The Impact of the Code Drugs: Cardioactive Medications in Cardiac Arrest Resuscitation

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• Cardiac arrest • Anti-arrhythmic agent • Vasopressor

Approximately 325,000 cardiac arrests occur each year in the United States; primary cardiac events represent the precipitating cause in 75% of all episodes of sudden death. Most of these cardiac arrests (250,000) occur outside of a hospital annually. Despite innumerable advancements in medical treatments and technology, survival of individuals after an out-of-hospital cardiac arrest remains low, averaging less than 7%.[1]

The human circulatory system is a complex vascular network, and dysfunction rapidly leads to impaired oxygen delivery, progressive cellular dysfunction, organ failure, and ultimately patient death. Therefore, interventions for victims of cardiac arrest must be performed rapidly and efficiently to maximize the chance of a favorable cardiac and neurologic outcome. In an attempt to address this dysfunction and

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alter its natural history, the American Heart Association (AHA) has proposed a 4-step chain of survival to improve the outcomes of patients who experience an out-of-hospital cardiac arrest. The survival benefit of the first 3 steps, which include early access to medical care, early initiation of cardiopulmonary resuscitation (CPR), and early defibrillation, have been established in the literature and are discussed elsewhere in this issue. The incremental benefit of the fourth step in the chain of survival, which is early access to advanced care including airway management and the use of cardioactive intravenous (IV) medications, has not yet been well established, and there have been few advances in the pharmacologic component of the chain of survival.

The impact of advanced care has been questioned. Stiell and colleagues[2] concluded that the use of cardioactive medications during cardiac arrest does not improve survival to hospital discharge or the resulting neurologic status despite an increase in the return of spontaneous circulation (ROSC) and survival to hospital admission. The OPALS (Ontario Prehospital Advanced Life Support) trial examined the incremental effect on the rate of survival of individuals after cardiac arrest of adding advanced life support to an already present rapid defibrillation program. The multicenter, controlled, clinical trial reviewed the cases of 5638 patients. The investigators concluded that although the addition of cardioactive medications increased survival to hospital admission, it did not affect survival to hospital discharge. Further work by Stiell and colleagues[3] examined the relative importance of interventions in cardiac arrest with the determination of the value added by these therapies; selected odds ratios supporting survival from cardiac arrest include the following: witnessed arrest (4.4), any form of bystander CPR (3.7), electrical defibrillation less than 8 minutes into arrest (3.4), and advanced life support with cardioactive medications (1.1). This data set does not suggest that the advanced interventions offer significant benefit when compared with the basic therapies such as CPR and defibrillation. Furthermore, medication administration should not interfere with other lifesaving interventions such as chest compressions and defibrillation.

Despite this less-than-impressive database supporting their use, the various cardioactive medications, or code drugs, remain prominently placed in the AHA's Advanced Cardiac Life Support (ACLS) Guidelines 2010 (G2010).[4] There are several categories of medications used during cardiac arrest: vasopressor medications (epinephrine, vasopressin, and atropine), antiarrhythmic medications (amiodarone and lidocaine), and adjunct medications (sodium bicarbonate, calcium, magnesium, and fibrinolytics). This review discusses the evidence for their use and notes their current position in the AHA G2010.[4]

VASOPRESSOR MEDICATIONS

Vasopressors, namely epinephrine and vasopressin, are routinely administered during cardiac arrest, and there is evidence to suggest that this usage positively affects ROSC. There are, however, no published placebo-controlled clinical trials demonstrating that the administration of any vasopressor medication at any stage in the management of pulseless ventricular tachycardia (VT), ventricular fibrillation (VF), pulseless electrical activity (PEA), or asystole increases the rate of neurologically intact survival to hospital discharge.[4]

Epinephrine is one of the most widely used drugs in the ACLS regimen, indicated for VF, pulseless VT, PEA, and asystolic arrests. Epinephrine is a sympathomimetic agent that serves as a potent adrenergic agonist stimulating both α and β receptors. Stimulation of the α_1 and α_2 receptors causes arterial vasoconstriction, which is deemed