JACC Vol. 28, No. 3
September 1996:700–6

Effects of Oral Propafenone Administration Before Electrical Cardioversion of Chronic Atrial Fibrillation: A Placebo-Controlled Study

LEOPOLDO BIANCONI, MD, MAURO MENNUNI, MD, VJERICA LUKIC, MD, ANTONIO CASTRO, MD, MARA CHIEFFI, MD, MASSIMO SANTINI, MD, FACC

Rome, Italy

Objectives. **Our aim was to evaluate the benefits and risks of administering propafenone before electrical defibrillation for chronic atrial fibrillation.**

Background. **In this context, an antiarrhythmic drug—although potentially useful in preventing early recurrence of arrhythmia—could adversely affect the defibrillation threshold and reduce the cardioversion success rate.**

Methods. **We randomly assigned 100 patients with chronic atrial fibrillation to oral treatment with either placebo (51 patients) or 750 mg/day of propafenone (49 patients) for 48 h before administration of direct current shock. After successful cardioversion, all patients received propafenone therapy and were followed up for 48 h.**

Results. **Before defibrillation, three patients in the propafenone group (6.1%) had reversion to sinus rhythm and one had sustained ventricular tachycardia. Shock efficacy (82.4% vs. 84.4%) and the cumulative effective energy (395 ± 258 vs. 421 ± 236 J) were not different between the placebo and propafenone groups. In the propafenone group, 11 patients had their arrhythmia transformed into atrial flutter and required a lower energy level for arrhythmia conversion than did the other patients with continued atrial fibrillation (245 ± 197 vs. 493 ± 215 J, $p < 0.01$); the latter patients showed a trend ($p < 0.10$) toward higher energy requirements than that of patients who received placebo. The incidence of asymptomatic bradyarrhythmias was higher in the propafenone group (28.9% vs. 7.1%, $p < 0.02$), but more patients who received placebo had early recurrence of atrial fibrillation (16.7% vs. 0%, $p < 0.02$). Two days after cardioversion, more patients given propafenone (73.5% vs. 52.9%, $p < 0.05$) were discharged from the hospital with sinus rhythm. During the in-hospital stay, propafenone was withdrawn from six patients (6.6%) because of side effects.**

Conclusions. **Propafenone, given before electrical cardioversion for chronic atrial fibrillation does not affect the mean defibrillation threshold or the rate of successful arrhythmia conversion. It decreases the recurrence of atrial fibrillation early after shock, thus allowing more patients to be discharged from the hospital with sinus rhythm.**

(J Am Coll Cardiol 1996;28:700–6)

It is well established that some antiarrhythmic drugs are useful for long-term maintenance of sinus rhythm after electrical cardioversion of chronic atrial fibrillation (1,2). Whether the antiarrhythmic treatment should be started before or after cardioversion has been insufficiently investigated. There is evidence that antiarrhythmic drugs may increase the energy required for ventricular defibrillation (3–8). This observation raises the concern that the same drugs could also increase the atrial defibrillation threshold, thereby reducing the likelihood of restoration of sinus rhythm. In addition, ventricular proarrhythmic effects as well as bradyarrhythmias have been described after cardioversion preceded by antiarrhythmic drug administration (9,10). However, some antiarrhythmic agents have been shown to reduce the incidence of supraventricular premature beats—possible harbingers of recurrence of atrial fibrillation—but whether they actually reduce the recurrence of the arrhythmia is an unresolved and largely speculative issue.

There are only a few published studies (9–16) on the effects of treatment with antiarrhythmic drugs in patients undergoing elective transthoracic cardioversion for chronic atrial fibrillation. No data are available on propafenone, a class IC drug that has been found useful in treating this arrhythmia (17–20). The purpose of the present study was to assess the risk/benefit ratio of administering propafenone before attempted cardioversion in patients with chronic atrial fibrillation.

Methods

Study patients. All patients with chronic (>1 month) atrial fibrillation scheduled for cardioversion between April 1992 and March 1994 were considered for the study. A complete clinical examination, 12-lead electrocardiogram (ECG), 24-h

From the Department of Heart Diseases, San Filippo Neri Hospital, Rome, Italy.

Manuscript received November 30, 1995; revised manuscript received March 14, 1996, accepted May 3, 1996.

