

VASOPRESSIN IN CARDIAC ARREST

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Introduction

- Cardiac arrest is a major cause of morbidity and mortality both out of hospital and in-hospital setting.
- US: 30,000 patients suffer out hospital cardiac arrest and 92% of them die each year.
- It is associated with very high mortality and also a high incidence of neurological injury to the survivors.

Introduction

- CPR with chest compression is the recommended management of cardiac arrest.
- AHA 2010: none of vasopressor agents increases the rate of neurologically intact or survival to hospital discharge but it is associated with an increased rate of ROSC.
- ACC/AHA guidelines: epinephrine.
- ACLS protocol: vasopressin may replace the first or second dose of epinephrine during CPR.

Physiology of Vasopressin

- Vasopressin [ADH] is synthesised by the hypothalamus and released by the posterior pituitary gland.
- Responsible for multiple physiologic functions: vasoconstriction and osmoregulation.
- Many receptor: V1 vascular; V2 renal; V3 pituitary; oxytocin and purinergic receptor.

Physiology of Vasopressin

- V1 receptor: releasing Ca → vasoconstriction in small arterioles.
- In a hemodynamically stable person this has little effect, but when hemodynamics are threatened vasopressin causes **profound vasoconstriction** of skin, skeletal muscle and intestine.
- Less vasoconstriction at the coronary, pulmonary, renal and cerebral vasculature → **maintenance of Cerebral Perfusion Pressure and oxygenation.**

Physiology of Vasopressin

- In comparison with adrenalin it has several advantages:
 - V1-mediated effects increase arterial peripheral resistance without causing direct myocardial stimulation.
 - Longer half-life (10– 20 minutes vs. 3–5 minutes).
 - More resistant to acidosis.

Why vasopressin has been proposed as an alternative to epinephrine in cardiac arrest?

Interest in the use of vasopressin as a therapy for ventricular fibrillation was triggered by the observation that vasopressin levels were significantly higher in resuscitated rather than in nonresuscitated patients undergoing CPR for out-of-hospital cardiac arrest [PubMed: 1329579]

Why vasopressin has been proposed as an alternative to epinephrine in cardiac arrest?

- Vasopressin is superior to epi for increasing vital organ blood flow; in particular coronary and cerebral flow [Pubmed 1329579].
- Experimental and animal studies suggested that vasopressin may have a favorable survival profile during CPR [pubmed 7805205].
- Prior experimental data suggest that vasopressin improves vital organ perfusion during CPR, post-ROSC survival, and neurological recovery.

Published evidence



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Lancet. 1997 Feb 22;349(9051):535-7.

Randomised comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation.

Lindner KH¹, Dirks B, Strohmer HU, Prenzel AW, Lindner IM, Lurie KG.

Author information

¹Department of Anesthesiology and Critical Care Medicine, University of Ulm, Germany.

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- In a prospective study of 40 patients with out-of-hospital VF, resistant to defibrillation, **a significantly larger number** of patients who received 40 units of vasopressin intravenously compared to 1 mg of epinephrine, **were successfully resuscitated and survived for 24 hours.**

Abstract

Send to:

Lancet. 2001 Jul 14;358(9276):105-9.

Vasopressin versus epinephrine for inhospital cardiac arrest: a randomised controlled trial.

Stiell IG¹, Hébert PC, Wells GA, Vandemheen KL, Tang AS, Higginson LA, Dreyer JF, Clement C, Battram E, Watpool J, Mason S, Klassen T, Weitzman BN.

+ Author information

- This triple blind randomized controlled trial **failed to** demonstrate a survival advantage for vasopressin over epinephrine.
- This was challenged by other authors:
 - ❖ 50% cases had PEA, which had a poor prognosis.
 - ❖ The mean time to study drug administration in the in-hospital study was about half that of the out-of-hospital study.

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A Comparison of Vasopressin and Epinephrine for Out-of-Hospital Cardiopulmonary Resuscitation

Volker Wenzel, M.D., Anette C. Krismer, M.D., H. Richard Arntz, M.D.,
Helmut Sitter, Ph.D., Karl H. Stadlbauer, M.D., and Karl H. Lindner, M.D.,
for the European Resuscitation Council Vasopressor during Cardiopulmonary Resuscitation Study Group*

CONCLUSIONS

The effects of vasopressin were similar to those of epinephrine in the management of ventricular fibrillation and pulseless electrical activity, but vasopressin was superior to epinephrine in patients with asystole. Vasopressin followed by epinephrine may be more effective than epinephrine alone in the treatment of refractory cardiac arrest.

