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Alameda County Emergency Medical Service District
Riverside County Emergency Medical Services Agency

Report
Amiodarone Pilot Study

Alameda and Riverside Counties
State of California

EMS Commission

August 28, 2002

I. Progress of the study a methodology

A. Methodology

1) Duration December 1, 2000 through May 31, 2002.

2) Indication for use of Amiodarone: Pulseless refractory ventricular fibrillation/tachycardia (after 3 shocks).

3) Procedure: After 1 milligram of 1:10,000 IV Epinephrine, 300 milligrams of Amiodarone IV was administered. The dose was followed by a 10cc Saline flush. No other changes were made in the pulseless refractory ventricular fibrillation/tachycardia procedure. Other cardiac drugs were administered as per advanced cardiac life support guidelines.

4) Data collected.

a. Date and time

b. Amiodarone dose

c. Transported to hospital "yes or no"

d. Hospital survival to admission "yes or no"

e. Hospital survival to discharge "yes or no"

f. Other medications administered

g. Cost of drug

5) This was <u>not</u> a clinical trial. There was no comparative data available and there was no control group. The pilot study simply gathered the data indicated for an 18-month period.

II. Number of patients: In Alameda County, 139 patients received the study drug during the trial interval. In Riverside County, 139 patients received the study drug in the trial interval. The totals for the two counties are 278patients for the 18-month period.

III. Beneficial effects: In Alameda County, 135 of 139 patients were transported to the hospital. Thirty-eight were admitted to the hospital (28%), and 11 were discharged from the hospital (8%). In Riverside County 134 patients were transported, 21 patients survived to hospital admission (16%), and 6 patients were discharged from the hospital (4%).

IV. Adverse reactions and complications. No adverse reactions or complications were noted. Paramedics did express difficulty in using the amiodarone in its vial formulation. The drug is packaged in 150-milligram vials and is not currently available in a "tubex" or needleless format. No injuries were reported due to the formulation during the trial.

V. Statistical Evaluation. Two major clinical trials have been performed involving amiodarone. Kudenchuk et al. compared amiodarone to placebo in out of hospital cardiac arrest due to ventricular fibrillation. (Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *NEJM* 1999;341:871-878.) These authors found that 108 of 246 patients who received amiodarone (44%) survived to hospital admission compared to 89 of 258 patients (34%) who received placebo. The study was not "powered" sufficiently to address survival to hospital discharge. However, 33 of 246 patients (13%) who received amiodarone survived to hospital discharge as compared to 34 of 258 patients (13%) who received the placebo.

Dorian et al. compared amiodarone with lidocaine for out-of-hospital ventricular fibrillation. (Dorian P, et al. Amiodarone as compared with lidocaine for shock resistant ventricular fibrillation. *NEJM* 2002;346:884-890.) Dorian found 41 of 180 (23%) patients who received amiodarone survived to hospital admission compared with 20 of 167 (12%) who received lidocaine. Again, this study was not powered sufficiently to address survival to hospital discharge. However, Dorian's data show that 9 of 180 patients (5%) received amiodarone survived to hospital discharge as compared with 5 of 167 patients (3%) with lidocaine. The survival to hospital admission and the survival to hospital discharge data for the pilot study in Alameda and Riverside Counties compare favorably with the numbers obtained in the two clinical trials mentioned above.

Cost considerations. Amiodarone costs approximately $140/300-milligram dose. The average charge for an advance life support transport in Alameda and Riverside Counties is approximately $900/patient. Thus, the cost for amiodarone represents approximately 13% of the charge for the average ALS transport. First responder involvement is not included in these cost figures. In general, first responders do not bill for their services if the patient is subsequently transported. Wyeth Pharmaceuticals provided both EMS Agencies with educational grants that were used to buy the initial 400 doses of amiodarone in each county free of charge. Of notice, the fact that the Centers for Medi-care and Medicaid (CMS) services disallow charges for individual medications.

VI. Conclusion. The pilot study has provided data regarding survival to hospital admission and survival to hospital discharge, which is in line with previously published studies. The pilot study was not designed as a clinical trial; therefore, no inferences can be made from these data regarding its relative efficacy in the treatment of refractive ventricular fibrillation/tachycardia.

Unfortunately, there are few alternatives to amiodarone and the treatment of this usually fatal dysrhythmia. Lidocaine, the standard of care for many years in this condition, may be dangerous. Several authors including Sadowski, et al. has reported that prophylactic lidocaine increases mortality rates in myocardial infarction. Weaver, et al. reported that lidocaine increased the incidence of asystole as compared to epinephrine. Even though the data regarding amiodarone's effect on long-term survival are sparse at best, the data for lidocaine and regularly-used ACLS drugs is even more limited. The cost and logistics involved in a randomized clinical trial that would be powered sufficiently to demonstrate an effect on survival to hospital discharge are daunting without significant financial support. The Kudenchuk and Dorian studies were both funded by the manufacturer of Amiodarone.

Compared with placebo and lidocaine, the amiodarone *does* appear to increase the patient survival to hospital admission. While this may be reminiscent of the case with high-dose epinephrine, obviously the patients must survive to hospital admission to be able to survive to hospital discharge. Perhaps with advances in cardio pulmonary resuscitation techniques, the effect of amiodarone can be clarified.

VII. Recommendation. We recommend that amiodarone be added to the local optional scope of practice. We realize the limitations and cost of amiodarone, the alternatives for this usually fatal dysrhythmia are no more efficacious and perhaps more dangerous. Fortunately, the drug is relatively infrequently used, and its cost will decrease as the patent expires this year.