

# Amiodarone maintained sinus rhythm better than did sotalol or placebo in atrial fibrillation, but adverse effects were more frequent

Kochiadakis GE, Igoumenidis NE, Marketou ME, et al. Low dose amiodarone and sotalol in the treatment of recurrent, symptomatic atrial fibrillation: a comparative, placebo controlled study. *Heart*. 2000 Sep;84:251-7.

## QUESTION

In patients with recurrent atrial fibrillation (AF), are amiodarone and sotalol safe and effective for maintaining sinus rhythm?

## DESIGN

Randomized (allocation not concealed\*), blinded (patients),\* placebo-controlled trial with mean follow-up of 22 months.

## SETTING

A tertiary cardiac referral center in a university hospital in Greece.

## PATIENTS

186 patients (mean age 63 y, 52% men) who had symptomatic chronic or paroxysmal AF confirmed by electrocardiography. Inclusion criteria were > 18 years of age and successful chemical or electrical cardioversion to sinus rhythm. Exclusion criteria were recent acute myocardial infarction, cardiogenic shock, transient AF related to an ongoing disease or condition, unstable hepatic or renal function, ejection fraction < 40%, hyperthyroidism, life expectancy < 1 year, or previous exposure to study drugs. Follow-up was 100%.

## INTERVENTION

After restoration of sinus rhythm and initiation of optimal treatment for underlying heart disease, antiarrhythmic agents were

stopped. 65 patients were allocated to amiodarone, 15 mg/kg of body weight/d for the first 7 days, 10 mg/kg per day for the next 7 days, and titrated to 200 mg/d during the next 7 to 12 days. 61 patients were allocated to sotalol, 80 mg twice a day with titration to a maximum of 480 mg/d in increments of 40 to 80 mg/d every 48 to 72 hours. 60 patients were allocated to placebo.

## MAIN OUTCOME MEASURES

Rates of and time to AF or intolerable adverse effects.

## MAIN RESULTS

Mean time to recurrence of AF was 6 months for patients in the amiodarone group, 8 months for those in the sotalol group, and 4 months for those in the placebo group. Patients in the amiodarone group had lower rates of recurrence of AF than did patients in the sotalol or placebo groups

( $P < 0.001$ ); the sotalol and placebo groups did not differ for rate of recurrence ( $P = 0.08$ ) (Table). The mean monthly progression rate to recurrent AF or intolerable adverse effects was 4.9% for amiodarone, 8.3% for sotalol, and 14.7% for placebo. Amiodarone had a higher rate of intolerable adverse effects (23% vs 3% for sotalol and 0% for placebo,  $P < 0.001$ ).

## CONCLUSION

Amiodarone had a higher rate of maintenance of sinus rhythm than did sotalol or placebo in patients who had had atrial fibrillation but had more intolerable adverse effects.

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*For correspondence:* Professor P.E. Vardas, Cardiology Department, University Hospital of Heraklion, P.O. Box 1352, Heraklion, Crete, Greece. FAX 30-81-542111.

\*See Glossary.

## Amiodarone, sotalol, or placebo for prevention of recurrence of atrial fibrillation†

Comparison at 4 to 8 mo	Event rates	RRR (95% CI)	NNT (CI)
Amiodarone vs placebo	48% vs 88%	46% (31 to 60)	3 (2 to 4)
Sotalol vs placebo	77% vs 88%	13% (-3 to 27)	Not significant
Amiodarone vs sotalol	48% vs 77%	38% (18 to 54)	4 (3 to 8)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

## COMMENTARY

The results of the study by Kochiadakis and colleagues are consistent with my clinical judgment that amiodarone is more effective than sotalol in maintaining sinus rhythm, although neither drug is completely adequate.

Substantial side effects were seen in 23% of the patients in the amiodarone group, only 3% in the sotalol group, and none in the placebo group. Side effects with amiodarone were more common in women, with a frequent side effect being hypothyroidism. Sotalol tolerance may have been enhanced by excluding patients with ejection fractions < 40% who have more serious cardiac disease and are potentially more prone to having adverse effects with sotalol.

The authors concluded that amiodarone may be more effective but that it also has more side effects than does sotalol. They did not

consider the cost of the 2 drugs. According to our hospital pharmacy, the cost of amiodarone, 200 mg/d, is approximately U.S. \$8.10. Sotalol, 160 mg (80 mg twice/d), is approximately \$9.70 a day. With titration of sotalol up to 3 times to 480 mg/d, the cost would be over \$28/d, substantially more than the cost of amiodarone.

Clinically, the greater effectiveness of amiodarone and its lower cost favor its use over sotalol, provided the practitioner is able to recognize and manage the side effects from amiodarone.

*Stephen R. Yarnall, MD  
Private Practice  
Lynnwood, Washington, USA*