

WORKSHEET for Evidence-Based Review of Science for Veterinary CPR

1. Basic Demographics

Worksheet author(s)

Yonaira Cortes	Date Submitted for review:

2. Clinical question:

In dogs and cats with ROSC after cardiac arrest who have cardiovascular dysfunction (hypotension, hypoperfusion) (P), does IV fluid administration (I) compared to no fluids (or another fluid) (C), result in improved outcome (O) (survival to discharge neurological function)?

3. Conflict of interest specific to this question:

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?
NO

4. Search strategy (including electronic databases searched):

4a. Databases

- MEDLINE via PUBMED (1950 to May 2011)
- 1. Cardiac arrest OR Cardiovascular dysfunction
- 3. IV fluids or infusions or fluid resuscitation
- 4. hypotension
- 5. hypoperfusion
- 6. cat
- 7. dog

Cardiopulmonary resuscitation OR cardiac arrest OR return of circulation OR ROSC OR cardiac arrest syndrome OR post-cardiac arrest syndrome AND (intravenous fluids OR colloids OR infusions OR IV fluids OR fluid resuscitation) AND hypotension OR hypoperfusion OR cardiovascular dysfunction): total of 253 hits

(dogs OR cats) And (Cardiopulmonary resuscitation OR cardiac arrest OR OR return of circulation OR ROSC OR cardiac arrest syndrome OR post-cardiac arrest syndrome) AND (intravenous fluids OR colloids OR infusions OR IV fluids OR fluid resuscitation) AND hypotension OR hypoperfusion OR cardiovascular dysfunction): 36 hits

CAB search for the following keywords:
Resuscitation or CPR or ROSC AND hypotension or hypoperfusion or cardiovascular dysfunction AND intravenous fluids
No hits

Of the 289 hits above 6 were relevant

4b. Other sources

Human ILCOR 2010 Worksheet was reviewed for additional articles

4c. State inclusion and exclusion criteria for choosing studies and list number of studies excluded per criterion

Inclusion criteria

Articles dealing with cardiac arrest with hypotension or hypoperfusion and fluid therapy in humans, dogs, and cats.

Exclusion criteria

Abstracts only. Editorials, Articles in language other than English

4d. Number of articles/sources meeting criteria for further review:

- 2 canine studies were identified Capone et al 1996 and Leonov et al 1992
- 8 human studies Gaieski et al, 2009, Sunde et al 2007, Kim et al 2007, Kliegel et al 2005, Nordmark et al 2009, Bernard et al 2003, Jacobshagen et al 2009, Kim et al 2005
- 3 porcine studies were identified Kaakinen et al 2006, Bertsch et al 2001, Kreiter et al 2002,

5. Summary of evidence

Evidence Supporting Clinical Question

Good						
Fair						
Poor						
	1	2	3	4	5	6
Level of evidence (P)						

A = Return of spontaneous circulation
 B = Survival of event

C = Survival to hospital discharge
 D = Intact neurological survival

E = Other endpoint
Italics = Non-target species studies

Evidence Neutral to Clinical question

Good			<i>Capone 1996 DE</i>			<i>Gaieski, 2009 CD Kaakinen, 2006 E Kreiter 2002 E Sunde 2007 CD</i>
Fair			<i>Leonov, 1992 E</i>			<i>Bertsch, 2001 E Kim 2007 CE Kliegel 2005 CDE Nordmark 2009 E</i>
Poor						<i>Bernard, 2003 C Jacobshagen 2009 E Kim, 2005 E</i>
	1	2	3	4	5	6
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event

C = Survival to hospital discharge
D = Intact neurological survival

E = Other endpoint
Italics = Non-target species studies

Evidence Opposing Clinical Question

Good						
Fair						
Poor						
	1	2	3	4	5	6
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event

C = Survival to hospital discharge
D = Intact neurological survival

E = Other endpoint
Italics = Non-target species studies

6. REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

None of the studies evaluated directly answered the question asked by evaluating fluids alone vs no fluids after CPR. Similar to the human ILCOR worksheet 2010, an assumption was made that all patients have some degree of cardiovascular dysfunction following ROSC.

The studies reviewed for the most part do not show clear benefit of fluids, similarly to do not show clear harm from the infusions.

One canine study (Leonov, 1992) used 10 dogs given fluids to induce haemodilution with 50 ml/kg of dextran 40 in 0.9% NaCl while removing blood via cardiopulmonary bypass. The dogs were maintained with a higher mean arterial pressure than the control group with norepinephrine infusion. Global cerebral blood flow was lower in the control group versus the interventional group. Oxygen delivery was the same in both groups due to a lower arterial oxygen content with the hemodilution. The study is fair, but there was no randomization. It did not show a benefit, but also no harm.

The other canine study (Capone 1996) used cardiopulmonary bypass to induce profound hypothermic circulatory arrest (PHCA) in 10 dogs, with 10 controls. This study found that when dogs were given fluids and blood to resuscitate from a MAP of 40mmHg vs 30mmHg, there was improved survival. It is unclear from the study how much fluid each group received during the resuscitative period. All dogs received fluid resuscitation, no group received no fluids.

