

WORKSHEET for Evidence-Based Review of Science for Veterinary CPR

1. Basic Demographics

Worksheet author(s)

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2. Clinical question:

PA04:

In dogs and cats with ROSC (P), does the institution of mild hypertension via the use of any particular cardio-active drug/vasopressor (I) compared to standard care (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 2009)

1. hypertension
2. resuscitation
3. cardiac arrest
4. outcome
5. vasopressor

1 and 2: 5 relevant hits out of 83 total hits (7.7.2011)

1, 3,4 and 5: 2 additional relevant hits out of 19 total hits (12.7.2011)

1, 3 and 4: 5 additional relevant hits out of 294 total hits (12.7.2011)

Pubmed related citations (Hachimi-Idrissi et al, 2001): 1 additional relevant hit out of 191 total hits (11.7.2011)

-CAB (1910 to Feb 2011)

Report as for Medline

4b. Other sources

-In addition all references of identified articles and in particular the references of relevant review articles will be checked:

-References of 2010 "Circulation" CPR guidelines reviewed: no additional relevant articles

-References of Hachimi-Idrissi (2001): 1 additional relevant hit

-References of Gisvold (1996): 3 additional relevant hits → all abstracts

-References of Müllner (1996): 2 additional relevant hits → all abstracts

-References of Leonov (1992): no additional relevant hits

-References of Sterz (1990): no additional relevant hits

-References of Safar (1996): no additional relevant hits

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

Inclusion criteria

Induction of hypertension in the post-resuscitation period

Exclusion criteria

Reviews, abstracts only, case reports

4d. Number of articles/sources meeting criteria for further review: 8

5. Summary of evidence

Evidence Supporting Clinical Question

Good			Stertz, 1990 D			
Fair			Safar, 1976 D Safar, 1996 D			<i>Hachimi-Idrissi, 2001 D</i>
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						
Fair			Leonov, 1992 E			
Poor						<i>Mullner, 1996 D</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						<i>Angelos, 1994 E</i> <i>Bleyaert, 1980 D</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

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

7. Conclusion

DISCUSSION:

At the moment it is difficult to conclude if induced hypertension after ROSC plays a role in improved neurological outcome. In this review there are only two studies that evaluated hypertension as a singular treatment option with neurological outcome as the endpoint, an experimental study in dogs⁸ and a retrospective study in humans⁵.

- The human study⁵ used a relatively low MAP (100 mmHg) to define hypertension (this was a control value in the dog studies) and did not see a significant difference between groups. In addition, hypertension was not purposefully induced, just retrospectively evaluated. Of note, 5 of the 6 patients with a MAP > 150 mmHg had good neurological outcome.
- The majority of the studies involving induced hypertension were performed in a consistent dog model by what is now the Safar Center for Resuscitation Research. Only one study evaluated hypertension alone⁸, and the other studies included hypertension as part of a cerebral blood flow promotion strategy including mild hemodilution and normocapnia^{4, 6-7}. The use of a cerebral blood promotion strategy (including an obligatory bout of systolic hypertension > 200 mmHg which when not spontaneous was induced with norepinephrine), especially when combined with mild induced hypothermia provided the best neurological outcome in the dog model they developed⁷. Interestingly, all but one dog in the control group of this study achieved this hypertension spontaneously and there was only a significant difference in MAP between groups at 15 minutes after ROSC. Therefore it is not likely that the induction of hypertension was as important as the other therapeutic measures initiated. Cerebral blood flow was also improved with hypertensive hemodilution, but cerebral oxygen delivery was not improved due to a decrease in oxygen content⁴. In the study specifically looking at hypertension⁸, dogs were resuscitated after 12 minutes of arrest using cardiopulmonary bypass. Three groups were studied, a control which received epinephrine during bypass and norepinephrine following bypass to achieve a MAP of 100 mmHg. A second group was given the same treatment but to a MAP of 140 mmHg and a third group received both hypertension and hemodilution. Groups 2 and 3 were maintained at 140 mmHg for the first hour, 130 mmHg for the second hour, 120 mmHg for the third hour and 110 mmHg for the fourth hour and then 100 mmHg thereafter. Group 1 (control) was supposed to remain at 100 mmHg but unintentionally also experienced hypertension due to the investigators' reluctance to administer a hypotensive agent. Therefore the MAP was not significantly different between the groups (100-150 mmHg) except for an initial higher spontaneous reperfusion pressure in groups 2 and 3. Data analysis revealed that the dogs with the best neurological outcome had a brief hypertensive bout with a MAP \geq 200 mmHg just after ROSC.
- In a monkey model², severe repetitive hypertension (increase of MAP with norepinephrine to 150-190 mmHg for 3-5 minute periods repeatedly during the first 48 hours post ischemia) was associated with a worse neurological outcome when compared to the normotensive control group. Further analysis of the data revealed that moderate hypertension (< 160 mmHg) did not seem to worsen neurological outcome. When the authors' reexamined the data, preliminary results concluded that if MAP was raised rapidly to normal levels after ROSC and then maintained at a normal or slightly elevated level, neurological outcome is better when compared to situation where the MAP was raised slowly or was low for prolonged periods after reperfusion.
- In a swine model¹, looking at the effect of norepinephrine induced hypertension on myocardial oxygen use, 9 of 10 animals achieved a spontaneous hypertension bout immediately after ROSC. Induction of

