



clinical investigations

Amiodarone as a First-Choice Drug for Restoring Sinus Rhythm in Patients With Atrial Fibrillation*

A Randomized, Controlled Study

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Study objectives: To investigate the efficacy and safety of amiodarone administered as the drug of first choice in the conversion of atrial fibrillation, regardless of its duration.

Design: Prospective, randomized, controlled clinical study.

Setting: Tertiary cardiac referral center.

Patients: Two-hundred eight consecutive patients (102 men; mean [\pm SD] age, 65 ± 10 years) with atrial fibrillation.

Interventions: One-hundred eight patients received amiodarone, and 100 patients received placebo treatment. Patients randomized to amiodarone received 300 mg IV for 1 h, and then 20 mg/kg for 24 h. They were also given 600 mg/d orally, divided into three doses, for 1 week, and thereafter 400 mg/d for 3 weeks. Patients randomized to placebo treatment received an identical amount of saline solution IV over 24 h, and oral placebo treatment for 1 month.

Measurements and results: Baseline clinical characteristics were similar in the two groups. Conversion to sinus rhythm was achieved in 87 of 108 patients (80.05%) who received amiodarone, and in 40 of 100 patients (40%) in the placebo group ($p < 0.0001$). Statistical analysis showed that the duration of the arrhythmia and the size of the left atrium affected both the likelihood of conversion to sinus rhythm and the time to conversion in both groups. No side effects requiring discontinuation of treatment were observed in either group.

Conclusions: Amiodarone appears to be safe and effective in the termination of atrial fibrillation. However, extreme cases with a large left atrium and long-lasting arrhythmia need long-term therapy. (CHEST 2000; 117:1538-1545)

Key words: amiodarone; atrial fibrillation; cardioversion; left atrial diameter

Abbreviations: CI=confidence interval; LVEF = left ventricular ejection fraction; NS = not significant

Amiodarone, with use in the United States approved only for life-threatening ventricular arrhythmias, is in widespread use elsewhere, in particular in southern Europe, for the treatment of atrial

fibrillation. However, studies of its effectiveness in restoring sinus rhythm have produced conflicting results, with success rates ranging from 16% to as

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high as 92%.¹⁻¹² Most of these earlier studies were not randomized and included either short- or long-lasting atrial fibrillation, using various administration protocols. Furthermore, amiodarone was generally the second-choice drug, as an alternative to a conventional, mainly class I, antiarrhythmic compound,

and so its true efficacy in the cardioversion of atrial fibrillation may sometimes have been wrongly estimated.

In the present prospective, randomized, controlled study, we aimed to assess the effectiveness and safety of amiodarone as a first-choice drug in the treatment of patients with atrial fibrillation of either long or short duration, administered during the loading phase in a combination of IV and oral doses. The combined method of administration was chosen in order to achieve a rapid onset of action by means of an initial IV dose, and to assess the role of the long-term administration of oral amiodarone in the conversion of atrial fibrillation in cases resistant to the short-term treatment.

MATERIALS AND METHODS

Patients

Two-hundred eight consecutive patients (102 men and 106 women) aged 27 to 78 years (mean [\pm SD], 65 ± 10 years), with symptoms of atrial fibrillation, who came to the emergency department or were treated in our clinic, were included in this study. Patients with a recent myocardial infarction, heart surgery within the last 6 months, unstable angina, acute myocarditis, acute pericarditis, severe uncontrolled heart failure (ejection fraction $< 30\%$), or cardiogenic shock were excluded, as were those with significant COPD, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, pregnancy or lactation, and age < 18 years. Also excluded were patients with sick sinus syndrome, a history of second- or third-degree atrioventricular block, as well as those who had taken any other antiarrhythmic drug apart from digoxin within a period prior to the study of less than five half-lives of the drug in question.

Study Protocol

The study was approved by the Ethics Committee of the hospital. After giving informed consent, patients were random-

ized to receive either amiodarone or placebo treatment. Patients randomized to amiodarone received 300 mg IV for 1 h, and then 20 mg/kg for 24 h. In addition, they were given 600 mg/d orally, divided into three doses, for the first week, and thereafter 400 mg/d for 3 weeks. Patients in the placebo group received an identical amount of saline solution the first day. They also took three placebo tablets per day for 1 week and two per day for 3 weeks. Digoxin, 0.5 mg IV initially, followed by 0.25 mg at 2 h and 0.25 mg every 6 h thereafter, was administered for 24 h to all patients who had not previously received it. Subsequently, the digoxin dose was adjusted to maintain therapeutic serum concentrations in all patients.

