

## Original Paper

## Compare the Effects of Epinephrine and Vasopressin in Return of Spontaneous Circulation

Samad Shams Vahdati<sup>1\*</sup>, Azra Nejabatian<sup>2</sup>, Farzad Rahmani<sup>3</sup>, Paria Habibollahi<sup>4</sup>, Pegah Sepehri Majd<sup>5</sup><sup>1</sup>Associate Professor of Emergency Medicine, Fellowship of Emergency Neurovascular, Emergency Medicine Research Team And Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran<sup>2</sup>Resident of Emergency Medicine, Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran<sup>3</sup>Assistant Professor of Emergency Medicine, Emergency Medicine Research Team, Tabriz University of Medical Sciences, Tabriz, Iran,<sup>4</sup>PhD Student of Toxicology, Pharmacology And Toxicology Department, Emergency Medicine Research Team, Tabriz University of Medical Sciences, Tabriz, Iran<sup>5</sup>Medical Student, Emergency Medicine Research Team, Tabriz University of Medical Sciences, Tabriz, Iran

Co responding Author: Samad Shams Vahdati, E-mail: sshamsv@gmail.com/shams@tbzmed.ac.ir

## ARTICLE INFO

## Article history

Received: March 14, 2018

Accepted: June 07, 2018

Published: July 31, 2018

Volume: 6 Issue: 3

Conflicts of interest: None

Funding: None

## Key words:

Cardiopulmonary  
Resuscitation (CPR),  
Return of Spontaneous  
Circulation (ROSC),  
Epinephrine,  
Vasopressin

## ABSTRACT

**Background:** There is a conflict in the superiority of each of the vasopressin and epinephrine compared to the other. Vasopressin has a vasoconstrictive action that results in an increase of the coronary perfusion pressure. Due to the expensive and sometimes scarce of vasopressin in most hospitals, this study aims to evaluate the response rate of vasopressin compared with epinephrine, in return of ROSC. **Methods:** In this descriptive-analytical study all patients in the emergency medicine department were enrolled in the study suffered a cardiopulmonary arrest and resuscitation will be done instantly for them (According to the guidelines AHA 2010). Their data were extracted from the hospital records and the success rate of recovery, 3-month survival and complications in patients recovering from the drug used during the CPR were analyzed. **Results:** A total of 61 patients record were analyzed. 31 patients had received epinephrine alone and 30 patients received a combination of epinephrine and vasopressin. No significant difference was observed between the two groups in terms of sex, sepsis, hypovolemia, renal failure, cancers, drug toxicity, brady, dysrhythmia, PEA, VT, VF, defibrillator, duration of CPR and three month outcome. The mean time of CPR in combination of epinephrine and vasopressin group was  $27.26 \pm 12.72$  and the mean time of CPR in epinephrine group was  $27.24 \pm 13.510$  (p-value= 0.99). **Conclusion:** Among patients with in-hospital cardiopulmonary arrest in this study no statistically significant difference was obtained between the results of treatment with epinephrine alone and combination of epinephrine and vasopressin.

## INTRODUCTION

Cardiac arrest affects more than 700,000 people in Europe. Ventricular fibrillation, most cases that require electrical defibrillation immediate action and CPR. (1-7) Clinical randomized controlled trials (RCTs) proved that advances in methods and techniques for CPR are still the most important topics (7-13). Cardiac arrest is a high stress state that is associated with SIRS-like response. Cardiac arrest was reduced Adrenal glands perfusion and due to low levels of cortisol during and after CPR is the effects of vasoconstrictors. (10-13)

The difference between the diastolic aortic pressure and right atrial pressure during cardiopulmonary resuscitation caused coronary artery perfusion. Epinephrine with vasoconstrictor effect leading to rise aortic pressure and CPP and is used for many years in the treatment of VF (8-10)

its acts on  $\alpha$ - and  $\beta$ -receptors, increase peripheral vasoconstriction and cardiac stimulation. (4-5) Vasopressin also has a vasoconstrictive action these results in an increase of the coronary perfusion pressure and increase of blood flow to the vital organs without causing a dramatic increase in the myocardial oxygen consumption and it has a longer half-life, and its effect is not diminished by acidosis, common in prolonged cardiac arrest. (8-10)

The use of vasopressor during cardiopulmonary resuscitation (CPR) after cardiac arrest (CA) increase in diastolic aortic pressure and finally coronary perfusion pressure and blood flow, as well as cerebral blood flow.

