Acid base, electrolyte, glucose, and lactate values during cardiopulmonary resuscitation in dogs and cats

Kate Hopper, BVSc, PhD, DACVECC; Angela Borchers, DVM, DACVIM, DACVECC and Steven E. Epstein, DVM, DACVECC

Abstract

Objective – To report acid base, electrolyte, glucose, and lactate values collected during or immediately after cardiopulmonary resuscitation (CPR) in dogs and cats.

Design – Retrospective study.

Setting – University Teaching Hospital.

Animals – Thirty-two dogs and 10 cats.

Interventions – None.

Measurements and Main Results – Blood gas, electrolyte, glucose, and lactate values measured during CPR or within 5 minutes of return of spontaneous circulation (ROSC) were retrospectively evaluated. The time of blood collection with respect to the occurrence of cardiopulmonary arrest (CPA), the initiation of CPR or ROSC was noted. Forty-two venous blood samples were analyzed, 24 collected during CPR and 18 samples were collected within 5 minutes of ROSC. Metabolic acidosis and hyperlactatemia were evident in all samples in the study while an increased PvCO\(_2\) occurred in 88% of samples collected during CPR and in 61% of samples collected following ROSC. Hyperkalemia occurred in 65% of all cases, decreased ionized calcium was evident in 18%, hypoglycemia was evident in 21% while hyperglycemia was evident in 62%. There was no significant difference in any parameter evaluated between dogs and cats during CPR.

There was no significant difference of any variable measured during the first 15 minutes of CPA versus those measured more than 15 minutes following CPA. When the values measured during the first 5 minutes of ROSC were compared to those measured during CPR, the pH and PvO\(_2\) were significantly lower in the CPR group.

Conclusions – Biochemical abnormalities including metabolic acidosis, hyperkalemia, ionized hypocalcemia, hypoglycemia, and hyperglycemia can be identified during CPR and immediately following ROSC. The therapeutic and prognostic relevance of these changes are yet to be defined and may prove to be useful to guide patient management in the future.


Keywords: hypercapnia, hyperkalemia, hypocalcemia, metabolic acidosis

Introduction

Cardiopulmonary arrest (CPA) is associated with numerous biochemical changes including metabolic acidosis, electrolyte abnormalities, and glucose derangements.\(^1\)\(^\text{-6}\) Evaluation of blood gas, electrolyte, lactate, and glucose concentrations during resuscitation may provide insight as to the cause of the arrest, can have the potential to guide therapy and may have prognostic value.\(^1\)\(^,\)\(^\text{7}\)

Acid base and electrolyte changes during CPA and CPR have been described in several experimental animal studies and a few small groups of human clinical patients. Commonly reported abnormalities include hyperkalemia, metabolic acidosis, hyperlactatemia, and

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>CPA</td>
<td>cardiopulmonary arrest</td>
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<tr>
<td>CPR</td>
<td>cardiopulmonary resuscitation</td>
</tr>
<tr>
<td>ROSC</td>
<td>return of spontaneous circulation</td>
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</tbody>
</table>

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The authors declare no conflicts of interests.

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ionized hypocalcemia. Some studies have suggested that therapy directed toward correcting these abnormalities could improve outcome from CPR. In addition, the degree of elevation of potassium and lactate may reflect the duration of CPA and the likelihood of return of spontaneous circulation (ROSC). No description of biochemical abnormalities occurring during CPA and CPR have been reported to date in clinical veterinary patients. With the advent of rapid point of care testing of acid base balance and electrolytes there may be a useful role for monitoring these parameters during CPR.

The recent RECOVER project identified changes in blood gas and electrolyte values following CPA and CPR as current knowledge gaps in veterinary patients. The aim of this study was to report the acid base, electrolyte, lactate, and glucose values in canine and feline patients during naturally occurring CPA and resuscitation.

Materials and Methods

All naturally occurring small animal CPR episodes that occurred at a veterinary teaching hospital over a 36-month period were enrolled in a prospective study recording details of cause of CPA, CPR techniques performed and outcome. This included emergency room patients, intensive care unit patients, hospitalized animals in the wards, and patients under general anesthesia. Patients with CPA were identified by the presence of the 3 following criteria: unresponsive, absence of effective respiratory efforts (agonal breathing was not considered effective respiratory efforts) and the lack of a detectable pulse or heartbeat.