[Crit Care Med.](#) 2008 Sep;36(9):2641-50. doi: 10.1097/CCM.0b013e3181847af3.

Tissue oxygenation during management of cerebral perfusion pressure with phenylephrine or vasopressin.

[Dudkiewicz M¹](#), [Proctor KG](#).

Author information

Abstract

OBJECTIVE: Phenylephrine is often used for management of cerebral perfusion pressure after traumatic brain injury, but can have undesirable actions. Few studies have evaluated alternatives. The hypothesis was that arginine vasopressin was as effective as phenylephrine for maintaining tissue oxygenation during cerebral perfusion pressure management.

- Dudkiewicz evaluated vasopressin after traumatic brain injury for maintaining cerebral perfusion pressure and reported that intracranial pressure and brain tissue oxygenation were improved at the expense of the periphery, suggesting that vasopressin does have a role in preserving cerebral perfusion pressure in critically ill patients.



Vasopressin administered with epinephrine is associated with a return of a pulse in out-of-hospital cardiac arrest

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outcomes. *Results:* During the study period, data were available for 298 subjects receiving epinephrine-only ($n = 231$, 78%), a combination of 40 IU vasopressin and epinephrine ($n = 37$, 12%) or no vasopressor drugs ($n = 30$, 10%). Among patients receiving vasopressor drugs, pulse was restored for 74 subjects (28%), and 56 subjects (21%) had a pulse on arrival at the hospital. Return of pulses was associated with witnessed collapse, bystander CPR, and an initial ECG rhythm of ventricular fibrillation or tachycardia. Subjects receiving vasopressin and epinephrine were more likely to have a return of pulses during the resuscitation (LR: 2.73; 95% CI: 1.24, 6.03) and at hospital arrival (3.85; 1.71, 8.65) than subjects treated with epinephrine alone. *Conclusions:* There is an association between using vasopressin in combination with epinephrine and restoration of circulation after out-of-hospital cardiac arrest.

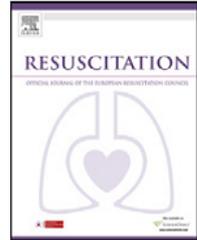


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Clinical paper

A randomised, double-blind, multi-centre trial comparing vasopressin and adrenaline in patients with cardiac arrest presenting to or in the Emergency Department^{☆,☆☆}

Main results: The study recruited 727 participants (adrenaline = 353; vasopressin = 374). Baseline characteristics of the two groups were comparable. Eight participants (2.3%) from adrenaline and 11 (2.9%) from vasopressin group survived to hospital discharge with no significant difference between groups ($p = 0.27$, RR = 1.72, 95% CI = 0.65–4.51). After adjustment for race, medical history, bystander CPR and prior adrenaline given, more participants survived to hospital admission with vasopressin (22.2%) than with adrenaline (16.7%) ($p = 0.05$, RR = 1.43, 95% CI = 1.02–2.04). Sub-group analysis suggested improved outcomes for vasopressin in participants with prolonged arrest times.

Conclusions: Combination of vasopressin and adrenaline did not improve long term survival but seemed to improve survival to admission in patients with prolonged cardiac arrest. Further studies on the effect of vasopressin combined with therapeutic hypothermia on patients with prolonged cardiac arrest are needed.



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Clinical paper

Vasopressin for cardiac arrest: Meta-analysis of randomized controlled trials[☆]

Spyros D. Mentzelopoulos^{a,*,d}, Spyros G. Zakyntinos^{a,d}, Ilias Siempos^{a,d},
Sotiris Malachias^a, Hanno Ulmer^b, Volker Wenzel^c

5. Conclusions

According to the pooled results of 6 RCTs with high methodological quality, vasopressin use in the resuscitation of cardiac arrest patients is not associated with any overall benefit or harm. However, vasopressin may improve the long-term survival of asystolic patients, especially when average T_{DRUG} is <20 min. New RCTs specifically assessing vasopressin effects on subgroup neurological outcome are warranted.

Table 1

Main characteristics of 8 potentially eligible trials.