The combination of vasopressin and epinephrine is the return of spontaneous circulation.

Due to lack of evidence in the superiority of each of the vasopressin and epinephrine compared to the other and ex-

pensive and sometimes scarce of vasopressin in most hospitals, this study aims to evaluate the response rate of vasopressin compared with epinephrine, in return of ROSC.

## METHODS

**Population:** All patients who experience cardiac arrest in the emergency department of Imam Reza Hospital, between 23 July 2014 and 22 October 2014 were enrolled in the study. Patients under 16 years old, end stage disease, trauma, Cancer, No IV access, hemorrhagic shock, pregnant and with any certification shows 'do not resuscitation' were excluded.

**Planning:** Patients record was divided into two groups of those who received epinephrine alone and those who have received vasopressin instead of the first or second dose of epinephrine. The vital status of patients after 24 and 72 hours was measured through their medical records. In order to 3-month follow up, in cases that were hospitalized data was extracted from the hospital record and for those who were discharged data was collected by phone call. According to ACLS guidelines for patients with VT Pulseless rhythm and VF Defibrillator was used and for patients with PEA and asystol also first performed chest compression and then 40 units of vasopressin or epinephrine were injected, and cardiopulmonary resuscitation continued. Those who responded to resuscitation were treated with ACLS guidelines AHA2010 and then admitted to the Intensive Care Unit.

It is noteworthy that only one dose of vasopressin (40 IU) was replaced first or second dose of epinephrine (According to the guidelines AHA 2010)

**Analysis:** all data were inserted into SPSS (version 15.0; SPSS, Chicago, Ill); quantitative variables were analyzed with T-test and qualitative variables were analyzed with chi – square.

**Must be deleted:** (*Ethic Approval:* this study was accepted by local ethic committee of Tabriz University of medical science with no.: 5/4/10871)

## RESULTS

To evaluate the effects of epinephrine and vasopressin in CPR 61 patients' record were studied.

30 patients (15 males, 15 females) were in vasopressin and epinephrine group and 31 patients (13 males, 18 females) were in epinephrine group. No significant difference was observed between the two groups in terms of sex ( $p$  value = 0.527)

In terms of sepsis in the vasopressin and epinephrine group 25 patients were without sepsis and sepsis was observed in 5 patients. In the epinephrine group 25 patients were without sepsis and sepsis was in 6 patients. No significant difference was observed between the two groups in terms of sepsis ( $p$  value =0.785)

In terms of cardiogenic events in the vasopressin and epinephrine group 24 patients were without cardiogenic events and cardiogenic events were observed in 6 patients. In the epinephrine group 26 patients were without cardiogenic events and it was observed in 5 patients. No significant difference was observed between the two groups in terms of cardiogenic events ( $p$  value =0.694)

In terms of hypovolemia in the vasopressin and epinephrine group 29 patients were without hypovolemia and 1 patient had it. In the epinephrine group 29 patients were without hypovolemia and it was in 2 patients. No significant difference was observed between the two groups in terms of hypovolemia ( $p$  value = 0.573)

In terms of renal failure in the vasopressin and epinephrine group 27 patients were without renal failure and it was in 3 patients. In the epinephrine group 25 patients were without renal failure and it was in 6 patients. No significant difference was observed between the two groups in terms of renal failure ( $p$  value = 0.303)

In terms of cancers in the vasopressin and epinephrine group 28 patients were without cancers and 2 patients had it. In the epinephrine group 30 patients without cancers and it was in 1 patient. No significant difference was observed between the two groups in terms of cancers ( $p$  value = 0.534)

