

# WORKSHEET for Evidence-Based Review of Science for Veterinary CPR

## 1. Basic Demographics

Amelia Munsterman	Date Submitted for review:

## 2. Clinical question:

PA18: In dogs and cats with ROSC after cardiac arrest (P), does maintaining a pH goal with buffers (e.g. NaHCO<sub>3</sub>) (I) compared to no pH control (C), result in improved outcome (O) (survival to discharge and/or 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. Textword searches only (1946 to present, performed on June 27<sup>th</sup> 2011)

1. canine resuscitation
2. feline resuscitation
3. sodium bicarbonate
4. THAM
5. Carbicarb
6. Tribonat
7. buffers

1 and 7: 10 relevant hits out of 64 total hits

2 and 7: no relevant hits

1 and 3: 4 additional hits out of 46 total hits

2 and 3: no additional hits

1 and 4: no additional hits

2 and 4: no additional hits

1 and 5: no additional hits

2 and 5: no additional hits

1 and 6: no additional hits

2 and 6: no additional hits

-CAB (1910 to week 24, 2011) (performed on June 27<sup>th</sup>, 2011)

Report as for Medline same relevant articles. No additions.

### 4b. Other sources

-GOOGLE SCHOLAR (performed on August 5<sup>th</sup> 2010)

Report as for Medline



A = Return of spontaneous circulation  
 B = Survival of event  
*species studies*

C = Survival to hospital discharge  
 D = Intact neurological survival

E = Other endpoint  
*Italics = Non-target*

## Evidence Neutral to Clinical question

<b>Good</b>			<b>Sanders1988</b> (controlled) E-time  <b>Guerci 1986</b> (controlled, random) A, B  <b>Sheikh 1986</b> (controlled, randomized) E-time			
<b>Fair</b>			<b>Blecic 1991</b> (controlled, randomized) A  <b>Minuck 1977</b> (controlled, randomized) A  <b>Bleske 1992,</b> <b>1994</b> (randomized, blinded, controlled) E-time  <b>Bishop 1976</b> (controlled) E-time			
<b>Poor</b>						
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>
<b>Level of evidence (P)</b>						

A = Return of spontaneous circulation  
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*species studies*

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 D = Intact neurological survival

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*Italics = Non-target*

## Evidence Opposing Clinical Question

<b>Good</b>						
<b>Fair</b>						
<b>Poor</b>						
	1	2	3	4	5	6
<b>Level of evidence (P)</b>						

A = Return of spontaneous circulation  
 B = Survival of event  
*species studies*

C = Survival to hospital discharge  
 D = Intact neurological survival

E = Other endpoint  
*Italics = Non-target*

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

Acidosis that develops during CPR may depress myocardial function, and reduce the cardiac response to catecholamines. However, there is belief that buffers can alter coronary hemodynamics, result in myocardial ischemia, and decrease cardiac output. In addition, there have been questions to the fact that while buffer administration results in increased levels of venous PCO<sub>2</sub>, paradoxical intracellular, arterial, and cerebral spinal fluid acidosis may result. Additional complications can include hyponatremia and hyperosmolality.

After a review of the literature, the effects of pH control on ROSC and successful outcomes after CPR is still unclear, due to the small study groups and a lack of documented clinical data in companion animals. Buffers such as THAM, bicarbonate and Carbicarb were shown to increase the arterial and venous pH and correct metabolic acidosis during a CPR event (Bar Joseph 1998, Bleske 1992, 1994, Sanders 1988, 1990, Guerci 1986, Kirlimli 1969, Leong 2001, Minuck 1977). Lactate values however, were unaffected by buffer administration (Bar Joseph 1998). While three studies provided support for the fact that buffers such as Carbicarb and bicarbonate may not change PaCO<sub>2</sub>, and PvCO<sub>2</sub> (Bar Joseph 1998, Bleicic 1991, Sanders 1988), others noted a significant increase in arterial and/or venous PCO<sub>2</sub> (Bleske 1992, 1994, Sanders 1988, Guerci 1986, Leong 2001). In contrast, THAM may result in a lower PaCO<sub>2</sub> and PvCO<sub>2</sub>, but it may also produced a lower serum bicarbonate level. Alkalinization by THAM was not as effective as bicarbonate (Bar Joseph 1998, Minuck 1977), possibly due to reduced arterial and coronary perfusion (Bar Joseph 1998).

In regards to outcome, buffers have been shown to reduce the time to successful ROSC and improve resuscitability in general from ventricular fibrillation (Bar Joseph 1998, Leong 2001, Sanders 1990, Kirlimli 1969, Vukmir 1995). Successful resuscitation was predicted by increased pH and a reduction in base deficit (Bar Joseph 1998). Dogs administered buffers also required significantly fewer defibrillation shocks to attain ROSC (Leong 2001). This may be due to improved mean arterial and coronary perfusion pressures (Vukmir 1995, Leong 2001). Bicarbonate provided the best response in terms of ROSC (Bar Joseph 1998), however these dogs remained comatose until 6 hours post-resuscitation, with only 1 out of twenty showing any higher brain function (Bar-Joseph 1998). Other studies were even less positive, showing no improvement in ROSC or survival (Bleske 1992, Guerci 1986, Minuck 1977, Teluvio 1968). Based on one study, outcome after CPR may be improved by delaying defibrillation after administration of the buffer during CPR to allow for the medication to have an effect on the acidosis (Leong 2001).