Another study (Kaakinen, 2006) in pigs evaluated the use of hypertonic saline dextran after hypothermic circulatory arrest. The pigs received normal saline or hypertonic saline dextran, however no group did not receive any fluid. The study showed benefit of hypertonic fluid over 0.9% NaCl. There was increased 7 day survival, faster neurologic recovery, lower intracranial pressures and less ischaemia on histopathology scoring.

There were 6 human studies evaluating rapid infusion of cold intravenous fluids to induce therapeutic hypothermia. These studies were Bernard, 2003; Jacobshagen, 2009; Kim 2005; Kim 2007; Kliegel 2005; Nordmark 2009. Five of the papers showed no harm to fluid administration, while one (Kliegel 2005) did find that 2 patients had pulmonary edema. The infusions were continued in those patients as they were not deemed to be compromised. Kim 2005 looked at ejection fraction with echocardiography and did not find significantly different values among study groups. These studies show that fluid infusions are tolerated, but do not show a benefit of survival from use. Another study (Jacobshagen, 2009) looked at infusions of 3427+/-210mL on respiratory function as measured by PaO₂/FiO₂ ratio. The infusions did not cause a statistically significant deterioration in respiratory function.

There were two studies (Gaieski, 2009 and Sunde 2007) that evaluated the inclusion of fluid as part of the post-cardiac arrest early goal directed therapy. The studies used cold normal saline to induce hypothermia and further intravenous fluids to maintain CVP>8. There was no control group that did not receive fluids. Gaeski showed an improvement in survival to discharge when compared to a historical control group that used early goal-directed therapy, but this was not statistically significant. Sunde found an improved survival however, no true control of other variables was accounted for and therefore survival cannot be attributed to fluids alone.

Three porcine studies (Bertch, 2001, Kaakinen, 2006, Kreiter, 2002) evaluated the use of hypertonic fluid after ROSC. Again, none of these studies had a group that did not receive any fluids. All studies found that hypertonic fluids was more beneficial than 0.9% NaCl. Kaakinen 2006 found that hypertonic saline increased 7 day survival after cardiac arrest, and showed faster neurologic recovery, lower intracranial pressures and

higher cerebral perfusion pressures. Kreiter found lower levels of protein s-100 and cTroponin I in the animals given hypertonic saline, indicating less neurologic and cardiac damage.

The limited studies show that fluids appear to be well tolerated in post-ROSC patients. There is not sufficient evidence showing a benefit of their use, however there was no study found that evaluated no fluids in the post-ROSC patient. There is really not enough evidence to recommend the use or not of fluid post-ROSC following cardiac arrest. The studies showed harm in very few patients, and is likely safe given the information found.

7. Conclusion

CONSENSUS ON SCIENCE:

Two canine studies, LOE 3 [Capone,1996 and Leonov 1992] evaluated cardiopulmonary bypass to evaluate resuscitation and neurologic recovery and found better survival and increases in cerebral blood flow in those animals that had haemodilution and higher blood pressures.

Three porcine studies, LOE 6, [Bertsch 2001, Kakkinen, 2006, Kreiter, 2002] found hypertonic fluid to provide neurological and cardiac protection compared to normal saline.

Two human studies, LOE 6, [Gaieski 2009, Sunde 2007] used fluids as part of their post-arrest protocols (in addition to therapeutic hypothermia). Both studies found no harm to the fluid administration, and Sunde found improved survival with favorable neurological outcome.

Five human studies, LOE 6, [Bernard 2003, Kim 2005, Kim 2007, Kliegel 2005, Nordmark 2009] showed rapid infusions of fluids to induce therapeutic hypothermia after ROSC did little harm. One study, LOE 6, [Jacobshagen 2009] showed deterioration in oxygenation after ROSC that was not significantly affected by large volumes of cold fluid (3427 ml +/-210ml).

TREATMENT RECOMMENDATION:

There is not enough evidence to make a definitive conclusion in regards to the benefits of fluid therapy post ROSC. There were no canine or feline studies that evaluated fluids vs no fluids in post cardiopulmonary arrest patients. Available studies indicate little harm from fluids infused post ROSC and possible benefit. The use of fluids in the post arrest patient should be considered and used cautiously as indicated by evaluation of haemodynamic variables and cardiovascular parameters. Future study is required to evaluate appropriate fluid doses after ROSC and effects of fluids on cardiovascular function.

8. Acknowledgement

9. Citation list

Induced hypothermia using large volume, ice-cold intravenous fluid in comatose survivors of out-of-hospital cardiac arrest: a preliminary report.

[Bernard S](#), [Buist M](#), [Monteiro O](#), [Smith K](#). Resuscitation. 2003; 56(1):9-13.

Source

The Intensive Care Unit, Dandenong Hospital, David St, Victoria 3175, Dandenong, Australia. stephen.bernard@dhs.vic.gov.au

Abstract

STUDY HYPOTHESIS:

Recent studies have shown that induced hypothermia for twelve to twenty four hours improves outcome in patients who are resuscitated from out-of-hospital cardiac arrest. These studies used surface cooling, but this technique provided for relatively slow

decreases in core temperature. Results from animal models suggest that further improvements in outcome may be possible if hypothermia is induced earlier after resuscitation from cardiac arrest. We hypothesized that a rapid infusion of large volume (30 ml/kg), ice-cold (4 degrees C) intravenous fluid would be a safe, rapid and inexpensive technique to induce mild hypothermia in comatose survivors of out-of-hospital cardiac arrest.

