Prophylactic and therapeutic efficacy of drug therapy in different common clinical conditions

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PREVALENCE OF IC COMMON-TYPE ATRIAL FLUTTER AND COMBINED EFFICACY OF RADIOFREQUENCY ISTHMUS ABLATION AND CHRONIC ANTIARRHYTHMIC DRUG TREATMENT IN PATIENTS WITH ATRIAL FIBRILLATION

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Aims. **The purpose of this study was to evaluate the clinical outcome in patients with recurrent atrial fibrillation (AF) and drug-related typical atrial flutter (AFL) undergoing cavotricuspid isthmus ablation.**

Methods. **The study population consisted of 53 consecutive patients (36 men, 17 women, mean age 61 ± 11 years) with recurrent AF (paroxysmal 62%, persistent 21%, paroxysmal and persistent 17%) and typical AFL while receiving class IC (79%) or class III (21%) antiarrhythmic drugs. All the patients underwent successful cavotricuspid isthmus ablation and continued the preexisting antiarrhythmic drug treatment.**

Results. **Within the first month after the procedure, AFL recurred in 4 patients who were successfully re-ablated. During a mean follow-up of 14 ± 9 months, AF recurred in 29 patients (55%), paroxysmal in 26, and persistent in 3. In these patients, however, the incidence (23 ± 44 episodes per year before ablation vs 6 ± 5 episodes per year after ablation, respectively, p = 0.02) was significantly lower compared to the year preceding the ablation. Moreover, compared with the pre-ablation period, fewer patients needed hospitalization for arrhythmic problems (50 vs 12%, p = 0.001) and electrical cardioversion (28 vs 2%, p = 0.001). Overall, 88% of the patients had an improvement in quality of life, 10% no change, and 2% had a worsening. One patient had a fatal stroke.**

Conclusions. **In patients with recurrent AF and typical AFL related to class IC and III antiarrhythmic drugs, cavotricuspid isthmus ablation and continuation of drug treatment eliminate AFL and reduce AF recurrences. As a consequence, a clinical benefit is observed.**

Introduction

Spontaneous organization of atrial fibrillation (AF) into atrial flutter (AFL) has been observed in human and animal studies[1-3]. Antiarrhythmic drugs can promote this organization probably by slowing isthmus conduction and limiting transverse conduction across the crista terminalis[4-6]. This may prevent the simultaneous occurrence of the multiple reentrant circuits necessary for perpetuation of AF, resulting in a single AFL reentrant circuit[7]. The incidence of AFL in patients taking antiarrhythmic drugs for recurrent AF has been reported to range 3.5-24%[8-10]. In these patients, a hybrid therapy consisting in a combination of cavotricuspid isthmus ablation and continuation of antiarrhythmic drugs, has been reported to prevent or reduce the recurrences of arrhythmic events[11-19]. The aim of the present study was to evaluate the long-term efficacy of this approach in a series of patients with recurrent AF and drug-induced typical AFL documented on the surface ECG.

Methods

Study population. During the recruitment period, which extended from August 2000 to October 2002, a total of 135 patients underwent cavotricuspid isthmus ablation for the treatment of AFL. Of these, 53 patients (36 men, 17 women, mean age 61 ± 11 years), who had been symptomatic with recurrent episodes of AF for 5.6 ± 5.8 years (range 6 months to 30 years), and who developed a

typical AFL while taking a class IC (79%) or class III (21%) antiarrhythmic drug, represented the study population. AF was paroxysmal in 33 patients (62%), persistent in 11 (21%), and paroxysmal/persistent in 9 (17%). Forty-three patients were taking propafenone (300-900 mg/day) or flecainide (50-100 mg/day), and 10 patients were taking amiodarone (200 mg/day) or sotalol (120-160 mg/day) when organization to AFL was observed; 1:1 atrioventricular conduction was observed in 8 (15%) patients, resulting in hemodynamic detriment in 3 patients, which required cardioversion under deep sedation. Typical AFL was documented with 12-lead surface ECG and was defined as the presence of regular flutter waves showing negative deflections (or predominantly negative with a terminal positive part) in the inferior leads, and an entirely or predominantly positive flutter wave in lead V_1. AFL was never documented before the use of antiarrhythmic drugs and was the only pre-ablation atrial arrhythmia documented in 9 of 53 patients (17%). In the remaining 44 patients (83%) accompanying pre-ablation AF episodes (AF on antiarrhythmic drug therapy) were observed. Structural heart disease was present in 28 (53%) patients, and the mean ejection fraction was 52 ± 8%. The mean left atrial dimension was 4.2 ± 0.7 cm.