In terms of drug toxicity in the vasopressin and epinephrine group 22 patients without drug toxicity and it were in 8 patients. In the epinephrine group 22 patients without drug toxicity and it were in 9 patients. No significant difference was observed between the two groups in terms of drug toxicity ( $p$  value = 0.837)

In terms of brady in the vasopressin and epinephrine group 17 patients were without brady and it was in 13 patients. In the epinephrine group 18 patients without brady and it were in 13 patients. No significant difference was observed between the two groups in terms of brady ( $p$  value = 0.912)

In terms of dysrhythmia in the vasopressin and epinephrine group 21 patients were without dysrhythmia and it was in 9 patients. In the epinephrine group 22 patients were without dysrhythmia and it was in 9 patients. No significant difference was observed between the two groups in terms of dysrhythmia ( $p$  value = 0.934)

In terms of bradycardia did not happen in any of the two groups' epinephrine and vasopressin and epinephrine group. No significant difference was observed between the two groups in terms of bradycardia.

In terms of PEA in the vasopressin and epinephrine group 24 patients were without PEA and it was in 6 patients. In the epinephrine group 25 patients were without PEA and it was in 6 patients. No significant difference was observed between the two groups in terms of PEA ( $p$  value = 0.949)

In terms of VT in the vasopressin and epinephrine group 29 patients were without VT and it was in 1 patient. In the epinephrine group 29 patients were without VT and it was in 2 patients. No significant difference was observed between the two groups in terms of VT ( $p$  value = 0.573)

In terms of VF in the vasopressin and epinephrine group 29 patients were without VF and it was in 1 patient. In the epinephrine group 30 patients were without VF and it was in 1 patient. No significant difference was observed between the two groups in terms of VF ( $p$  value = 0.981)

In terms of arrest did not happen in any of the two group's epinephrine and vasopressin and epinephrine group. No significant difference was observed between the two groups in terms of arrest.

In terms of defibrillator in the vasopressin and epinephrine group 28 patients did not use the defibrillator and 2 pa-

tients use it. In the epinephrine group 29 patients did not use the defibrillator and 2 patients use it. No significant difference was observed between the two groups in use of defibrillator (p value = 0.973)

In terms of CPR result in the vasopressin and epinephrine group 6 of the 30 patients had mortality. In the epinephrine group 11 of the 31 patients had mortality. No significant difference was observed between the two groups in terms of Result. CPR (p value = 0.178)

In terms of 3-month outcome in the vasopressin and epinephrine group 7 patients had a mortality of 24 patients survived. In the epinephrine group 9 patients had a mortality of 20 patients survived. No significant difference was observed between the two groups in terms of 3-month outcome (p value= 0.277)

The mean age of vasopressin and epinephrine group was  $44.07 \pm 20.02$  and the mean age of epinephrine group was  $53.32 \pm 18.86$ . No significant difference was observed between the two groups in terms of age (p value = 0.068) (Min=19, Max=88, CI=95%)

The average hospitalization time in vasopressin and epinephrine group was  $11.84 \pm 12.29$  and in epinephrine group was  $8.30 \pm 10.12$ . No significant difference was observed between the two groups in terms of hospitalization time (P value=0.306)

The mean time of CPR in vasopressin and epinephrine group was  $27.26 \pm 12.72$  and the mean time of CPR in epinephrine group was  $27.24 \pm 13.51$ . No significant difference was observed between the two groups in terms of time of CPR. (P value= 0.994) (Min=10, Max=60, CI=95%)

## DISCUSSION

Cardiac arrest is associated with significant mortality in the hospital, and about 20% of patients with in-hospital cardiac arrest are alive at the time of discharge from the hospital. Cardiac arrest affects more than 700,000 people in Europe. Ventricular fibrillation, most cases that require electrical defibrillation immediate action and CPR During resuscitation from cardiac arrest, coronary perfusion pressure is driven by the difference between aortic diastolic pressure and right atrial pressure. (1-7) CPR in hospital was more successful in the hospitals with emergency specialist or residents (14).