METHODS:

We enrolled 22 patients who were comatose following resuscitation from out-of-hospital cardiac arrest. After initial evaluation in the Emergency Department (ED), a large volume (30 ml/kg) of ice-cold (4 degrees C) lactated Ringers solution was infused intravenously over 30 min. Data on vital signs, arterial blood gas, electrolyte and hematological was collected immediately before and after the infusion.

RESULTS:

The rapid infusion of large volume, ice-cold crystalloid fluid resulted in a significant decrease in median core temperature from 35.5 to 33.8 degrees C. There were also significant improvements in mean arterial blood pressure, renal function and acid-base analysis. No patient developed pulmonary odema.

CONCLUSION:

A rapid infusion of large volume, ice-cold crystalloid fluid is an inexpensive and effective method of inducing mild hypothermia in comatose survivors of out-of-hospital cardiac arrest, and is associated with beneficial haemodynamic, renal and acid-base effects. Further studies of this technique are warranted.

LOE 6. Human study.

Poor, Neutral results

Historical controls. 22 patients given 30ml/kg of 4 degrees celcius lactated ringers over 30minutes

No adverse effects, survival do discharge was 8/14 ventricular arrest and 2/8 of other rhythms

Hypertonic-hyperoncotic solutions decrease cardiac troponin I concentrations in peripheral blood in a porcine ischemia-reperfusion model.

[Bertsch T](#), [Denz C](#), [Janke C](#), [Weiss M](#), [Fassbender K](#), [Luiz T](#), [Ellinger K](#), [Krieter H](#). *Exp Toxicol Pathol.* 2001;53(2-3):153-6.

Source

Institute for Clinical Chemistry, Klinikum Mannheim gGmbH, Faculty of Clinical Medicine Mannheim of the University of Heidelberg, Germany. thomas.bertsch@ikc.ma.uni-heidelberg.de

Abstract

In this study we addressed the question of whether the measurement of cardiac Troponin I (cTnI) is able to reflect beneficial effects of hypertonic-hyperoncotic solutions after transient cardiac arrest. Ten pigs were anaesthetized and cardiac arrest was induced by electric fibrillation. After 5 minutes of global ischemia, cardiac arrest was reversed by electric defibrillation. Upon return of spontaneous circulation 5 animals received hypertonic-hyperoncotic solutions (10% Hydroxyethylstarch 200/0.5 and 7.2% NaCl). The other animals received equivalent volumes of physiological saline. We observed that cTnI serum levels of animals treated with hypertonic-hyperoncotic solutions were significantly lower than those treated with saline. We conclude that hypertonic-hyperoncotic solutions may have cardioprotective effects.

LOE 6, Porcine model. Control group, non-randomized

Outcome = troponin. No pig did not receive no fluids.

10 animals, 5 hypertonic, 5 normal saline

Lower troponin in hypertonic group

Complete recovery after normothermic hemorrhagic shock and profound hypothermic circulatory arrest of 60 minutes in dogs.

[Capone A](#), [Safar P](#), [Radovsky A](#), [Wang YF](#), [Peitzman A](#), [Tisherman SA](#). *J of Trauma.* 1996;40(3):388-395.

Source

Safar Center for Resuscitation Research, University of Pittsburgh, PA 15260, USA.

Abstract

OBJECTIVE:

We hypothesize that during severe normothermic hemorrhagic shock (HS), induction of profound hypothermic circulatory arrest (PHCA) of 60 minutes to allow repair of otherwise lethal injuries in a bloodless field, can be survived without brain damage. In previous dog studies, normothermic HS with mean arterial pressure (MAP) of 40 mm Hg for 30 minutes, followed by PHCA of 2 hours at brain (tympanic membrane) temperature of 5 to 10 degrees C and core temperature of 10 degrees C, induced and reversed

with cardiopulmonary bypass, resulted in survival with mild histopathologic brain damage. This study was designed to determine the severity of HS that can safely allow 1 hour of PHCA. In pilot studies with HS at MAP 30 mm Hg for 90 minutes with or without subsequent PHCA of 60 minutes there were no survivors.

METHODS:

In the definitive study, outcomes in four groups of five dogs each were compared: group I, HS at MAP 30 mm Hg for 60 minutes and normothermic fluid resuscitation; group II, HS at MAP 30 mm Hg for 60 minutes, PHCA for 60 minutes, and resuscitation; group III, HS at MAP 40 mm Hg for 60 minutes and normothermic fluid resuscitation; and group IV, HS at MAP 40 mm Hg for 60 minutes, PHCA for 60 minutes, and resuscitation. Controlled ventilation was maintained for at least 20 hours and intensive care for 72 hours.

RESULTS:

In groups I and II, two of five dogs in each group survived to 72 hours. In groups III and IV, all ten dogs survived. All survivors were functionally normal, with neurologic deficit scores (0% = normal, 100% = brain dead) of < 10%. Light microscopic scoring of 18 brain regions revealed no ischemic changes. All nonsurvivors had a severe metabolic acidemia after HS and developed multiple organ failure, including pulmonary edema, pneumonia, and intestinal necrosis.