Electrophysiological study and radiofrequency ablation. Three electrode catheters were inserted from femoral veins and basilic or subclavian veins: a tetrapolar catheter was positioned in the coronary sinus, a 10-polar catheter in the right atrium around the tricuspid annulus, and an 8-mm tip ablation catheter was positioned in the cavotricuspid isthmus. Activation sequence mapping and entrainment mapping were performed only in those subjects who were in AFL at the time of electrophysiological testing. In the majority of patients, who were in sinus rhythm during the procedure, no efforts were made to induce AFL before the ablation. The anatomical approach with a goal of producing a line of block between the tricuspid annulus and the inferior vena cava was used for radiofrequency ablation. The procedure was considered successful if the criteria for bidirectional isthmus conduction block were reached: modification of the sequence activation of the lateral and posterior wall of the right atrium during pacing from the coronary sinus and the low lateral wall[20] and local criteria[21]. Patients were followed for recurrences for any atrial arrhythmias via clinic visit, contacts with primary physicians and telephone interviews. Whenever the patients had symptoms suggestive of arrhythmia they were advised to seek consultation from the ambulatory arrhythmia clinic or contact their physicians to evidence the eventual arrhythmia relapse. In case of AFL recurrence, the patients were hospitalized and re-ablation was offered. In patients with AF recurrences, the incidence of arrhythmia episodes in the year before and after the ablation procedure was compared. In addition hospital admissions because of a rhythm problem and need for electrical cardioversion before and after the ablation procedure were evaluated. Patients scored their general quality of life at the end of follow-up by defining their conditions better, unchanged or worse in respect of the period before ablation.

Statistical analysis. Data are presented as means ± SD, percentage or range. Incidence of AF episodes throughout the year before ablation and during the follow-up was compared with non-parametric test (Wilcoxon test). Nominal values were compared with the χ^2 test. Results were considered to be significant at $p < 0.05$.

Results

Electrophysiological data and acute ablation results. At the time of electrophysiological testing 48 patients (91%) presented with sinus rhythm and 5 patients (9%) were in counterclockwise typical AFL. Criteria for bidirectional block were achieved in all 53 patients. Mean fluoroscopy time was 28 ± 21 min. Mean number of radiofrequency applications was 23 ± 15 deliveries. Thirty-six (68%) patients were discharged with warfarin, while aspirin was prescribed in 17 (32%). All the patients continued the preexisting antiarrhythmic drug treatment: 43 (81%) patients were discharged on propafenone (450-600 mg/day) or flecainide (50-100 mg/day) and 10 (19%) on amiodarone (200 mg/day) or sotalol (80-160 mg/day).

Follow-up. Fifty-three patients were followed for a mean of 14 ± 9 months. Within the first month after the procedure, typical AFL recurred in 4 patients that were successfully re-ablated. During the follow-up, 24 patients (45%) were free of AF recurrences; 29 patients (55%) presented AF relapses, paroxysmal in 26 and persistent in 3. In these patients, however, the incidence (23 ± 44 episodes per year before ablation vs 6 ± 5 episodes per year after ablation, respectively, $p = 0.02$) was significantly lower compared to the year preceding the ablation. AF recurred in 4 of 9 (45%) patients with only AFL after antiarrhythmic therapy and in 25 of 44 (57%) patients with accompanying pre-ablation AF episodes (p = NS). Compared with the pre-ablation period, fewer patients needed hospitalization for arrhythmic problems (50 vs 12%, $p = 0.001$) and electrical cardioversion (28 vs 2%, $p = 0.001$).

Overall, 88% of the patients had an improvement in quality of life, 10% no change and 2% had a worsening. There was no significant difference in the rate of post-ablation AF between the treatment groups (51% class IC group vs 70% class III group, p = NS) and between patients with paroxysmal or persistent AF. One patient had a fatal stroke.

Discussion

Development of AFL due to administration of antiarrhythmic drugs for AF is a well-known phenomenon. Antiarrhythmic drugs can promote this phenomenon by modifying the electrophysiological properties of atrial tissue. In patients who convert from AF to AFL on antiarrhythmic drugs, a significant portion demonstrates isthmus-dependent AFL amenable to ablation[11].