Animal models of cardiac arrest should be cautiously interpreted. Some studies performed multiple resuscitation events in the same dogs, which may have reduced the ability to achieve ROSC and compare individual resuscitation events (Bleske 1992, 1994). Ventricular fibrillation may have been unrealistically short (induced for less than 5 minutes without CPR) (Guerci 1986, Bleicic 1991, Bleske 1992, 1994, Teluvio 1968, Minuck 1977, Kirlimli 1969, Bishop 1976), the CPR event brief (Bleske 1992, 1994, Guerci 1986, Minuck 1977, Bishop 1976), or the bicarbonate administered unrealistically early in CPR or even before fibrillation occurred (Bleske 1992, 1994, Sanders 1990, Kirlimli 1969, Minuck 1977, Bishop 1976). Inappropriately

high doses of buffers may also have been used, and if epinephrine was not provided, perfusion pressures and resuscitation rates may both be reduced (Bleske 1992, 1994, Sanders 1988, 1990, Kirlimli 1969). Finally, all studies evaluated used small numbers of normal healthy dogs, precluding extrapolation to the general clinical population.

## **7. Conclusion**

### CONSENSUS ON SCIENCE:

Four studies (LOE 3) noted increased resuscitability in terms of ROSC with buffer administration (Bar Joseph 1998, Vukmir 1995, Leong 2001, Sanders 1990) with improved short term survival. Vukmir et al noted improvement only in dogs treated with bicarbonate after prolonged arrest (15 minutes) while dogs treated after shorter periods of fibrillation (5 minutes) were equivalent to the control. Leong et al was similar, in that all dogs treated with bicarbonate had improved ROSC and survival after 10 minutes of arrest. Improved neurologic outcomes were only assessed in one study, where bicarbonate reduced neurologic deficits in dogs with prolonged arrest but had no effect on brain histology versus a control (Vukmir 1995).

The positive effects of bicarbonate may relate to improved coronary and systemic perfusion pressures noted in the treated dogs (Vukmir 1995, Leong 2001). Improvement in base deficit and pH with buffers also was shown to improve the success of defibrillation (Bar Joseph 1998) and bicarbonate may reduce the number of shocks required for defibrillation (Leong 2001).

As the studies were small and lacked statistical power to detect a true influence on clinical outcomes, it may be concluded that although there is no definite proof of a harmful effect of buffer therapy, there is also no definitive proof of its benefits in regards to ROSC and improved outcome (neurological and discharge from hospital).

## **8. Acknowledgement**

None.

## **9. Citation list**

**Bar-Joseph G., T. Weinberger, et al. (1998). "Comparison of sodium bicarbonate, Carbicarb, and THAM during cardiopulmonary resuscitation in dogs." Crit Care Med 26(8):1397-408.**

### **Abstract:**

Objectives: During cardiopulmonary resuscitation (CPR), elimination of CO<sub>2</sub> was shown to be limited by low tissue perfusion, especially when very low perfusion pressures were generated. It has therefore been suggested that sodium bicarbonate (NaHCO<sub>3</sub>), by producing CO<sub>2</sub>, might aggravate the hypercarbic component of the existing acidosis and thereby worsen CPR outcome. The objectives of this study were to evaluate the effects of CO<sub>2</sub> producing and non-CO<sub>2</sub> producing buffers in a canine model of prolonged ventricular fibrillation followed by effective CPR.

Design: Prospective, randomized, controlled, blinded trial.

Setting: Experimental animal research laboratory in a university research center.

Subjects: Thirty-eight adult dogs, weighing 20 to 35 kg.

Interventions: Animals were prepared for study with thiopental followed by halothane, diazepam, and pancuronium. Ventricular fibrillation was electrically induced, and after 10 mins, CPR was initiated, including ventilation with an FIO<sub>2</sub> of 1.0, manual chest compressions, administration of epinephrine (0.1 mg/kg every 5 mins), and defibrillation. A dose of buffer, equivalent to 1 mmol/kg of NaHCO<sub>3</sub>, was administered every 10 mins from start of CPR. Animals were randomized to receive either NaHCO<sub>3</sub>, Carbicarb, THAM, or 0.9% sodium chloride (NaCl). CPR was continued for up to 40 mins or until return of spontaneous circulation. Measurements and Main Results: Buffer-treated animals had a higher resuscitability rate compared with NaCl controls. Spontaneous circulation returned earlier and at a significantly higher rate after NaHCO<sub>3</sub> (in seven of nine dogs), and after Carbicarb (six of ten dogs) compared with NaCl controls (two of ten dogs). Spontaneous circulation was achieved twice as fast after NaHCO<sub>3</sub> compared with NaCl (14.6 vs. 28 mins, respectively). Hydrogen ion (H<sup>+</sup>) concentration and base excess, obtained 2 mins after the first buffer dose, were the best predictors of resuscitability. Arterial and mixed venous PCO<sub>2</sub> did not increase after NaHCO<sub>3</sub> or Carbicarb compared with NaCl.

Conclusions: Buffer therapy promotes successful resuscitation after prolonged cardiac arrest, regardless of coronary perfusion pressure. NaHCO<sub>3</sub>, and to a lesser degree, Carbicarb, are beneficial in promoting early return of spontaneous circulation. When epinephrine is used to promote tissue perfusion, there is no evidence for hypercarbic venous acidosis associated with the use of these CO<sub>2</sub> generating buffers.

