

Low-dose amiodarone was better than sotalol or propafenone for preventing first recurrence of atrial fibrillation

Roy D, Talajic M, Dorian P, et al., for the Canadian Trial of Atrial Fibrillation Investigators. Amiodarone to prevent recurrence of atrial fibrillation. *N Engl J Med*. 2000 Mar 30;342:913-20.

QUESTION

In patients with atrial fibrillation (AF), is low-dose amiodarone better than antiarrhythmic therapy with sotalol or propafenone for preventing recurrence of AF?

DESIGN

Randomized {allocation concealed*}†, unblinded,* controlled trial with a mean follow-up of 468 days.

SETTING

19 cardiology centers in Canada.

PATIENTS

403 patients (mean age 65 y, 56% men) who had had ≥ 1 episode of symptomatic AF (confirmed by electrocardiogram [ECG]) lasting ≥ 10 minutes in the previous 6 months for which long-term antiarrhythmic therapy was planned. Exclusion criteria included continuous presence of AF for ≥ 6 months, myocardial infarction in the previous 6 months, moderate or severe cardiac disability, AF associated with an acute reversible condition, chronic lung disease requiring bronchodilators, the Wolff-Parkinson-White syndrome, previous long-term therapy with or intolerance to the study drugs, untreated hypothyroidism, serum creatinine level $> 250 \mu\text{mol/L}$, serum alanine aminotransferase level > 2.5 times the upper limit of normal, corrected QT interval > 480 msec (uncorrected > 500

msec in the absence of bundle-branch block), or bradycardia. Follow-up was 98%.

INTERVENTION

Patients were allocated to amiodarone, 10 mg/kg of body weight daily for 14 days, 300 mg/d for 4 weeks, and 200 mg/d thereafter ($n = 201$), or to sotalol ($n = 101$) or propafenone ($n = 101$). Sotalol was given in doses of 160 mg every 12 hours (men ≤ 70 y of age with creatinine level $\leq 130 \mu\text{mol/L}$); 80 mg every 8 hours (men ≥ 70 y of age or with creatinine level $> 130 \mu\text{mol/dL}$, men weighing < 70 kg, and women ≤ 70 y of age with creatinine level $\leq 110 \mu\text{mol/L}$); and 80 mg every 12 hours (women ≥ 70 y of age or with creatinine level $> 110 \mu\text{mol/L}$). Propafenone was given in doses of 300 mg every 12 hours or 150 mg every 6 hours to patients who were ≤ 70 y of age and weighed ≥ 70 kg; it was given in doses of 150 mg every 8 hours to all others.

MAIN OUTCOME MEASURES

Time to first recurrence of AF confirmed on ECG.

MAIN RESULTS

Analysis was by intention to treat. Amiodarone led to fewer patients with recurrence of AF than did sotalol or propafenone ($P < 0.001$) (Table). The median time to recurrence was 98 days for patients who received sotalol or propafenone and > 468 days for those who received amiodarone. A trend existed toward greater study withdrawal because of adverse effects in the amiodarone group than in the group treated with sotalol or propafenone (18% vs 11%, $P = 0.06$).

CONCLUSION

In patients with AF, low-dose amiodarone was better than sotalol or propafenone for preventing first recurrence of AF.

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*See Glossary.

†Information provided by author.

Amiodarone vs sotalol or propafenone (control) for atrial fibrillation†

Outcome at mean follow-up of 468 d	Amiodarone	Control	RRR (95% CI)	NNT (CI)
First recurrence of atrial fibrillation	35%	63%	44% (31 to 55)	4 (3 to 6)

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

COMMENTARY

This interesting trial by Roy and colleagues showed that amiodarone, in low doses by North American standards, was more effective than either propafenone or sotalol in preventing a first recurrence of AF. Amiodarone was also better tolerated than the other 2 drugs, as judged by continuation rates. However, the report does not provide an overall assessment of tolerability, integrating all major and minor events. The relatively small sample size does not allow for further conclusions.

The trial is well done, and the results are convincing as far as they go. Regrettably, the potential interaction with β -blockers (1) was not examined among the many subgroups in the secondary analysis.

What do the results show? Low-dose amiodarone can prevent recurrence of AF better than can sotalol or propafenone, with a relative risk reduction of 57%. But recurrence of AF assessed by ECG is not a proper therapeutic outcome (2). It is at best a surrogate outcome. We cannot estimate the size of amiodarone efficacy over the

comparison drugs on clinical outcomes that matter to patients, such as death, embolism, quality of life, and episodes of heart failure. A much larger study would be needed to assess these end points. Thus, although this report is interesting and useful for scientists, it adds little evidence for the practitioner.

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References

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