CONCLUSIONS:

The critical level of hypotension during 60 minutes normothermic HS that is compatible with survival in dogs is a MAP of between 30 and 40 mm Hg. After otherwise survivable severe normothermic HS of 60 minutes, PHCA of 60 minutes does not add brain damage or mortality, and may allow survival from injuries that would otherwise be irreparable.

LOE 3. Canine study

Good.

N=20, four groups of 5 dogs.

Group 1 normothermic hemorrhagic shock at MAP 30mmHg followed by normothermic fluids

Group 2 normothermic HS at MAP 30mmHg followed by hypothermic circulatory arrest for 60min followed by reperfusion/rewarming

Group 3 was similar to group 1 at MAP 40mmHg, Group 4 was similar to group 2 at 40mmHg

Resuscitation in groups 1 and 3 received lactated ringer's IV as needed to maintain a MAP > or = to 90mmHg as well as reinfusing shed blood.

Group 2 and 3 additionally were given epinephrine boluses or norepinephrine infusions as needed to maintain MAP

Group 1 3/5 died, group 2 3/5 died; Group 3 and 4 all 10 dogs survived. All dogs that survived from all groups had normal neurologic scores.

Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest.

[Gaieski DF](#), [Band RA](#), [Abella BS](#), [Neumar RW](#), [Fuchs BD](#), [Kolansky DM](#), [Merchant RM](#), [Carr BG](#), [Becker LB](#), [Maguire C](#), [Klair A](#), [Hylton J](#), [Goyal M](#). Resuscitation. 2009;80(4):418-24.

Source

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Abstract

BACKGROUND:

Comatose survivors of out-of-hospital cardiac arrest (OHCA) have high in-hospital mortality due to a complex pathophysiology that includes cardiovascular dysfunction, inflammation, coagulopathy, brain injury and persistence of the precipitating pathology. Therapeutic hypothermia (TH) is the only intervention that has been shown to improve outcomes in this patient population. Due to the similarities between the post-cardiac arrest state and severe sepsis, it has been postulated that early goal-directed hemodynamic optimization (EGDHO) combined with TH would improve outcome of comatose cardiac arrest survivors.

OBJECTIVE:

We examined the feasibility of establishing an integrated post-cardiac arrest resuscitation (PCAR) algorithm combining TH and EGDHO within 6h of emergency department (ED) presentation.

METHODS:

In May, 2005 we began prospectively identifying comatose (Glasgow Motor Score<6) survivors of OHCA treated with our PCAR protocol. The PCAR patients were compared to matched historic controls from a cardiac arrest database maintained at our institution.

RESULTS:

Between May, 2005 and January, 2008, 18/20 (90%) eligible patients were enrolled in the PCAR protocol. They were compared to historic controls from 2001 to 2005, during which time 18 patients met inclusion criteria for the PCAR protocol. Mean time from initiation of TH to target temperature (33 degrees C) was 2.8h (range 0.8-23.2; SD=h); 78% (14/18) had interventions based upon EGDHO parameters; 72% (13/18) of patients achieved their EGDHO goals within 6h of return of spontaneous circulation (ROSC). Mortality for historic controls who qualified for the PCAR protocol was 78% (14/18); mortality for those treated with the PCAR protocol was 50% (9/18) (p=0.15).

CONCLUSIONS:

In patients with ROSC after OHCA, EGDHO and TH can be implemented simultaneously.

LOE 6. Human study. Good quality, retrospective control.

No group did not receive fluids. Neutral results.

20 patients following protocol for goal directed therapy.

Improved survival in 50% compared to 22% in historical controls (not statistically significant)

Effects of large volume, ice-cold intravenous fluid infusion on respiratory function in cardiac arrest survivors.

[Jacobshagen C](#), [Pax A](#), [Unsöld BW](#), [Seidler T](#), [Schmidt-Schweda S](#), [Hasenfuss G](#), [Maier LS](#). Resuscitation. 2009. 80:1223-1228.

Source

Department of Cardiology and Pneumology, Georg-August-University, Göttingen, Germany. jacobshagen@med.uni-goettingen.de

Abstract

International guidelines for cardiopulmonary resuscitation recommend mild hypothermia (32-34 degrees C) for 12-24h in comatose survivors of cardiac arrest. To induce therapeutic hypothermia a variety of external and intravascular cooling devices are available. A cheap and effective method for inducing hypothermia is the infusion of large volume, ice-cold intravenous fluid. There are concerns regarding the effects of rapid infusion of large volumes of fluid on respiratory function in cardiac arrest survivors. We have retrospectively studied the effects of high volume cold fluid infusion on respiratory function in 52 resuscitated cardiac arrest patients. The target temperature of 32-34 degrees C was achieved after 4.1+/-0.5h (cooling rate 0.48 degrees C/h). During this period 3427+/-210 mL ice-cold fluid was infused. Despite significantly reduced LV-function (EF 35.8+/-2.2%) the respiratory status of these patients did not deteriorate significantly. On intensive care unit admission the mean PaO(2) was 231.4+/-20.6 mmHg at a F(i)O(2) of 0.82+/-0.03 (PaO(2)/F(i)O(2)=290.0+/-24.1) and a PEEP level of 7.14+/-0.31 mbar. Until reaching the target temperature of <or=34 degrees C the F(i)O(2) could be significantly reduced to 0.63+/-0.03 with unchanged PEEP level (7.23+/-0.36 mbar). Under these conditions the PaO(2)/F(i)O(2) ratio slightly decreased to 247.5+/-18.5 (P=0.0893). Continuing the saline infusion to achieve a body temperature of 33 degrees C, the F(i)O(2) could be further reduced with unchanged PEEP. The infusion of large volume, ice-cold fluid is an effective and inexpensive method for inducing therapeutic hypothermia. Resuscitation from cardiac arrest is associated with a deterioration in respiratory function. The infusion of large volumes of cold fluid does not cause a statistically significant further deterioration in respiratory function. A larger, randomized and prospective study is required to assess the efficacy and safety of ice-cold fluid infusion for the induction of therapeutic hypothermia.