Previous studies[11-19] have shown that cavotricuspid isthmus ablation and continuation of drug therapy are highly effective in reducing AF episodes in patients with recurrent AF and drug-related AFL, with an improvement of nearly 80% on the natural course of AF during the follow-up. In the majority of these studies AFL was demonstrated isthmus-dependent at the electrophysiological study and was the only or prevalent arrhythmia on antiarrhythmic drugs. Conversely, the population of the present study was less rigorously selected. In fact, in the majority of our patients, AFL was defined typical only on the basis of the surface ECG and nearly two thirds of the patients presented AF episodes during antiarrhythmic therapy. Nevertheless, a significant clinical benefit was seen during the follow-up: almost half of the patients were completely free from arrhythmia recurrence during a long-term follow-up and the remaining patients showed a significant improvement in the incidence of AF episodes. There was also a statistically significant reduction in hospital admissions for AF and in the need for electrical cardioversion following the procedure. Overall, 88% of the patients had an improvement in quality of life, 10% no change, and 2% had a worsening.

A recent report by Reithmann et al.[19] on patients undergoing hybrid therapy showed that only the presence of accompanying pre-ablation episodes of AF and a decreased left ventricular ejection fraction were significant and independent predictors of post-ablation AF on continued antiarrhythmic medication. In contrast with these authors, we also observed a higher recurrence rate in patients without coexistent AF. Admittedly, as this subgroup was very small, a type II error cannot be excluded in our series. Similarly to Reithmann et al., the recurrence rate of AF during the long-term follow-up was not statistically different between patients treated with antiarrhythmic drugs of class IC or class III or in patients presenting paroxysmal or persistent AF pre-ablation.

Study limitation. This is an observational study and a randomized evaluation would be more appropriate to answer the question if hybrid therapy is the better treatment for drug-induced AFL. Electrophysiological characterization of the AFL circuit was not performed in the majority of the patients. This may explain the higher rate of AF recurrences with respect to other previous studies. It is possible that some asymptomatic recurrences of AF were missed. There is a large difference in the number of patients treated with the various antiarrhythmic drugs. It is possible that in larger or more equal groups of patients, drug-specific differences in the recurrence rate of AF may be identified.

Conclusion

Cavotricuspid isthmus ablation and continuation of antiarrhythmic drugs is a safe and effective therapy in patients with recurrent AF and drug-related typical AFL. Also patients less rigorously selected, presenting accompanying pre-ablation AF after initiation of antiarrhythmic drug therapy, showed a significant clinical benefit from hybrid therapy.

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INCIDENCE OF FULL RECOVERY TO PERMANENT SINUS RHYTHM AFTER ORAL ANTIARRHYTHMIC DRUGS IN PATIENTS WITH ATRIAL FIBRILLATION AND NO HEART DISEASE

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In managing atrial fibrillation, the main pharmacological strategies include rate control or termination of the arrhythmia by electrical cardioversion or antiarrhythmic drugs and prevention of recurrences by antiarrhythmic agents. Recent trials comparing rate and rhythm control strategies were not able to show a superiority of rhythm control. However, these trials investigated relatively old patients with atrial fibrillation, the vast majority suffering from organic heart disease. Thus, the impact of these studies for the treatment of patients with atrial fibrillation in the absence of organic heart disease is limited. However, valid data on the efficacy of antiarrhythmic drugs in this patient subset are lacking. Most studies aiming on the efficacy of antiarrhythmic drugs to prevent atrial fibrillation included heterogeneous patient cohorts, i.e. patients with and without organic heart disease and only very few studies meet current standards of good clinical practice. In addition, the mode and intensity of follow-up differs from study to study and many investigators rely on so-called symptom-based follow-up. Since many recurrences of atrial fibrillation are asymptomatic, symptom-based follow-up strategies may not be adequate. This is of particular importance when full recovery to sinus rhythm, i.e. complete freedom from atrial fibrillation, is the defined goal of therapy. Based on the limited data available from the literature, the efficacy rate with class I antiarrhythmic drugs may not exceed 50-60% over a period of 1 year. However, antiarrhythmic drug treatment of patients with atrial fibrillation without organic heart is safe, there is no evidence for an increased mortality in this patient subset. Prospective studies with well defined endpoints and a high quality follow up (e.g. digital long-term recorders) are needed to reliably assess the incidence of full-recovery to permanent sinus rhythm by antiarrhythmic drugs in patients with atrial fibrillation and no organic heart disease. However, as we have seen with all other supraventricular arrhythmias, antiarrhythmic drug therapy will surely be replaced by curative treatment strategies such as percutaneous catheter ablation as a first-line treatment strategy in the near future.

