Need to Know: CJEM Journal Club

Epinephrine in cardiac arrest: The PARAMEDIC2 trial

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Abstract Link: http://www.nejm.org/doi/10.1056/NEJMoa1806842
Full citation: Perkins GD, Ji C, Deakin CD, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. *N Engl J Med* 2018; epub, NEJMoa1806842.
Article type: Therapy
Ratings: Methods – 4/5 Usefulness – 3.5/5

INTRODUCTION

Background

There is clinical uncertainty regarding the safety and efficacy of epinephrine administration in out-of-hospital cardiac arrest (OHCA).[1]

Objective

The aim of this study was to assess, in a more definitive manner than prior research, the effect of epinephrine in OHCA and its safety and efficacy.

METHODS

Design

Randomized, double-blind trial

Setting

Five UK National Health Service ambulance services

Subjects

Adults (≥ 16 years of age) with OHCA in whom initial cardiopulmonary resuscitation (CPR) and defibrillation were unsuccessful. Exclusion criteria included suspected pregnancy, cardiac arrest from anaphylaxis or asthma, and epinephrine before the arrival of trial-trained paramedics. Traumatic arrests were excluded at one site.

Intervention

IV or intraosseous epinephrine, 1 mg, or 0.9% normal saline placebo every 3–5 minutes.

Outcomes

Primary outcomes included rate of survival at 30 days. Secondary outcomes included rates of survival until hospital admission, at-hospital discharge and 3-months, lengths of hospital and intensive care unit (ICU) stay, and neurologic outcome at hospital discharge.

RESULTS

Results of the study are shown in Table 1.

APPRAISAL

Strengths

- Large, multicentre, double-blind randomized controlled trial (RCT), expanding upon previously observational research
- Outcomes clearly defined and clinically relevant
- Primary outcome in accordance with International Liaison Committee on Resuscitation (ILCOR) guidelines
- Well-defined population

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Table 1. Primary and secondary outcomes (from Table 2 in Perkins et al., 2017, "A randomized trial of epinephrine in out-of-hospital cardiac arrest")

Outcome	Epinephrine (N = 4012)	Placebo (N = 3995)	Adjusted
Primary outcome			
Survival at 30-days (%)	3.2	2.4	1.8 (1.1-2.0)
Secondary outcomes			
Survival until hospital admission (%)	23.8	8	3.8 (3.3-4.4)
Median length of stay in ICU – days			
Patients who survived	7.5	7.0	NA
Patients who died	2.0	3.0	NA
Median length of hospital stay – days			
Patients who survived	21.0	20.0	NA
Patients who died	0	0	NA
Survival until hospital discharge (%)	3.2	2.3	1.5 (1.1-2.0)
Favourable neurologic outcomes at hospital discharge (%)	2.2	1.9	1.2 (0.9-1.7)
Survival at 3-months (%)	3.0	2.2	1.5 (1.1-2.0)
Favourable neurologic outcomes at 3-months (%)	2.1	1.6	1.4 (1.0-2.0)

- Similar baseline characteristics between groups
- CPR data included when available

Limitations

- Emergency department and hospital care not defined by the study protocol, which could distort the accuracy or generalizability of the results
- Overall rate of survival following cardiac arrest significantly lower than anticipated
- Median time to administration of study agent > 21 minutes, which could distort the accuracy or generalizability of the results
- No discussion on shockable versus non-shockable rhythms included (However, a subgroup analysis reported in the supplementary material found no significant differences.)
- CPR quality during resuscitation efforts known to contribute heavily to outcomes and not assessed
- Not necessarily generalizable to other epinephrine dosing strategies

CONTEXT

Multiple cohort studies with conflicting results on the efficacy and safety of epinephrine in OHCA have been published. In 2011, Jacobs et al. published the only other RCT on this topic; however, it was terminated early with incomplete enrolment.[2] Current Advanced Cardiac Life Support guidelines recommend the routine administration of 1-mg (standard dose) epinephrine every 3–5 minutes in OHCA, despite a lack of strong evidence to support this practice.[3] Trials focused on different epinephrine doses and frequencies, infusions, or other vasopressor agents would be helpful.

BOTTOM LINE

The results of this study provide persuasive evidence to reconsider current epinephrine guidelines in OHCA. Although epinephrine was associated with increased 30-day survival, it did not increase the probability of survival with good neurologic outcome owing to an increased rate of severe neurologic disability in the treatment group. The number needed to treat in this trial to obtain one additional survivor was 112. The slight increased survival coupled with worsened neurologic outcome in the treatment group does not support the routine use of epinephrine in OHCA; however, the possibility of benefit in subgroups remains, and further research is required. Clinicians should continue to use epinephrine in OHCA until such time that society and national guidelines are revised.

Keywords: ACLS, cardiac arrest, epinephrine, resuscitation, ROSC

Competing interests: None declared.

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https://doi.org/10.1017/cem.2019.354 Published online by Cambridge University Press