Drugs in Out-of-Hospital Cardiac Arrest

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KEYWORDS

• Cardiac arrest • Emergency medical services • Medications • Advanced cardiac life support

KEY POINTS

- Limited evidence exists regarding the optimal medical therapy for the management of out-of-hospital cardiac arrest.
- Epinephrine is the only recommended medication for all cardiac arrests.
- Amiodarone or lidocaine is recommended for refractory ventricular fibrillation or ventricular tachycardia.
- Although there is evidence that these medications increase short-term survival, there are few data that they affect long-term outcome measures.
- Other medications should only be considered for use in special situations during out-of-hospital cardiac arrest.

INTRODUCTION

More than 350,000 people suffer out-of-hospital cardiac arrest (OHCA) in the United States each year,[1] and 60% of these patients are treated by emergency medical services (EMS).[2] Despite medical advancements, overall survival to hospital discharge continues to be only 11%.[1] Recognition of cardiac arrest and early application of quality cardiopulmonary resuscitation and defibrillation remain the crucial steps to survival from OHCA. Yet, improvements in medical therapies for cardiac arrest have the potential to save tens of thousands of lives every year.

Management of OHCA has distinct differences compared with in-hospital cardiac arrest, including lengthy response times of trained personnel, limited resources on scene, and multiple challenges to implementation of treatment guidelines.[3] Additionally, logistical considerations for EMS-administered medications include ease of administration, storage space, temperature stability, and cost. For example, medications supplied in pre-filled syringes and administered by bolus are more feasible to administer quickly than medications requiring mixing with a diluent or administered by infusion. Unproven or equivalent medical therapies can become distractors in the out-of-hospital setting, where simplified algorithms emphasizing the most important aspects of resuscitation are more likely to result in a return of spontaneous circulation (ROSC) and good patient outcomes. Current evidence-based guidelines for OHCA remain limited by the low quality of available evidence, and most recommendations are based on metaanalyses and systematic reviews of primarily retrospective studies.[4,5] Newer randomized controlled trials (RCTs) performed outside of the hospital have advanced our knowledge substantially, yet RCTs remain a minority of studies on OHCA owing to multiple logistical barriers and high cost.

In this article, we review the literature and highlight some of the key studies that have evaluated

specific medications for the treatment of OHCA. We also summarize evidence-based guidelines from the American Heart Association (AHA),[4,5] which form the basis for EMS protocols for OHCA management in the United States (Tables 1 and 2).

VASOPRESSORS
Epinephrine

Epinephrine is an adrenergic agonist that has been used for resuscitation of cardiac arrest since the earliest standardized guidelines.[6] Early animal studies of epinephrine demonstrated improved rates of ROSC[7,8] and improved cerebral and myocardial blood flow during cardiopulmonary resuscitation.[9] The evidence for patient-centered outcomes has been more limited, with the majority of human data being observational. RCTs comparing epinephrine against placebo have been difficult to perform because its use in cardiac arrest has become the standard of care in many areas.

A large observational study in Japan questioned the value of epinephrine in OHCA.[10] In this study of 400,000 cases of OHCA, epinephrine use increased the chance of prehospital ROSC, but there was a negative association between epinephrine and both 1-month survival and 1-month functional outcomes. This study was followed by the only prehospital RCT comparing epinephrine with placebo, performed in Western Australia, which found that epinephrine was significantly associated with prehospital ROSC.[11] Additionally, twice as many patients in the epinephrine group survived to hospital discharge, but this was not statistically significant, possibly owing to the trial being underpowered for this outcome and raising questions

Table 1
American Heart Association recommendations for medications in cardiac arrest

Category	Medication	Indication	IV/IO Dosing	Recommendation (LOE)
Vasopressor	Epinephrine	Any rhythm	1 mg every 3–5 min	Recommended (class IIb, LOE B)
	Vasopressin	Any rhythm	40 U (replacing first or second dose of epinephrine)	No benefit over epinephrine (class IIb, LOE B)
Antiarrhythmic	Amiodarone	VF/pVT	300 mg (first dose) 150 mg (second dose)	Recommended (class IIb, LOE B)
	Lidocaine	VF/pVT	1.5 mg/kg	Recommended (class IIb, LOE C)
	Magnesium sulfate	Polymorphic VT (torsades de pointes)[a]	1–2 g diluted in 10 mL D5W	Recommended (class IIb, LOE C)
		VF/pVT	Not recommended	Not Recommended (class III: no benefit, LOE B)
	Procainamide	VF/pVT (as second agent)	500 mg, repeated up to 17 mg/kg	Uncertain benefit (not addressed)
	Calcium chloride	Any rhythm	500–1000 mg	Not recommended (class III, LOE B)
	Atropine	Asystole, PEA	1 mg	Not recommended (class IIb, LOE B)
	Sotalol	VF/pVT	1.5 mg/kg	Not addressed
Other	Sodium bicarbonate	Any rhythm	1 mEq/kg	Not recommended (class III, LOE B)
	Naloxone	Any rhythm	2 mg	No Recommendation[b]

Abbreviations: D5W, dextrose 5% in water; LOE, level of evidence; PEA, pulseless electrical activity; pVT, pulseless ventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.
   [a] Recommended only when polymorphic VT is associated with a long QT interval.
   [b] No recommendation for confirmed cardiac arrest.
   Data from Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132(18 Suppl 2):S444–64.