

Washington University Emergency Medicine Journal Club
Amiodarone: Wonder Drug or Wonder Why?

Vignette

Working in TCC can be draining, and on one particularly busy afternoon, you begin to suspect your own sanity. After back-to-back cardiac arrest patients, you wonder if perhaps you should have done something less stressful with your life, like maybe become a lobster boat captain or an ice road trucker.

Your first code is a middle-aged female who suffered cardiac arrest while watching Alabama beat Clemson during the Sugar Bowl (yeah...that's right!!!). She was initially noted to be in ventricular fibrillation (VF), and remained so after three rounds of defibrillation. As she arrives in the trauma room, you immediately continue CPR and set up to shock her again. Your attending orders amiodarone, and even though you remember hearing that this may not be very effective, you realize it's not the time to argue. The patient ends up with ROSC and goes to the cath lab when her ECG reveals an anterior STEMI.

Your second patient is an elderly male who was initially found to be in PEA by EMS, but then later developed fine VF after three rounds of epinephrine en route. You shock him three times in the trauma room without effect, and once again your attending calls for amiodarone. After twenty more minutes of CPR, the patient reverts to asystole and the code is soon called.

You end up giving amiodarone twice more in your shift, once to a patient with new-onset a-fib who ends up getting admitted after not converting to a sinus rhythm, and later to a patient with stable, wide-complex tachycardia (which you're pretty sure was ventricular tachycardia [VT]), and you start to wonder if your attending owns stock in the company that makes it. You search online after your shift and find an excellent rundown on the limits of amiodarone on [RebeLEM](#), which prompts you to perform your own literature search.

PICO Question

Population: Adults patients with either new-onset atrial fibrillation, hemodynamically stable ventricular tachycardia (VT), or cardiac arrest due to ventricular fibrillation (VF) or VT

Intervention: IV Amiodarone

Comparison: Placebo or any alternative antiarrhythmic

Outcome: Conversion to normal sinus rhythm, need for hospital admission, survival, functional neurologic outcome, hypotension.

Search Strategy

Three articles were chosen from the RebeLEM blog ([Ortiz 2017](#), [Chevalier 2003](#), [Kudenchuk 2016](#)). A fourth article was chosen by reviewing the "similar articles" list for the Kudenchuk article ([Kudenchuk 2017](#)).

Article 1: [Ortiz M, Martín A, Arribas F, et al; PROCAMIO Study Investigators. Randomized comparison of intravenous procainamide vs. intravenous amiodarone for the acute treatment of tolerated wide QRS tachycardia: the PROCAMIO study. Eur Heart J. 2017 May 1;38\(17\):1329-1335. Answer Key.](#)

Article 2: [Chevalier P, Durand-Dubief A, Burri H, Cucherat M, Kirkorian G, Touboul P. Amiodarone versus placebo and class Ic drugs for cardioversion of recent-onset atrial fibrillation: a meta-analysis. J Am Coll Cardiol. 2003 Jan 15;41\(2\):255-62. Answer Key.](#)

Article 3: [Kudenchuk PJ, Brown SP, Daya M, et al; Resuscitation Outcomes Consortium Investigators. Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest. N Engl J Med. 2016 May 5;374\(18\):1711-22. Answer Key.](#)

Article 4: [Kudenchuk PJ, Leroux BG, Daya M, et al; Resuscitation Outcomes Consortium Investigators. Antiarrhythmic Drugs for Nonshockable-Turned-Shockable Out-of-Hospital Cardiac Arrest: The ALPS Study \(Amiodarone, Lidocaine, or Placebo\). Circulation. 2017 Nov 28;136\(22\):2119-2131. Answer Key.](#)

Bottom Line

Amiodarone, which was first approved by the FDA in 1985, became a mainstay of arrhythmia management after being added to the [ACLS guidelines in 2000](#). At that time, amiodarone was recommended ahead of lidocaine for management of hemodynamically stable wide-complex tachycardia but was only included as a consideration for refractory VF and pulseless VT. In the 2010 update, amiodarone was recommended as a “first line anti arrhythmic agent” in refractory VF/pulseless VT, based on limited evidence for improved rates of ROSC and hospital admission. In addition, amiodarone been recommended for use in recent-onset AF for over twenty years ([Hou 1995](#)). Given the rise in prominence of procainamide use in AF (see [Ottawa Aggressive Protocol by Stiell et al](#)), and an increased focus on [longer term outcomes in cardiac arrest](#), we decided to review evidence for a variety of amiodarone indications frequently seen in the ED.