### **Level 3, Good quality (blinded, randomized, controlled study), Supportive.**

Funding: Supported, in part, by grant 184-115 from the Israel Ministry of Defense, grant 184-142 from the Chief Scientist, Israel Ministry of Health, and grant 184-147 from the Technion, Israel Institute of Technology.

#### **Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation. Standardized resuscitation per the ACLS guidelines using manual compressions was applied to compare saline, bicarbonate, Carbicarb and THAM using epinephrine in the resuscitation protocol. Epinephrine was used as well. Sodium chloride, and to a lesser extent Carbicarb, significantly increased resuscitation rates and reduced time to ROSC by half. All animals remained comatose, and only one of 20 that had ROSC regained PLR and corneal reflexes. There was no significant increase in PvCO<sub>2</sub>, suggesting that no tissue accumulation of CO<sub>2</sub> occurred after the administration of CO<sub>2</sub> generating buffers.

**Bishop R.L., M.L. Weisfeldt. (1976). "Sodium bicarbonate administration during cardiac arrest. Effect on arterial pH PCO<sub>2</sub>, and osmolality." 235(5); 506-509.**

#### **Abstract:**

Arterial pH, Pco<sub>2</sub>, and osmolality were determined serially during cardiac resuscitation in patients and in dogs, with and without administration of sodium bicarbonate. These studies demonstrate that (1) in the absence of preexisting acidosis, severe acidosis can be prevented by adequate ventilation alone; (2) sodium bicarbonate administration results in a significant rise in arterial Pco<sub>2</sub>, which parallels the rise in pH despite adequate ventilation; (3) during prolonged

cardiac and resuscitation, there is a rise in arterial osmolality that is accentuated by sodium bicarbonate. These studies suggest that sodium bicarbonate should not be used during resuscitation (1) in the absence of effective hyperventilation or where carbon dioxide removal is inadequate despite adequate ventilation, (2) in repeated doses, without confirmation of substantial acidosis, or (3) when cardiac arrest has been of brief duration and preexisting acidosis is unlikely. These studies also point to the need for a reappraisal of other buffers that do not elevate the arterial Pco<sub>2</sub>.

**Level 3, Fair quality (controlled study), Neutral.**

Funding: Supported by Myocardial Infarction Research Unit contract PH 43, NHLI 67-1444 from the National Heart and Lung Institute, Bethesda, MD.

**Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation and manual compressions. Epinephrine was administered. Arterial pH, PCO<sub>2</sub> and osmolality were all significantly increased by bicarbonate versus controls. ROSC was not evaluated.

**Blecic S. D DeBacker, et al. (1991). "Correction of metabolic acidosis in experimental CPR: a comparative study of sodium bicarbonate, carbicarb, and dextrose." Ann Emerg Med 20(3): 235-8.**

**Abstract:**

**STUDY OBJECTIVE:**

Carbicarb, sodium bicarbonate, and 5% dextrose were compared for effects on resuscitability in a canine model of electromechanical dissociation after ventricular fibrillation.

**DESIGN/INTERVENTIONS:** 21 healthy mongrel dogs were anesthetized with pentobarbital, intubated, and mechanically supported. They were instrumented to measure heart rate, arterial pressure, pulmonary artery pressure, right atrial pressure, cardiac output, and arterial and mixed venous blood gases. The dogs were then subjected to a protocol that consisted of three successive CPR episodes. During each episode they were treated with repeated injections of one of the three substances, randomly chosen. After two minutes of ventricular fibrillation and four minutes of electromechanical dissociation, CPR was started with a thumper (rate, 60; duty cycle, 50%). If recovery was not obtained after five minutes of CPR, 1 mEq/kg carbicarb or sodium bicarbonate or 5 mL D5W was injected in the right atrium. Half the dose of the same substance was injected every five minutes thereafter; 1 mg epinephrine was also injected every five minutes until recovery. Hemodynamic and gasometric evaluations were performed five and 20 minutes after recovery. This later evaluation served as baseline for the next CPR episode.

**MEASUREMENTS AND MAIN RESULTS:**

The duration and success rates of CPR are similar in the three CPR groups. Hemodynamic parameters were also similar during recovery. Bicarbicarb and sodium bicarbonate increased bicarbonate levels and corrected pH in the arterial and mixed venous blood. There was no difference in the blood gas values after carbicarb and sodium bicarbonate.

**CONCLUSION:**

In this model of cardiac arrest, carbicarb was not superior to sodium bicarbonate in the correction of metabolic acidosis during CPR.

**Level 3, Fair quality (randomized, controlled study), Neutral.**

Funding: none listed.

**Key points:**

This was an experimental model of cardiac arrest using defibrillation and electromechanical dissociation in dogs. Each dog served as its own control and all treatments were applied to each of the dogs. A mechanical compressor and ventilator were used. Epinephrine was administered. Endpoints ROSC or lack thereof (death). The success decreased with each successive resuscitation for each dog. CPR resulted in acidosis in all dogs, which was not corrected by bicarbonate or carbicarb. Recovery and PCO<sub>2</sub> was also not affected.