Address for correspondence: Dr. Leopoldo Bianconi, Via San Sotero 12, 00165, Rome, Italy.

0735-1097/96/$15.00
PII S0735-1097(96)00230-6

ambulatory ECG (Holter) recording, color Doppler echocardiogram and baseline assessment of renal, hepatic and thyroid function were performed. Exclusion criteria were bifascicular block, mean daytime ventricular rate <80 beats/min in patients not receiving digitalis or other drugs depressing atrioventricular (AV) node conduction, sinus node dysfunction (sinus bradycardia ≤50 beats/min, sinus pauses or sinoatrial block documented before atrial fibrillation onset), uncontrolled hyperthyroidism, major hepatic or renal dysfunction, and clinical signs of cardiac or respiratory insufficiency. Patients who met the preceding criteria, accepted participation in the study and gave written informed consent were considered eligible for the trial.

No study patient had been receiving any class I, III or IV antiarrhythmic agent for ≥5 half-lives or amiodarone for ≥3 months. All patients had had full anticoagulation with warfarin or acenocoumarin for ≥3 weeks.

Study design. The trial was designed as a single-blind, randomized, placebo-controlled study. The study protocol was approved by the review board of our institution.

A regimen in which the drug was administered both before and after cardioversion, was compared with a second regimen in which the patients received the drug only after the direct current (DC) shock. We then sought to assess which of the two regimens was preferable with respect to conversion to sinus rhythm, energy requirement for cardioversion, postshock arrhythmias, predischarge maintenance of sinus rhythm and untoward effects.

The patients were prospectively allocated, according to a randomization table, to receive propafenone, 750 mg/day orally in three divided doses of 300, 150 and 300 mg, or three daily doses of placebo (vitamin B_1 tablets, matching the appearance of propafenone tablets). After 48 h the patients who still had atrial fibrillation underwent transthoracic electrical defibrillation.

All cardioversions were performed with the patient in the fasting state during the morning. Propofol, 100 to 150 mg intravenously, was used for anesthesia. A Temtech defibrillator (Temtech Ltd., Bangor, Northern Ireland, United Kingdom) with hand-held paddle electrodes (7 × 11 cm) was used. The paddles were placed in the right upper parasternal border and over the left ventricular apex. Synchronized DC shocks were delivered at increasing energy levels: 100, 200, and 300 J, the last administered twice. The procedure was ended after restoration of sinus rhythm or delivery of two 300-J shocks. A rhythm strip was obtained during defibrillation and for 1 min thereafter. Then, oscilloscopic monitoring was continued for 10 min. A 12-lead ECG was recorded immediately before and after cardioversion.

All ECGs were independently analyzed in blinded manner by two experienced cardiologists. Controversial readings were resolved by collegial discussion. Atrial fibrillation was diagnosed by ECG when atrial activity was represented by small, irregular baseline undulations of variable amplitude and configuration (f waves) at rates >350/min. Partial regularization of f waves (fibrillo-flutter) was classified as atrial fibrillation. Atrial flutter was diagnosed when identically recurring regular atrial waves at a rate <350/min (F waves) were present. Because the flutter waves may be slowed by class IC drugs, we did not set a lower limit for the F wave rate. The following were considered arrhythmic complications: severe sinus bradycardia (≤45 beats/min, lasting >10 s), second-degree sinoatrial block, pauses >2 s, junctional rhythm (regular rhythm of ≥3 beats at a rate <50 beats/min without identifiable P waves), AV block of any degree, frequent (≥10/min) or complex (couplets, runs or self-limiting episodes of atrial fibrillation) atrial premature beats, recurrence of stable atrial fibrillation, and any number of premature ventricular beats.

After successful cardioversion the patients already receiving propafenone continued to receive the drug; patients in the placebo group were given propafenone, 750 mg/day orally, starting with 300 mg 1 h after the procedure. An ECG was obtained 24 and 48 h after DC shock. In the absence of complications, the patients who still had sinus rhythm were discharged from the hospital 48 h after cardioversion.

Statistical analysis. The results were expressed as mean value ± SD. Differences in continuous variables were analyzed by one-way analysis of variance, and groups were compared with use of the multiple Bonferroni test. Differences in categoric variables were analyzed by the two-sided Fisher exact test or chi-square test, with Yates correction if needed. Recurrence curves of atrial fibrillation in the placebo and propafenone groups were compared by the method of Mantel and Cox and the risk of relapse of arrhythmia at each observation time was assessed by relative risk analysis (21). The energy necessary for cardioversion in the placebo and propafenone groups was compared by Mann-Whitney U test. All statistical tests were performed with use of BMPD statistical software. A p value < 0.05 was considered significant.

