



Evidence for Lidocaine and Amiodarone in Cardiac Arrest Due to VF/Pulseless VT

Introduction

- Evidence supporting the use of lidocaine and amiodarone for advanced cardiac life support was considered by international experts at the 2000 ACLS Guidelines Conference.¹
- Studies involving the antiarrhythmic agents, dating back in some cases to the 1950s, were considered. All evidence was reviewed, including both English and non-English sources.¹

Lidocaine: Level of Evidence

Supporting (10)

- Level 4 (1)
- Level 6 (1)
- Level 7 (7)
- Level 8 (1)



Neutral/Opposing (17)

- Neutral (5)
 - Level 2 (2)
 - Level 3 (1)
 - Level 6 (1)
 - Level 7 (1)
- Opposing (12)
 - Level 1 (1)
 - Level 4 (2)
 - Level 6 (7)
 - Level 7 (2)

Level 1 = prospective, randomized controlled trial (RCT)

Level 2 = neutral RCT

Level 3 = prospective nonrandomized observational study with control

Level 4 = retrospective nonrandomized observational study with control

Level 5 = case series with no control

Level 6 = animal/mechanical models

Level 7 = reasonable extrapolations from data gathered for other purposes

Level 8 = common practices before evidence-based guidelines

Quality and Level of Evidence Supporting Lidocaine

- The quality of the evidence supporting lidocaine was considered to be “fair” in all cases.
- The level of evidence was more rigorous than Level 6 in only one case. This was a large (N = 1,360), controlled, Level-4 study² that showed improved resuscitation rates and survival to hospital admission (but not discharge) in patients receiving lidocaine.
- The other nine supporting sources used methodologies that were considered less rigorous (Levels 6, 7, and 8). For example, one study evaluated the prophylactic use of lidocaine to prevent VF in patients with myocardial infarction (MI).³ Extrapolations from the results of this study became the basis of assumptions that lidocaine offered potential benefit in treating VF.¹

Quality and Level of Neutral/Opposing Evidence for Lidocaine

- The quality of the neutral/opposing evidence for lidocaine was considered “good” in 15 of the 17 sources.
- The level of evidence was more rigorous than Level 6 in 6 of the 17 sources.

Quality and Level of Evidence Supporting Amiodarone

- Examination of the supporting evidence showed the following:
 - One randomized, placebo-controlled, Level-1 study—the ARREST trial,⁴ the only study to show a benefit for any antiarrhythmic agent versus placebo.
 - A placebo-control group was included in 3 of the 16 sources.

Quality and Level of Neutral/Opposing Evidence for Amiodarone

- Two of the three sources were dose-ranging studies designed to establish the most appropriate treatment regimen for IV amiodarone. Because amiodarone was compared only with other doses of amiodarone, these studies could not, by design, show a benefit for amiodarone versus any other regimen. Therefore, these studies were assigned to the “neutral or opposing” category.

Amiodarone: Level of Evidence

Supporting (16)

- Level 1 (2)
- Level 2 (1)
- Level 5 (10)
- Level 6 (2)
- Level 7 (1)



Neutral/Opposing (3)

- Neutral (2)
 - Level 2 (2)
- Opposing (1)
 - Level 7 (1)

Level 1 = prospective, randomized controlled trial (RCT)

Level 2 = neutral RCT

Level 3 = prospective nonrandomized observational study with control

Level 4 = retrospective nonrandomized observational study with control

Level 5 = case series with no control

Level 6 = animal/mechanical models

Level 7 = reasonable extrapolations from data gathered for other purposes

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- The third source was a Level-7 animal study conducted by Zhou et al in 1998 in 24 dogs. The aim was to study the effect of amiodarone on cardiac electrophysiological properties and on the VF threshold in induced congestive heart failure (CHF). Whereas the investigators concluded that amiodarone normalizes cardiac electrophysiological properties, neither survival nor medical benefits were evaluated in this study, nor was amiodarone compared with any other pharmacological agent. This study was also considered “neutral or opposing” because amiodarone provided no mortality or morbidity benefit.

Evidence-Based Results for Lidocaine and Amiodarone	
Lidocaine	Amiodarone HCl
<ul style="list-style-type: none"> • Suffered during new emphasis on evidence 	<ul style="list-style-type: none"> • Respected and effective agent
<ul style="list-style-type: none"> • Evidence supporting efficacy is poor and methodologically weak (one supporting study of Level 5 or better) for shock-refractory VF and pulseless VT 	<ul style="list-style-type: none"> • Better evidence-based support than any other antiarrhythmic (13 supporting studies of Level 5 or better)
<ul style="list-style-type: none"> • No proven short- or long-term efficacy in cardiac arrest 	<ul style="list-style-type: none"> • Strong supporting evidence justifies use before lidocaine in shock-refractory VF and pulseless VT
<ul style="list-style-type: none"> • Class Indeterminate: <ul style="list-style-type: none"> - Remains a second choice after other agents (amiodarone, procainamide, sotalol) in VF and pulseless VT that persists after defibrillation and epinephrine 	<ul style="list-style-type: none"> • Class IIb: <ul style="list-style-type: none"> - Recommended ahead of other agents after defibrillation and epinephrine in cardiac arrest with persistent VF/pulseless VT
<ul style="list-style-type: none"> - For control of hemodynamically compromising premature ventricular complexes and hemodynamically stable VT (Class IIb) 	<ul style="list-style-type: none"> - First-choice antiarrhythmic for shock-refractory cardiac arrest due to persistent VF/pulseless VT

Data from American Heart Association.¹

- The guidelines emphasize that the only proper evaluation of new resuscitation agents is with prospective, randomized clinical studies with placebo as the only acceptable control group. If new drugs are compared with standard therapy and if both therapies make the cardiac arrest victims worse, valid results can never be obtained.¹

IV amiodarone is indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients refractory to other therapy.

IV amiodarone can also be used to treat patients with VT/VF for whom oral amiodarone is indicated, but who are unable to take oral medication.

IV amiodarone is contraindicated in patients with cardiogenic shock, marked sinus bradycardia, and second- or third-degree AV block in the absence of a functioning pacemaker.

IV amiodarone should be administered only by physicians who are experienced in the treatment of life-threatening arrhythmias, who are thoroughly familiar with the risks and benefits of amiodarone therapy, and who have access to facilities adequate for monitoring the effectiveness and side effects of treatment.

Hypotension is the most common adverse effect seen with IV amiodarone and may be related to the rate of infusion. Hypotension should be treated by slowing the infusion or with standard therapy: vasopressor drugs, positive inotropic agents, and volume expansion.

In clinical trials, the most important treatment-emergent adverse effects were hypotension (16%), bradycardia (4.9%), liver function test abnormalities (3.4%), cardiac arrest (2.9%), VT (2.4%), congestive heart failure (2.1%), cardiogenic shock (1.3%), and AV block (0.5%).

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REFERENCES

1. American Heart Association. Guidelines 2000 for cardiopulmonary resuscitation and emergency cardiac care. *Circulation*. 2000;102 (suppl): I-86, I-87, I-116, I-117, I-149.
2. Herlitz J, Ekstrom L, Wennerblom B, et al. Lidocaine in out-of-hospital ventricular fibrillation: does it improve survival? *Resuscitation*. 1997;33:199-205.
3. Lie KI, Wellens HJ, van Cappelle FJ, et al. Lidocaine in the prevention of primary ventricular fibrillation: a double-blind, randomized study of 212 consecutive patients. *N Engl J Med*. 1974;291:1324-1326.
4. 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;341:871-878.