Introduction

In managing atrial fibrillation, the main pharmacological strategies include rate control or termination of the arrhythmia by electrical cardioversion or antiarrhythmic drugs and prevention of recurrences by antiarrhythmic agents. In general, rate control drugs have only little efficacy in suppressing recurrences of atrial fibrillation[1]. The theoretical benefits of maintaining sinus rhythm using antiarrhythmic drugs include prevention of atrial electrical remodeling and thus slowing down progression of the disease as well as hemodynamic improvement and relief of symptoms. However, antiarrhythmic drug therapy to prevent recurrences of atrial fibrillation carries significant risks of which the occurrence of drug-induced proarrhythmia is the most frequent and serious one[2,3]. Thus, safety and efficacy are important considerations in choosing an antiarrhythmic drug for the treatment of atrial fibrillation. The risk of drug-induced life-threatening arrhythmias is highest in patients with severe structural heart disease while patients without structural heart disease may not be at risk. Because of this high risk observed in patients with organic heart disease, antiarrhythmic drug therapy for the treatment of patients with atrial fibrillation with class I antiarrhythmic agents has almost abandoned from clinical practice[3]. However, in patients with atrial fibrillation in the absence of organic heart disease, antiarrhythmic drug therapy still is an accepted treatment option. This article will review the role of antiarrhythmic drug therapy in this subset of patients with respect to efficacy and safety.

Efficacy of antiarrhythmic drugs for the treatment of atrial fibrillation: general considerations

Over the past decades, many studies on the efficacy of antiarrhythmic drugs to convert atrial fibrillation to sinus rhythm and/or to prevent arrhythmia recurrences have been published with quite divergent results[3-5]. The number and the quality of studies with each drug are limited and few studies meet current standards of good clinical practice[5]. The difficulties to judge on the efficacy of antiarrhythmic drugs to prevent recurrences of atrial fibrillation are multiple. In most studies published, heterogeneous patient populations have been investigated with respect to arrhythmia presentation (paroxysmal or permanent atrial fibrillation) or presence or absence of organic heart disease (so-called lone atrial fibrillation). Various endpoints to assess drug efficacy have been defined such as freedom from atrial fibrillation over a certain and from study to study variable time period, time to the first relapse of the arrhythmia or reduction of the time being in atrial fibrillation, i.e. the burden of atrial fibrillation. Moreover, the clinical presentation of atrial fibrillation covers a wide spectrum: the arrhythmia may be symptomatic or asymptomatic, frequent or infrequent, or both. In addition, patients with symptomatic atrial fibrillation may develop asymptomatic arrhythmia recurrences following initiation of antiarrhythmic drug therapy especially in combination with beta-blockers or calcium antagonists. Thus, the mode and intensity of follow-up is of utmost importance to assess the true efficacy of antiarrhythmic drugs to prevent recurrences of atrial fibrillation both symptomatic and asymptomatic attacks. In the PAFAC study (Prevention of Atrial Fibrillation After Cardioversion) 848 patients underwent electrical cardioversion and were treated with sotalol (n = 383), quinidine plus verapamil (n = 377) or placebo (n = 88) to prevent recurrences of atrial fibrillation6. Follow-up was performed using daily transtelephonic ECG transmission. After 1 year of follow-up, 28% of placebo treated patients and approximately only 40% of patients on sotalol or quinidine/verapamil were free from documented recurrence of atrial fibrillation. Most interestingly, about 70% of all recurrences of atrial fibrillation were asymptomatic[6]. Thus, a symptom-based follow-up presumably would have resulted in a significant underestimation of arrhythmia recurrences and overestimation of drug efficacy. Recent data from Piorkowski et al.[7] obtained in highly symptomatic patients with atrial fibrillation assessed with long-term digital Holter-ECGs following catheter ablation for atrial fibrillation also showed a high incidence of asymptomatic recurrences of the arrhythmia during follow-up. Thus, the results of antiarrhythmic drug therapy to prevent recurrences of atrial fibrillation reported in the literature need to be critically reviewed with respect to patient selection, study endpoints as well as with respect to the mode and intensity of follow-up in order to judge on the data quality. This is of particular importance when full recovery to sinus rhythm, i.e. complete freedom from atrial fibrillation, is the defined goal of therapy.