Results

Patient characteristics. The study group consisted of 100 patients, 51 assigned to placebo and 49 to propafenone treatment. The groups were comparable in age, gender, body weight, left atrial dimensions, duration of atrial fibrillation and underlying heart disease (Table 1 and 2). Twenty-two patients, 10 in the placebo and 12 in the propafenone group, had had previous cardioversion with subsequent recurrence of the arrhythmia; in 17 the arrhythmia had recurred while they were receiving an antiarrhythmic drug: quinidine (n = 8), sotalol (n = 3), amiodarone (n = 2), flecainide (n = 2) or low dose propafenone (n = 2).

Outcome before DC shock. Before the scheduled cardioversion, no patient in the placebo group and three (6.1%) in the propafenone group had conversion to sinus rhythm (p = NS). During day 2 of propafenone administration, one patient had an episode of sustained ventricular tachycardia, symptomatic for presyncope; the arrhythmia subsided before any intervention and the drug was discontinued.

In 11 patients in the propafenone group, the ECG obtained immediately before the cardioversion attempt documented the

Table 1. Baseline Characteristics of the Study Patients

	Placebo Group (n = 51)	Propafenone Group (n = 49)	p Value
Age (yr)	63.8 ± 10.7	67.3 ± 11.2	0.12
Male/female	26/25	28/21	0.67
Body weight (kg)	77 ± 17.1	76.9 ± 14	0.92
Left atrial dimension (long axis, mm)	46.4 ± 7.6	46.4 ± 6.3	0.98
Atrial fibrillation duration (mo)	7.6 ± 6.8	9.7 ± 18.6	0.45
Patients with previous direct current shock	10	12	0.72

Data presented are mean value ± SD or number of patients.

appearance of atrial flutter ($p < 0.01$ vs. the placebo group) (Fig. 1). The mean rate of F waves was 257 ± 52/min. There were no cases of 1:1 atrioventricular conduction.

No clinical events or significant ECG modifications were observed in the placebo group.

Cardioversion: efficacy and energy requirements. Sinus rhythm was restored in 42 (82.4%) of the 51 patients given placebo and in 38 (84.4%) of the 45 patients given propafenone who underwent DC shock (p = NS). With inclusion of the three patients with chemical cardioversion, sinus rhythm was obtained in 41 (83.7%) of the 49 patients in the propafenone group. There was no difference in cardioversion success rate between patients undergoing their first cardioversion (62 [83.8%] of 74) and those undergoing their second cardioversion (18 [81.8%] of 22).

No significant difference emerged between the two treatment groups in the number of patients with conversion or the cumulative conversion rate at each energy level (Fig. 2). The cumulative energy required for cardioversion was 395 ± 258 J in the placebo and 421 ± 236 J in the propafenone group (p = NS).

In the propafenone group, all 11 patients whose atrial fibrillation was transformed into atrial flutter had successful cardioversion, and the cumulative energy required was significantly lower than that in the other 34 patients who continued to have atrial fibrillation (245 ± 197 vs. 493 ± 215 J, $p < 0.02$). In these latter patients the cumulative effective energy was higher than that in the placebo group ($p = < 0.10$, NS). Figure 3 compares the number of patients with arrhythmia conversion and the cumulative conversion rate at each energy level among patients with atrial flutter or atrial fibrillation in the propafenone group and patients given placebo.

Atrial fibrillation recurrence. The rate of maintenance of sinus rhythm at the predefined observation times after successful cardioversion in the two treatment groups is shown in Figure 4. The curves are significantly divergent in favor of the patients pretreated with propafenone ($p < 0.01$).

The most relevant finding was that, within 10 min after DC shock, no patient given propafenone had recurrence of atrial fibrillation, whereas the arrhythmia recurred in seven (16.7%) patients given placebo (p = 0.012).