To prevent thromboembolic episodes in all patients who had atrial fibrillation lasting > 48 h, or of unknown onset, and who were not already taking anticoagulant medication, acenocoumarol (international normalized ratio, 2–3) was given for > 21 days before cardioversion was attempted. This treatment was continued for 21 days after successful cardioversion, or indefinitely when cardioversion was not achieved.

Monitoring and Follow-up

During the first 24 h, while the drug was being administered IV, all patients were kept in the coronary care unit under continuous monitoring of ECG and BP. They were then kept under observation in the Cardiology Department for at least another 2 days before being discharged from the hospital. Patients were evaluated in the clinic after completion of 30 days of treatment.

Before the patient's entry into the study and at the 30-day follow-up visit, a full history was taken and the following examinations were carried out: physical assessment, 12-lead ECG, chest roentgenogram, and tests of thyroid and liver function.

Blood samples were taken for the measurement of plasma amiodarone, desethylamiodarone, and digoxin immediately after cardioversion was achieved, or at 1 h, 24 h, and 30 days if treatment was unsuccessful. Serum levels of amiodarone were determined using high-performance liquid chromatography. Digoxin serum levels were determined by radioimmunoassay.

One- and two-dimensional echocardiographic examinations were used to determine left atrial size and left ventricular ejection fraction (LVEF), and were performed in all patients either within 24 h after conversion or at the end of the study period. All echocardiographic recordings were reviewed by two experienced operators.

Table 1—Baseline Patient Characteristics*

Characteristics	Placebo Group (n = 100)	Amiodarone Group (n = 108)	p Value
Sex, % men	49	49.1	0.99
Age, yr	65 ± 9	64 ± 10	0.72
Left atrial diameter, mm	42.9 ± 6.6	43.9 ± 6.3	0.27
LVEF, %	50 ± 8	51 ± 9	0.40
Baseline heart rate, beats/min	120 ± 25	122 ± 24	0.73
Systolic BP, mm Hg	130 ± 25	125 ± 30	0.56
Underlying heart disease, %	45	41	0.67
Median AF duration, h	28	24	0.42
AF type			
Recent-onset	49	57	0.48
Persistent	27	25	0.84
Chronic	24	26	0.73

*Values given as mean \pm SD, unless otherwise indicated. AF = atrial fibrillation.

Table 2—Plasma Concentration of Amiodarone and Desethylamiodarone*

Drugs	1 h	24 h	30 d	On Conversion
Amiodarone, µg/mL	2.676 ± 1.201	2.967 ± 1.311	1.02 ± 0.5†	2.541 ± 1.321
Desethylamiodarone, µg/mL	0.257 ± 0.0367	0.41 ± 0.17	0.98 ± 0.31†	0.34 ± 0.241

*Values given as mean ± SD.

†p < 0.05 vs 1 h.

Definition of Terms

Atrial fibrillation was considered chronic when its duration was at least 1 month, and of recent onset when its duration was < 24 h. The remaining cases were considered as persistent atrial fibrillation.

For the precise determination of the onset of atrial fibrillation, we took into account the electrocardiographically proven time of onset (for patients treated in our clinic), or the clearly determined time of onset of symptoms such as palpitations, dyspnea, chest congestion (for those patients who came to the emergency department). When the precise time of onset could not be determined (12 patients), the duration of the arrhythmia was considered to be 48 h, and these patients received anticoagulation therapy for 21 days before cardioversion was attempted.

Treatment was considered successful if conversion to sinus rhythm was achieved within the study period. In patients who did not convert to sinus rhythm, conversion was attempted using other antiarrhythmic drugs or current cardioversion.

Statistical Analysis

Patients eligible for the study were allocated to treatment using a computer-generated random number algorithm; *t* tests and χ^2 tests were used for continuous and categorical variables, respectively, to ascertain that the two patient groups were comparable with respect to potentially important predictors of conversion, including sex, age, left atrial size, LVEF, duration of atrial fibrillation, baseline heart rate, baseline systolic BP, and underlying heart disease.