LOE6. Human Study.

Fair, neutral results

Evaluated IV fluids after arrest on respiratory function as seen by PaO2/FiO2 ratio

Found that ratios dropped slightly but not statistically significant, ratios were poor to begin with.

Retrospective study

Hypertonic saline dextran improves outcome after hypothermic circulatory arrest: a study in a surviving porcine model.

[Kaakinen T](#), [Alaoja H](#), [Heikkinen J](#), [Dahlbacka S](#), [Laurila P](#), [Kiviluoma K](#), [Salomäki T](#), [Tuominen H](#), [Ohtonen P](#), [Biancari F](#), [Juvonen T](#). Ann Thorac Surg. 2006; 81(1):183-90.

Source

Department of Surgery, Oulu University Hospital, University of Oulu, Oulu, Finland.

Abstract**BACKGROUND:**

Hypertonic saline dextran (HSD) has been shown to have neuroprotective properties. In the present study we have assessed its potential neuroprotective efficacy in the setting of hypothermic circulatory arrest in a surviving porcine model.

METHODS:

Twenty-four pigs were randomized to receive two 5-minute intravenous infusions (4 mL/kg) of either HSD (7.5 % saline, 6% dextran 70) or normal saline immediately after and 4 hours after a 75-minute period of hypothermic circulatory arrest at a brain temperature of 18 degrees C.

RESULTS:

The 7-day survival was 75% in the HSD group and 66% in the control group ($p > 0.9$). Brain total histopathologic score was lower in the HSD group ($p = 0.01$). Postoperative behavioral scores were higher in the HSD group on the second day after surgery ($p = 0.03$). Intracranial pressure was lower in the HSD group from 45 minutes to 8 hours after hypothermic circulatory arrest ($p = 0.03$). Cerebral perfusion pressure was higher in the HSD group from 45 minutes to 3 hours after hypothermic circulatory arrest ($p = 0.06$). Brain lactate concentration was lower in the HSD group when compared with controls ($p = 0.05$). Furthermore, brain glucose levels tended to be higher and brain lactate-pyruvate ratio and lactate-glucose ratio were lower in the HSD group. Brain tissue oxygen partial pressures were somewhat higher in the HSD group ($p = 0.08$).

CONCLUSIONS:

The use of HSD in experimental hypothermic circulatory arrest is associated with significantly better neurologic recovery, better histopathology, lower intracranial pressure, higher cerebral perfusion pressure, and better preservation of brain metabolism.

LOE 6. Porcine study

Good, neutral

No group did not receive fluid

24 pigs after hypothermic arrest received 4ml/kg hypertonic saline dextran or 0.9% saline post ROSC and 4 hours post initiation of reperfusion and received ringer's acetate

7 day survival with HSD was 75% vs 66.7% in the saline group

Faster recovery in the HSD group for neurologic

Pilot Randomized Clinical Trial of Prehospital Induction of Mild Hypothermia in Out-of-Hospital Cardiac Arrest Patients With a Rapid Infusion of 4°C Normal Saline

[Francis Kim](#), MD; [Michele Olsufka](#), RN; [W.T. Longstreth Jr](#), MD; [Charles Maynard](#), PhD; [David Carlbom](#), MD; [Steven Deem](#), MD; [Peter Kudenchuk](#), MD; [Michael K. Copass](#), MD; [Leonard A. Cobb](#), MD

Circulation. 2007;115(24):3064-70.

Abstract

Background— Although delayed hospital cooling has been demonstrated to improve outcome after cardiac arrest, in-field cooling started immediately after the return of spontaneous circulation may be more beneficial. The aims of the present pilot study were to assess the feasibility, safety, and effectiveness of in-field cooling.

Methods and Results— We determined the effect on esophageal temperature, before hospital arrival, of infusing up to 2 L of 4°C normal saline as soon as possible after resuscitation from out-of-hospital cardiac arrest. A total of 125 such patients were randomized to receive standard care with or without intravenous cooling. Of the 63 patients randomized to cooling, 49 (78%) received an infusion of 500 to 2000 mL of 4°C normal saline before hospital arrival. These 63 patients experienced a mean temperature decrease of $1.24 \pm 1^\circ\text{C}$ with a hospital arrival temperature of 34.7°C , whereas the 62 patients not randomized to cooling experienced a mean temperature increase of $0.10 \pm 0.94^\circ\text{C}$ ($P < 0.0001$) with a hospital arrival temperature of 35.7°C . In-field cooling was not associated with adverse consequences in terms of blood pressure, heart rate, arterial oxygenation, evidence for pulmonary edema on initial chest x-ray, or rearrest. Secondary end points of awakening and discharged alive from hospital trended toward improvement in ventricular fibrillation patients randomized to in-field cooling.