If a blood sample for blood gas analysis was collected during CPR or in the 5 minutes following ROSC on any of the patients in the prospective study, the timing of the blood sample with respect to CPA, initiation of CPR or ROSC was recorded. The decision to perform blood work was left to the discretion of the supervising clinician and the timing of blood samples was not controlled. This blood work was retrospectively analyzed as it represents a convenience sampling from patients in the prospective study and not an a priori goal of that study. For the purposes of this study, a CPR event was defined to be from the time of detection of CPA until either the time when resuscitation efforts were halted or until 5 minutes after the time of ROSC. In cases in which more than one blood sample during a CPR event was analyzed, the first sample only was included. If an animal experienced more than one CPR event, a single blood sample from each event was included, providing the CPR events occurred more than 24 hours apart.

Heparinized blood samples for pH, PCO₂, PO₂, sodium, chloride, potassium, ionized calcium, lactate, and glucose values were all measured within 5 minutes of sample collection on a point of care machine. Biocarbonate and standard base excess were calculated by the analyzer. All samples were collected anaerobically as whole blood and immediately transferred to 125 μL clinitubes coated with dry, electrolyte balanced heparin, purpose-made for the blood gas machine.

Statistical Methods

Data were tested for normality with Kolmogorov–Smirnov test. The dataset was not found to be normally distributed and descriptive statistics were reported as median with range. A Mann–Whitney-test was used to compare values from samples collected during CPR with samples collected during the first 5 minutes of ROSC. Patients with blood samples collected during CPR were stratified into those that had successful ROSC and a non-ROSC group. Values in these 2 groups as well as the values from the first 5 minutes of ROSC were compared with Kruskal–Wallis with Dunn post-hoc comparison tests. All measured variables during CPR were compared between cats and dogs using the Mann–Whitney U-test.

To look for any effect of time elapsed since CPA, samples were grouped as those taken within 15 minutes of CPA or samples collected greater than 15 minutes after CPA. All measured parameters were compared using a Mann–Whitney U-test. All statistics were performed using a commercially available software package.

Results

A total of 43 patients had blood samples collected during CPR or within 5 minutes of ROSC in the study period. One arterial sample was excluded from the study, leaving 42 venous blood samples for analysis, 24 of which were collected during CPR (8 cats and 16 dogs) and 18 of which were collected within 5 minutes of ROSC (2 cats and 16 dogs). Nineteen of the 42 samples were central venous samples; the rest were collected from peripheral veins.

No animals included in the study had more than one CPR event. Three patients had a second blood sample analyzed during the specified time period; only the first sample was included in analysis. The median (range) body weight of dogs was 11.5 kg (0.5–60 kg) and of cats was 5 kg (4–11 kg). The cause of CPA as determined by the supervising clinician was hypovolemia (n = 11), sepsis (7), hypoxemia (3), hyperkalemia (3), upper airway obstruction (3), brain disease (2), dysrhythmia (2), pericardial effusion (2), anemia (1), diabetic ketoacidosis (1), kidney failure (1), anesthesia related (2), and unknown
Thirty-nine of the 42 animals were successfully endotracheally intubated and ventilated with 100% oxygen. The median ventilation rate was 10/min with a range of 9–30/min. Three animals were not able to be endotracheally intubated at the time of arrest and received no ventilation. All animals received chest compressions; the median chest compression rate was 120/min with a range of 70–160 compressions/min. Thirty-nine animals received atropine, six animals received 1 or more epinephrine doses, and 13 received vasopressin during CPR. Six animals received no fluid administration during CPR beyond that needed to flush in administered drugs. Thirty-three animals were rapidly administered an isotonic crystalloid during resuscitation at a median dose of 25 mL/kg, range of 2–170 mL/kg. Seven animals received hetastarch doses, and 13 received vasopressin during CPR. Six animals received no fluid administration during CPR but the recent veterinary consensus statement on CPR, the RECOVER project recommends venous versus arterial blood sampling. There is some debate regarding the superiority of venous versus arterial blood sampling during CPR but the recent veterinary consensus statement on CPR, the RECOVER project recommends venous blood gas analysis over arterial samples.

Of the samples collected during CPR, the median time from CPA to sample collection was 13.5 minutes with a range of 2–40 minutes. Of the 24 patients with samples collected during CPR, 15 animals attained ROSC and 9 did not. There was no significant difference in any parameter evaluated between dogs and cats during CPR. There were insufficient numbers of samples from cats in the within 5 minutes of ROSC group to perform a comparison with dogs. Of the samples collected during ROSC, the median time from CPA to sample collection was 6 minutes with a range of 5–8 minutes.