The analysis then proceeded in two phases. First, we checked at the univariate level which factors were significantly associated with conversion, by comparing the appropriate parameters between patients who converted and those who did not. Following the univariate screen, we employed a multivariate step-wise logistic regression analysis of the significant univariate factors, with conversion outcome as the dependent variable, to determine which of them contained independent prognostic value in predicting conversion. The thresholds for entry into and removal

from the model were 5% and 10%, respectively. Time-specific conversion rates were also computed at 1 h (the end of the loading phase), at 24 h (when IV administration was stopped), and after 30 days of treatment. A *p* value < 5% was the criterion for significance throughout.

RESULTS

Of the 208 patients who were enrolled, 108 patients were randomized to amiodarone and 100 to placebo treatment. There were no significant differences between the amiodarone and placebo groups in baseline patient characteristics (Table 1). Echocardiographic studies were performed in 97 patients while they were in atrial fibrillation (37 receiving amiodarone and 60 receiving placebo treatment), and in 111 patients while they were in sinus rhythm (within 24 h after conversion). In 31 patients, echocardiographic recordings were made both in sinus rhythm and during atrial fibrillation; in these patients, there was no significant difference in the left atrial size (38.1 ± 5.1 mm vs 39.2 ± 5.5 mm; *p* = not significant [NS]), nor in the LVEF (51.0 ± 7.2% vs 49.2 ± 7.5%; *p* = NS) as measured during the two studies.

Conversion to Sinus Rhythm

Forty-one of the patients (38%) receiving amiodarone and 25 of those receiving placebo treatment (25%) converted to sinus rhythm within the first hour (odds ratio, 1.84; 95% confidence interval [CI], 1.01 to 3.33; *p* < 0.05). Another 25 patients in the

Table 3—Univariate Assessment of Factors for Conversion in the Two Groups*

Characteristics	Placebo Group		Amiodarone Group	
	Converted	Nonconverted	Converted	Nonconverted
Sex, % men	50.0	48.3	50.6	42.9
Age, yr	63.35 ± 9.7	64.9 ± 8.8	63.8 ± 10.5	63.5 ± 8.8
Left atrial size, mm	37.9 ± 5.1	46.3 ± 5.2†	42.5 ± 5.6	49.8 ± 5.9†
LVEF, %	51.0 ± 7.9	49.0 ± 8.4	52.0 ± 9.2	49.0 ± 7.5
Baseline heart rate, beats/min	121 ± 17	119 ± 22	122 ± 21	121 ± 17
Median AF duration, h	11	105†	14	1,440†
Underlying heart disease, %	42	46	40	42

*Values given as mean ± SD. See Table 1 for abbreviation.

†p < 0.001 compared to those who converted.

Table 4—Univariate Assessment of Factors for Conversion Time*

Characteristics	Conversion by Placebo			Conversion by Amiodarone		
	1 h	24 h	30 d	1 h	24 h	30 d
Patients, No.	25	15	—	41	25	21
Sex, % men	56	40	—	51	40	62
Age, yr	61.4 ± 10.6	66.4 ± 7.4	—	62.1 ± 11.6	65.6 ± 9.6	65.6 ± 8.9
Left atrial size, mm	35.9 ± 3.1	41.3 ± 6.1†	—	39.8 ± 3.7	45.5 ± 3.8†	44.3 ± 7.6†
LVEF, %	52.8 ± 9.14	50.6 ± 5.6	—	51.3 ± 11.1	51.8 ± 6.1	52.8 ± 8.8
Baseline heart rate, beats/min	122 ± 14	120 ± 22	—	122 ± 15	120 ± 16	118 ± 22
Median AF duration, h	8	20†	—	8	8	120†

*Values given as mean ± SD. Since the conversion rate showed significant differences between the two groups at each of the time points, the predictors of conversion were examined separately. See Table 1 for abbreviation.

†p < 0.001 compared to those who converted within 1 h in each group.

amiodarone group and 15 control subjects converted between 1 h and 24 h from the start of the study, so that by the end of the first day, 61.1% of the amiodarone group and 40% of the placebo group had converted (odds ratio, 2.35; 95% CI, 1.35 to 41.1; p < 0.001).

Between 24 h and 30 days after the start of continuous oral administration, another 21 amiodarone-treated patients had converted to sinus rhythm, 5 of them before their discharge from the hospital. No more of the patients in the placebo group converted. Thus, by the end of the 30 days, 87 of the amiodarone group (80.5%) and 40 of the control group (40%) had converted to sinus rhythm (odds ratio, 6.21; 95% CI, 3.33 to 11.57; p < 0.0001).

