Vasopressin for cardiac arrest: meta-analysis of randomized controlled trials
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CRD summary
The review concluded that vasopressin use in the resuscitation of cardiac arrest patients was not associated with any overall benefit or harm, but may have improved long-term survival in asystolic patients. The authors’ conclusions reflect the evidence presented and appear likely to be reliable.

Authors' objectives
To determine the overall and/or selective benefit for vasopressin in cardiac arrest with respect to sustained restoration of spontaneous circulation, long-term survival and neurological outcome.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched until June 2010 for studies in English; search terms were reported. Reference lists of retrieved articles were also examined to identify further studies. Studies published only as abstracts were excluded.

Study selection
Randomised controlled trials (RCTs) were eligible if they compared a vasopressin-containing regimen to adrenaline (epinephrine) alone for adult patients with out-of-hospital or in-hospital cardiac arrest, and reported on survival. Studies that fulfilled a pre-specified criterion for high risk of bias (see below) were excluded.

Most studies were of out-of-hospital cardiac arrests. The mean reported frequency of witnessed cardiac arrest was 70%. The initial cardiac rhythm was asystole in two-thirds of patients. The average time between cardiovascular collapse and advanced life support was less than three minutes within hospital and 15 to 17 minutes out of hospital. The average time between cardiovascular collapse and drug treatment was less than five to six minutes within hospital and between 15 and 22 minutes out of hospital. All studies compared vasopressin plus adrenaline with placebo plus adrenaline, except for one study which added corticosteroids to the vasopressin treatment. In all studies, the average vasopressin dose was within 40 to 80IU. Co-interventions were used in approximately a fifth of patients. All studies took place in Europe or North America. Outcomes included: restoration of spontaneous circulation for at least 15 minutes (in hospital trials) or until hospital admission, long-term survival (patient survives to at least 30 days post-randomisation, or to hospital discharge), and favourable neurological outcome (patient achieves long-term survival and has a Glasgow–Pittsburgh Cerebral Performance Category score of 1 or 2).

Two reviewers independently selected studies for inclusion, with disagreements resolved by discussion.

Assessment of study quality
Two reviewers independently evaluated study quality by assessing likely sources of bias as described in the Cochrane Handbook for Systematic Reviews. The authors added assessments for power calculations, and differences between groups in co-interventions (of greater than 5%). Studies were judged to be at high risk of bias if this judgement was made for one or more domain, or if an unclear risk of bias judgement was made for two or more domains.

Data extraction
Two reviewers independently extracted intention-to-treat data in order to calculate odds ratios (OR) with 95% confidence intervals (CI). Authors were contacted for data not reported in the papers.

Methods of synthesis
Meta-analyses were performed to calculate pooled odds ratios and 95% confidence intervals using a random-effects model; if heterogeneity was less than 25% (when assessed using $I^2$), a fixed-effect model was used. Pre-specified analyses assessed the effect of vasopressin in the asystole, ventricular fibrillation/tachycardia and pulseless electrical activity subgroups. Another subgroup analysis was conducted based on initial rhythm and the time from cardiovascular collapse to first study-drug injection being less than 20 minutes. A sensitivity analysis examined the
effect of including two studies excluded during the quality assessment and two excluded for reasons of language or publication status.

Results of the review
Six RCTs were eligible including 4,745 patients (range 40 to 2,894). Studies had a low risk of bias for all domains, except for one study with an unclear risk of detection bias, and a different study having an unclear risk of attrition bias.

There were no significant differences between groups for overall rates of sustained restoration of spontaneous circulation, long-term survival or favourable neurological outcome.

In the subgroup analyses, for patients in asystole, vasopressin treatment was associated with higher long-term survival (OR 1.80, 95% CI 1.04 to 3.12, P=9%; five RCTs). In asystolic patients of trials with mean time from cardiovascular collapse to first study-drug injection being less than 20 minutes, vasopressin increased the rates of sustained restoration of spontaneous circulation (OR 1.70, 95% CI 1.17 to 2.47, P=0%; two RCTs) and long-term survival (OR 2.84, 95% CI 1.19 to 6.79, P=17%; three RCTs).

Sensitivity analysis results were similar to the primary analysis results.

Authors' conclusions
Vasopressin use in the resuscitation of cardiac arrest patients was not associated with any overall benefit or harm. However, vasopressin may have improved the long-term survival of asystolic patients, especially when average time from cardiovascular collapse to first study-drug injection was less than 20 minutes.

CRD commentary
The review addressed a clear question and was supported by reproducible eligibility criteria. Attempts to identify relevant studies were undertaken by searching electronic databases and checking references. The exclusion of articles not written in English and studies published only as abstracts meant that relevant studies might have been missed and the review may have been subject to language and publication bias. Authors noted when such studies were excluded, and conducted sensitivity analyses that included the results of the studies where possible.

Suitable methods were employed to reduce the risks of reviewer error and bias during the review study selection, data extraction and quality assessment processes. Study quality was assessed and was used when selecting studies for inclusion; studies generally had a low risk of bias. Sufficient study details were provided; appropriate methods were used to pool data and assess heterogeneity.

The authors' conclusions reflect the evidence presented and appear likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that new randomised trials that specifically assessed vasopressin effects on subgroup neurological outcome were warranted.

Funding
No external funding.

Bibliographic details

PubMedID
21787738

DOI
10.1016/j.resuscitation.2011.07.015
Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Cardiopulmonary Resuscitation/methods; Global Health; Heart Arrest/mortality/therapy; Humans; Randomized Controlled Trials as Topic; Survival Rate/trends; Vasoconstrictor Agents/therapeutic use; Vasopressins/therapeutic use

AccessionNumber
12012000288

Date bibliographic record published
20/03/2012

Date abstract record published
26/10/2012

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.