hypertension with norepinephrine for 15 minutes (mean aortic pressure 95 mmHg vs. 73 mmHg in the control group) significantly increased oxygen use in the myocardium

- Increased survival at 7 days after ROSC was seen in a rat model. The treatment group received both mild hypothermia and induced hypertension.³

CONSENSUS ON SCIENCE STATEMENT

Evidence from one experimental study (LOE 3)⁸ in dogs and supported indirectly by two experimental studies in dogs (LOE 3)⁶⁻⁷ indicate that a MAP of greater than 150 mmHg immediately after ROSC may be associated with better neurological outcome. In these studies most animals achieved this hypertension spontaneously. There is no conclusion regarding the use of vasopressor therapy as the only study specifically evaluating this, did not achieve a difference in MAP between the control and experimental groups. Further experimental and clinical trials are needed. Given the evidence, the use of epinephrine or norepinephrine immediately after ROSC to guarantee a hypertensive spike, should be evaluated.

TREATMENT RECOMMENDATION

At this time, no treatment recommendation can be made.

8. Acknowledgement

none

9. Citation list

1. Angelos MG, Ward KR, Beckley PD. (1994). "Norepinephrine-induced hypertension following cardiac arrest: effects on myocardial oxygen use in a swine model." *Ann Emerg Med.* Nov;24(5):907-14.

STUDY OBJECTIVE: Recent studies suggest that norepinephrine-induced hypertension early after cardiac arrest ameliorates cerebral hypoperfusion and improves neurologic outcome. The purpose of this study was to evaluate the effects of early norepinephrine-induced hypertension on postresuscitation myocardial blood flow and oxygen use.

DESIGN: Prospective, controlled laboratory study.

PARTICIPANTS: Ten swine.

INTERVENTIONS: All animals underwent 10 minutes of ventricular fibrillation cardiac arrest followed by 5 minutes of low-flow cardiopulmonary bypass (10 mL/kg.min), norepinephrine (0.12 mg/kg), and defibrillation. Animals then were assigned to a hypertension group (mean aortic pressure, 95 mm Hg) or a control group (mean aortic pressure, 75 mm Hg) by titrating a norepinephrine infusion to attain the prescribed aortic pressure.

RESULTS: Myocardial blood flow, perfusion pressure, and oxygen metabolism were compared between groups at different times using analysis of variance with a post-hoc Tukey test. Groups had similar myocardial blood flow during ventricular fibrillation, total defibrillation energy, and time to restoration of spontaneous circulation. Fifteen minutes after restoration of spontaneous circulation, the hypertension group had significantly elevated myocardial blood flow, 965 +/- 314 mL/min.100 g versus 325 +/- 67 mL/min.100 g in the control group (P < .001), myocardial oxygen consumption of 51.2 +/- 26.9 mL O₂/min.100 g versus 6.4 +/- 3.4 mL O₂/min.100 g (P < .001), and myocardial oxygen extraction of 46% +/- 20% versus 14% +/- 4% (P < .01).