Efficacy of antiarrhythmic drugs for the prevention of atrial fibrillation in patients without organic heart disease

As discussed above, most studies on the efficacy of antiarrhythmic drugs to prevent atrial fibrillation recurrences were performed in heterogeneous study groups, i.e. patients with and without organic heart disease. Attempts to identify studies solely focusing on patients without organic heart disease including a Medline literature search failed. Thus, the results of studies at least mainly including patients without organic heart disease are reported and discussed below.

In the FAPIS study (Flecainide and Propafenone Italian Study) 200 patients with paroxysmal atrial fibrillation and no history of organic heart disease were randomly assigned to treatment with flecainide (200-300 mg/day) or propafenone (450-900 mg/day)[8]. Detailed analysis of the patient population studied revealed that some patients had a history of hypertension (10% of patients on flecainide and 15% of patients on propafenone) and that few patients (n = 14) with reduced left ventricular ejection fraction (< 50%) were also included in the study. An intention-to-treat analysis showed a probability of 12 months safe and effective treatment of 77% for flecainide and 75% for propafenone[8]. However, follow-up in the FAPIS study was based on symptoms and a single Holter recording at the end of the study period only. Thus, the true incidence of arrhythmia recurrences may have been significantly higher than reported. The UK Propafenone PVST study included 48 patients with paroxysmal atrial fibrillation treated with 600-900 mg propafenone to prevent arrhythmia recurrences in a double-blind placebo-controlled fashion. Eleven patients had a cardiovascular history while the other 39 patients had no detectable heart disease[9]. Follow-up was performed using transtelephonic ECG recordings. The probability of freedom from atrial fibrillation at 100 days of follow-up was significantly higher on propafenone therapy (600 and 900 mg/day) vs placebo and the time to arrhythmia recurrence was significantly prolonged. However, due to the crossover design of the study the follow-up period of the patients was very short. Clementy et al.[10] report on 500 patients with paroxysmal atrial fibrillation treated with flecainide (mean dosage 190 ± 34 mg/day) to prevent arrhythmia recurrence. Approximately 50% of the patients had no organic heart disease. Follow-up evaluation was based on Holter recording every 3 months. After 9 months of follow-up, 65% of the patients were free from arrhythmia recurrence. Amiodarone is

believed to be the most efficient drug to prevent atrial fibrillation recurrences. However, due to the well know end-organ toxicity of amiodarone, the drug has not been systematically used in patients with atrial fibrillation without organic heart disease. In the CTAF study (Canadian Trial of Atrial Fibrillation), amiodarone (mean dosage ≈200 mg/day following oral drug loading for 21 days) was compared to propafenone (mean dosage ≈500 mg/day) or sotalol (mean dosage ≈240 mg/day) in 403 patients with atrial fibrillation. Only 35% of the patients had no organic heart disease[11]. Over the course of a mean follow-up period of 468 ± 150 days, 35% of patients assigned to amiodarone had first recurrence of atrial fibrillation, as did 63% on propafenone or sotalol. Interestingly, a subgroup analysis identified patients without structural heart disease to profit even more form amiodarone therapy when compared to the other patients.

Safety of antiarrhythmic drugs for the prevention of atrial fibrillation in patients without organic heart disease

The results of the CAST trial (Cardiac Arrhythmias Suppression Trial) as well as other studies have raised important issues regarding the safety of antiarrhythmic drugs to suppress arrhythmias or prevent arrhythmia recurrences[2,12]. These studies demonstrated a significantly higher mortality in patients on class I antiarrhythmic drugs compared to placebo presumably due to proarrhythmic effects of the antiarrhythmic drugs. However, patients included in these studies suffered from severe organic heart disease. In contrast to patients with organic heart disease, the incidence of severe side effects of class I antiarrhythmic drugs in patients without organic heart disease seems to be low. In a meta-analysis, Wehling[13] assessed the incidence of side effects in 4811 patients treated in 122 prospective studies with flecainide for supraventricular tachycardia. The vast majority of the patients had no or only moderate cardiovascular disease. Proarrhythmic events were seen more frequent on flecainide (120 patients on flecainide compared to 88 patients on placebo, $p < 0.001$) but total mortality rate was not different ($p = 0.46$)[13]. In other studies on the use of class I antiarrhythmic drugs for the treatment of supraventricular tachycardia the rate of side effects leading to drug discontinuation was around 10-15%[8-10]. However, proarrhythmic effects were rare in these patients and it is unlikely that class I antiarrhythmic drugs have a negative impact on mortality when given to patients without organic heart disease[8-10]. The risk-to-benefit ratio of amiodarone is uncertain because of the relative high incidence of non-cardiac side effects and the drugs well-known end-organ toxicity. Studies on the use of amiodarone in patients without organic heart disease are lacking.

