires the combined use of digitalis with β-blocker or class Ia antiarrhythmic drugs.19 However, digitalis must be avoided when preexcitation is suspected, and class Ia agents, which facilitate atrioventricular nodal transport, must never be used without digitalis, and are usually not well tolerated.19,20 Chemical cardioversion may also be achieved by short-term high-dose intravenous amiodarone therapy.21

Propafenone has been shown to be effective for the control of supraventricular and ventricular arrhythmias,13-15,22,23 most probably because of its property of prolonging atrial and ventricular refractory periods and slowing conduction velocity in all regions of the heart.24 Animal studies have shown that propafenone is a class Ic antiarrhythmic agent that decreases the maximal upstroke velocity during phase 0 of the action potential, shortens the action potential duration in atrial and ventricular muscle,25 and produces modest inhibition of β-receptors and the calcium channel.11,12 Hammill and coworkers26 also found that for prophylaxis of recurrences of AF, propafenone is very effective and well tolerated.

Although many patients in the present study had AF longer than 24 h duration, they were not anticoagulated, since anticoagulation therapy was
not yet included in our protocol of treating paroxysmal AF when this study was started.

In conclusion, oral propafenone is an effective and safe agent for the conversion of recent-onset AF to normal sinus rhythm in patients with no cardiovascular decompensation, and might be continued for the prophylaxis of recurrences of AF with no expected serious side effects.

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