**Bleske B.E., M.S. Chow MS, et al. (1992). "Effects of different dosages and modes of sodium bicarbonate administration during cardiopulmonary resuscitation." Am J Emerg Med 10(6): 525-532.**

**Abstract:**

Systemic acidosis occurs during cardiac arrest and cardiopulmonary resuscitation (CPR). The present study investigated the effect of different modes of sodium bicarbonate administration on blood gas parameters during CPR. Arterial and venous blood gases were obtained during 10 minutes of CPR which was preceded by 3 minutes of unassisted ventricular fibrillation in 36 dogs. Following 1 minute of CPR, the animals received one of four treatments in a randomized and blinded manner: normal saline (NS), sodium bicarbonate bolus dose 1 mEq/kg (B), sodium bicarbonate continuous infusion 0.1 mEq/kg/min (I), and sodium bicarbonate bolus dose (0.5 mEq/kg) plus continuous infusion 0.1 mEq/kg/min (L+I). Eleven dogs completed NS, 8 B, 8 I, and 9 L+I protocol. Following NS infusion, both arterial and venous pH declined consistently over time. Significant differences compared with NS treatment in venous pH were observed at 12 minutes of ventricular fibrillation (L+I, 7.27 +/- 0.05; NS, 7.15 +/- 0.05; B, 7.20 +/- 0.05; I, 7.24 +/- 0.04, each bicarbonate treatment versus NS, and L+I versus B, (P < .05). The B group had an elevated venous PCO<sub>2</sub> (mm Hg) concentration following 6 minutes of ventricular fibrillation compared with NS, L+I, and I groups (81 +/- 14 versus 69 +/- 10 versus 68 +/- 10 versus 71 +/- 8, respectively, (P = .07). Arterial pH and PCO<sub>2</sub> values showed a similar trend as the venous data with the L+I group demonstrating arterial alkalosis (pH > 7.45) at 12 minutes of ventricular fibrillation.

The authors conclude: 1) venous acidosis developed during NS treatment and worsened with duration of CPR; 2) the L+I group showed significantly improved venous pH at 12 minutes of ventricular fibrillation as compared with NS and B but at the expense of arterial alkalosis; 3) the I group also had a greater effect on venous pH than the NS and B groups, but without causing arterial alkalosis at 12 minutes of ventricular fibrillation; and 4) a continuous infusion of sodium bicarbonate may be the most desirable mode of administration for the prevention of venous acidosis during CPR; however arterial alkalosis may occur when an additional small bolus of bicarbonate is administered.

**Level 3, Fair quality (blinded, randomized study), Neutral**

Funding: None listed.

**Key points:**

The researchers used a canine model of cardiac arrest as well as a mechanical chest compressor. Epinephrine was not provided and end tidal CO<sub>2</sub> was not assessed. The endpoint was timed and the dog never recovered from fibrillation. The model showed that pH decreases without bicarbonate, and is more significant in the venous circulation. Bolus are less physiologic and can increase both arterial and venous PCO<sub>2</sub> short term, whereas CRI infusions of buffer did not increase CO<sub>2</sub> concentrations despite increases in venous pH. Arterial alkalosis did occur with the bolus and CRI, possibly reducing tissue oxygenation, therefore the CRI was the best method of the three assessed. However, it is important to note that the study used dogs that had already undergone a resuscitation event, the bicarbonate was administered very early in CPR, and the CPR event was extremely short. PH was altered by bicarbonate, but ROSC and outcome were not assessed.

**Bleske, B.E., T.L. Rice, et al. (1994). "An alternative sodium bicarbonate regimen during cardiac arrest and cardiopulmonary resuscitation in a canine model." *Pharmacotherapy* 14(1): 95-99.**

**Abstract:**

We evaluated the effect of frequent, early bolus administration of low-dose sodium bicarbonate (NaHCO<sub>3</sub>) on blood gas values during ventricular fibrillation and cardiopulmonary resuscitation (CPR) compared with normal saline and standard bolus doses of NaHCO<sub>3</sub>. This was a randomized laboratory investigation involving 13 mongrel dogs and 18 experiments (5 dogs were used in a crossover manner). Each dog underwent 3 minutes of ventricular fibrillation, followed by 15 minutes of CPR. Animals were randomly assigned to one of three treatments administered early in the resuscitation effort: NaHCO<sub>3</sub> 0.5 mEq/kg at 5, 10, and 15 minutes of ventricular fibrillation (SB); NaHCO<sub>3</sub> 1 mEq/kg at 5 minutes and 0.5 mEq/kg at 15 minutes of fibrillation (SB); or 0.9% NaCl 1 ml/kg at 5 minutes and 0.5 ml/kg at 15 minutes of fibrillation (P). A total of 15 experiments were included for analysis. Arterial and venous blood gases were sampled at 4, 8, 13, and 18 minutes of fibrillation. The SB group demonstrated the highest arterial partial pressures of carbon dioxide (pCO<sub>2</sub>) at each sampling point after NaHCO<sub>3</sub>, including the 18-minute sample: 42 +/- 12, 29 +/- 11, and 35 +/- 10 torr for SB, P, and B, respectively. In addition, SB produced arterial alkalemia (pH > 7.45) after NaHCO<sub>3</sub> administration. The arterial pH at 18 minutes of fibrillation for SB, P, and B was 7.46 +/- 0.14, 7.29 +/- 0.07, and 7.41 +/- 0.1, respectively. Similar trends for pCO<sub>2</sub> and pH were observed for venous samples. Early, frequent administration of low-dose NaHCO<sub>3</sub> during CPR is associated with elevated pCO<sub>2</sub> and pH (alkalotic) values that may be potentially detrimental in this setting. It appears that this mode of administration offers no advantage over B with regard to blood gas values during CPR in this canine model.