First author, reference no.	Year of publication; country	Study design ^a	Study population, ^b (n)	Setting	Intervention in vasopressin group ^c	Intervention in control group ^c	Dosage of vasopressin	Number of enrolled patients; male (%)	CPR by bystander-no./total no. (%) ^d	Initial cardiac rhythm (%)
Mentzelopoulos ²	2009; Greece	Single-centre double-blind RCT	Adult patients (≥ 18 years) with cardiac arrest (n=100)	In-hospital	Vasopressin and epinephrine and corticosteroids ^e	Epinephrine and placebos	20–100 IU ^f	100; (59%)	Not applicable	VF/VT: 14% PEA: 25% Asystole: 61%
Gueugniaud ¹	2008; France	Multi-centre double-blind RCT	Adult patients (≥ 18 years) with cardiac arrest (n=2894)	Out-of-hospital	Vasopressin and epinephrine ^e	Epinephrine and placebo	40–80 IU ^g	2894; (74%)	400/1442 (28%) vs 377/1452 (26%)	VF/VT: 9% PEA: 8% Asystole: 83%
Callaway ²⁵	2006; USA	Multi-centre double-blind RCT	Adult patients (≥ 18 years) with cardiac arrest (n=325)	Out-of-hospital	Vasopressin and epinephrine ^e	Epinephrine and placebo	40–80 IU ^g	325; (61%)	52/167 (31%) vs 56/158 (35%)	VF/VT: 15% PEA: 22% Asystole: 51%
Wenzel ⁴	2004; Austria, Germany, Switzerland	Multi-centre double-blind RCT	Adult patients (≥ 18 years) with cardiac arrest (n=1186)	Out-of-hospital	Vasopressin followed by epinephrine	Epinephrine and placebo	40–80 IU ^g	1186; (69%)	111/589 (19%) vs 107/597 (18%)	VF/VT: 40% PEA: 16% Asystole: 45%
Stiell ¹⁹	2001; Canada	Multi-centre double-blind RCT	Adult patients (≥ 16 years) with cardiac arrest (n=200)	In-hospital	Vasopressin followed by epinephrine	Epinephrine and placebo	40 IU ^g	200; (63%)	Not applicable	VF/VT: 21% PEA: 48% Asystole: 31%
Lindner ¹⁸	1997; Germany	Single-centre double-blind RCT	Adult patients (≥ 18 years) with DC-countershock-refractory VF/VT (n=40)	Out-of-hospital	Vasopressin followed by epinephrine	Epinephrine and placebo	40 IU ^g	40; (73%)	4/20 (20%) vs 5/20 (25%)	VF/VT: 100% PEA: 0% Asystole: 0%

Conclusions: Vasopressin use in the resuscitation of cardiac arrest patients is not associated with any overall benefit or harm. However, vasopressin may improve the long-term survival of asystolic patients, especially when average T_{DRUG} is <20 min.



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Review article

Efficacy of vasopressin during cardio-pulmonary resuscitation in adult patients: A meta-analysis



Amitava Layek^a, Souvik Maitra^b, Sugata Pal^c, Sulagna Bhattacharjee^{b,*}, Dalim K. Baidya^d

Results: A total of 6120 patients from 10 RCTs were included in this meta-analysis. Vasopressin use during CPR has no beneficial impact in an unselected population in ROSC [OR 1.19, 95% CI 0.93, 1.52], survival to hospital discharge [OR 1.13, 95% CI 0.89, 1.43], survival to hospital admission [OR 1.12, 95% CI 0.99, 1.27] and favorable neurological outcome [OR 1.02, 95% CI 0.75, 1.38]. ROSC in “in-hospital” cardiac arrest setting [OR 2.20, 95% CI 1.08, 4.47] is higher patients receiving vasopressin. Subgroup analyses revealed equal or higher chance of ROSC [OR 2.15, 95% CI 1.00, 4.61], higher possibility of survival to hospital discharge [OR 2.39, 95% CI 1.34, 4.27] and favorable neurological outcome [OR 2.58, 95% CI 1.39, 4.79] when vasopressin was used as repeated boluses of 4–5 times titrating desired effects during CPR.

Conclusion: ROSC in “in-hospital” cardiac arrest patients is significantly better when vasopressin was used. A subgroup analysis of this meta-analysis found that ROSC, survival to hospital admission and discharge and favorable neurological outcome may be better when vasopressin was used as repeated boluses of 4–5 times titrated to desired effects; however, overall no beneficial effect was noted in unselected cardiac arrest population.

