

Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest

TO THE EDITOR: It is unclear why Kudenchuk et al. (May 5 issue)¹ report that neither lidocaine nor amiodarone resulted in a significantly higher rate of survival to hospital discharge than the rate with placebo among patients with out-of-hospital cardiac arrest in the Resuscitation Outcomes Consortium (ROC) trial. A previous study showed that amiodarone increased survival to hospital admission among patients with cardiac arrest that was witnessed,² and another study showed that as long-term therapy, amiodarone was as effective as an implantable defibrillator more than 24 months after the cardiac arrest.³

The extreme pharmacokinetic properties of amiodarone are seldom well understood. Its elim-

ination half-life of 55 days and volume of distribution of more than 10,000 liters⁴ mandate a loading dose of more than 10 g to maintain effect; achieving this takes considerable time. However, its distribution half-life of less than 17 hours between the central and peripheral compartments means that initial concentrations decrease rapidly after parenteral administration, since adipose tissue competes with cardiac tissue for amiodarone as blood concentrations decrease. Continuous replacement of the drug in the central compartment for more than 24 to 48 hours after an initial bolus may be required in order to obtain the full benefit.

Exploration of the time course of amiodarone exposure with serial measurement of amiodarone

concentrations after intravenous administration could improve administration protocols. Amiodarone might be efficacious with improved administration of this drug.

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1. Kudenchuk PJ, Brown SP, Daya M, et al. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med* 2016;374:1711-22.
2. Kudenchuk PJ, Cobb LA, Copass MK, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med* 1999;341:871-8.
3. Connolly SJ, Gent M, Roberts RS, et al. Canadian Implantable Defibrillator Study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation* 2000;101:1297-302.
4. Pollak PT, Bouillon T, Shafer SL. Population pharmacokinetics of long-term oral amiodarone therapy. *Clin Pharmacol Ther* 2000;67:642-52.

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