Conclusions— These pilot data suggest that infusion of up to 2 L of 4°C normal saline in the field is feasible, safe, and effective in lowering temperature. We propose that the effect of this cooling method on neurological outcome after cardiac arrest be studied in larger numbers of patients, especially those whose initial rhythm is ventricular fibrillation.

LOE 6. RCT, Fair. Neutral

N=125, most of these received fluids. The test group received 2L 4 degree celcius 0.9% NaCl; of the other 63, 8 did not get fluids and 6 got < 500ml. It is unclear how much fluids the control group received.

Outcome VF group improved survival to discharge than PEA with cold fluids compared to control, the PEA group had worse survival with cold fluids

Fluids were not associated with adverse effects

Pilot Study of Rapid Infusion of 2 L of 4°C Normal Saline for Induction of Mild Hypothermia in Hospitalized, Comatose Survivors of Out-of-Hospital Cardiac Arrest

[Francis Kim](#), MD; [Michele Olsufka](#), RN; [David Carlbom](#), MD; [Steven Deem](#), MD; [W.T. Longstreth Jr](#), MD; [Margret Hanrahan](#), RN; [Charles Maynard](#), PhD; [Michael K. Copass](#), MD; [Leonard A. Cobb](#), MD

Circulation. 2005;112(5):715-9.

Abstract

Background— Recent clinical studies have demonstrated that mild hypothermia (32°C to 34°C) induced by surface cooling improves neurological outcome after resuscitation from out-of-hospital cardiac arrest. Results from animal models suggest that the effectiveness of mild hypothermia could be improved if initiated as soon as possible after return of spontaneous circulation. Infusion of cold, intravenous fluid has been proposed as a safe, effective, and inexpensive technique to induce mild hypothermia after cardiac arrest.

Methods and Results— In 17 hospitalized survivors of out-of-hospital cardiac arrest, we determined the effect on temperature and hemodynamics of infusing 2 L of 4°C cold, normal saline during 20 to 30 minutes into a peripheral vein with a high-pressure bag. Data on vital signs, electrolytes, arterial blood gases, and coagulation were collected before and after fluid infusion. Cardiac function was assessed by transthoracic echocardiography before fluid administration and 1 hour after infusion. Passive (fans, leaving patient uncovered) or active (cooling blankets, neuromuscular blockade) cooling measures were used to maintain mild hypothermia for 24 hours. Infusion of 2 L of 4°C cold, normal saline resulted in a mean temperature drop of 1.4°C 30 minutes after the initiation of infusion. Rapid infusion of fluid was not associated with clinically important changes in vital signs, electrolytes, arterial blood gases, or coagulation parameters. The initial mean ejection fraction was 34%, and fluid infusion did not affect ejection fraction or increase central venous pressure, pulmonary pressures, or left atrial filling pressures as assessed by echocardiography. Passive measures were ineffective in maintaining hypothermia compared with active measures.

Conclusions— Infusion of 2 L of 4°C cold, normal saline is safe and effective in rapidly lowering body temperature in survivors of out-of-hospital cardiac arrest.

LOE 6. Poor. Neutral.

N=17. All patients got 2L of 4 degrees celcius NaCl over 20-30min

No adverse effects noted, no worsening of cardiac hemodynamics noted

Cold simple intravenous infusions preceding special endovascular cooling for faster induction of mild hypothermia after cardiac arrest--a feasibility study.

[Kliegel A](#), [Losert H](#), [Sterz F](#), [Kliegel M](#), [Holzer M](#), [Uray T](#), [Domanovits H](#). Resuscitation. 2005;64(3):347-51.

Source

Department of Emergency Medicine, Medical University Vienna, 1090 Wien, Austria.

Abstract

OBJECTIVE:

Mild therapeutic hypothermia has shown to improve neurological outcome after cardiac arrest. Our study investigated the efficacy and safety of cold simple intravenous infusions for induction of hypothermia after cardiac arrest preceding further cooling and maintenance of hypothermia by specialised endovascular cooling.

METHODS:

All patients admitted after cardiac arrest of presumed cardiac aetiology were screened. Patients enrolled received 2000 ml of ice-cold (4 degrees C) fluids via peripheral venous catheters. As soon as possible endovascular cooling was applied even if the cold infusions were not completed. The target temperature was defined as 33 +/- 1 degrees C. All temperatures recorded were measured via bladder-temperature probes. The primary endpoint was the time from return of spontaneous circulation to reaching the target temperature. Secondary endpoints were changes in haemodynamic variables, oxygenation, haemoglobin, clotting variables and neurological outcome.

RESULTS:

Out of 167 screened patients 26 (15%) were included. With a total amount of 24 +/- 7 ml/kg cold fluid at 4 degrees C the temperature could be lowered from 35.6 +/- 1.3 degrees C on admission to 33.8 +/- 1.1 degrees C. The target temperature was reached 185 +/- 119 min after return of spontaneous circulation, 135 +/- 112 min after start of infusion, and 83 +/- 85 min after start of endovascular cooling. Except for two patients showing radiographic signs of mild pulmonary edema no complications attributable to the infusions could be observed. Thirteen patients (50%) survived with favourable neurological outcome.