In the propafenone group the relative risk (RR) of recurrence of atrial fibrillation was significantly lower both at 24 h (RR 0.17, 95% confidence interval [CI] 0.04 to 0.72, $p < 0.01$) and at 48 h (RR 0.31, CI 0.14 to 0.81, $p < 0.05$). At this latter time, 64.2% of patients with cardioversion in the placebo group and 87.8% of propafenone-treated patients with cardioversion had sinus rhythm ($p < 0.05$) (Fig. 4). There was no difference in the rate of recurrence of arrhythmia between patients undergoing a first cardioversion (13 [21%] of 62) and those with a second cardioversion (4 [22.2%] of 18).

Of the initial study group, 27 (52.9%) of the 51 patients who received placebo and 36 patients (73.5%) who received propafenone had sinus rhythm ($p < 0.05$).

Regardless of the protocol, in five of the seven in placebo-treated patients whose atrial fibrillation recurred ≤10 min after cardioversion, received an intravenous bolus of 1.5 mg/kg body weight of propafenone followed in 5 min by a new DC shock. All five had stable sinus rhythm until discharge. For the purpose of the study, they were classified in the placebo failure group.

Complications. Table 3 lists the complications that occurred during the 10 min of ECG monitoring after shock delivery. Patients in the placebo group had a significantly higher incidence of frequent and complex supraventricular premature beats (52.4% vs. 18.4%, p = 0.002). They also had a higher incidence of isolated ventricular premature beats (13.4% vs. 2.1%, p = NS). No frequent or complex ventricular arrhythmias were observed in either group.

The overall incidence of sinus node dysfunction (severe sinus bradycardia, sinoatrial block or sinus pauses, junctional rhythm) after cardioversion was higher in the propafenone than in the placebo group (28.9% vs. 7.1%, p = 0.017); intranodal AV conduction disturbances (first-degree and Mobitz 1 type second-degree AV block) had a similar incidence in the two groups (7.1% vs. 10.2%). All the excitation/conduction disorders observed during the initial 10 min of monitoring were asymptomatic. These disorders were typically short-lasting except in four patients in the propafenone group: two with sinus node dysfunction, one with first-degree AV block (PR interval 0.40 s) and one with intranodal second-degree AV block. The first two patients, because of persistent bradyarrhythmia 48 h after propafenone withdrawal received a permanent pacemaker (AAI and DDD, respectively); in the

Table 2. Heart Disease Associated With Atrial Fibrillation in the Study Patients*

Heart Disease	Placebo Group (n = 51)	Propafenone Group (n = 49)
Hypertensive	16	22
Valvular	15	10
Ischemic	4	7
Cardiomyopathy	3	0
Idiopathic	13	10

*There were no significant differences between groups.