Over the years, Advanced Cardiac Life Support algorithms recommended epinephrine as the standard vasopressor. The acts of epinephrine on  $\alpha$  and  $\beta$  receptors, increasing peripheral vasoconstriction and cardiac stimulation. (4-5) Increase myocardial and cerebral blood flow and facilitating return of spontaneous circulation (ROSC) may be created by alpha-adrenergic effects of epinephrine. The other effects of epinephrine ( $\beta$ -effects) may worsen post-resuscitation myocardial dysfunction and increase myocardial oxygen consumption which can't be beneficial during or after cardiac arrest.

Vasopressin, an endogenous peptide synthesized in the hypothalamus, and in Cardiac arrest used as adjuvant treatment with epinephrine. Vasopressin causes vasoconstriction effects, thus increasing peripheral arterial resistance, these effects are mediated via V1 receptors, but unlike epinephrine, vasopressin has no direct effects on the myocardium.

Common in prolonged cardiac arrest vasopressin has a longer half-life, dilates cerebral blood vessels to a greater extent than epinephrine and its effect is not diminished by acidosis. (8-10) neurological survival in the post-CPR period can be predicted by serum cortisol levels (15)

Our results confirm previous data that showed there is no statistically significant difference in survival after CPR between vasopressin and epinephrine group with epinephrine group (16, 17)

The effects of vasopressin were similar to those of epinephrine in the management of cardiac arrest and pulseless electrical activity (PEA).

The combination of vasopressin and epinephrine is the return of spontaneous circulation.

For patients receiving vasopressin and epinephrine, survival rates are not significantly different (18) and in long-term human cardiac arrest, 40% of patients receiving vasopressin had a significant increase in CPP (14). Vasopressin has no therapeutic advantage over epinephrine, but it can be used as an alternative to epinephrine. This finding is consistent with our study results.

After induction of ventricular fibrillation and discontinuation of electrical pulse generation on laboratory animals, it showed that lab animals respond to vasopressin regeneration better than epinephrine also, a much lower number of animals after the first dose of vasopressin than the first dose of epinephrine required re-injection of the same drug (19). Our study results are similar between two groups in terms of comparison of cardiac dysrhythmia, but the results of this study are not consistent with our study about the time of CPR.

In the long run, there is no significant difference between the two groups of patients treated with epinephrine and vasopressin. In our study, similar results were obtained. It is also noted in the study that the effects of these two groups of drugs are short term and it is more effective at the initial recovery of patients (18)

Our study had some important limitations, including time constraints and limitations of the statistical society and descriptive-analytical method for doing.

## CONCLUSION

Our study showed that there is no significant difference in the results of treatment between vasopressin and epinephrine in patients with cardiopulmonary arrest. Despite the relative superiority of vasopressin to epinephrine in some cases, this superiority was not statistically significant. Considering the studies agree and oppose our study there is still a lot of questions to ask about the effectiveness of each of these two drugs.

## REFERENCES

1. Kesteloot H, Sans S, Kromhout D: Dynamics of cardiovascular and all-cause mortality in Western and Eastern Europe between 1970 and 2000. *Eur Heart J* 2006, 27:107-113.
2. Goff DC, Brass L, Braun LT, Croft JB, Flesch JD, Fowkes FGR, Hong Y, Howard V, Huston S, Jencks SF,

