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


**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 µmol/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 ≤ 130 µmol/L); 80 mg every 8 hours (men ≥ 70 y of age or with creatinine level > 130 µmol/L), men weighing < 70 kg, and women ≤ 70 y of age with creatinine level ≤ 110 µmol/L); and 80 mg every 12 hours (women ≥ 70 y of age or with creatinine level > 110 µmol/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.

**Source of funding:** Medical Research Council of Canada.

For correspondence: Dr. D. Roy, Montreal Heart Institute, 5000 Belanger Street East, Montreal, Quebec H1T 1C8, Canada. FAX 514-593-2581.

*See Glossary.
†Information provided by author.

**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.

Jean-Pierre Boissel, MD
Claude Bernard University
Lyon, France

**References**