**Level 3, Fair quality (blinded, randomized controlled study), Neutral**  
Funding: none listed.

**Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation as well as a mechanical chest compressor. Epinephrine was not provided. The endpoint was timed and the dog never recovered from fibrillation. The model showed that bicarbonate does result in alkalemia after the boluses of bicarbonate. PH, however, was not significantly different between

dogs administered buffer and the placebo. Both arterial and venous PCO<sub>2</sub> trended towards an increase after buffer administration, and low dose bicarbonate significantly increased pCO<sub>2</sub>. However, it is important to note that the study used dogs that had already undergone a resuscitation event, the bicarbonate was administered very early in CPR, and the CPR event was extremely short. PH was altered by bicarbonate, but ROSC and outcome were not assessed.

**Guerci A.D., N. Chandra, et al. (1986). "Failure of sodium bicarbonate to improve resuscitation from ventricular fibrillation in dogs." *Circulation* 74(6 Pt 2): IV75-79.**

**Abstract:**

To determine the value of sodium bicarbonate in resuscitation from ventricular fibrillation and the prevention of spontaneous refrillation, sodium bicarbonate (1 meq/kg) or placebo was administered on a random basis to 16 pentobarbital-anesthetized dogs 18 min after the induction of ventricular fibrillation and cardiopulmonary resuscitation. Defibrillation was attempted 2 min after the administration of bicarbonate or placebo. All animals were successfully defibrillated, but three of eight bicarbonate-treated and two of eight control animals died in electromechanical dissociation (p = NS). Spontaneous refrillation occurred in three animals in each group (p = NS). Successful resuscitation was not dependent on treatment, arterial or mixed venous Pco<sub>2</sub>, or arterial or mixed venous pH but correlated strongly with coronary perfusion pressure (p less than .003). Spontaneous refrillation occurred without relation to any identifiable variable. The gradient between diastolic aortic and right atrial pressures was 24 +/- 2 mm Hg in controls and 23 +/- 2 mm Hg in treated animals over the entire 20 min of cardiopulmonary resuscitation (p = NS). However, among animals successfully resuscitated, mean diastolic coronary perfusion pressure averaged 27 +/- 2 mm Hg compared with 20 +/- 1 mm Hg among those dying in electromechanical dissociation (p less than .02). For the final 2 min of resuscitation, after drug administration, these gradients were 31 +/- 2 and 23 +/- 2 mm Hg, respectively (p less than .01). Microsphere determined myocardial perfusion correlated with the diastolic aortic-right atrial perfusion pressure gradient (r = .86) and was 0.43 +/- 0.03 ml/min/g in survivors and 0.22 +/- 0.01 ml/min/g in nonsurvivors (p less than .01). Microsphere determined myocardial perfusion correlated with the diastolic aortic-right atrial perfusion pressure gradient (r=0.86) and was 0.43 +/- 0.03 ml/min/g in survivors and 0.22 +/- 0.01 ml/min/g in nonsurvivors (p<0.01). These data do not suggest a primary role for bicarbonate in the treatment of ventricular fibrillation. Efforts should be made to maximize coronary artery perfusion pressure during cardiopulmonary resuscitation.

**Level 3, Good quality (randomized, controlled study), Neutral**

Funding: Supported by the NHLBI Ischemic Heart Disease SCOR grant 5P50-H: 17655.

**Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation as well as a mechanical chest compressor. Epinephrine was provided. The endpoint was timed and the dogs were defibrillated and resuscitated for ROSC. The dogs were killed 10 minutes after successful resuscitation. Bicarbonate increased venous pH at a dose of 1mEq/kg. The model showed that bicarbonate administered towards the end of a CPR event did not make a difference versus

saline on number of defibrillations to return to normal rhythm, refribrillation events and success of defibrillation.

**Kirlimli B. L.C. Harris, et al. (1969). "Evaluation of Sodium Bicarbonate and Epinephrine in Cardiopulmonary Resuscitation ." Anesthesia Analgesia 48(4): 649-658.**

**Abstract:** None available

**Summary:**

The effect of 2.5 mEq/kg. of sodium bicarbonate, 0.5 mg. of epinephrine, and both combined, administered intravenously during resuscitation from electrically-induced ventricular fibrillation, was investigated in 4 groups of 5 dogs each under controlled conditions. After 5 minutes of cardiac arrest and 4 minutes of cardiopulmonary resuscitation (9 minutes of V.F.), defibrillation by graded D.C. shocks was attempted. Dogs given bicarbonate required less D.C. energy for defibrillation and had significantly better carotid flows during the postresuscitation period.

**Level 3, Fair quality (controlled study), Positive.**

Funding: None stated.

**Key points:** The researchers used a canine model of cardiac arrest as well as a mechanical chest compressor/ventilator. Comparisons were made between resuscitation with 1) saline, 2) saline and epi 3) bicarbonate and saline, and 4) bicarbonate and epinephrine. Bicarbonate was administered early and epinephrine was provided. defibrillation was attempted one minute after epi and two minutes after bicarbonate. The process was repeated if ROSC was present for 30 minutes. Bicarbonate reduced the minimum shock energy for defibrillation. It also improved success of defibrillation. Only the dogs administered epinephrine and bicarbonate were 100% successful for ROSC for all 3 fibrillation events. Bicarbonate also improved carotid artery perfusion. PH was also normalized short term in dogs receiving bicarbonate after successful defibrillation, versus those that did not. The one drawback is the small sample size, and the repetition of the experimental protocol up to three times in the same dogs.