- Luepker R, Manolio T, O'Donnell C, Robertson RM, Rosamond W, Rumsfeld J, Sidney S, Zheng ZJ: Essential features of a surveillance system to support the prevention and management of heart disease and stroke: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Stroke and Cardiovascular Nursing and the Interdisciplinary Working Groups on Quality of Care and Outcomes Research and Atherosclerotic Vascular Disease. *Circulation* 2007, 115:127-155.
3. Sans S, Kesteloot H, Kromhout D: The burden of cardiovascular diseases mortality in Europe. Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. *Eur Heart J* 1997, 18:1231-1248.
  4. Cobb LA, Fahrenbruch CE, Olsufka M, Copass MK: Changing incidence of out-of-hospital ventricular fibrillation 1980–2000. *JAMA* 2002, 288:3008-3013.
  5. Rea TD, Eisenberg MS, Sinibaldi G, White RD: Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. *Resuscitation* 2004, 63:17-24.
  6. Rosamond W, Flegal K, Friday G, Furie K, Go Alan, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y: Heart disease and stroke statistics – 2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2007, 115:69-171.
  7. Handley AJ, Koster R, Monsieurs K, Perkins GD, Davies S, Bossaert L: European Resuscitation Council Guidelines for Resuscitation 2005. Section 2. Adult basic life support and use of automated external defibrillators. *Resuscitation* 2005, 67:S7-S23.
  8. Lindner KH, Strohmenger HU, Ensinger H, Hetzel WD, Ahnefeld FW, Georgieff M: Stress hormone response during and after cardiopulmonary resuscitation. *Anesthesiology* 1992, 77:662.
  9. Lindner KH, Brinkmann A, Pfenninger EG, Lurie KG, Goertz A, Lindner IM: Effect of vasopressin on hemodynamic variables, organ blood flow, and acid-base status in a pig model of cardiopulmonary resuscitation.
  10. Adrie C, Adib-Conquy M, Laurent I, Monchi M, Vinsonneau C, Fitting C, Fraisse F, Dinh-Xuan AT, Carli P, Spaulding C, Dhainaut JF, Cavaillon JM: Successful cardiopulmonary resuscitation after cardiac arrest as a 'sepsis-like' syndrome. *Circulation* 2002, 106:562–568.
  11. Zhong JQ, Dorian P: Epinephrine and vasopressin during cardiopulmonary resuscitation. *Resuscitation* 2005, 66:263–269.
  12. Lindner KH, Haak T, Keller A, Bothner U, Lurie KG: Release of endogenous vasopressors during and after cardiopulmonary resuscitation. *Br Heart J* 1996, 75:145–150.
  13. Hékimian G, Baugnon T, Thuong M, Monchi M, Dabbane H, Jaby D, Rhaoui A, Laurent I, Moret G, Fraisse F, Adrie C: Cortisol levels and adrenal reserve after successful cardiac arrest resuscitation. *Shock* 2004, 22:116–119.
  14. Ghaffarzadeh A, Shams Vahdati S, Salmasi S. Assessment of emergency medicine residents' cardiopulmonary resuscitation team in imam reza hospital. *J Cardiovasc Thorac Res.* 2012 Sep 30;4(3):85-6.
  15. Tavakoli N, Bidari A, Vahdati SS. Serum Cortisol Levels as a Predictor of Neurologic Survival in Successfully Resuscitated Victims of Cardiopulmonary Arrest. *Journal of cardiovascular and thoracic research.* 2012;4(4):107.
  16. Wenzel V, Krismer AC, Arntz HR, Sitter H, Stadlbauer KH, Lindner KH. A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. *New England Journal of Medicine.* 2004; 350(2):105-13.
  17. Babar SI, Berg RA, Hilwig RW, Kern KB, Ewy GA. Vasopressin versus epinephrine during cardiopulmonary resuscitation: a randomized swine outcome study. *Resuscitation.* 1999; 41(2):185-92.
  18. Stiell IG, Hébert PC, Wells GA, Vandemheen KL, Tang AS, Higginson LA, et al. Vasopressin versus epinephrine for in-hospital cardiac arrest: a randomised controlled trial. *The Lancet.* 2001;358(9276):105-9.
  19. Lindner K, Prengel A, Pfenninger E, Lindner I, Strohmenger H, Georgieff M, et al. Vasopressin improves vital organ blood flow during closed-chest cardiopulmonary resuscitation in pigs: *Circulation* 1995; 91/1; 215–221. *Resuscitation.* 1995;30(1):81.