The blood concentrations of amiodarone were sufficiently high at 1 h, and 1 month later had decreased progressively. Conversely, the levels of desethylamiodarone showed a gradual increase during this period (Table 2). There was no difference in the plasma levels of amiodarone, desethylamiodarone, or digoxin between patients who converted and those who did not at any of the time points (data not shown).

Univariate Predictors of Conversion

As can be seen in Table 3, patients who converted to sinus rhythm had atrial fibrillation of shorter

duration and smaller atria than those who did not in both groups. Duration of atrial fibrillation and left atrial size also significantly affected the time to conversion in both groups. The patients who converted during the first hour had significantly smaller atria and atrial fibrillation of shorter duration than those who did not (Table 4).

Tables 5 and 6 display the time-specific conversions and conversion rates in both groups by duration of atrial fibrillation and left atrial size, respectively. The shorter the duration of the atrial fibrillation and/or the smaller the left atrium, the higher the conversion rate and the more rapidly conversion was likely to be achieved by both treatments.

Multivariate Predictors of Conversion

Multiple logistic regression analysis revealed that treatment, left atrial size, and atrial fibrillation duration were the only significant independent predictors for conversion, in decreasing order of importance ($\chi^2 = 37.1, 64.6, \text{ and } 22.5$, respectively; p < 0.0001 for all). In Table 7, the estimated probabilities (percent) of conversion by duration and left atrial size in the two groups are displayed, as computed by multiple logistic regression. Patients with recent-onset atrial fibrillation had excellent chances of converting, regardless of left atrial size, while the

Table 5—Time-Specific Conversions and Conversion Rates by Duration of Atrial Fibrillation*

AF Type	Treatment, No.		Conversion Rate							
			1 h		1–24 h		24 h–30 d		Overall	
	PI	A	PI	A	PI	A	PI	A	PI	A
Recent-onset (n = 106)	49	57	44.9 (22)	61.4 (35)	18.4 (9)	31.6 (18)	—	3.5 (2)	63.3 (31)	96.5 (55)†
Persistent (n = 52)	27	25	11.1 (3)	24.0 (6)	22.2 (6)	28.0 (7)	—	40 (10)	33.3 (9)	92.0 (23)†
Chronic (n = 50)	24	26	—	—	—	—	—	34.6 (9)	—	34.6 (9)

*Values given as % (No. of patients), unless otherwise indicated. A = amiodarone; PI = placebo. See Table 1 for other abbreviation.

†p < 0.05 amiodarone vs placebo treatment.

Table 6—Specific Conversions and Conversion Rates by Left Atrial Size*

Left Atrial Diameter	Treatments, No.		Conversion Rate							
			1 h		1–24 h		24 h–30 d		Overall	
	PI	A	PI	A	PI	A	PI	A	PI	A
≤ 41 mm (n = 68)	38	30	65.8 (25)	66.7 (20)	18.4 (7)	10 (3)	—	16.7 (5)	84.2 (32)	93.3 (28)
41–46 mm (n = 69)	31	38	—	50 (19)	16.1 (5)	34.2 (13)	—	7.9 (3)	16.1 (5)	92.1 (35)†
> 46 mm (n = 71)	31	40	—	5 (2)	9.7 (3)	22.5 (9)	—	32.5 (13)	9.7 (3)	60 (24)†

*Values given as % (No. of patients), unless otherwise indicated. To examine the role of left atrial size in conversion, we divided the left atrial diameter into three tertiles and computed the conversion rate in each group. See Table 5 for abbreviations.

†p < 0.05 amiodarone vs placebo treatment.

latter factor became more important as the duration of the arrhythmia increased.

For rapid conversion (within 1 h), a separate subanalysis showed that the independent prognostic factors were the same, but had a different order of importance, where a small left atrium and atrial fibrillation of short duration played a more significant role than the kind of treatment provided ($\chi^2 = 73.5, 43.6, \text{ and } 13.5$, respectively; $p < 0.0001$ for all).

Adverse Effects of Amiodarone

A significant decrease in systolic BP (< 90 mm Hg) was observed in 12 patients during the first hour of IV drug administration. All patients did well after IV fluids, and no additional treatment was required.

Phlebitis over the site of amiodarone infusion was observed in 17 patients. In all cases, the administration was continued at a more central site.