Metabolic acidosis and hyperlactatemia were evident in all samples in the study while an elevated PvCO2 occurred in 88% of samples collected during CPR and in 61% of samples collected following ROSC (Table 1). Hyperkalemia was a common abnormality, occurring in 65% of cases (60% of all cases when patients with known preexisting hyperkalemia were excluded), decreased ionized calcium was evident in 18% of cases, hypoglycemia was evident in 21%, while hyperglycemia was evident in 62% (Table 1).

When the values measured during the first 5 minutes of ROSC were compared to those measured during CPR only the pH (P = 0.038) and PvO2 (P = 0.013) were significantly different (Table 1). When the values measured during CPR of patients that did not attain ROSC were compared to those that did attain ROSC, no significant differences were identified (Table 2). There was no significant difference of any variable measured during the first 15 minutes of CPA versus those measured more than 15 minutes following CPA.

On review of the patient records, only 10 of the 42 cases had blood work evaluated within the 10 hours before CPA. As this blood work was collected at variable times and therapy was provided between the time of the blood work and CPA, comparison of these results with those obtained during resuscitation was not performed.

### Discussion

This is the first clinical veterinary study to describe abnormalities in acid base, electrolyte, lactate, and glucose levels in clinical patients during CPA and resuscitation. Despite variability in the timing of the blood samples collected during CPR in this study, in general the abnormalities found were consistent across all samples. A moderate to severe metabolic acidosis was evident in all cases with a concurrent respiratory acidosis present in 88% and hyperkalemia present in 65%. This study only included venous blood samples. There is some debate regarding the superiority of venous versus arterial blood sampling during CPR but the recent veterinary consensus statement on CPR, the RECOVER project recommends venous blood gas analysis over arterial samples.

Metabolic acidosis is an expected abnormality following CPA as a consequence of global ischemia and subsequent lactic acidosis. Lactate maybe further elevated by the administration of epinephrine that increases

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<table>
<thead>
<tr>
<th>Parameter</th>
<th>During CPR (N = 24)</th>
<th>Within 5 minutes of ROSC (N = 18)</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCO2 mm Hg</td>
<td>63.7 (23.5–111)</td>
<td>48.1 (28.3–103)</td>
<td>37–45</td>
</tr>
<tr>
<td>PVCO2 mm Hg</td>
<td>27.4 (11.8–99.6)</td>
<td>48.4* (20.8–160)</td>
<td>30–50</td>
</tr>
<tr>
<td>HCO3 mmol/L</td>
<td>8.9 (3.7–20.7)</td>
<td>10.7 (7.1–18.6)</td>
<td>18–26</td>
</tr>
<tr>
<td>SBE mmol/L</td>
<td>–22.8 (–28.5 to –8.9)</td>
<td>–17.9 (–27 to –8.4)</td>
<td>–3 to 2</td>
</tr>
<tr>
<td>Lactate mmol/L</td>
<td>16 (4–23)</td>
<td>12.8 (4.1–27)</td>
<td>2.0</td>
</tr>
<tr>
<td>Sodium mmol/L</td>
<td>144 (113–171)</td>
<td>150 (130–160)</td>
<td>144–152</td>
</tr>
<tr>
<td>Potassium mmol/L</td>
<td>5.4 (2.6–12.2)</td>
<td>5.3 (2.9–7.7)</td>
<td>3.6–4.7</td>
</tr>
<tr>
<td>i-Ca mmol/L</td>
<td>1.21 (0.68–1.59)</td>
<td>1.3 (1.01–1.54)</td>
<td>1.1–1.5</td>
</tr>
<tr>
<td>Chloride mmol/L</td>
<td>115 (98–149)</td>
<td>117 (99–125)</td>
<td>111–112</td>
</tr>
<tr>
<td>Glucose mg/dL</td>
<td>250 (6–1415)</td>
<td>209 (12–411)</td>
<td>80–120</td>
</tr>
</tbody>
</table>

SBE, standardized base excess; i-Ca, ionized calcium.

*Values significantly different from the during CPR value (P < 0.05).
lactate production by accelerating the rate of glycolysis. The degree of lactate elevation may reflect the effectiveness of the resuscitative efforts. A human clinical study showed no significant change in arterial lactate levels during CPR in patients who ultimately achieved ROSC but there were significant increases in lactate concentration during CPR in patients who did not attain ROSC. Lactate may be a valuable parameter to monitor during CPR but further investigations are needed to better define its role.