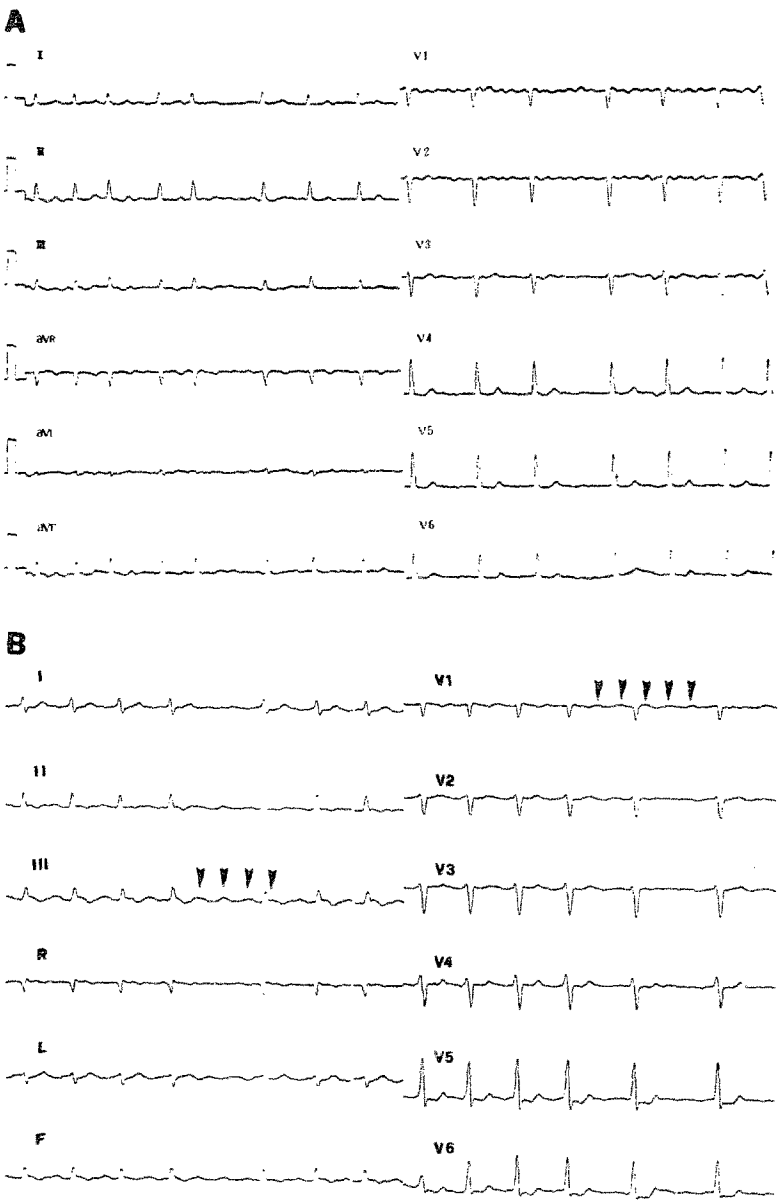


Figure 1. Twelve-lead electrocardiograms demonstrating the transformation of atrial fibrillation into atrial flutter by propafenone. **A,** Atrial fibrillation before treatment. **B,** After 48 h of propafenone therapy. Discrete and regular F waves at a rate of 200/min are present **(arrowheads),** indicating the appearance of slow atrial flutter. F = lead aVF; L = lead aVL; R = lead aVR.

patients with intranodal conduction delay propafenone dosage was reduced to 450 mg/day.

During the in-hospital stay after cardioversion, propafenone dosage was reduced in five more patients (three of whom had been receiving the drug before cardioversion) because of new onset second-degree AV block (n = 1) or QRS widening >120 ms (n = 4). The drug was withdrawn because of side effects in five patients, two of whom were treated with placebo before DC shock. The untoward effects were: presyncope (n = 1), heart failure (n = 2), asthma (n = 1), first-degree AV block of 0.40 s (n = 1). Thus, with inclusion of the patient who had ventricular tachycardia before DC shock, propafenone was withdrawn in 6 (6.6%) of the 91 patients exposed to it.

Discussion

Why an antiarrhythmic drug before electrical cardioversion? A brief course of antiarrhythmic drug therapy is frequently used in clinical practice before cardioversion, but few studies have examined whether such a practice is justified in terms of risk/benefit ratio. From a theoretic point of view, such pretreatment offers at least two advantages: The drug may result in chemical cardioversion in some patients—hence, avoiding the need for electrical defibrillation—and may prevent early recurrence of the arrhythmia. However, the drug could raise the defibrillation threshold and bring about postcardioversion bradyarrhythmias or tachyarrhythmias.

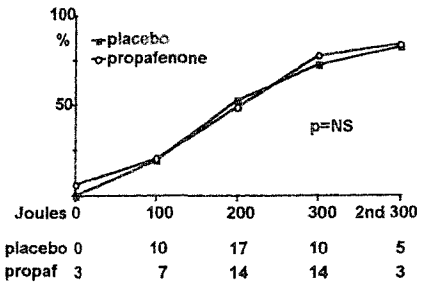


Figure 2. Cumulative percent of patients with cardioversion at each energy level in the placebo and propafenone (propaf) groups. The patients who had reversion to sinus rhythm before the scheduled electrical cardioversion are reported at 0 J. The curves of the two patient groups are similar. The absolute number of patients with conversion at each energy step is shown below the graph.

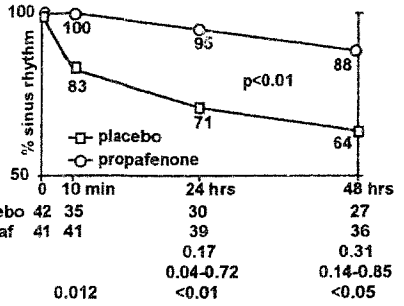
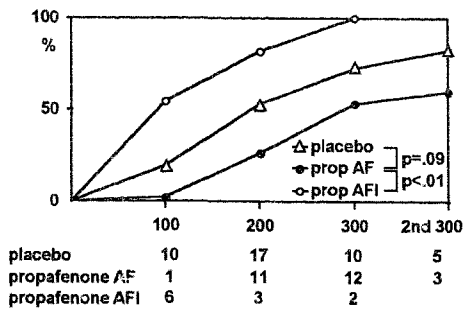


Figure 4. The percent of each treatment group with sinus rhythm at the preestablished observation times. The curves are significantly different ($p < 0.01$). The absolute number of patients with atrial fibrillation recurrence, the relative risk of recurrence (RR) and the confidence intervals (CI) at the same preestablished times are shown below the graph. propaf = propafenone.