**Leong E.C., J.C. Bendall JC, et al. (2001). "Sodium bicarbonate improves the chance of resuscitation after 10 minutes of cardiac arrest in dogs." Resuscitation 51(3)L 309-315.**

**Abstract:**

The likelihood of successful defibrillation and resuscitation decreases as the duration of cardiac arrest increases. Prolonged cardiac arrest is also associated with the development of acidosis. These experiments were designed to determine whether administration of sodium bicarbonate and/or adrenaline in combination with a brief period of cardiopulmonary resuscitation (CPR) prior to defibrillation would improve the outcome of prolonged cardiac arrest in dogs. Ventricular fibrillation (VF) was induced by a.c. shock in anaesthetised dogs. After 10 min of VF, animals received either immediate defibrillation (followed by treatment with bicarbonate or control) or immediate treatment with bicarbonate or saline (followed by defibrillation). Treatment with bicarbonate was associated with increased rates of restoration of spontaneous circulation. This was achieved with fewer shocks and in a

shorter time. Coronary perfusion pressure was significantly higher in NaHCO<sub>3</sub>-treated animals than in control animals. There were smaller decreases in venous pH in NaHCO<sub>3</sub>-treated animals than in controls. The best outcome in this study was achieved when defibrillation was delayed for approximately 2 min, during which time NaHCO<sub>3</sub> and adrenaline were administered with CPR. The results of the present study indicate that in prolonged arrests bicarbonate therapy and a period of perfusion prior to defibrillation may increase survival.

**Level 3, Good quality (randomized, blinded, controlled study), Positive.**

Funding: Funding provided by Laerdal Foundation for Acute Medicine, Stavanger, Norway, Michigan Instruments, and Acute Care Systems.

**Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation as well as a mechanical chest compressor/ventilator. ROSC was defined as a blood pressure of 60 mmHg, for 10 min, and survival was a ROSC for 30 minutes. ROSC and survival were higher in bicarbonate treated animals and was attained quicker than untreated dogs when treated before defibrillation. Fewer shocks were required for ROSC. Coronary perfusion pressure were also higher in bicarbonate treated animals. Venous PCO<sub>2</sub> did increase significantly if bicarbonate was provided. One drawback was that neurological outcome was not assessed.

**Minuck M., G.P. Sharma. (1977). Comparison of THAM and sodium bicarbonate in resuscitation of the heart after ventricular fibrillation in dogs. *Anesthesia and Analgesia* 56(1) 38-45.**

**Abstract:**

Tris (hydroxymethyl) aminomethane (tromethamine or THAM) has been suggested as an effective substitute for sodium bicarbonate (NaHCO<sub>3</sub>) in the treatment of metabolic acidosis accompanying cardiac arrest. Even though several reports on its appraisal have been published, there is still no clear agreement on its therapeutic value. A double-blind study was therefore undertaken to compare in 36 dogs the effectiveness of 0.6 M THAM, 0.3 M THAM, and NaHCO<sub>3</sub> (0.892 mEq/ml) to correct metabolic acidosis produced during 3 minutes of cardiac fibrillation, followed by a 3-minute period of cardiac compression. The dogs were then defibrillated and observed for 45 minutes. One group of 8 dogs was treated with 0.9 percent NaCl infusion. Compared with 0.9 percent NaCl, both THAM and NaHCO<sub>3</sub> were equally effective in correcting metabolic acidosis (p less than 0.05). Initially, 0.6 M THAM produced a more pronounced (p less than 0.05) elevation of blood pH, but this effect was not sustained during the later post defibrillation period. There was little difference in the effect of either of these drugs on mean aortic pressure and total peripheral vascular resistance. It is concluded that adequate ventilation and effective cardiac compression are still the chief criteria on which the final outcome of cardiac resuscitation depends. Correction of metabolic acidosis is important supportive therapy, but either THAM or NaHCO<sub>3</sub> can be used with comparatively equivalent effect.

**Level 3, Fair quality (randomized, blinded, controlled study), Neutral**

Funding: Supported in part by the Department of National Health and Welfare (Grant for project #606-7-135), the St . Boniface General Hospital, Winnipeg, Manitoba, and Abbott Laboratories (Canada) Ltd.

**Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation, as well as internal defibrillation and massage. The study continued for 40 minutes and all animals recovered from ventricular fibrillation. There was no difference in rates of ROSC for any buffer compared to the controls. Both THAM and bicarbonate significantly increased arterial pH, and base excess, but did not change hemodynamic parameters. One drawback is the short duration of the CPR and fibrillation events, since acidosis was not allowed to occur prior to treatment.

