

Mixed results on benefits of antiarrhythmic drugs for out-of-hospital cardiac arrest

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Paramedics often give heart rhythm stabilizing drugs to patients who are suffering out-of-hospital cardiac arrest when they fail to regain a stable heart rhythm after electrical shock treatment. In a study presented at the American College of Cardiology's 65th Annual Scientific Session, these drugs, specifically amiodarone and lidocaine, did not significantly improve such patients' likelihood of surviving to hospital discharge overall. However, among patients whose cardiac arrest was witnessed by a bystander, those who received either amiodarone or lidocaine during resuscitation had a 5 percent greater chance of survival to hospital discharge compared with those who received a placebo, which was a statistically significant difference. Witnessed cardiac arrests represented more than half of the study's population.

This trial is the first and largest randomized, double-blind, placebo-controlled study to assess the impact of amiodarone and [lidocaine](#) on survival to hospital discharge after out-of-hospital [cardiac arrest](#) triggered by two types of dangerous [heart rhythms](#) known as ventricular fibrillation and pulseless ventricular tachycardia. More than 80,000 cardiac arrest cases per year are specifically caused by these heart rhythms, and in more than half of these cases, paramedics are unable to restore a stable heart rhythm using defibrillator shocks alone. Amiodarone and lidocaine are thought to work by stabilizing the electrical signaling within the heart.

Among all study participants, [patients](#) receiving amiodarone fared slightly better in terms of survival to hospital discharge, the study's

primary endpoint, but did not achieve statistical significance. The finding that both these drugs significantly improved rates of survival to hospital discharge when the cardiac arrest was witnessed by a bystander suggests their benefit may be linked to how quickly such events are recognized and [drug](#) treatment is started.

"You can see these results as a cup half empty or a cup half full," said Peter Kudenchuk, M.D., a cardiac electrophysiologist and professor of medicine at the University of Washington and the study's lead author. "From a statistical perspective, neither drug significantly improved survival to hospital discharge in the overall group of treated patients. Still, a beneficial clinical effect from these medications is undeniable. Both drugs significantly improved the chances of survival to hospital admission, so they clearly did their job in stabilizing dangerous heart rhythms and getting patients to the hospital alive."

Surviving cardiac arrest requires cardiopulmonary resuscitation (CPR) and immediate medical attention. Patients whose cardiac arrest is witnessed by a bystander are believed to have a better chance of survival because they are recognized sooner after their collapse and less likely to have already sustained fatal organ damage upon receiving medical attention.

"If you look at patients who had a witnessed cardiac arrest, a group with the best hope of being saved by effective treatments, the drugs significantly improved survival," Kudenchuk said. "By comparison, in persons whose cardiac arrest was not witnessed, many of whom may not have been discovered until long after their collapse, antiarrhythmic drugs had no significant effect, probably because there was so little chance of survival by that point anyway. When outcomes from these two groups were added together, the absence of any benefit from drug therapy in patients with an unwitnessed arrest may have muted the significant benefit seen in those with a witnessed cardiac arrest, resulting in the

marginal overall outcome of the study."

Paramedics across 10 communities in the United States and Canada were trained on the study's protocols and screened nearly 38,000 out-of-hospital cardiac arrest patients for possible inclusion in the trial. Study participation was restricted to patients with either ventricular fibrillation or ventricular tachycardia who did not achieve a stable heart rhythm after at least one defibrillator shock and, therefore, represent the typical group of those who receive such medications for cardiac arrest in clinical practice. Children, persons with advance (do-not-resuscitate) directives, and patients in protected groups such as prisoners and pregnant women were excluded.

After screening, the trial randomized 3,026 study participants to receive up to 450 milligrams of amiodarone, up to 180 milligrams of lidocaine or a saline placebo. The drugs and placebo were provided to paramedics in indistinguishable boxes containing three syringes, each containing a third of the maximum total dose, to ensure that neither patients nor care providers knew which treatment was used for a given patient. In total, 974 patients received amiodarone, 993 received lidocaine and 1,059 received a placebo. Paramedics used a standard monitoring device to objectively track and record heart rhythms and other parameters during resuscitation.

Survival to hospital discharge among the 1,934 study participants whose cardiac arrest was witnessed by a bystander was improved from about 23 percent for those taking placebo to 28 percent for patients taking either drug, results that were statistically significant.

"If you assume these drugs might improve survival rates by just 3 percent overall or by 5 percent in witnessed cardiac arrest events, this means they could save 1,800 additional patients every year in the United States alone from out-of-hospital cardiac arrest. That's a huge potential

impact on the single greatest killer of men and women with heart disease," Kudenchuk said.

The antiarrhythmic drugs also showed some benefits for other outcomes. Among all patients, those receiving either amiodarone or lidocaine required significantly fewer shocks to achieve a stable heart rhythm and were significantly more likely to survive to hospital admission. There was a low frequency of adverse side effects for both amiodarone and lidocaine. Favorable neurological outcome did not differ between the drug and placebo treatment groups. Overall, patients who survived to [hospital discharge](#) left with at most only a slight disability.

The patients randomized in the trial across the three patient groups were similar in terms of their demographic characteristics, the quality of CPR that was administered and the treatments they received after being admitted to the hospital.

Kudenchuk noted that one limitation of the study is that drug treatment was relatively late, which may have lessened its effectiveness. The trial also did not compare the effects of different doses or drug protocols and did not assess amiodarone and lidocaine when used in combination. Kudenchuk said the study is an important step toward elucidating potential benefits of antiarrhythmic drugs for out-of-hospital cardiac arrest, but the size of the study may have been insufficient to establish these benefits with greater statistical certainty. Additional study could shed light on how different approaches could further improve outcomes.

Cardiac arrest is a leading cause of death in the United States and worldwide. More than 326,000 people experience cardiac arrest outside of a hospital setting in the United States each year, and just 10 percent survive overall. Coronary artery disease, or the buildup of plaque and blockages in the heart's arteries, is the most common cause of cardiac arrest, though it can also be caused by other forms of heart disease as

well as some genetic diseases and other conditions.

Provided by American College of Cardiology

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