

How Effective Are Epinephrine and Vasopressin for Improving Survival Among Patients in Cardiac Arrest?



TAKE-HOME MESSAGE

Epinephrine is associated with improved overall survival rates, but no difference noted in favorable neurologic outcomes.

METHODS

DATA SOURCES

Authors of this review conducted a thorough search of the Cochrane Central Register of Controlled Trials, the Database of Abstracts of Reviews of Effects, MEDLINE, Ovid, and EMBASE from inception and through May 2018. Authors also searched the International Liaison Committee on Resuscitation 2015 Advanced Life Support Consensus on Science and Treatment Recommendations, ClinicalTrials.gov, the ISRCTN registry, the World Health Organization International Clinical Trials Registry Platform, and the NHS Clinical Trials and Medical Research database.

STUDY SELECTION

Two reviewers independently read the title and abstract, and, if in doubt, read the entire article for inclusion. Disagreements were resolved through discussion between these reviewers and the other 2 authors. There were no language restrictions and translators were used for non-English studies. Authors included all randomized controlled trials comparing standard-dose (or high-

EBEM Commentators

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Finn J, Jacobs I, Williams TA, et al. Adrenaline and vasopressin for cardiac arrest. *Cochrane Database Syst Rev.* 2019;(1):CD003179.**

Results

Comparison of epinephrine versus placebo in cardiac arrest.

| Outcome | No. of Studies (No. of Participants) | Relative Effect (95% CI) | I ² , % |
|--------------------------------|---|-----------------------------|--------------------|
| ROSC | 3 (8,663) | 2.86 (2.21-3.71) | 33 |
| Survival to hospital admission | 2 (8,489) | 2.51 (1.67-3.76) | 77 |
| Survival to hospital discharge | 2 (8,538) | 1.44 (1.11-1.86) | 0 |
| Favorable neurologic outcome | 2 (8,535) | 1.21 (0.90-1.62) | 0 |

CI, Confidence interval; ROSC, return of spontaneous circulation.

The search strategy identified 2,056 articles, of which the authors included 26 studies (n=21,704 participants). Studies were conducted between 1991 and 2008 in a variety of countries, with the United States, France, and Germany composing half of the involved countries. Sixteen studies occurred in the out-of-hospital setting and 6 in the hospital setting. Study populations ranged from 30 to 8,104 participants. In

the adult studies, patients had a mean age of 62 years and 66% were men. In the pediatric studies, the mean age was 4.6 years, with 56% male patients.

Compared with placebo, epinephrine increased return of spontaneous circulation, survival to hospital admission, and survival to hospital discharge (Table). However, there was no difference noted in favorable neurologic

dose) epinephrine versus placebo, standard-dose epinephrine versus high-dose epinephrine, or epinephrine versus vasopressin (alone or in combination with epinephrine). Both adult and pediatric patients were included, as well as those with cardiac arrests either outside of the hospital or during hospitalization. Peer-reviewed abstracts and letters to the editor of peer-reviewed journals were also included. Authors excluded animal studies. Primary outcomes included survival to hospital discharge, survival to hospital admission, and neurologic outcome. Return of spontaneous circulation was assessed as a secondary outcome.

DATA EXTRACTION AND SYNTHESIS

Two reviewers extracted the data, with differences resolved through discussion in consultation with an additional reviewer. Authors used risk ratios with 95% confidence intervals to compare dichotomous outcomes. Authors dichotomized the neurologic outcomes. Among studies using the Cerebral Performance Category tool, scores less than or equal to 2 were considered a favorable neurologic outcome and those greater than 2 were considered a poor one. Among studies using the modified Rankin Scale, a score less than or equal to 3 was considered a favorable neurologic outcome, whereas a score greater than 3 was considered a poor one. Study quality was assessed with the Cochrane Risk of Bias tool. Articles written by authors of the review were evaluated for bias by 3 independent reviewers. Studies were examined for heterogeneity with χ^2 and I^2 statistics. Publication bias was assessed with forest plots.

outcomes between epinephrine and placebo. When standard-dose epinephrine was compared with high-dose epinephrine, there was an increase in return of spontaneous circulation and survival to hospital admission, but no difference in survival to hospital discharge or favorable neurologic outcomes. When standard-dose epinephrine was compared with vasopressin, there was an increase in survival to hospital admission, but no difference in any of the other outcomes. When standard-dose epinephrine was compared with standard-dose epinephrine and vasopressin, no difference was noted in any of the outcomes.

Commentary

Each year, hundreds of thousands of people around the world sustain a cardiac arrest.^{1,2} However, only approximately 7% of all patients survive one.¹ High-quality cardiopulmonary resuscitation (CPR) and early defibrillation have been associated with improved survival rates.³ Meanwhile, epinephrine has been more controversial despite being included in the advanced cardiac life support (ACLS) guidelines.^{4,5} Vasopressin was first studied as a potential adjunct in cardiac arrest in the 1990s and was included in the ACLS guidelines until 2015.⁵ However, a number of recent studies have been published on the utility of epinephrine and vasopressin in cardiac arrest, prompting this review.

Overall, the authors found that epinephrine was associated with improved overall survival, but no difference noted in favorable neurologic outcomes. Because survival with a favorable neurologic outcome is important to patients

and their families, it is imperative to consider this in light of the other findings.

It is important to consider several limitations with respect to this review. First, there was significant heterogeneity in the studies, including differences in patient populations, study protocols, and timing of medication administration. The inclusion of both adult and pediatric patients, as well as inhospital and out-of-hospital cardiac arrest patients, may have further contributed to this. Additional confounders include differences in rates of shockable rhythms and bystander CPR. Moreover, the overall quality of the data was low for most outcomes, limiting the strength of recommendations that could be made. Finally, many studies were conducted greater than 20 years earlier. Since then, there have been significant changes in cardiac arrest care and postarrest management, which may influence the applicability to current practice.

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