**Sanders AB, C.W. Otto, et al. (1988). “Acid-base balance in a canine model of cardiac arrest.” *Ann Emerg Med* 17(7): 667-671.**

**Abstract:**

Our study was performed to determine the pattern of arterial, venous, and cerebral spinal fluid (CSF) acidosis in a canine model of cardiac arrest and resuscitation; and the effect of bicarbonate treatment on arterial, venous, and CSF acidosis. Animals were instrumented to sample arterial blood, mixed venous blood, and CSF through a cisternal catheter. Following six minutes of ventricular fibrillation, manual CPR efforts were begun and continued for 30 minutes of cardiac arrest. Arterial, mixed venous, and CS fluids were sampled at baseline, six, 12, 18, 24, 27, and 30 minutes. Ten experimental dogs received sodium bicarbonate (2 mEq/kg) at 20 minutes of cardiac arrest, while ten animals in the control group received no alkali treatment. The experimental group showed a significantly higher arterial (7.79 +/- 0.20 vs 7.46 +/- 0.16 at 30 minutes) and venous pH (7.34 +/- 0.12 vs 7.19 +/- 0.10 at 24 minutes) following bicarbonate administration. This higher pH occurred despite a concomitant increase in arterial (31 +/- 10 vs 19 +/- 9 mm Hg at 27 minutes; 31 +/- 9 vs 10 +/- 8 at 30 minutes) and venous (104 +/- 30 vs 63 +/- 10 mm Hg at 24 minutes) pCO<sub>2</sub>. CSF analysis showed a gradually worsening acidosis. However, CSF pH (7.12 +/- 0.14 vs 7.16 +/- 0.23 at 30 minutes) and pCO<sub>2</sub> were not significantly changed by the administration of bicarbonate.

**Level 3, Good quality (controlled study), Neutral.**

Funding: None listed.

**Key points:**

The researchers used a canine model of cardiac arrest followed by manual compressions for CPR. Epinephrine was not provided. The endpoint was timed and the dog never recovered from fibrillation. The model showed that venous pH increases with bicarbonate bolus. Bicarbonate increased both arterial and venous PCO<sub>2</sub> short term, whereas CSF fluid was not changed.

**Sanders A.B., K.B. Kern, et al. (1990). “The role of bicarbonate and fluid loading in improving resuscitation from prolonged cardiac arrest with rapid manual chest compression CPR.” *Ann Emerg Med* 19(1): 1-7.**

**Abstract:**

Rapid manual chest compression (120 compressions/min) CPR has been shown to improve hemodynamics and survival when compared with standard CPR (60 compressions/min) in a canine model of prolonged cardiac arrest. The study showing improved survival with rapid manual CPR empirically included treatment with bicarbonate and initial fluid loading. To determine the role of bicarbonate and fluid loading in the success of rapid manual chest compression CPR, 31 mongrel dogs were studied. After instrumentation with micromanometer-tipped catheters to measure aortic and right atrial pressures, the animals were assigned sequentially to three treatment groups. Group A underwent rapid manual chest compressions at 120 compressions/min, bicarbonate treatment, and initial fluid loading. Group B underwent rapid manual compressions at 120 compressions/min without bicarbonate or fluid loading. Group C underwent standard CPR at 80 compressions/min with bicarbonate and fluid loading. After 30 minutes of ventricular fibrillation, defibrillation was attempted. Seven of 11 dogs in group A survived 24 hours. None of the animals in group B resuscitated or survived. Three of the ten dogs in group C survived 24 hours. Survival with rapid manual CPR without bicarbonate and initial fluid loading was significantly less than when these interventions were used (P less than .01). To examine the separate contribution of bicarbonate and fluid therapy, two additional groups of animals were studied. Fourteen animals (group D) received rapid manual CPR with bicarbonate therapy, and 12 (group E) received rapid manual CPR with fluid loading only. Three of 14 in group D and two of 12 in group E survived 24 hours. This study confirmed the benefit of using rapid manual chest compression CPR compared with standard CPR. However, use of bicarbonate and fluid loading is necessary to achieve improved outcome with rapid manual chest compression CPR.

**Level 3, Fair quality (controlled study), Supportive.**

Funding: Supported by grants from the American Heart Association , Arizona Affiliate, and The Flinn Foundation, Phoenix, Arizona. .

**Key points:**

The researchers used a canine model of cardiac arrest followed by manual compressions for CPR. Epinephrine was not provided. Bicarbonate was provided in small boluses prior to ventricular fibrillation and during CPR. The endpoint was timed and the dogs were defibrillated to provide ROSC. Dogs were monitored for 24 hours afterwards, weaned from mechanical ventilation, and then euthanized. The model showed that bicarbonate and fluid loading to maintain right atrial pressures significantly improved survival with a model of rapid compressions (120/min). Prognosis is better when bicarbonate is combined with fluid resuscitation but fluid loading or bicarbonate alone was not as successful. One drawback was that the dogs were fluid loaded prior to arrest.

**Sheikh A., G. Fleisher, et al. (1986). "Effect of dichloroacetate in the treatment of anoxic lactic acidosis in dogs. Crit Care Med 14(11): 970-973.**

**Abstract:**

Lactic acidosis is seen frequently after severe anoxia and circulatory failure. Because dichloroacetate (DCA) has been shown to be effective in the treatment of lactic acidosis, we studied its effect on lactate levels and pH in arterial and sagittal sinus blood

specimens in a pediatric canine model of anoxic cardiac arrest followed by CPR. Lactate levels rose steadily in all puppies receiving DCA alone (group 1), DCA plus bicarbonate (group 2), bicarbonate alone (group 3), or neither drug (group 4). Arterial and sagittal-sinus lactate levels were in the range of 2 mmol/L during the baseline period, 6 mmol/L after anoxic arrest, and 10 mmol/L after 20 min of CPR. Bicarbonate, but not DCA, significantly raised arterial pH. Neither drug reversed the progression of acidosis in the sagittal sinus; mean pH ranged from 6.85 to 6.92 among the four groups after 20 min of CPR. We speculate that DCA did not decrease lactate levels or raise the pH in either the peripheral circulation or the CNS (sagittal sinus) because of poor perfusion achieved during closed-chest cardiac compression.