CONCLUSION: In the early resuscitation period, increasing the norepinephrine dose to induce mild hypertension significantly increases oxygen use in the postischemic myocardium.

LOE 6. Opposing. Poor.

Experimental study in swine evaluation the effects of norepinephrine induced hypertension on myocardial oxygen use. Not randomized. Hypertension was defined as a mean aortic pressure of 95 mmHg for 15 minutes after ROSC. The control group was kept with a mean aortic pressure of 75 mmHg. Nine out of the 10 animals (both groups) experienced a spontaneous hypertensive surge (187 mmHg for the five animals in the control group and 168 mmHg for the four animals in the experimental group). Increasing the norepinephrine dose to achieve mild hypertension for 15 minutes was associated with increased oxygen use in the myocardium.

Funding supported by the William H Davis Scholarship Fund for Medical Research and an Emergency Medicine Foundation Research Fellowship

2. Bleyaert A, Safar P, et al. (1980). "Effect of postcirculatory-arrest life-support on neurological recovery in monkeys." Crit Care Med. Mar;8(3):153-6.

The existence of treatable postischemic (PI) changes which influence neurological outcome has been documented by this group before. A global brain ischemia model without cardiac arrest was developed in monkeys. It includes high-pressure neck tourniquet inflation plus hypotension for a reproducible ischemic insult; survival with reproducible neurological deficit (ND) under continuous PI life-support for 7 days with control of extracranial variables; and new ND and histopathological damage scoring systems. Hypoxemia, hypercarbia, hypotension, uremia, sepsis, and other extracranial complications PI in 50 unsatisfactory experiments led to immediate worsening in ND and brain death (ND = 100%) in most of these monkeys. In contrast, all monkeys with the same initial insult, with life-support according to protocol, survived with a 7 day ND of 60% or less. In 46 experiments of seven treatment groups, after 16 or 18 min ischemia, life support was according to protocol for 7 days. The control 1 protocol (spontaneous breathing when feasible) resulted in a mean 7-day ND score of 53% (including quadriplegia). Immobilization with pancuronium and controlled ventilation ameliorate deficit to an ND score of 19% (P less than 0.05) (including quadriparesis); this became control 2 protocol. Immobilization resulted in less neuronal damage in the neocortex. Severe repetitive hypertension worsened ND to 46%, versus 19% in controls (P less than 0.05). In separate series, neither heparinization over 72 hours PI, nor hemodilution to hematocrit 25% with dextran 40, changed final ND significantly from that of their control groups. Histopathological damage scores correlated with ND scores.

LOE 6. Poor. Opposing.

Experimental study in monkeys. Not randomized. Hypertension was defined as raising the MAP 150-190 mmHg for 3 to 5 minute periods repeatedly during the first 48 hours after ROSC. In the control group it was unclear from the methods how the blood pressure was controlled and what the MAP was in comparison. The treated monkeys had a significantly higher 7 day neurological deficit score when compared to the control group. When the authors' reexamined their data, preliminary results concluded that if MAP was raised rapidly to normal levels after ROSC and then maintained at a normal or slightly elevated level, neurological outcome was better when compared to the situation where the MAP was raised slowly or was low for prolonged periods after reperfusion.

Funding through a NIH grant.

3. Hachimi-Idrissi S, Corne L, Huyghens L. (2001). "The effect of mild hypothermia and induced hypertension on long term survival rate and neurological outcome after asphyxial cardiac arrest in rats." Resuscitation. Apr;49(1):73-82.

STUDY OBJECTIVE: we studied the long-term effect of a combined treatment with resuscitative mild hypothermia and induced hypertension on survival rate and neurological outcome after asphyxial cardiac arrest (CA) in rats.

METHODS: 36 male Wistar rats, were randomised into three groups: Group I (n=10): anaesthetised with halothane and N(2)O/O(2) (70/30%) had vessel cannulation but no asphyxial CA; mechanical ventilation was continued to 1 h. Group II (n=13): under the same anaesthetic conditions and vessel cannulation, was subjected to asphyxial CA of 8 min, reversed by brief external heart massage and followed by mechanical ventilation to 1 h post restoration of spontaneous circulation (ROSC). Group III (n=13): received the same insult and resuscitation as described in group II, but in contrast to the previous group, a combination treatment of hypothermia (34 degrees C) and induced hypertension was started immediately after ROSC and maintained for 60 min ROSC. Survival rate and neurological deficit (ND) scores were determined before arrest, at 2 and 24 h, and each 24-h up to 4 weeks after ROSC.

