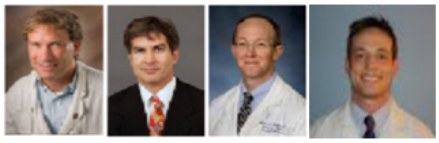
critical care perspectives in emergency medicine



Is Epinephrine Useful in OHCA?

Key Article

Perkins GD, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. N Engl J Med. 2018; 379:711-21.

- Background
  - Epi has potential beneficial effects in cardiac arrest
    - Alpha-adrenergic effects: increases aortic diastolic BP during CPR and augments coronary blood flow, increasing the chances of ROSC; can cause platelet activation which promotes thrombosis and impairs microvascular blood flow
    - Beta-adrenergic effects: can cause dysrhythmias and increased myocardial oxygen demand, increases the risk of recurrent cardiac arrest
  - Observational trials involving more than 500,000 patients have reported higher rates of ROSC but worse neurologic outcomes in patients treated with epi
  - These studies have produced conflicting results
  - ILCOR called for the initiation of a placebo-controlled trial to establish whether epi is safe and effective in cardiac arrest
- Objective
  - Determine whether epinephrine is beneficial or harmful as a treatment for OHCA
- Study
  - Multicenter, randomized, double-blind, placebo-controlled trial
  - 5 National Health Service ambulance services in the UK
  - Patients
    - Inclusion
      - Adults with OHCA for which ALS was provided by trial-trained paramedics
    - Exclusion
      - Pregnancy
      - Age < 16 years
      - Anaphylaxis or asthma as etiology
      - Administration of epi prior to arrival of trial-trained paramedic
  - Randomization and Treatment
    - If initial attempts at resuscitation (CPR and defibrillation) were unsuccessful, patient randomly assigned to receive epi or saline placebo
    - Trial packs (10 prefilled syringes) of 1 mg of epi or 0.9% saline
    - Single doses given every 3 to 5 minutes
    - Assigned in a ratio of 1:1
    - Treatment was continued until a sustained pulse was achieved, resus discontinued, or care handed over to clinicians in the hospital
    - Hospital care (TTM, hemodynamic, oxygenation/ventilation, prognostication) not specified
  - Primary outcome: 30-day survival

- Secondary outcomes
  - Rate of survival until hospital admission
  - ICU and hospital LOS
  - Rates of survival at hospital DC and at 3 months
  - Neurologic outcomes at hospital DC and 3 months (defined using mRS)
- Results
  - 8014 patients assigned (8103 of 10,623 eligible and trial packets opened)
    - Epi group: 4015 patients
    - Placebo group: 3999 patients
    - Characteristics well balanced
    - Concurrent treatments similar
    - Median time from call to EMS arrival 6.6 minutes
    - Median time from arrival to trial agent administration 13.8 minutes
    - Proportion of patients with ROSC during prehospital phase 36.3% vs. 11.7%
  - Primary Outcome
    - 30-day survival
      - Epi group: 130/4012 patients: 3.2%
      - Placebo group: 94/3995 patients: 2.4%
      - p=0.02
      - NNT with Epi to prevent one death at 30-days: 112
  - Secondary Outcomes
    - Proportion of patients who survived to hospital DC with favorable neurologic outcome
      - Epi group: 87/4007 patients: 2.2%
      - Placebo group: 74/3994 patients: 1.9%
    - Severe neurologic impairment
      - Epi group: 39/126 patients: 31%
      - Placebo group: 16/90 patients: 17.8%
    - No difference in survival at 3 months and neurologic outcomes at 3 months
    - No difference in LOS in the hospital or ICU
    - No evidence of difference in treatment effect based on age, witnessed cardiac arrest, bystander CPR, initial rhythm, or response time to trial agent administration
- Limitations
  - Earlier administration may have influenced results?
  - Did not collect info on patient's baseline neuro status
  - Information about quality of CPR only during first 5 minutes and in less than 5% of cases
  - No information or specification of hospital care
- **Take Home Point**
  - **In patients with OHCA, use of epi resulted in higher rate of 30-day survival but no difference in rate of favorable neuro outcome with more severe impairment**