Previous studies. Earlier studies (12,15) reported that quinidine obtained reversion to sinus rhythm in 12% to 13% of patients before scheduled electrical cardioversion. The energy required for cardioversion was reported to be lowered (12,15) or at least not increased (13) by the drug. The incidence of atrial premature beats after cardioversion was decreased (11,12,15), but serious arrhythmias—ventricular tachycardia or fibrillation—were reported after restoration of sinus rhythm (9,10). Whether quinidine prevents very early recurrence of atrial fibrillation is not known, although Rossi and Lown (12) observed a nonsignificant trend supporting this assumption: Within 1 minute after cardioversion, 30% of patients who had received placebo and only 4% of those given quinidine had a recurrence of atrial fibrillation.

Amiodarone obtained chemical cardioversion at a rate similar to that of quinidine and did not raise the defibrillation threshold (10). Its intravenous use was associated with a higher incidence of postshock bradyarrhythmias (38.6% vs. 12%) and ventricular premature beats (14% vs. 4%) (10). Flecainide was reported to significantly increase the energy required for cardioversion when given either orally (16) or intravenously (14), without affecting the success rate of the procedure (14).

Figure 3. Cumulative percent of patients in the placebo and propafenone groups submitted to direct current shock who had cardioversion at each energy level. The propafenone group is separated into those whose arrhythmia was transformed into atrial flutter (AFl) and those with continued atrial fibrillation (AF). The absolute number of patients with conversion at each energy step is shown below the graph.



Propafenone effects on DC shock efficacy and energy requirements. In our total group of patients, propafenone did not appear to have any significant effect on the total energy required for cardioversion or on the success rate of the procedure. In the patients pretreated with propafenone the effect of the drug on the defibrillation threshold was contradictory, depending on whether the ECG obtained immediately before DC shock showed atrial flutter or atrial fibrillation. The energy required for cardioversion was significantly decreased in the patients who had atrial fibrillation transformed into atrial flutter by propafenone, whereas, in those with continued atrial fibrillation, the required energy level tended to be higher than in the placebo group. This observation suggests that

Table 3. Arrhythmic Complications Occurring Within 10 Minutes of Continuous Electrocardiographic Monitoring After Direct Current Shock in Patients With Cardioversion

	Placebo Group (n = 42)	Propafenone Group (n = 38)	p Value
Frequent or complex atrial premature beats	22 (52.4%)	7 (18.4%)	0.002
Atrial fibrillation relapse	7 (16.7%)	0	0.012
Ventricular premature beats	6 (14.3%)	1 (2.6%)	NS
Sinus node disturbances			
Sinus bradycardia (<45 beats/min)	0	2 (5.3%)	NS
Pauses (>2 s)	2 (4.8%)	6 (15.8%)	NS
Sinoatrial block	0	2 (5.3%)	NS
Junctional rhythm	1 (2.4%)	3 (7.9%)	NS
Total*	3 (7.1%)	11 (28.9%)	0.017
AV block			
1st degree	1 (2.4%)	3 (7.9%)	NS
2nd degree	2 (4.8%)	1 (2.6%)	NS
Total	3 (7.1%)	4 (10.5%)	NS

*Some patients had more than one type of bradyarrhythmia. Data presented are number (%) of patients.

propafenone has a dual effect: a rise in defibrillation threshold that is often counterbalanced by the drug's ability to "organize" (22–24) the atrial electrical activity, a condition in which less energy is usually required to terminate the arrhythmia (25). Indeed, it should be kept in mind that higher energy levels may be required for cardioversion in patients who have persistent atrial fibrillation while receiving propafenone.