Hyperlactatemia ranging from 2 to 12 times the normal value was evident in all the samples evaluated in this study, although lactate concentration measured during CPR was not different in patients that had ROSC compared to those that did not. The variable timing of sample collection during CPR in this study may have prevented any association with ROSC being identified. Many of the blood samples included in this study were collected from a peripheral vein. In healthy dogs there are very small differences between arterial, central venous, and peripheral venous lactate levels. Unfortunately, there have been very few studies evaluating lactate during CPR and most have measured arterial blood lactate. The correlation between arterial and peripheral venous lactate during CPR is unknown. Studies that compared arterial with mixed or central venous lactate concentration and arterial with mixed venous lactate concentration during CPR reported no difference in the values.

An elevated venous PCO\textsubscript{2} was the second most common abnormality found with the median value during CPR of 64 mm Hg and the highest recorded value being 111 mm Hg. The interpretation of venous PCO\textsubscript{2} in CPR may differ than in the usual clinical patient. In the clinical setting, changes in PaCO\textsubscript{2} are generally interpreted as a marker of changes in alveolar minute ventilation. Venous PCO\textsubscript{2} has been shown to correlate closely to arterial PCO\textsubscript{2}, running approximately 4–5 mm Hg higher. In states of low cardiac output, such as hypovolemic shock or CPR, CO\textsubscript{2} accumulates in the tissues and leads to high venous PCO\textsubscript{2} levels, reflecting the low blood flow state, rather than alveolar ventilation. End tidal CO\textsubscript{2} during CPR reflects pulmonary blood flow and as such can be used as a measure of effectiveness of chest compressions. In a manner similar to venous PCO\textsubscript{2}, ETCO\textsubscript{2} is not an accurate measure of alveolar ventilation during CPR. Arterial PCO\textsubscript{2} in low flow states will still reflect alveolar ventilation and the buildup of CO\textsubscript{2} leads to an increase in the arterio-venous PCO\textsubscript{2} gradient. The arterio-venous PCO\textsubscript{2} gradient has been found to correlate to cardiac output in numerous disease states in human medicine including CPR. It is important that venous hypercapnia during CPR is not mistaken for hypoventilation that could prompt rescuers to increase the ventilation rate. Not only would an increased ventilation rate fail to change the magnitude of venous hypercapnia, it has been shown to have negative cardiovascular consequences during CPR.

Venous oxygen levels can be used clinically as a measure of the balance between oxygen delivery and oxygen consumption. Low mixed venous and central venous oxygen levels suggest inadequate oxygen delivery to the tissues and improvements in this value have been found to be excellent end points in shock resuscitation. In the current study, the median partial pressure of venous oxygen (PvO\textsubscript{2}) measured during CPR was 27 mm Hg for all samples and 34 mm Hg when the central venous samples were analyzed separately. These values are similar to that reported in a previous study of human CPR patients. It is not surprising that venous oxygen levels are low during CPR as a consequence of very low oxygen delivery. It is interesting that venous oxygen was significantly higher within 5 minutes following ROSC in this study and likely reflects the rapid improvement in oxygen delivery to the tissues.

In our study venous oxygen was not different in patients with ROSC and those not achieving ROSC. To the authors’ knowledge, there is only 1 study to date that

### Table 2: Median and range of blood gas, electrolyte, glucose, and lactate values of dogs and cats measured during cardiopulmonary resuscitation (CPR) in which return of spontaneous circulation (ROSC) occurred versus those in which it did not. No significant differences were evident between groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>During CPR–ROSC (N = 15)</th>
<th>During CPR–no ROSC (N = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PvCO\textsubscript{2} mm Hg</td>
<td>72.8 (26.2–111)</td>
<td>51.3 (23.5–94.7)</td>
</tr>
<tr>
<td>PvO\textsubscript{2} mm Hg</td>
<td>27.4 (11.8–99.6)</td>
<td>29.9 (14.8–56.2)</td>
</tr>
<tr>
<td>HCO\textsubscript{3} mmol/L</td>
<td>8.7 (4.5–20.7)</td>
<td>9.0 (3.7–17.9)</td>
</tr>
<tr>
<td>SBE mmol/L</td>
<td>–23.2 (–27.0 to –9.1)</td>
<td>–22.7 (–28.5 to –8.9)</td>
</tr>
<tr>
<td>Lactate mmol/L</td>
<td>13.6 (4–23)</td>
<td>17.5 (7.1–21)</td>
</tr>
<tr>
<td>Sodium mmol/L</td>
<td>145 (131–160)</td>
<td>142.5 (113–171)</td>
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<td>Potassium mmol/L</td>
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<td>i-Ca mmol/L</td>
<td>1.26 (0.68–1.59)</td>
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<td>Chloride mmol/L</td>
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<td>116 (98–149)</td>
</tr>
<tr>
<td>Glucose mg/dL</td>
<td>351 (6–875)</td>
<td>157 (29–1,415)</td>
</tr>
</tbody>
</table>

