

Vasopressin was not better than epinephrine for out-of-hospital cardiac arrest

Wenzel V, Krismer AC, Arntz H, et al. A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. *N Engl J Med*. 2004;350:105-13.

QUESTION

In patients with out-of-hospital cardiac arrest, is vasopressin more effective than epinephrine for survival to hospital admission?

DESIGN

Randomized (unclear allocation concealment*), blinded (clinicians and patients)*, controlled trial with follow-up to hospital discharge.

SETTING

33 communities involving 44 emergency medical service units in Austria, Germany, and Switzerland.

PATIENTS

1219 patients with an out-of-hospital cardiac arrest who presented with ventricular fibrillation, pulseless electrical activity, or asystole requiring cardiopulmonary resuscitation (CPR) with vasopressor therapy. Exclusion criteria were successful defibrillation without a vasopressor, terminal illness, no intravenous access, hemorrhagic shock, cardiac arrest after trauma, pregnancy, age < 18 years, or presence of a do-not-resuscitate order. 1186 patients (97%) completed the study (mean age 66 y, 70% men).

INTERVENTION

Patients were allocated to vasopressin (Pitressin), 40 IU ($n = 589$), or epinephrine (Suprarenin), 1 mg ($n = 597$). If circulation was not restored in 3 minutes, the same drug at the same dose was injected again. If circulation was still not restored, patients received an additional injection of epinephrine at the discretion of the emergency physician managing the CPR attempt.

MAIN OUTCOME MEASURES

Survival to hospital admission. The secondary outcome was survival to hospital discharge.

MAIN RESULTS

Analysis was by intention to treat. The rate of hospital admission was not higher among patients who received vasopressin than those

who received epinephrine (Table). Groups also did not differ for rate of hospital discharge (Table).

CONCLUSION

In patients with out-of-hospital cardiac arrest, vasopressin was not more effective than epinephrine for survival to hospital admission.

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*See Glossary.

Vasopressin vs epinephrine for out-of-hospital cardiac arrest†

Outcomes	Vasopressin	Epinephrine	RBI (95% CI)	NNT
Survival to hospital admission	36.3%	31.2%	15% (0 to 31)	Not significant‡
Survival to hospital discharge	9.9%	9.9%	0% (-43 to 28)	Not significant

†Abbreviations defined in Glossary; RBI, NNT, and CI calculated from odds ratio in article.

‡ $P = 0.06$.

COMMENTARY

Vasopressin has shown promising results in various resuscitation studies on animal models, porcine in particular. The first human randomized controlled trial (RCT) comparing vasopressin with epinephrine for cardiac arrest involved 40 out-of-hospital patients with ventricular fibrillation and found no difference in either survival to hospital discharge or neurologic function (1). The second RCT involved 200 in-hospital patients and showed similar results (2). The trial by Wenzel and colleagues is the third randomized comparison of epinephrine and vasopressin in patients with cardiac arrest and the third to show that vasopressin does not improve survival to hospital discharge.

This large multicenter RCT used survival to hospital admission as the primary outcome rather than the more clinically relevant endpoints of survival to hospital discharge and neurologic function. This allows for a much smaller number of patients to meet the sample size requirements than the rare outcome of hospital discharge.

Wenzel and colleagues concluded that “vasopressin was superior to epinephrine in patients with asystole.” This is based on a subgroup analysis (1 of 29 statistical comparisons) that was not hypothesized a priori, did not include any statistical correction for the multiplicity of comparisons, and did not include a sensitivity analysis for the 33 patients excluded from analysis because of a missing study-drug code or

who were lost to follow-up before hospital discharge. Most important, this finding contradicts the overall study results and those of the only other RCT involving patients with asystole (2). At best, the findings of this study support the need for additional trials focusing on patients with asystole.

Overall, RCTs evaluating the performance of vasopressin as a replacement vasopressor in patients with cardiac arrest have consistently shown disappointing results. Until the results from high-quality RCTs show vasopressin to be at least equivalent to epinephrine with respect to clinically important outcomes, the American Heart Association should consider removing its recommendation of vasopressin in the Advance Cardiac Life Support Guideline as a treatment for patients in cardiac arrest.

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References

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