Atrial fibrillation recurrence. Propafenone decreased the incidence of frequent or complex atrial premature beats after cardioversion and, most important, it reduced the likelihood of early recurrence of atrial fibrillation. Indeed, in the very early minutes after cardioversion, atrial fibrillation frequently recurs, because atrial irritability is high (as expressed by the frequency of atrial premature beats) and the refractory periods of atrial cells are still extremely short (26). Such arrhythmogenic conditions explain why the effect of an antiarrhythmic agent is especially desirable in this period.

The efficacy of propafenone in preventing early recurrence of atrial fibrillation is also supported by the fact that all five placebo-treated patients who had early recurrence of the arrhythmia and underwent a second cardioversion immediately after a bolus of intravenous propafenone were discharged with stable sinus rhythm. All five would otherwise have been considered resistant to cardioversion and their atrial fibrillation would have remained intact.

This initial advantage in preserving sinus rhythm obtained by pretreatment with propafenone was maintained during in-hospital observation and the percent of patients with sinus rhythm at 48 h was significantly higher in the patients who had received the drug before cardioversion than in those who received it only immediately thereafter.

Untoward effects. The increased incidence of postcardioversion sinus node disturbances caused by propafenone, a finding already described with flecainide (16) and amiodarone (10), can be related to the depressant action of the drug on the sinus node; this effect, although weak, can unmask latent sinus node dysfunction (27). Of importance, all excitation/conduction disturbances were asymptomatic. They were usually transient and required no treatment, except in a few patients who needed a reduction in drug dosage and two who had a permanent pacemaker implanted, because the bradyarrhythmia persisted after drug discontinuation.

Propafenone was usually well tolerated, but it needed to be discontinued in 6.6% of patients because of adverse effects. As with other class I drugs, serious side effects often occur within the first days of drug administration, thus suggesting that it is preferable to institute such therapy during a hospital stay.

Clinical implications. Our results indicate that treatment with oral propafenone before electrical cardioversion is preferable to starting treatment after reversion to sinus rhythm, because pretreatment with propafenone reduces early recurrence of the arrhythmia, thus allowing more patients to be discharged with sinus rhythm. This advantage is counterbalanced by the cost of admitting patients to the hospital some days before cardioversion to start the antiarrhythmic therapy. A more cost-effective strategy might be to administer the drug intravenously just before the DC shock and then continue with oral administration. Alternatively, intravenous propafenone loading might be given immediately after delivery of the DC shock. However, this strategy might not be optimal, because—owing to the lag between drug administration and its electrophysiologic effect—the antiarrhythmic action of the drug would be foregone, just in the immediate period after cardioversion, when the risk of the arrhythmia recurrence is maximal. However, none of the two aforementioned alternatives is directly supported by our data, and further studies would be required to assess their validity.

Conclusions. The results of this study support the accumulating evidence that electrical cardioversion of chronic atrial fibrillation should be preceded by the administration of an antiarrhythmic drug. In this setting, propafenone, despite a direct action that seems to increase the energy required for atrial defibrillation, actually decreases it in a substantial proportion of patients, by transforming the original arrhythmia into atrial flutter. On balance, both the energy required for cardioversion and the immediate success rate of the procedure are not affected by the drug. Moreover, pretreatment with propafenone significantly decreases the postcardioversion incidence of complex premature supraventricular beats as well as the early recurrence of atrial fibrillation, thus improving the likelihood of maintenance of sinus rhythm, at least in a short-term follow-up period.