RESULTS: Baseline variables were the same in the three groups. Comparison of the asphyxial CA groups (groups II and III), showed an increased, although not statistically significant, survival rate at 72 h after ROSC in group III, and it became highly significant at 4 weeks after ROSC. The ND scores were the same in both asphyxial CA groups (groups II and III).

CONCLUSIONS: Resuscitative mild hypothermia and induced hypertension after asphyxial CA in rats is associated with a better survival rate. This beneficial effect persisted for 4 weeks after ROSC.

LOE 6. Fair. Supportive.

Experimental study in rats. Randomized. Three groups were studied. Group 1 was a sham group that was only anesthetized. Group 2 was subjected to 8 min asphyxiation and then CPR and group 3 was additionally treated with mild hypothermia and hypertension. Hypertension was defined as a MAP of 140 mmHg for 60 minutes after ROSC using norepinephrine. Group 3 improved survival rate at 72 hours only numerically and survival rate was statistically improved 7 days after the insult.

No comment about funding.

4. Leonov Y, Sterz F, et al. (1992). "Hypertension with hemodilution prevents multifocal cerebral hypoperfusion after cardiac arrest in dogs." *Stroke*. Jan;23(1):45-53.

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 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. Fair. Neutral.

Randomized experimental study in dogs to evaluate the effect of hypertensive hemodilution on cerebral oxygen delivery. Group 1 (control) was given epinephrine after ventricular fibrillation and during cardiopulmonary bypass resuscitation to maintain a MAP of 100 mmHg and then titrated to 100mm Hg with norepinephrine after ROSC throughout the experiment (4 hours post arrest). Group 2 received epinephrine during bypass to achieve a MAP of 140 mmHg and then was given norepinephrine to a MAP of 140 mmHg after ROSC for the first hour, 120 mmHg for the second, 120 for the third and 110 for the fourth hour. Hemodilution was also induced in group 2. In the treatment group cerebral blood flow improved but oxygen delivery did not due to the decrease in oxygen content caused by the hemodilution. Funding through a NIH grant.

5. Müllner M, Sterz F, et al. (1996). „Arterial blood pressure after human cardiac arrest and neurological recovery.” *Stroke*. Jan;27(1):59-62.

BACKGROUND AND PURPOSE: In animal cardiac arrest studies, outcome has been improved by inducing arterial hypertension early after return of spontaneous circulation. The aim of our study was to evaluate whether arterial blood pressure within the first minutes and hours after return of spontaneous circulation influences neurological recovery in human cardiac arrest survivors.

METHODS: Of 136 retrospectively evaluated patients after sudden cardiac death, two groups were defined: group 1, mean arterial blood pressure (MABP) within 5 minutes after return of spontaneous circulation above 100 mm Hg; group 2, MABP of 100 mm Hg or less. Thereafter MABP was measured every 5 minutes until 2 hours after return of spontaneous circulation. The groups were compared in regard to age, sex, in/out of hospital, witnessed/not witnessed, first electrocardiographic rhythm, time from cardiac arrest to beginning of life support and to return of spontaneous circulation, cumulative epinephrine dose administered, and best neurological outcome within 6 months.

RESULTS: In group 1 (n = 54) good neurological recovery was observed in 63% and in group 2 (n = 82) in 55% (chi 2 = 0.87, P = NS). Both groups exhibited comparable baseline values except that time intervals from beginning of life support to return of spontaneous circulation were shorter in group 1. After we controlled for this difference with Spearman's partial rank correlation (rs), there was no association between MABP measured within the first 5 minutes and outcome (rs = -.023; P = NS). Good neurological recovery was independently and directly related to MABP measured during 2 hours after return of spontaneous circulation (rs = .26; P < .01).