CONCLUSION:

Our results indicate that induction of mild hypothermia with infusion of cold fluids preceding endovascular cooling is safe and effective.

LOE 6, Human study.

Fair, no patients did not receive fluids.

N=26

No relevant changes in haemodynamic variables or Hb, 2 patients developed pulmonary edema but did not require stopping the fluid administration

Survival to discharge was 54%, Neurologic outcome was 50%

Hypertonic-Hyperoncotic Solutions Reduce the Release of Cardiac Troponin I and S-100 After Successful Cardiopulmonary Resuscitation in Pigs

[Heiner Krieter](#), MD DEAA*, [Christof Denz](#), MD*, [Christoph Janke](#), MD*, [Thomas Bertsch](#), MD†, [Thomas Luiz](#), MD*, [Klaus Ellinger](#), MD* and [Klaus van Ackern](#), MD*

Anesth Analg. 2002;95(4):1031-6.

Abstract

In some patients, cardiopulmonary resuscitation (CPR) can revive spontaneous circulation (ROSC). However, neurological outcome often remains poor. Hypertonic-hyperoncotic solutions (HHS) have been shown to improve microvascular conductivity after regional and global ischemia. We investigated the effect of infusion of HHS in a porcine CPR model. Cardiac arrest was induced by ventricular fibrillation. Advanced cardiac life support was begun after 4 min of nonintervention and 1 min of basic life support. Upon ROSC, the animals randomly received 125 mL of either normal saline (placebo, $n = 8$) or 7.2% NaCl and 10% hydroxyethyl starch 200,000/0.5 (HHS, $n = 7$). Myocardial and cerebral damage were assessed by serum concentrations of cardiac troponin I and astroglial protein S-100, respectively, up to 240 min after ROSC. In all animals, the levels of cardiac troponin I and S-100 increased after ROSC ($P < 0.01$). This increase was significantly blunted in animals that received HHS instead of placebo. The use of HHS in the setting of CPR may provide a new option in reducing cell damage in postischemic myocardial and cerebral tissues.

Abstract

IMPLICATIONS: Infusion of hypertonic-hyperoncotic solutions (HHS) after successful cardiopulmonary resuscitation in pigs significantly reduced the release of cardiac troponin I and cerebral protein S-100, which are sensitive and specific markers of cell damage. Treatment with HHS may provide a new option to improve the outcome of cardiopulmonary resuscitation.

LOE 6. Porcine study.

Good. Neutral.

N=16. Randomized and blinded study, pigs were given either 125ml of 0.9% NaCl or 125ml of 7.2%NaCl with 10% hydroxyethyl starch both infusions given at 12.5ml/min. No group did not receive any fluids.

No differences in haemodynamic variables between groups. Protein s-100 (seen with brain tissue injury) and cardiac troponin I both increased in all groups, but the increase was less in the groups treated with the hypertonic fluid.

Hypertension with hemodilution prevents multifocal cerebral hypoperfusion after cardiac arrest in dogs.

[Leonov Y](#), [Sterz F](#), [Safar P](#), [Johnson DW](#), [Tisherman SA](#), [Oku K](#). Stroke. 1992;23(1):45-53.

Source

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Abstract

BACKGROUND:

Improved neurological outcome with postarrest hypertensive hemodilution in an earlier study could be the result of more homogeneous cerebral perfusion and improved O₂ delivery. We explored global, regional, and local cerebral blood flow by stable xenon-enhanced computed tomography and global cerebral metabolic metabolism in our dog cardiac arrest model.

METHODS:

Ventricular fibrillation cardiac arrest of 12.5 minutes was reversed by brief cardiopulmonary bypass, followed by life support to 4 hours postarrest. We compared control group I ($n = 5$; mean arterial blood pressure, 100 mm Hg; hematocrit, greater than or equal to 35%) with immediately postarrest reflow-promoted group II ($n = 5$; mean arterial blood pressure, 140-110 mm Hg; hypervolemic hemodilution with plasma substitute to hematocrit, 20-25%).

RESULTS:

After initial hyperemia in both groups, during the "delayed hypoperfusion phase" at 1-4 hours postarrest, global cerebral blood flow was 51-60% of baseline in group I versus 85-100% of baseline in group II (p less than 0.01). Percentages of brain tissue voxels with no flow, trickle flow, or low flow were lower (p less than 0.01) and mean regional cerebral blood flow values were higher in group II (p less than 0.01). Global cerebral oxygen uptake recovered to near baseline values at 3-4 hours postarrest in both groups. Postarrest arterial O₂ content, however, in hemodiluted group II was 40-50% of that in group I. Thus, the O₂ uptake/delivery ratio was increased (worsened) in both groups at 2-4 hours postarrest.

CONCLUSIONS:

After prolonged cardiac arrest, immediately induced moderate hypertensive hemodilution to hematocrit 20-25% can normalize cerebral blood flow patterns (improve homogeneity of cerebral perfusion), but does not improve cerebral O₂ delivery, since the flow benefit is offset by decreased arterial O₂ content. Individualized titration of hematocrit or hemodilution with acellular O₂ carrying blood substitute (stroma-free hemoglobin or fluorocarbon solution) would be required to improve O₂ uptake/delivery ratio.

