Amiodarone reduced ventricular fibrillation or arrhythmic death in MI with frequent ventricular premature depolarizations


Objective
To assess the effect of amiodarone on the risk for resuscitated ventricular fibrillation (RVF) or arrhythmic death in survivors of a myocardial infarction (MI) with frequent or repetitive ventricular premature depolarizations (VPDs).

Design
Randomized, double-blind, placebo-controlled trial with mean 1.79-year follow-up.

Setting
36 acute-care hospitals in Canada.

Patients
1202 patients > 19 years of age (mean age 64 y, 82% men) who had had an acute MI within the previous 6 to 45 days and had frequent (≥ 10/h) or repetitive (≥ 1 run of ventricular tachycardia) VPDs. Exclusion criteria were contraindications to amiodarone, need for antiarhythmic therapy or tricyclic antidepressants, concurrent severe disease, or factors that made study participation impractical.

Intervention
606 patients were allocated to amiodarone, 10 mg/kg daily for 2 weeks followed by 300 to 400 mg/kg daily for 3.5 months, then 200 to 300 mg/kg daily for 4 months, and then 200 mg/kg for 5 to 7 days/wk for 16 months. 596 patients were allocated to placebo.

Main outcome measures
The primary outcome was RVF or arrhythmic death. The secondary outcomes were arrhythmic, cardiac, and all-cause mortality.

Main results
By efficacy and intention-to-treat (ITT) analysis, RVF or arrhythmic death occurred less often in patients in the amiodarone group compared with those in the placebo group (P = 0.016 and P = 0.029, respectively) (Table). Arrhythmic death, cardiac mortality, and all-cause mortality (P = 0.129) (Table) did not differ between the treatment groups.

Conclusion
Amiodarone reduced the incidence of ventricular fibrillation or arrhythmic death among survivors of myocardial infarction with frequent or repetitive ventricular premature depolarizations.

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Amiodarone vs placebo*

<table>
<thead>
<tr>
<th>Outcome at 2 years</th>
<th>Amiodarone</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>ARR (1EER-CER) (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVF or arrhythmic death (ITT analysis)</td>
<td>4.5%</td>
<td>6.9%</td>
<td>34.3%</td>
<td>2.4% (-1.7 to 6.5)</td>
</tr>
<tr>
<td>Efficacy analysis</td>
<td>3.3%</td>
<td>6.0%</td>
<td>45.3%</td>
<td>2.7% (0 to 5.4)</td>
</tr>
<tr>
<td>All-cause mortality (ITT analysis)</td>
<td>9.4%</td>
<td>11.4%</td>
<td>17.6%</td>
<td>2.0% (-1.4 to 5.5)</td>
</tr>
</tbody>
</table>

*ITT = intention-to-treat; RVF = resuscitated ventricular fibrillation. Other abbreviations defined in Glossary; RRR, ARR, and CI supplied by the author.

Commentary
Physicians desire adjunctive drugs to prolong life in survivors of acute MI, especially those with poor left ventricular function. Of the strategies evaluated to date, adrenergic receptor blockade and angiotensin-converting enzyme (ACE) inhibition clearly improve survival (1). However, some strategies that were thought to promote electrical stability (e.g., sodium-channel blockers) actually shorten life (2), even in low-risk patients. Earlier studies suggested that high-risk patients might benefit from antiarhythmic therapy with amiodarone. Besides prolonging the ventricular refractory period, amiodarone has adrenergic blocking and anti-ischemic actions. These 2 trials, the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT) and the European Myocardial Infarct Amiodarone Trial (EMIAT), show that the outcome of treatment with amiodarone is complex and not readily predictable.

CAMIAT focused on patients with frequent ventricular ectopy, and EMIAT focused on patients with left ventricular dysfunction. In CAMIAT, the primary outcome measure was arrhythmic death or RVF and the results were assessed using a 1-tailed t-test. Patients withdrew at high and unequal rates, 36% of patients in the amiodarone group and 25% in the placebo group, possibly confounding the results. In the ITT analysis, amiodarone did not show a statistically significant decrease in total mortality or nonarhythmic cardiac mortality. Taken together, these factors weaken the authors’ conclusion that amiodarone produces “a clinically important reduction in arrhythmic death and RVF.” Although the design of EMIAT was better, the trials’ 33% increase in nonarrhythmic death, which may have been caused by amiodarone, offset the 35% reduction in risk for arrhythmic death. 42 (CAMIAT) and 44 (EMIAT) patients would need to be treated to prevent 1 arrhythmic death.

The 2 trials remind us of the weakness of arrhythmic death as an outcome measure. (continued on page 143)