CONCLUSIONS: In human cardiac arrest survivors, good functional neurological recovery was independently and positively associated with arterial blood pressure during the first 2 hours after human cardiac arrest but not with hypertensive reperfusion within the first minutes after return of spontaneous circulation.

Level 6. Neutral. Poor.

Retrospective human study. Hypertension was defined as a MAP >100 mmHg which is much lower than what was used in the dog studies (MAP >150 mmHg). Some of dog studies in fact used a MAP > 100 mmHg for their control group. In the discussion the authors' mention this and say that 5 of the 6 patients with a MAP > 150 had a good neurological outcome. The protocol in both groups involved use of low dose dopamine (1.5 mcg/kg/hr) and epinephrine to maintain MAP more than 70 mmHg. No mention of industry funding but did not have access to PDF of this article.

6. Safar P, Stezoski W, Nemoto EM. (1976). "Amelioration of brain damage after 12 minutes' cardiac arrest in dogs." Arch Neurol. Feb;33(2):91-5.

To determine the efficacy of cerebral microcirculation promoting therapy in postischemic brain failure, 11 dogs awakening from methohexital sodium anesthesia were subjected to 12 minutes of reversible circulatory arrest by ventricular fibrillation. Physiological variables were controlled for six hours after resuscitation, and the dogs were observed for seven days. Six dogs without the special postresuscitative therapy did not awaken, and either died within 36 hours or remained comatose for seven days. In five dogs, a combination of the following measures was applied: (1) mean arterial pressure was raised to 150 to 180 mm Hg with norepinephrine for six hours; (2) heparinization; (3) rapid intra-aortic injection of dextran 40 (10 ml/kg body weight); and (4) normovolemic hemodilution with dextran 40 to a hematocrit reading of 25% to 30%. All five treated dogs awakened within 24 hours and appeared normal on the seventh day. Therapy enhanced constriction of pupils and normalization of the electroencephalogram (P less than .05). Postischemic neurological deficit is at least partially due to impaired reperfusion and can be ameliorated or prevented by blood flowing-promoting therapy.

LOE 3. Fair. Supportive

Experimental study in dogs. Not randomized. Hypertension was defined as a MAP between 150 and 180 mmHg for 6 hours after ROSC using norepinephrine. Additionally, the experimental group received heparin, a dextran flush and normovolemic hemodilution. The control group received norepinephrine to a MAP of 80 to 100 mmHg. All 5 dogs in the experimental group survived and were considered neurologically normal by the 7th day. The control group experienced 3 deaths and a significantly higher neurological deficit score.

No funding mentioned.

7. Safar P, Xiao F, et al. 1996. "Improved cerebral resuscitation from cardiac arrest in dogs with mild hypothermia plus blood flow promotion." Stroke. Jan;27(1):105-13.

BACKGROUND AND PURPOSE: In past studies, cerebral outcome after normothermic cardiac arrest of 10 or 12.5 minutes in dogs was improved but not normalized by resuscitative (postarrest) treatment with either mild hypothermia or hypertension plus hemodilution. We hypothesized that a multifaceted combination treatment would achieve complete cerebral recovery.

METHODS: With our established dog outcome model, normothermic ventricular fibrillation of 11 minutes (without blood flow) was followed by controlled reperfusion (with brief normothermic cardiopulmonary bypass simulating low flow and low PaO₂ of external cardiopulmonary resuscitation) and defibrillation at < 2 minutes. Controlled ventilation was provided to 20 hours and intensive care to 96 hours. Control group 1 (n = 8) was kept normothermic (37.5 degrees C), normotensive, and hypocapnic throughout. Experimental group 2 (n = 8) received mild resuscitative hypothermia (34 degrees C) from about 10 minutes to 12 hours (by external and peritoneal cooling) plus cerebral blood flow promotion with induced moderate hypertension, mild hemodilution, and normocapnia.

RESULTS: All 16 dogs in the protocol survived. At 96 hours, all 8 dogs in control group 1 achieved overall performance categories 3 (severe disability) or 4 (coma). In group 2, 6 of 8 dogs achieved overall performance category 1 (normal); 1 dog achieved category 2 (moderate disability), and 1 dog achieved category 3 (P < .001). Final neurological deficit scores (0% [normal] to 100% [brain death]) at 96 hours were 38 +/- 10% (22% to 45%) in group 1 versus 8 +/- 9% (0% to 27%) in group 2 (P < .001).