Stable Ventricular Tachycardia

[PROCAMIO](#), a small, multicenter randomized controlled trial conducted at several hospitals in Spain enrolled 74 patients with hemodynamically stable, wide-complex tachycardia and randomized them to receive either IV amiodarone or IV procainamide over twenty minutes. Major cardiac events (clinical signs of hypoperfusion, dyspnea, hypotension, or acceleration of heart rate) occurred less frequently among patients receiving procainamide (OR 0.1; 95% CI 0.03 to 0.6). These patients also had a much higher rate of cardioversion (OR 3.3; 95% CI 1.2 to 9.3). Unfortunately, this was a very small study in which only a fifth of the number of planned patients was actually enrolled. Despite this limitation, it seems reasonable to use procainamide as a first line agent for hemodynamically stable wide-complex tachycardia rather than amiodarone.

Recent Onset Atrial Fibrillation

Procainamide has been used successfully in the management of recent-onset AF, with a previously documented conversion rate of around 60%, occurring at a median of 3 hours following drug infusion ([Stiell 2010](#)). In one systematic review and meta-analysis comparing IV amiodarone to placebo and class Ic antiarrhythmics ([Chevalier 2003](#)), amiodarone did not have a significantly higher rate of cardioversion compared to placebo at 1 to 2 hours, but did have a higher rate at 6 to 8 and 24 hours. Compared to class Ic antiarrhythmics, amiodarone was less effective at 1 to 2 and 6 to 8 hours, but had similar efficacy at 24 hours. Cardioversion with amiodarone by 6 to 8 hours occurred in 48-62% patients (depending on the individual study), which is fairly comparable to previously reported rates for procainamide. Given the lack of studies comparing procainamide to amiodarone head-to-head, it seems reasonable to consider either drug, though concerns regarding [hypotension with amiodarone](#) may sway many to use procainamide instead.

Refractory VF or Pulseless VT

[A recent multicenter, randomized controlled trial](#) conducted at 55 EMS services in North America sought to compare the effectiveness of amiodarone, lidocaine, and placebo in patients with out of hospital cardiac arrest (OHCA) due to refractory VF/pulseless VT. After excluding patients whose initial rhythm was not VF or VT, 3026 patients were enrolled and evenly split between groups. The authors found no significant difference in survival to hospital discharge between patients receiving amiodarone and placebo (ARR 3.2%; 95% CI -0.4% to 7.0%) and no difference between those receiving lidocaine and placebo (ARR 2.6%; 95% CI -1.0% to 6.3%). Unfortunately, despite the large number of patients enrolled, the outcome was fairly rare, which resulted in relatively wide 95% CIs. As a result, a potentially clinically meaningful survival improvement (3.2% for amiodarone and 2.6% for lidocaine) could not be shown to be statistically significant.

[In a follow-up study](#), the authors of the previous study also looked at those patients initially enrolled but excluded because VF/pulseless VT was not their initial rhythm (i.e. those patients with an initially non-shockable rhythm). Again, they did not observe any statistically significant difference in survival to discharge between the three groups (1.9% for the placebo group, 3.1% for the lidocaine group, and 4.1% for the amiodarone group). Also, despite not finding a statistically significant difference, the study was not [sufficiently powered](#) to detect a potentially clinically significant improvement in mortality of 2% with amiodarone. Given this limitation for the last two studies, and the lack of any downside in this subset of patients, it seems reasonable to continue amiodarone use for patients with refractory VF/pulseless VT for both OHCA and in-hospital arrest.