References

1. Antman EM, Beamer AD, Cantillon C, McGowan N, Goldman N, Friedman PL. Long term oral propafenone therapy for suppression of refractory symptomatic atrial fibrillation and atrial flutter. J Am Coll Cardiol 1988;12:1005–11.
2. Coplen SE, Antman EM, Berlin JA, Hewitt P, Chalmers TC. Efficacy and safety of quinidine therapy for maintenance of sinus rhythm: a meta-analysis of randomized clinical trials. Circulation 1990;82:1106–16.
3. Fain ES, Dorian P, Davy JM, Kates R, Winkle R. Effects of encainide and its metabolites on energy requirements for defibrillation. Circulation 1986;73:1334–41.
4. Singer I, Guarnieri T, Kupersmith J. Implanted automatic defibrillators: effects of drugs and pacemakers: PACE 1988;11:2250–62.
5. Echt DS, Blank JN, Barbey JT, Coxe DR, Cato E. Evaluation of antiarrhythmic drugs on defibrillation energy requirements in dogs: sodium channel block and action potential prolongation. Circulation 1989;79:1106–17.
6. Hernandez R, Mann DE, Breckinridge S, Reiter MJ. Effects of flecainide on defibrillation threshold in the anesthetized dog. J Am Coll Cardiol 1989;14:777–81.
7. Peters W, Gang ES, Okazaky H, et al. Acute effects of intravenous propafenone on the internal ventricular defibrillation threshold in the anesthetized dog. Am Heart J 1991;122:1355–60.
8. Jung W, Manz M, Pizzulli L, Pfeiffer D, Luderitz B. Effects of chronic amiodarone therapy on defibrillation threshold. Am J Cardiol 1992;70:1023–7.
9. Szekely P, Wynne NA, Pearson DT, Batson GA, Sideris DA. Direct current shock and antidysrhythmic drugs. Br Heart J 1970;32:209–18.
10. Sagristà-Sauleda J, Permanyer-Miralda G, Soler-Soler J. Electrical cardioversion after amiodarone administration. Am Heart J 1992;123:1536–42.
11. Hall JI, Wood DR. Factors affecting cardioversion of atrial arrhythmias with special reference to quinidine. Br Heart J 1968;30:84–90.
12. Rossi M, Lown B. The use of quinidine in cardioversion. Am J Cardiol 1967;19:234–8.
13. Sodermark T, Edhag Y, Sjogren A, et al. Effect of quinidine on maintaining sinus rhythm after conversion of atrial fibrillation or flutter. A multicentre study from Stockholm. Br Heart J 1975;37:486–92.

14. Van Gelder IC, Crijns HJ, Van Gilst WH, De Langen CD, Van Wijk LM, Lie KI. Effects of flecainide on the atrial defibrillation threshold. Am J Cardiol 1989;63:112–6.
15. Sagristà-Sauleda J, Permanyer-Miralda G, Soler-Soler J. Cardioversion electrica bajo la action de la quinidina. Rev Esp Cardiol 1990;43:604–9.
16. Guarnieri T, Tomaselli G, Griffith LSC, Brinker J. The interaction of antiarrhythmic drugs and the energy for cardioversion of chronic atrial fibrillation. PACE 1991;14:1007–12.
17. Kerr CR, Klein GJ, Axelson JE, Cooper JC. Propafenone for prevention of recurrent atrial fibrillation. Am J Cardiol 1988;61:914–6.
18. Connolly SJ, Hoffert DL. Usefulness of propafenone for recurrent paroxysmal atrial fibrillation. Am J Cardiol 1989;63:819–9.
19. Antman EM, Beamer AD, Cantillon C, McGowan N, Friedman PL. Therapy of refractory atrial fibrillation and atrial flutter: a staged care approach with new antiarrhtyhmic drugs. J Am Coll Cardiol 1990;15:698–707.
20. Grey E, Silverman DI. Efficacy of type 1C antiarrhythmic agents for treatment of resistant atrial fibrillation. PACE 1993;16:2235–40.
21. Morris JA, Gardner RJ. Calculating confidence intervals for relative risk (odds ratio) and standardised ratios and rate. Br Med J 1988;296:1313–16.
22. Bianconi L, Boccadamo R, Pappalardo A, Broglia R, Pistolese M. Fibrillazione e flutter atriale. Controllo immediato e conversione a ritmo sinusale con propafenone endovena. G Ital Cardiol 1987;17:653–60.
23. Feld GK, Chen PS, Nicod P, Fleck P, Meier D. Possible atrial proarrhythmic effects of class IC antiarrhythmic drugs. Am J Cardiol 1990;66:378–83.
24. Murdoch CJ, Kyles AE, Yeung-Lai-Wah JA, Qi A, Vorderbrugge S, Kerr CR. Atrial flutter in patients treated for atrial fibrillation with propafenone. Am J Cardiol 1990;66:755–7.
25. Lown B. Electrical reversion of cardiac arrhythmias. Br Heart J 1967;29:469–87.
26. Kumagai K, Akimitsu S, Kawahira K, et al. Electrophysiological properties in chronic lone atrial fibrillation. Circulation 1991;84:1662–8.
27. Shlepper M. Propafenone, a review of its profile. Eur Heart J 1987;8 Suppl A:27–32.