Antiarrhythmic drugs for the prevention of atrial fibrillation in patients without organic heart disease: current status and future perspectives

Although several new treatment modalities (e.g. catheter ablation, preventive pacing) have been developed and are currently under clinical investigation, pharmacologic therapy still is the first-line therapy for most patients with atrial fibrillation. Recent trials comparing rate and rhythm control strategies were not able to show a superiority of rhythm control[1,13]. These studies, however, were performed in an old patient population (e.g. in the AFFIRM study 69 ± 9 years) with more than 80% of the patients suffering from organic heart disease[14]. Thus, the impact on the treatment strategies for patients without organic heart disease is limited. However, valid data on the efficacy of antiarrhythmic drugs to prevent recurrences of atrial fibrillation in this patient subset are lacking and the true rate of full recovery to sinus rhythm on antiarrhythmic drugs can only be estimated. Based on the limited data available from the literature, the efficacy rate with class I antiarrhythmic drugs may not exceed 40-50% over a period of 1 year follow-up. Whether or not new antiarrhythmic drugs such as dofetilide or ambasilide are more potent in maintaining sinus rhythm without increasing the risk of proarrhythmic events remains to be investigated. However, as we have seen with all other supraventricular arrhythmias, antiarrhythmic drug therapy for the treatment of atrial fibrillation will surely be replaced by curative treatment strategies such as percutaneous catheter ablation as a first-line treatment strategy in the near future.

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WHICH ARRHYTHMIAS ARE MOST SUITABLE FOR A "PILL IN THE POCKET" APPROACH? WHICH DRUGS SHOULD BE USED?

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Few data are available on clinical experience of outpatient treatment of patients with supraventricular arrhythmias instituted with the aim of minimizing the need for emergency hospital admission during recurrences of tachycardia. It has been tested the efficacy of two drug treatments, flecainide and the combination of diltiazem and propranolol, versus placebo, each administered as a single oral dose for termination of the arrhythmic episodes, as first-line treatment in patients with infrequent and well-tolerated episodes of paroxysmal reentrant supraventricular tachycardia. First the efficacy of different treatments has been evaluated during electrophysiological studies, administering the drugs in a random order after the induction of arrhythmia. Conversion to sinus rhythm occurred within 2 hours in 52, 61, and 94% of patients receiving placebo, flecainide, and diltiazem/propranolol, respectively ($p < 0.001$). Four patients (1 receiving placebo, 1 diltiazem/propranolol and 2 flecainide) had hypotension and 4 (3 treated with diltiazem/propranolol and 1 with flecainide) a sinus rate of < 50 b/min following interruption of the tachycardia. Patients were discharged home with a single oral dose of the drug treatment (flecainide or diltiazem/propranolol) found at the time of acute testing to be most effective. Twenty-six patients were discharged with diltiazem/propranolol, and 5 with flecainide. During 17 ± 12 months of follow-up, the treatment was successful in 81% of diltiazem/propranolol patients and in 80% of flecainide patients, as all the arrhythmic episodes were interrupted within 2 hours without admission to hospital. In the remaining patients, a failure occurred during one or more episodes because of drug ineffectiveness or drug unavailability. One patient had syncope after diltiazem/propranolol ingestion. During follow-up, the percentage of patients calling for emergency assistance was significantly lower than in the year before enrollment (9 vs 100%, $p < 0.0001$).

Flecainide (300 mg) and propafenone (600 mg) have been shown to be effective in the treatment of paroxysmal atrial fibrillation when administered orally, with success ranging from 60 to 90%. Up to now these drugs have been investigated only in hospital; large trials of out-of-hospital treatment are lacking. A study dealing with out-of-hospital treatment of paroxysmal atrial fibrillation utilizing oral flecainide or propafenone has been carried out with the endorsement of the Italian Association of Arrhythmology and Cardiostimulation. It was terminated in August 2003 and the results will be presented in January 2004.