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Vasopressin versus epinephrine in cardiac arrest: Where is the data?

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A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation

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Aim of Study

The objective of this study was to compare the outcome of victims of out-of-hospital cardiac arrest after the administration of either vasopressin 40 IU or epinephrine 1 mg, using survival to hospital admission and hospital discharge as primary outcome variables.

Methods

Wenzel and coworkers report a double-blind, prospective, multicenter, randomized, controlled clinical trial of 1219 patients who suffered out-of-hospital cardiac arrest, with ventricular fibrillation (VF), pulseless electrical activity (PEA), or asystole. Out of 1219 randomized patients, 33 were excluded because of missing study drug code. Of the 1186 patients remaining, 586 were assigned to receive vasopressin and 597 to receive epinephrine.

The criteria for exclusion were: Defibrillation without the administration of a vasopressor, documented terminal illness, a lack of intravenous access, hemorrhagic shock, pregnancy, cardiac arrest after trauma, age of less than 18 years, and the presence of a do-not-resuscitate order. Patients who presented with pulseless electrical activity or asystole were randomized immediately; patients with ventricular fibrillation were randomized after the first three attempts at defibrillation were unsuccessful. The study drugs, two ampules of 1 mg of epinephrine (Suprarenin) or two ampules of 40 IU of vasopressin (Pitressin) were kept in a container that was opened, and either 1 mg of epinephrine or 40 IU of vasopressin were administered. The same drug at the same dose was administered again if spontaneous circulation was not reestablished within three minutes after the first injection of the study. If spontaneous circulation was not established; the patient could receive additional doses of epinephrine at the discretion of the physician attending the patient.

Results

Baseline characteristics of the groups were similar: Age 66.5 Ø 14.4 (vasopressin group) and 65.9 Ø 14.2 (epinephrine group) [p=0.45]. Male gender 69.3 % (402 out

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of 580) in the vasopressin group and 71.2 % (421 out of 591) in the epinephrine group [p=0.47]. VF was present in 223 patients (37.9%) of the vasopressin group and in 249 patients (41.7%) of the epinephrine group [p=0.18]. PEA was observed in 104 patients (17.7%) in vasopressin group and in 82 patients (13.7 %) in epinephrine group [p=0.06]. Asystole victim totalled of 262 (44.5%) in the vasopressin group and 266 (44.6%) in epinephrine group [p=0.98]. A diagnosis of coronary artery disease was present in 176/467 (37.7%) of the vasopressin group and 189/463 (40.8%) in epinephrine group [p=0.33]. There were no significant differences in the rates of hospital admissions between the vasopressin group and the epinephrine group either among patients with VF (46.2 percent vs. 43.0 percent) [p=0.48] or among those with PEA (33.7 percent vs. 30.5 percent) [p=0.65]. However, those patients with asystole, vasopressin use was associated with significantly higher rates of hospital admission (29.0 percent vs. 20.3 percent in the epinephrine group), [p=0.02] and hospital discharge (4.7 percent vs. 1.5 percent) [p=0.04]. Of note, this statistical analysis was not corrected for multiple comparison. Among the 732 patients in whom spontaneous circulation was not restored with the two injections of study drug, additional treatment with epinephrine resulted in significant improvement in the rates of survival to hospital admission and hospital discharge in the vasopressin group, but not in the epinephrine group (hospital admission rate, 25.7 percent vs. 16.4 percent) [p=0.002].

Conclusion

The authors of this study conclude that the effects of vasopressin were similar to those of epinephrine in the management of VF and PEA, but vasopressin was superior to epinephrine in patients with asystole. In addition, the use of vasopressin followed by epinephrine may be more effective than the use of epinephrine alone in patients with refractory cardiac arrest.