No adverse effects necessitating drug discontinuation occurred. There were no proarrhythmic events, either in patients who converted to sinus rhythm or in those who remained in atrial fibrillation.

No side effects were observed in the placebo group during either the IV or the oral administration.

Conversion During Further Follow-up

After the end of the study period, 16 of the 21 nonresponders to amiodarone agreed to undergo

electrical cardioversion; 13 of these procedures (81%) were successful. The 60 nonconverters in the placebo group were first given other medication than amiodarone in a further attempt at chemical cardioversion, in accordance with our standard practice. Of these, 23 subsequently converted (9 with procainamide, 8 with propafenone, and 6 with flecainide). Twenty-four of the 37 patients who did not convert with drug treatment consented to electrical cardioversion; 18 of these patients (75%) were successfully cardioverted.

DISCUSSION

According to our findings, a patient receiving amiodarone has six times better odds of converting to sinus rhythm than a patient receiving placebo treatment. However, factors such as the duration of the arrhythmia and the size of the left atrium appear to influence the conversion rate of amiodarone, mainly in extreme cases. The overall conversion rate of amiodarone is very high (> 90%), but in patients with a very large left atrium and chronic atrial fibrillation, the rate falls to relatively low levels (61% and 34.6%, respectively).

When considering the above, however, it is important to keep in mind that those patients with a large left atrium and a long-lasting arrhythmia are precisely those for whom pharmaceutical conversion is most desirable, since their spontaneous conversion rate is extremely low (Tables 5, 6). Thus, for these difficult patients, amiodarone may be of great benefit.

Table 7—Estimated Probabilities of Conversion in Relation to Duration of Atrial Fibrillation and Left Atrial Diameter in the Two Groups*

AF Type	Left Atrium < 40 mm, %		Left Atrium 40–46 mm, %		Left Atrium > 46 mm, %	
	PI	A	PI	A	PI	A
Recent-onset	88.7	99.7	36.3	96.6	27.9	95.1
Persistent	69.2	99.1	14.1	88.9	9.9	84.5
Chronic	14.4	89.3	1.2	37.7	0.8	29.1

*Results from multivariate logistic regression. See Tables 1 and 5 for abbreviations.

In contrast, patients with a small left atrium and/or short-lasting atrial fibrillation have a very high spontaneous conversion rate, so the relative benefit of amiodarone is smaller. This is clearly shown if we consider cases with recent-onset atrial fibrillation and left atrial size < 41 mm: although amiodarone is likely to cause conversion to sinus rhythm in almost all patients (99.7%), we might expect that 9 of 10 would convert spontaneously.

Another factor, which affects the conversion rate of amiodarone, is the duration of treatment. According to our findings and those of other researchers, the longer the duration of amiodarone treatment, the higher the conversion rate. Kerin et al⁶ noted an increase in the conversion rate from 44% at 24 h to 67% after 9 months of amiodarone administration. This is probably related to the progressive increase we observed in serum desethylamiodarone levels. The finding of Tieleman et al,⁵ that for conversion of atrial fibrillation, plasma concentrations of desethylamiodarone are more important than those of the parent compound, further reinforces this hypothesis.

Treatment Duration

According to our results, the time required before amiodarone treatment is successful is affected by factors such as the duration of the atrial fibrillation and the size of the left atrium. The larger the left atrium and the longer the duration of the arrhythmia, the longer the treatment necessary to produce the desired result. In fact, all of our patients who converted and had chronic atrial fibrillation, as well as more than half of those with left atrial size > 46 mm, needed long-term therapy with amiodarone.

It should be noted that left atrial size and arrhythmia duration are the most important independent predictors of short-term conversion (< 1 h), with

treatment relegated to third place. This can also be seen from the fact that the difference between the conversion rates of amiodarone and placebo for the first hour following the start of treatment barely reaches statistical significance. From a practical point of view, this means that where rapid conversion to sinus rhythm is required, amiodarone is likely to be of little assistance and other means of conversion should be sought.

Comparison With Previous Studies

Studies of Recent-Onset Atrial Fibrillation: The results of our own study were more encouraging than any previously reported (Table 8).^{8,10,13-16} According to our findings, patients with atrial fibrillation lasting < 24 h had a high probability of conversion (> 95%) with amiodarone regardless of the left atrial size.

