Is the combination of vasopressin and epinephrine superior to repeated doses of epinephrine alone in the treatment of cardiac arrest? A systematic review

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CRD summary
The authors concluded that the combination of vasopressin and epinephrine found a trend towards better rate of spontaneous cardiac circulation, but equivocal effects on survival; there was inadequate evidence at the time of the review to advocate the sequential use of vasopressin and epinephrine for cardiac arrest. The authors’ conclusions reflect the evidence presented and are likely to be reliable.

Authors’ objectives
To assess the effectiveness of vasopressin and epinephrine together versus repeated doses of epinephrine alone in the treatment of cardiac arrest.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched without restriction on the basis of language or publication status, from 1950/1980 until April (or first quarter) of 2007. Search terms were reported. Reference lists of relevant articles were searched for additional studies. Authors were contacted for unpublished data or in press data.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion in the review if they: reported outcomes for survival to hospital discharge (primary outcome) and return of spontaneous circulation (ROSC) or survival to hospital admission (secondary outcomes); contained some patients who received both vasopressin and epinephrine; examined patients with non-traumatic cardiac arrest requiring administration of vasopressors.

Studies varied as to whether they were pre-hospital or in-hospital and as to whether the patient received epinephrine prior to randomisation.

Two independent reviewers selected studies for inclusion in the review.

Assessment of study quality
Study quality was assessed using the Jadad Scale of randomisation, blinding and treatment of withdrawals and dropouts (maximum score of 5). Studies were deemed high quality if they scored 3 or more points. Allocation concealment was assessed using the Cochrane Collaboration criteria (adequate, inadequate or unable to assess).

Two reviewers independently performed the study quality assessment.

Data extraction
Data were extracted in order to calculate relative risk (RR) and 95% confidence intervals (CI) using standardised forms.

Two independent reviewers performed the data extraction.

Methods of synthesis
The results were presented in narrative synthesis as the studies were too heterogeneous to perform a meta-analysis.

Results of the review
Three studies (n=1,226 patients) were included. Sample size ranged from 169 to 732 patients. All three studies were of
Survival to hospital discharge (two studies): One study showed that survival to hospital discharge was significantly improved for a combination of vasopressin and epinephrine versus repeated doses of epinephrine alone (RR 3.69, 95% CI 1.52 to 8.95). The other study showed no statistically significant difference (RR 0.88, 95% CI 0.26 to 2.92).

Rates of return of spontaneous circulation (three studies): One study showed a statistically significant improved rate of ROSC with a combination of vasopressin and epinephrine versus epinephrine alone (RR 1.42, 95% CI 1.14 to 1.77). Two studies showed no statistically significant difference (RR 1.10, 95% CI 0.82 to 1.46 and RR 1.02, 95% CI 0.74 to 1.42).

Survival to hospital admission (two studies): One study found that survival to hospital admission was significantly improved for the combination of vasopressin and epinephrine versus repeated doses of epinephrine (RR 1.57, 95% CI 1.17 to 2.09). The other study found no statistically significant difference (RR 0.79, 95% CI 0.52 to 1.21).

Authors’ conclusions
The combination of vasopressin and epinephrine found a trend towards better ROSC, but equivocal effects on survival. At the time of the review there was inadequate evidence to advocate the sequential use of vasopressin and epinephrine for cardiac arrest.

CRD commentary
The review addressed a clear research question and was supported by adequate inclusion criteria. The search strategy was adequate. There was no language restriction and attempts were made to locate unpublished material, which reduced the risk of language and publication biases. The study quality assessment tools were appropriate for the included study design. Given the heterogeneity of the included studies, it was appropriate that the results were presented in a narrative synthesis. The review process was carried out with sufficient attempts to minimise reviewer error and bias. The authors’ conclusions reflect the evidence presented and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that as the review did not support the use of the combination of vasopressin and epinephrine for cardiac arrest, practitioners should continue to follow advanced cardiac life support (ACLS) guidelines.

Research: The authors stated that there was a need for RCTs to evaluate the simultaneous use of vasopressin and epinephrine in cardiac arrest.

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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.