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Amiodarone for out-of-hospital cardiac arrest

Clinical question

Does intravenous amiodarone improve outcomes in patients with out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation (VF) or tachycardia (VT)?

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Article chosen

Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation or tachycardia. N Engl J Med 1999;341:871-8.

Objective

To determine, in out-of-hospital cardiac arrest patients with refractory VF or VT, whether intravenous amiodarone, given within a standard ACLS (advanced cardiac life support) protocol following a minimum of 3 shocks, increases survival to hospital with a perfusing rhythm.

Background

There are more than 250,000 cardiac deaths annually in the US, many due to ventricular fibrillation. ACLS guidelines state that antiarrhythmic medications are "acceptable and probably helpful" for patients with VF or pulseless VT persisting after 3 or more shocks.[1] However, to date, there is little supporting evidence for this statement.

Population studied

Victims of non-traumatic, out-of-hospital cardiac arrest in a city served by well trained emergency medical services (EMS) providers, including emergency medical technician (EMT)-defibrillation first responders and paramedics dispatched simultaneously for life-threatening calls.

Study design

This was a double-blind randomized clinical trial of single-dose intravenous amiodarone (300 mg) versus its diluent, polysorbate 80, as placebo. Eligible patients were those with persistent VF or pulseless VT following 3 or more precordial shocks, intubation and intravenous epinephrine (1 mg). All other resuscitative efforts were based on existing standard protocols. Data were collected from dispatch records, EMS records, ECG and defibrillator recorders, hospital records, and survivors or their family members.

Outcomes measured

The primary end point was admission to hospital with a spontaneously perfusing rhythm. Secondary end points were adverse effects, number of precordial shocks required after study drug administration, duration of resuscitative efforts, and the need for additional antiarrhythmics. Survival to discharge and functional neurological status at

discharge were documented but not considered as end points due to insufficient study power.

Results

During the study period, 507 of 667 eligible patients were enrolled, 246 in the amiodarone group and 258 in the placebo group. Clinical characteristics of "included" and "excluded" patients were similar, but minor differences were reported between amiodarone and placebo recipients. More witnessed arrests occured in the placebo group (77% vs. 70%), and bystander CPR was more common in the amiodarone group (68% vs. 59%).

With respect to the primary outcome, amiodarone was associated with increased survival to hospital admission (44% vs. 34%, $p < 0.03$); however, more amiodarone patients required inotropic support (59% vs. 48%, $p = 0.04$), and more amiodarone recipients developed bradycardia (41% vs. 25%, $p = 0.004$) and hypotension (mean systolic BP, 104 +/– 41 vs. 117 +/– 36, $p = 0.04$). Women were more likely to benefit from amiodarone than men (adjusted odds ratio for survival to hospital, 4.3 vs. 1.2). There was no difference between amiodarone and placebo in survival to hospital discharge (13.4% vs. 13.2%).

Study conclusions

The addition of amiodarone to prehospital advanced cardiac life-support measures resulted in greater survival rates to hospital (NNT = 10). There was no difference between the groups in discharge from the hospital, although the study was not powered to examine this outcome.

Commentary

New ACLS guidelines will be published this fall, and "reliable sources" say that amiodarone will be recommended as the first-line antiarrhythmic for refractory out-of-hospital ventricular tachydysrhythmias. This despite the fact that convincing evidence of survival benefit exists for only 2 interventions — timely precordial shocks and early CPR.[2,3]

The authors of this study conclude that in patients with VF or VT unresponsive to 3 defibrillations, amiodarone treatment generates one more survivor (to hospital) for every 10 patients treated. They acknowledge that the study was too small to compare survival to discharge, but it is worrisome that there was not even a trend toward improvement in the amiodarone group. As Ballew and Philbrick[4] point out, survival to hospital but not to hospital discharge would increase medical care costs without improving overall mortality.

Few trials have shown a significant survival benefit for amiodarone over placebo,[5] but a recent meta-analysis concluded that in high-risk patients with recent myocardial infarction or congestive heart failure, amiodarone treatment prevents arrhythmic sudden death and leads to a 13% reduction in overall mortality.[6]

In a recent Canadian trial comparing amiodarone to implantable cardioverter defibrillators (ICD), ICD therapy was associated with a 20% decrease in all-cause mortality and a 33% reduction in arrhythmic death, although these differences did not achieve statistical significance.[7] The data described above suggest that, given a choice, electricity is preferable and remains the treatment of choice.

Not long ago, we administered lidocaine to patients with suspected acute myocardial infarction and "high risk" premature ventricular contractions. Only later did we learn that this practice caused more harm than good.[8] Future studies will clarify whether or not amiodarone improves meaningful survival. Until this evidence appears, it seems premature to recommend amiodarone for all patients with refractory VF/VT cardiac arrest. Health care costs are an important concern, and the cost of equipping every advanced life support ambulance in the developed world with amiodarone will be more than substantial.

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