Our good results are probably due to the fact that in this study, amiodarone was used as the first-choice drug. Furthermore, the high serum levels of amiodarone and desethylamiodarone—higher than the levels reported by other studies—that we achieved after the first 24 h of treatment are also likely to have been a significant factor. In contrast, the duration of treatment does not appear to play a significant role in the cardioversion of recent-onset atrial fibrillation, since all our patients in this category who converted did so within the first 24 h.

Studies of Long-Lasting Atrial Fibrillation: For long-lasting atrial fibrillation, our conversion results were also higher than those reported for chemical agents in previous studies (Table 8).^{5-7,17} Only electrical cardioversion shows a higher conversion rate and works faster in these patients. However, that technique requires general anesthesia or heavy se-

Table 8—Studies of Amiodarone for Converting Atrial Fibrillation to Normal Sinus Rhythm*

Investigators	AF Type	Method of Administration	Patients, No.	Efficacy	p Value
Noc et al ¹⁶	Recent-onset (≤ 2 d)	IV	24	77% by 3 h	< 0.001 vs verapamil
Donovan et al ¹⁴	Recent-onset (≤ 3 d)	IV	32	59% by 8 h	NS vs placebo
Capucci et al ¹³	Recent-onset (≤ 7 d)	IV	19	37% by 8 h 89% by 24 h	NS vs placebo
Galve et al ^{10,15}	Recent-onset ≤ 7 d ≤ 1 d	IV	50	68% by 24 h 91%	NS vs placebo
Hou et al ⁸	Recent-onset (≤ 10 d)	IV	26	92% by 24 h	0.005 vs digoxin
Kerin et al ⁶	Chronic	IV and orally	27	44% by 48 h 67% by 9 mo	NS vs quinidine < 0.001 vs quinidine
Zehender et al ¹⁷	Chronic	IV	20	60%	NS vs quinidine
Tieleman et al ⁵	Chronic	Orally	126	18% by 4 wk	Noncontrolled trial
Gosselink et al ⁷	Chronic	Orally	89	16% by 4 wk	Noncontrolled trial

*See Table 1 for abbreviation.

dation. In addition, there is a potential risk of myocardial damage, ventricular tachyarrhythmia, or thromboembolism. It must be admitted that our good results were probably largely due to the long duration of treatment. It is indicative that no patient with chronic atrial fibrillation converted during the first 24 h: all required treatment for a longer period.

This is troublesome from one point of view, since the main goal of an antiarrhythmic agent in atrial fibrillation should be rapid conversion to sinus rhythm. However, in patients with long-lasting arrhythmia, the need for immediate cardioversion is rarely great. Furthermore, in these patients, cardioversion must in any case be delayed until after 21 days of anticoagulation treatment, so that delayed cardioversion would not appear to be a significant problem. To our knowledge, the only other drug for which the conversion rate for chronic atrial fibrillation has been found to increase with time is propafenone¹⁸; whether the same may hold true for other drugs remains to be confirmed.

Safety

In our study, although we used high doses of amiodarone and achieved high serum levels, the side effects observed were relatively few. This was probably due to the method of administration of the drug. By using a combination of oral and IV administration during the initial loading phase, we avoided most of the side effects associated with each route.

Although amiodarone is a drug that has been implicated in many cardiac and noncardiac side effects, it has been proven that the majority of side effects are related to the dose and the duration of treatment^{19–22}; it thus seems likely that the duration of amiodarone treatment in our study was not, in general, sufficient for the development of side effects.

Study Implications

Our results show that amiodarone is an effective and safe means for the treatment of atrial fibrillation and could be used as a drug of first choice, provided that rapid conversion is not required.

For short-duration atrial fibrillation, amiodarone is of great benefit, especially in extreme cases with a large left atrium. However, it appears that large doses of amiodarone, leading to high serum levels of amiodarone and desethylamiodarone, are necessary in order to achieve a good result. Although such large doses over a short time increase the risk of side effects, a combination of IV and oral administration seems to achieve the desired high serum levels, while minimizing the risk of side effects from both methods of administration.

For long-lasting atrial fibrillation, amiodarone appears to be a very promising agent for the restoration of sinus rhythm, although long-term therapy is needed in order to achieve a high conversion rate. It may be inferred from our findings and from those of Kerin et al,⁶ that the longer the duration of treatment, the higher the conversion rate. On the other hand, it must be admitted that the long-term administration of amiodarone also increases the risk of side effects, and this must be taken into account.

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