SBE, standardized base excess; i-Ca, ionized calcium.

mental studies of ventricular fibrillation induced cardiac and subsequent potassium efflux from cells. CPR, hyperkalemia occurs as a result of global ischemia potassium level during resuscitation. During CPA and during the resuscitation period and one had a normal prior to arrest; 2 of these had hyperkalemia recorded animals in this study were known to have hyperkalemia sis will impact serum potassium concentration. intracellular shifts of potassium, but respiratory acido-
vvelops during CPR may also exacerbate hyperkalemia. The remaining 7 patients had hypoglycemia as a result of their underlying disease. Interestingly, most of these patients achieved ROSC, including two dogs with a blood glucose less than 20 mg/dL (1.1 mmol/L). In human patients, hypoglycemia occurring during the 24 hours following CPR is associated with decreased odds of survival, although the influence of hypoglycemia on the likelihood of ROSC has not been evaluated.

Unlike hypoglycemia, hyperglycemia is expected during resuscitation as a result of the effects of endogenous and exogenous catecholamines. In an experimental canine study of ventricular fibrillation, blood glucose increased from normal levels prearrest to a mean of 232 mg/dL (12.9 mmol/L) after 8 to 12 minutes of CPR. Of the 42 animals in this study, 62% had hyperglycemia, excluding 4 patients that received exogenous dextrose therapy. Human studies have shown that hyperglycemia following ROSC can be detrimental to outcome and recommendations for glucose control have been made although the optimal strategy for glucose management is unknown. Further studies are needed to determine if there is a role for glucose control in the post-CPR veterinary patient.

This study has many limitations, the first being the relatively small number of samples included. Because of these low numbers, a difference between ROSC and non-ROSC groups may have existed, but could not be documented in our study. In addition these samples were collected in clinical cases as deemed indicated by the supervising clinician so the timing of the samples was variable. Blood sample collection during CPR was more likely to be performed in cases with longer CPR periods because the first few minutes of CPR are focused on basic and advanced life support procedures. Monitoring efforts such as blood sample evaluation are more likely to be performed later in the resuscitation period. If there is not rapid ROSC further evaluation such as blood sample evaluation maybe considered. As a result, the CPR group in this study may represent patients that are less likely to have a successful CPR than those in the ROSC group. This concern is supported by the difference in the
time between CPA and blood sample collection. Further, prearrest blood work was not available for comparison. Sequential blood samples at defined time points in individual patients during and after CPR would be an ideal design for a future prospective study.

Obtaining a blood sample during CPR is often challenging and venous blood samples are more likely to be available than arterial samples. Although the therapeutic and prognostic relevance of many of the changes that can occur during resuscitation is unknown, marked abnormalities such as hypoglycemia and hypocalcemia may warrant directed therapy. It is important to note that marked hyperkalemia can occur during CPR in animals that were normokalemic prior to CPA.

Conclusions

Further studies are required to better define the role of venous blood gas, electrolyte, glucose, and lactate monitoring during CPR in canine and feline patients. Specifically, research to determine the potential for venous oxygen, potassium, and lactate concentrations to be predictive of ROSC or survival, the clinical relevance of hyperkalemia that develops during CPR and the role of glucose monitoring in the CPR and postresuscitation patient is needed.

Footnotes

- ABL 705, Radiometer Medical A/S, Copenhagen, Denmark.
- GraphPad Prism 3.0, Graph Pad Software, La Jolla, CA.
- Atropine sulfate, 0.4 mg/mL, West-Ward, Eatontown, NJ.
- Epinephrine, 1:1000, IMS Ltd, El Monte, CA.
- Fitepressin, JHP Pharmaceuticals, Rochester, MI.
- Hetastarch (625/0.75) in 0.9% NaCl, Hospira, Lake Forest, IL.

References