Total brain histopathologic damage scores were 138 +/- 22 (110 to 176) in group 1 versus 43 +/- 9 (32 to 56) in group 2 (P < .001). Regional scores showed similar group differences.

CONCLUSIONS: After normothermic cardiac arrest of 11 minutes in dogs, resuscitative mild hypothermia plus cerebral blood flow promotion can achieve functional recovery with the least histological brain damage yet observed with the same model and comparable insults.

LOE 3. Supportive. Fair.

Experimental study in dogs. Hypertension was defined as a mandatory systolic peak ≥ 200 mmHg over one to five minutes after ROSC that if not spontaneous was induced with norepinephrine. Thereafter MAP was maintained to 140 mmHg until 4 hours post resuscitation, then 110 mmHg until 20 hours in the experimental group. In addition the experimental group received hemodilution and hypothermia. The control group was maintained with a MAP of 110 mmHg until 20 hours post resuscitation. After ROSC all but one dog (control group) experienced an initial hypertensive bout spontaneously (systolic arterial pressure peaks > 200 mmHg for ≤ 2 minutes). Only at 15 minutes post-resuscitation was there a significant difference in MAP between groups. The experimental group had a significantly better neurological outcome 96 hours after ROSC with 6 of 8 dogs considered normal.

Unsure of funding, but unable to access the PDF of this paper.

8. Sterz F, Leonov Y, et al. (1990). "Hypertension with or without hemodilution after cardiac arrest in dogs." Stroke. 1990 Aug;21(8):1178-84.

We studied blood flow-promoting therapies after cardiac arrest in 18 dogs. Our model consisted of ventricular fibrillation (no blood flow) lasting 12.5 minutes, controlled reperfusion with cardiopulmonary bypass and defibrillation within 5 minutes, controlled intermittent positive-pressure ventilation to 20 hours, and intensive care to 96 hours. Group I (control, n = 6) dogs were reperfused under conditions of normotension (mean arterial blood pressure 100 mm Hg) and normal hematocrit (greater than or equal to 35%). Group II (n = 6) and III (n = 6) dogs were treated with norepinephrine at the beginning of reperfusion to induce hypertension for 4 hours. In addition, group III dogs received hypervolemic hemodilution to a hematocrit of 20% using dextran 40. There were no differences in the time to recovery of electroencephalographic activity among groups. All six group I dogs remained severely disabled; in groups II and III combined, six of the 12 dogs achieved good outcome (p less than 0.01). Some regional histopathologic damage scores at 96 hours were better in groups II and/or III than in group I (neocortex: p less than 0.05 group II different from group I; hippocampus: p less than 0.01 both groups II and III different from group I). Total histopathologic damage scores were similar among the groups. A hypertensive bout with a peak mean arterial blood pressure of greater than or equal to 200 mm Hg beginning 1-5 minutes after the start of reperfusion was correlated with good outcome (p less than 0.01). Our results support the use of an initial bout of severe hypertension, but not the use of delayed hemodilution.

LOE 3. Good. Supportive.

Experimental study in dogs. Randomized.

The dogs were resuscitated after 12 minutes of arrest using cardiopulmonary bypass. Three groups were studied, a control which received epinephrine during bypass and norepinephrine following bypass to achieve a MAP of 100 mmHg. A second group was given the same treatment but to a MAP of 140 mmHg and a third group received both hypertension and hemodilution. Groups 2 and 3 were maintained at 140 mmHg for the first hour, 130 mmHg for the second hour, 120 mmHg for the third hour and 110 mmHg for the fourth hour and then 100 mmHg thereafter. Group 1 (control) was supposed to remain at 100 mmHg but unintentionally also experienced hypertension due to the investigators' reluctance to administer a

hypotensive agent. Therefore the MAP was not significantly different between the groups (100-150 mmHg) except for an initial higher spontaneous reperfusion pressure in groups 2 and 3. Data analysis revealed that the dogs with the best neurological outcome had a brief hypertensive bout with a MAP \geq 200 mmHg just after ROSC.

Funded with a NIH grant.