- The European Resuscitation Council recommends 40 units of vasopressin in adults as an initial vasopressor in case of shock-refractory ventricular fibrillation, as an alternative to 1 mg of epinephrine. (pubmed 11255370).
- The 2005 American Heart Association guidelines recommend 40 units of vasopress in intravenous or intraosseous, to replace the first or second dose of epinephrine in cardiac arrest, in adults.

Part 8: Adult Advanced Cardiovascular Life Support

2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Robert W. Neumar, Chair; Charles W. Otto; Mark S. Link; Steven L. Kronick;
Michael Shuster; Clifton W. Callaway; Peter J. Kudenchuk; Joseph P. Ornato; Bryan McNally;
Scott M. Silvers; Rod S. Passman; Roger D. White; Erik P. Hess; Wanchun Tang;
Daniel Davis; Elizabeth Sinz; Laurie J. Morrison

Because the effects of vasopressin have not been shown to differ from those of epinephrine in cardiac arrest, 1 dose of vasopressin 40 units IV/IO may replace either the first or second dose of epinephrine in the treatment of cardiac arrest (Class IIb, LOE A).

Abstract

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Resuscitation. 2002 Feb;52(2):149-56.

Beneficial effects of vasopressin in prolonged pediatric cardiac arrest: a case series.

Mann K¹, Berg RA, Nadkarni V.

- A retrospective case series of children with cardiac arrest suggested that vasopressin 0.4 units/kg/dose is beneficial during prolonged pediatric cardiac arrest, following the failure of conventional cardiopulmonary resuscitation.

Abstract

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Crit Care Med. 2007 Apr;35(4):1161-4.

Beneficial effects of terlipressin in prolonged pediatric cardiopulmonary resuscitation: a case series.

Matok I¹, Vardi A, Augarten A, Efrati O, Leibovitch L, Rubinshtein M, Paret G.

- A second retrospective case series of pediatric cardiac arrests, unresponsive to epinephrine, found that **ROSC was achieved in six of eight** episodes in patients treated with 15 to 20 mics/kg/dose of terlipressin and **four of these patients survived without neurological sequelae.**

Pediatr Crit Care Med. 2010 Jan;11(1):139-41. doi: 10.1097/PCC.0b013e3181ae7834.

Pediatric cardiac arrest refractory to advanced life support: is there a role for terlipressin?

Gil-Antón J¹, López-Herce J, Morteruel E, Carrillo A, Rodríguez-Núñez A.

Author information

Abstract

OBJECTIVE: Pediatric cardiac arrest unresponsive to advanced life support and several adrenaline doses has a very poor prognosis. Alternative vasopressors could improve the results of resuscitation in such cases. We report our experience with the compassionate administration of terlipressin in children who suffered in-pediatric intensive care unit cardiac arrest and did not respond to immediate advanced life support and at least three epinephrine doses.

MEASUREMENTS AND MAIN RESULTS: Sustained return of spontaneous circulation was achieved in four cases, two of them were declared dead 6 and 12 hrs later, and the remaining two survived without cardiopulmonary procedures-related sequelae and with good neurologic condition.

CONCLUSIONS: Terlipressin might contribute to obtain sustained return of spontaneous circulation in children with refractory in-hospital cardiac arrest. A randomized controlled clinical trial should be conducted to investigate the optimal drug treatment in pediatric cardiac arrest.

Abstract

See

Pediatr Crit Care Med. 2012 May;13(3):265-72. doi: 10.1097/PCC.0b013e31822f1569.

Vasopressin rescue for in-pediatric intensive care unit cardiopulmonary arrest refractory to initial epinephrine dosing: a prospective feasibility pilot trial.

Carroll TG¹, Dimas VV, Raymond TT.

doses of vasopressor, and did not receive arginine vasopressin (n = 20). Of 2,654 patients admitted to the pediatric intensive care unit, 29 (1.1%) had refractory cardiopulmonary arrest: five patients were excluded, 14 missed for inclusion, and ten were enrolled. There was increased 24-hr survival (80% vs. 30%, odds ratio 9.33, 95% confidence interval 1.51-57.65) in arginine vasopressin patients. There was no significant difference in return of spontaneous circulation, survival to hospital discharge, or favorable neurologic status at discharge.

CONCLUSIONS: These pilot data provide support for a larger randomized controlled trial of arginine vasopressin therapy during cardiopulmonary resuscitation for in-hospital pediatric cardiac arrest.

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