**Level 3, Good quality (randomized, controlled study), Neutral.**

Funding: Supported by grants from the American Heart Association , Arizona Affiliate, and The Flinn Foundation, Phoenix, Arizona. .

**Key points:**

The researchers used a canine model of anoxic cardiac arrest followed by mechanical compressions and ventilation for CPR. Epinephrine was not provided. Dogs received a bolus of DCA (100 mg/kg), DCA plus bicarbonate (1 Meq/kg), bicarbonate or nothing at the start of resuscitation. No dog was allowed to recover, and any cardiac activity noted was extinguished with potassium chloride. DCA provided a slight increase in MAP, PaO<sub>2</sub> and hematocrit. Bicarbonate significantly raised pH, but DCA had no effect. Lactate was not altered by any treatment.

**Telivuo, L., T. Maamies, et al. (1968). “Comparison of alkalinizing agents in resuscitation of the heart after ventricular fibrillation.” *Annales Chirurgiae et Gynaecologiae Fenniae* 57: 221-224.**

**Abstract:**

None available.

**Level 3, Poor quality (randomized study), Supportive.**

Funding: None specified.

**Key points:**

The researchers used a canine model of cardiac arrest using an open thoracotomy approach and ventricular fibrillation. All dogs underwent multiple fibrillation events, but the number per dog was random. Sodium bicarbonate, sodium carbonate or THAM were tested as a bolus, but with no consistency in testing and no controls. Half of the THAM treated animals converted spontaneously, but the number of treated events was also double those treated by sodium bicarbonate and almost triple the cases treated with sodium carbonate. In addition, the only non-survivors were those treated with THAM (2/11). All buffers tested had similar effects on acid-base status.

**Vukmir R.B., N.G.Bircher, et al. (1995). “Sodium bicarbonate may improve outcome in dogs with brief or prolonged cardiac arrest.” *Crit Care Med* 23(3): 515-522.**

**Abstract:****OBJECTIVE:**

Despite the absence of outcome evaluation, the use of sodium bicarbonate in cardiac arrest has declined based on advanced cardiac life-support guidelines. The effects of bicarbonate therapy on outcome in a canine model of ventricular fibrillation cardiac arrest of brief (5-min) and prolonged (15-min) duration were examined.

**DESIGN:**

Prospective, randomized, controlled trial.

**SETTING:**

Experimental animal laboratory in a university medical center.

**SUBJECTS:**

Thirty-two adult dogs, weighing 10 to 17 kg.

**INTERVENTIONS:**

The animals were prepared with ketamine, nitrous oxide/oxygen, halothane, and pancuronium. Ventricular fibrillation was then electrically induced and maintained in arrest for 5 mins (n = 12) or 15 mins (n = 20). Canine advanced cardiac life-support protocols were instituted, including defibrillation, cardiopulmonary resuscitation (CPR), and the administration of epinephrine (0.1 mg/kg), atropine, and lidocaine. The bicarbonate group received 1 mmol/kg of sodium bicarbonate initially, and base deficit was corrected to -5 mmol/L with additional bicarbonate, whereas acidemia was untreated in the control group. Cardiopulmonary values were recorded at intervals between 5 mins and 24 hrs, and the neurologic deficit score was determined at 24 hrs after CPR.

**MEASUREMENTS AND MAIN RESULTS:**

The treatment group received an additional 2 to 3 mmol/kg of bicarbonate in the early postresuscitation phase. Compared with controls, the bicarbonate group demonstrated equivalent (with brief arrest) or improved (with prolonged arrest) return of spontaneous circulation and survival to 24 hrs, with lessened neurologic deficit. The acidosis of arrest was decreased in the prolonged arrest group without hypercarbia. Improved coronary and systemic perfusion pressures were noted in the bicarbonate group with prolonged arrest, and the epinephrine requirement for return of spontaneous circulation was decreased.

**CONCLUSIONS:**

The empirical administration of bicarbonate improves the survival rate and neurologic outcome in a canine model of cardiac arrest.

**Level 3, Good quality (blinded, randomized, controlled).**

Funding: Supported, in part, by the Laerdal Foundation for Acute Medicine and the American Heart Association, Western Pennsylvania Affiliate.

**Key points:**

The researchers used a canine model of cardiac arrest using ventricular fibrillation, followed by defibrillation and a mechanical CPR thumper. Epinephrine was administered. Outcome variables of survival and graded neurological deficits were scored by a blinded observer. Survival and return to spontaneous circulation were significantly improved in dogs after prolonged arrest treated with bicarbonate. While neurologic deficits were reduced in the

bicarbonate treated dogs, histologic scores were similar to the controls. While acidosis was reduced by bicarbonate during long arrests, alkalemia, hypoxia and hypercarbia were not noted in either group treated with bicarbonate. Bicarbonate also improved MAP and coronary perfusion pressures after prolonged arrest.