

# Amiodarone maintained sinus rhythm better than 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

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

## Setting

A tertiary cardiac referral centre 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, anti-arrhythmic agents were stopped. 65 patients were allocated to amiodarone, 15 mg/kg of body weight/day for the first 7 days, 10 mg/kg/day for the next 7 days, and titrated to 200 mg/day 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/day in increments of 40 to 80 mg/day 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 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% v 3% for sotalol and 0% for placebo,  $p < 0.001$ ).

## Conclusion

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

\*See glossary.

## COMMENTARY

The results of the study by Kochiadakis *et al* 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 sotalol. They did not consider the cost of the 2 drugs. According to our hospital pharmacy, the cost of amiodarone, 200 mg/day, is approximately US \$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/day, the cost would be over \$28/day, substantially more than the cost of amiodarone.

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

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

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For correspondence: Professor P E Vardas, Cardiology Department, University Hospital of Heraklion, PO Box 1352, Heraklion, Crete, Greece. Fax +30 81 542111.

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

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

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