LOE 3. Canine study.**Fair. Neutral.****N=10**

Cardiopulmonary bypass post-arrest. Epinephrine/norepinephrine was used to maintain meant arterial blood pressure of 100mmHg in group 1 and 140/130/120/110 reducing by hour in group 2. Group 1 had bypass of 15ml/kg so hematocrit was >35%. Group 2 had 50ml/kg IV dextran 40 in 0.9% NaCl while 35 ml/kg of blood was removed, equaling a hematocrit of 20-25% until blood was reinfused after 2 hours.

Neurologic outcome: cerebral blood flow 1-4 hours post-arrest 21-60% in group 1 compared to 85-100% in group 2.

Assessment of intravascular volume by transthoracic echocardiography during therapeutic hypothermia and rewarming in cardiac arrest survivors.

[Nordmark J](#), [Johansson J](#), [Sandberg D](#), [Granstam SO](#), [Huzevka T](#), [Covaciu L](#), [Mörtberg E](#), [Rubertsson S](#). Resuscitation. 2009. 80:1234-1239.

Source

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Abstract**AIM:**

To study haemodynamic effects and changes in intravascular volume during hypothermia treatment, induced by ice-cold fluids and maintained by ice-packs followed by rewarming in patients after resuscitation from cardiac arrest.

MATERIALS AND METHODS:

In 24 patients following successful restoration of spontaneous circulation (ROSC), hypothermia was induced with infusion of 4 degrees C normal saline and maintained with ice-packs for 26 h after ROSC. This was followed by passive rewarming. Transthoracic echocardiography was performed at 12, 24 and 48 h after ROSC to evaluate ejection fraction and intravascular volume status. Central venous pressure (CVP), central venous oxygen saturation (ScvO(2)) and serum lactate were measured. Fluid balance was calculated.

RESULTS:

Twelve hours after ROSC, two separate raters independently estimated that 10 and 13 out of 23 patients had a decreased intravascular volume using transthoracic echocardiography. After 24 and 48 h this number had increased further to 14 and 13 out of 19 patients and 13 and 12 out of 21 patients. Calculated fluid balance was positive (4000 ml the day 1 and 2500 ml day 2). There was no difference in ejection fraction between the recording time points. Serum lactate and ScvO(2) were in the normal range when echocardiography exams were performed. CVP did not alter over time.

CONCLUSIONS:

Our results support the hypothesis that inducing hypothermia following cardiac arrest, using cold intravenous fluid infusion does not cause serious haemodynamic side effects. Serial transthoracic echocardiographic estimation of intravascular volume suggests that many patients are hypovolaemic during therapeutic hypothermia and rewarming in spite of a positive fluid balance.

LOE 6. Human study.**Fair. Neutral.****N=24, no control group that did not receive fluids****30ml/kg 4C saline for hypothermia.**

Serial echocardiogram, CVP, central venous saturation and lactate. The study group was generally intravascularly depleted post ROSC and fluid may be beneficial.

No detrimental effects of fluids given during cooling and rewarming.

Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest.

[Sunde K](#), [Pytte M](#), [Jacobsen D](#), [Mangschau A](#), [Jensen LP](#), [Smedsrud C](#), [Draegni T](#), [Steen PA](#). Resuscitation. 2007;73(1):29-39.

Source

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Abstract**BACKGROUND:**

Mortality among patients admitted to hospital after out-of-hospital cardiac arrest (OHCA) is high. Based on recent scientific evidence with a main goal of improving survival, we introduced and implemented a standardised post resuscitation protocol focusing on vital

organ function including therapeutic hypothermia, percutaneous coronary intervention (PCI), control of haemodynamics, blood glucose, ventilation and seizures.

METHODS:

All patients with OHCA of cardiac aetiology admitted to the ICU from September 2003 to May 2005 (intervention period) were included in a prospective, observational study and compared to controls from February 1996 to February 1998.

RESULTS:

In the control period 15/58 (26%) survived to hospital discharge with a favourable neurological outcome versus 34 of 61 (56%) in the intervention period (OR 3.61, CI 1.66-7.84, $p=0.001$). All survivors with a favourable neurological outcome in both groups were still alive 1 year after discharge. Two patients from the control period were revascularised with thrombolytics versus 30 (49%) receiving PCI treatment in the intervention period (47 patients (77%) underwent cardiac angiography). Therapeutic hypothermia was not used in the control period, but 40 of 52 (77%) comatose patients received this treatment in the intervention period.

CONCLUSIONS:

Discharge rate from hospital, neurological outcome and 1-year survival improved after standardisation of post resuscitation care. Based on a multivariate logistic analysis, hospital treatment in the intervention period was the most important independent predictor of survival.

LOE 6. Human study.

Good. Neutral.

1-3L of ice cold 0.9% NaCl given to induce hypothermia, followed by folume, vasopressors or diuretics to keep parameters at a MAP >65-70, CVP 8-12

Control group did not receive fluids to hypothermia but did receive fluids as standard post ROSC care. Fluid balance in control was +2300 +/-1200, intervention group +3455 +/-1594. Both groups had favourable neurologic outcome and still alive 1 year after discharge. There were more survivors during the intervention period vs the control, however both groups did receive fluids as part of the protocol. No adverse effects noted.