Objectives

1. Discuss the historical evidence supporting the use of Epinephrine, Vasopressin and Amiodorone in cardiac arrest.

2. Review recent publications evaluating the efficacy of Epinephrine, Vasopressin and Amiodorone.
2010 AHA ACLS Guidelines

- Bigger emphasis on compressions
- Early defibrillation
- Waveform Capnography
- Post resuscitation algorithm
- New guidelines in 2015

Which of the following medications has been shown to increase survival to discharge from cardiac arrest?

A. Epinephrine
B. Vasopressin
C. Bicarb
D. Amiodorone
E. None of the above

![Survey Results]
10/13/2014

Emergency medications – V-fib

- **Epinephrine** 1 mg every 3-5 min or
- **Vasopressin** 40 units instead of the 1st or 2nd Epi
- **Amiodorone**
  - 300 mg IV pulseless
  - 150 mg pulse

Circulation 2010, AHA ACLS Guidelines
Epinephrine

Current AHA guideline:
1 mg every 3 – 5 min in any pulseless rhythm

Rationale for use of Epinephrine

- Increased alpha 1 & alpha 2 effects
- Increased systemic vascular resistance
- Increased myocardial & cerebral blood flow
- Increased ROSC rates?
Does Epinephrine improve myocardial blood flow during cardiac arrest?

A. Yes
B. No
C. Sometimes

Improved myocardial blood flow?

- Decreased Cardiac Output with Epi
- CPP: 14 ± 4 mm Hg before Epi, 29 ± 6 mmHg after Epi
- P = < 0.01

Animal study evaluating CO in pigs

Improved cerebral blood flow?

- Animal study evaluating nine - 40 kg pigs
- Decreased microvascular perfusion with Epinephrine administration


Cerebral Blood Flow with Epi

Increases in CPP were not accompanied by increases in CBF

Japanese EMS introduction of Epi

Short term gain, but long term pain

N = 4

Increased ROSC rates, however,
Decreased chance of survival at 1 month & decreased neurologic outcomes

Japan EMS 2004 – Permitted to start IVs
2006 – Permitted to administer Epi

Hagihara et al (2012) JAMA

VSE Study

Mentzelopoulos (2013) JAMA

- RCT
- Vasopressin 20 IU + Epi 1mg q 3 min x 5 cycles + 40 mg Steroid - methylprednisolone (1st cycle)

Figure 2. Results on Survival Analysis
Epinephrine in Cardiac Surgery Patients

- Look for causes!
  - Tamponade? Bleeding?
  - Resternotomy
- If primary V-fib, defibrillation x 3 sequential
- Do not give Epinephrine unless a senior provider advises to do so!

What’s the risk?
- Severe rebound hypertension leading to possible:
  - Aortic rupture
  - Suture line disruption

-Cardiac Surgery Advanced Life Support Guidelines

Epinephrine – What’s the evidence?

- Alpha adrenergic effect
  - Increase coronary & cerebral perfusion pressure (animal study - dogs)
- No evidence linking to increased human survival
- Optimal dose? Who knows! NOT high dose!
  - Possibly < 30 – 45 mcg/kg (< 2 – 3 mg)
- Optimal interval? Who knows!

- High dose epip?
  - 0.1 – 0.2 mg/kg (3 mg, 5 mg doses)
- No difference in survival or neurologic outcomes

Paradis et al (1991) JAMA
Brown et al (1992) NEJM
Callaham et al (1992) JAMA
Brown et al (1992) NEJM
Stell et al (1992) NEJM
Is Epinephrine beneficial or does it cause harm?

- Current recommendation: 1 mg Q 3 – 5 min
- RCT Epi vs. Placebo
- Warwick University
- UK & Wales
- Enrollment started Sept 2014
- 8,000 subjects
- Out-of-Hospital Cardiac Arrest

Ventricular fibrillation

- Most successful treatment for v-fib is defibrillation!
- For every minute delay, survival decreases by 10%!!!


N = 13,053
Amiodorone vs. Placebo
(after 3 successive shocks in OHCA)

Kudenchuk et al (1999) NEJM

N = 504

Amiodorone vs. Lidocaine

Dorian et al (2002) NEJM

Early = < 24 min of dispatch call

Note: Survival to hospital admission
V-fib

Amiodorone

- 2 RCTs (OHCA) increased survival to hospital admission (vs. Lidocaine or placebo)
- Lacking evidence that it makes a difference in survival to discharge

- For REFRACTORY V-fib, use Amiodorone
- 300 mg, may re-bolus with 150 mg

Kudenchuk et al (1999) NEJM
Dorian et al (2002) NEJM

ALP Trial

- Amiodorone vs. Lidocaine vs. Placebo
- Out of hospital v-fib arrest
- Goal is drug administration < 10 minutes after arrival on scene

- Resuscitation Outcome Consortium (ROC) study group
- Multi-city EMS trial
- Still enrolling patients
- Goal: 3,000 patients
Torsades de Pointes

- Magnesium!!!
- Effective for termination of Torsades de Pointes associated with prolonged QT
  - Perticone et al (1986) AMJ

**Empiric dosing with Magnesium is not shown to be beneficial for in-hospital cardiac arrest**

Gone by the wayside?

- What happened to Lidocaine????!!!
  - Amiodorone was superior in out-of-hospital VF arrest

- What happened to Magnesium????!!!
  - No benefit, except in Torsades de Pointes

- What happened to Calcium Chloride
  - No benefit
PEA – Pulseless Electrical Activity & Asystole

- **Pump**
  - at least 100 cpm
  - 2 inch depth

- **Epi**
  - 1 mg Q 3 – 5 min

- **Assess**
  - the causes

- **Atropine?**
  - No longer recommended
  - Initial use was based on a case study of 8 patients

Symptomatic bradycardia

- **Atropine** 0.5 mg up to 3 mg
  - removed from algorithm (except in symptomatic bradycardia)
  - Do not give if the cause is heart block secondary to MI or any quickly reversible cause
  - Doses < 0.5 mg may cause paradoxical bradycardia

- 2nd line (not responsive to atropine):
  - Pacing
  - Dopamine infusion 5 – 20 mcg/kg/min or
  - Epinephrine infusion – 2 – 10 mcg/min

When is Bicarb appropriate?

- Hyperkalemia
- Acidosis that was bicarb responsive pre-arrest
- Tricyclic antidepressant overdose

- Not “JUST BECAUSE”!!!

Route of administration

- Abandoned endotracheal administration
  - Not effective
- Whatever route does not interrupt chest compressions!
  - IV
  - IO
Intra-osseous access

Summary on drugs...

- Some have demonstrated increased ROSC
- None have shown long term benefit in RCT
- Most studies are based on OHCA
- Lower doses of Epi are likely better than higher doses (> 5 mg)
- Amiodorone is better than Lidocaine, but no survival benefit
- Don’t give bicarb just because…
In conclusion…

- The focus of cardiac resuscitation should be on high quality CPR, minimal interruptions
- Defibrillate early, minimize pre/post shock pauses
- Incorporate waveform Capnography
- Control the temperature post arrest