Commentary

The principal cause of death in the United States is ischemic coronary disease, almost half of these deaths are originated by sudden out-of-hospital cardiac arrest [1]. Most of cardiac arrests occur outside the hospital [2]. The probability of surviving such events is poor, and the chances of surviving with normal neurologic status are even more remote [3]. For more than 80 years epinephrine has been the drug of choice in the treatment of cardiac arrest. The American Heart Association (AHA) guidelines for resuscitation accepted this drug in 1974 [4]. Unfortunately, epinephrine increases myocardial oxygen consumption, cardiac ischemia, coronary vasoconstriction, ventricular dysrrhythmias, and myocardial dysfunction [5,6]. Agents such as vasopressin have then been studied in attempts to improve outcome on epinephrine.

Previous studies indicated that endogenous vasopressin levels were higher in patients surviving cardiac arrest than in those patients who died. This data suggests vasopressin could be helpful in cardiac arrest [7].

Morris and coworkers reported that in four out of ten patients with extended CPR attempts, and that had received about 18 mg of epinephrine (for more than 40 minutes), return of spontaneous circulation occurred following the administration of vasopressin despite receiving approximate 18 mg of epinephrine [8]. Vasopressin has been previously reported to improve return of spontaneous circulation; improve blood flow to vital organs, increase oxygen delivery to the brain, and in greater resuscitation success and neurological recovery [9].

The American Heart Association (AHA) in combination with the International Liaison Committee on Resuscitation (ILCOR) currently recommend management with either vasopressin or epinephrine for patients who suffer cardiac arrest consequent to VF without conversion following a defibrillation. On the other hand, the European Resuscitation Council (ERC), which is an important contributor to ILCOR, did not include vasopressin in the universal algorithm due to a perceived lack of support evidence to support its recommendation.

The inclusion of vasopressin for ventricular fibrillation in the 2000 International Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care was classified as Class IIb (acceptable, not harmful, supported by fair evidence), and vasopressin use in asystolic cardiac arrest, was placed in the Indeterminate Class (not recommended, minimal evidence; preliminary research) [10]. At the current time, the lack of consistent evidence demonstrating efficacy of vasopressin in cardiac arrest is disconcerting. A clear understanding of the utility of vasopressin must await further study.

Conclusion

Firm recommendations on the use of vasopressin in cardiac arrest are problematic. The combination of vasopressin and epinephrine may be beneficial. However, the preponderance of the data does not support recommending one agent over the other.

References

1. Levine RL, Pepe PE, Fromm RE Jr, Curka PA, Clark PA (1992) Prospective evidence of a circadian rhythm for out-of-hospital cardiac arrests. JAMA 267:2935-37.
2. Hearne TR, Cummins RO (1988) Improved survival from cardiac arrest in the community. Pacing Clin Electrophysiol 11:1968-73.
3. Lombardi G, Gallagher E, Gennis P (1994) Outcome of out-of-hospital cardiac arrest in New York City. The Pre-Hospital Arrest Survival Evaluation (PHASE) Study. JAMA 271:678-83.
4. Varon J, Marik P, Fromm R (1998) Cardiopulmonary resuscitation: A review for clinicians. Resuscitation 36:133-45.
5. Paradis NA, Wenzel V, Southall J (2002) Pressor drugs in the treatment of cardiac arrest. Cardiol Clin 20:61-78.
6. Ditchey RV, Lindenfeld J (1988) Failure of epinephrine to improve the balance between myocardial oxygen supply and demand during closed-chest resuscitation in dogs. Circulation 78:382-89.
7. Lindner KH, Strohmenger HU, Ensinger H, Hetzel WD, Ahnefeld FW, Georgieff M (1992) Stress hormone response during and after cardiopulmonary resuscitation. Anesthesiology 77:662-8.
8. Morris DC, Dereczyk BE, Grzybowski M, Martin GB, Rivers EP, Wortsman J, Amico JA (1997) Vasopressin can increase coronary perfusion pressure during human cardiopulmonary resuscitation. Acad Emerg Med 4:878-83.
9. Lindner KH, Dirks B, Strohmeneger HU (1997) Randomised comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation. Lancet 349:535-7.
10. Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 6: Advanced cardiovascular life support: 7C: A guide to the International ACLS algorithms. The American Heart Association in collaboration with the International Liaison Committee on Resuscitation. Circulation 102 (8 Suppl):I142-57.