Original Article

The Effect of Electrolyte Imbalance on Weaning from Cardiopulmonary Bypass: An Experimental Study

Alfred H. Stammers, MSA, CCP; Nancy Mills, MPS, CCP; Scott A. Kmiecik, MPS, CCP; Craig M. Petterson, MPS, CCP; Jun-Li Liu, MD, PhD, CCP; Jeffery D. Nichols, MPS, CCP; Ryan J. Kohtz, MPS, CCP; Hong Zheng, MD; Lynette M. Hock, MS

Abstract: An imbalance in electrolyte concentration during separation from cardiopulmonary bypass (CPB) may lead to a disruption in excitation–contraction coupling resulting in a failure to wean. The etiology of myocardial dysfunction is multifactorial, and includes alterations in acid-base balance, glucose metabolism, and cellular function. The purpose of this study was to assess the effect of hyperkalemia on myocardial function during separation from CPB. A porcine model (n = 5) of hypothermic (32°C) CPB was used where hyperkalemia [K+ (6.5 ± 1.0)] was created before weaning. A 3-minute weaning process was initiated once normothermia was achieved. Mixed venous and arterial samples were obtained during CPB, weaning, and 10 minutes postbypass. Samples were assayed for [K+], [Ca++], glucose, pH, CPK-MB, and lactic acid levels. Hyperkalemia resulted in the generation of severe arrhythmias in all animals. During the immediate prewean period, there was a significant correlation between venous [K+] and pH (p < .01, r^2 = .891). Arterial pH did not change during the weaning or post-CPB period, while venous pH declined significantly throughout the same period (7.35 ± 0.75 to 7.20 ± 0.17, p < .05). No other measured variables correlated with hyperkalemia. In summary, hyperkalemia caused a significant decline in venous pH evidenced in the early separation period, but had no effect on other variables. Therefore, measurement of venous pH may be an early marker indicating myocardial dysfunction and dysrhythmia. Keywords: hyperkalemia, cardiopulmonary bypass, weaning.
MATERIALS AND METHODS

Animal Protocol
The research protocol was approved by the Institutional Animal Care Utilization Committee at the University of Nebraska Medical Center (UNMC). All five porcine subjects used in this study received humane care in compliance with the Guide for the Care and Use of Laboratory Animals as published by the National Institutes of Health (NIH Publication No. 85-23).

All procedures were conducted as acute studies. The swine were anesthetized with a mixture of ketamine (20 mg/kg) and xylazine (2 mg/kg) given intramuscularly. Electrocardiogram leads were placed, and the rhythm and rate were continuously monitored. Each subject was intubated with a 6.5 F endotracheal tube and ventilated with a tidal volume (20–30 mL/kg) at a rate of 15–20 breaths per minute. The femoral vein and artery were cannulated with 14-gauge needles. The subjects were intermittently dosed with pentothal (100 µg/kg) and pavulon (50 µg/kg). Before the midline sternotomy, bretylium (3 mg/kg) was administered.

A midline sternotomy was performed, and a bolus dose of 300 iu/kg of bovine lung heparin was administered. Purse string sutures were placed in the aorta and right atrial appendage. A 7.0-mm soft flow arterial cannula was placed in the aorta, and a dual stage 29/37 F venous cannula was placed in the atrial appendage.

Cardiopulmonary Bypass
Once an adequate ACT (> 480) was reached, the subjects were placed on CPB. The experimental period lasted approximately 120 minutes. A standard ECC was used that consisted of a hollow five membrane oxygenator, an soft-shell reservoir, a hard-shell cardiotomy reservoir, a 40-micron arterial line filter, polyvinylchloride tubing, and a centrifical biohead pump.

The circuit was primed with 1200 mL of Plasmalyte-A, 50 mL of 8.4% sodium bicarbonate (1 mEq/mL), and 2500 iu/L of bovine lung heparin. Upon the initiation of bypass, the perfusate temperature was decreased to and maintained at 32°C throughout the procedure up until rewarming was initiated.

Each subject was maintained within normal physiologic and hemodynamic parameters. The mean arterial blood pressure (50–80 mmHg) was maintained, if intervention was necessary, with pharmacological agents [neosynephrine (80 µg/mL) or sodium nitroprusside (200 µg/mL)]. The following variables were also controlled within normal parameters: central venous pressure (0–8 mmHg), arterial acid-base management (pH 7.35–7.45), PaCO2 (100–150 mmHg), HCO3 (22–26 mmol), anticoagulation (ACT > 480s) and hematocrit (20–25%). In line arterial and venous blood gas monitors were used. Arterial and venous blood gases, mixed venous saturations, electrocardiogram, and hemodynamics were continuously measured.

At the termination of each experiment, the animal was euthanized after the last blood sample was obtained. Barbiturate (1 mg/kg) and potassium chloride (20 mEq) were directly administered into the aortic root. The ventilator was turned off, and the endotracheal tube was removed.

Experimental Protocol
All five subjects were treated with the same protocol. Each subject was placed on a potassium drip 30 minutes before the termination of bypass. The dose of potassium was calculated according to the measured potassium utilizing the following equation for [K+] correction:

\[
\text{Additional K}^+ = \frac{(\text{kg BW} \times 0.3) \times [6.5\text{-measured (K+)]}}{2}
\]

Potassium measurements were taken every 15 minutes before rewarming and every 10 minutes during the rewarming process. Additional doses of potassium chloride were given until a potassium level of 6.5 ± 1.0 was maintained for at least 5 minutes before the weaning process.

Blood Sample Collection
Blood samples were drawn from the left ventricle and femoral artery catheter. Samples were drawn simultaneously every 15 minutes before rewarming, every 10 minutes during rewarming, at 0,1,2, and 3 minutes during the weaning period and then at 1,3,5,7, and 10 minutes post bypass. All samples were assayed for acid-base status, calcium, glucose, and potassium levels. Electrical activity was monitored throughout, and strip recordings were printed during each sample period.

Statistical Analysis
All data were recorded and entered into a computer database. Arterial and venous measurements of potassium, pH, glucose, and calcium were made on the five subjects at various time points, Pre-CPB, CPB before rewarming, rewarming, weaning, and post-CPB. Potassium was administered before and during the rewarming period. The weaning period included three different measurements, and the post-CPB period contained five different measurements. The three wean measurements and five post-CPB measurements were averaged within each pig, giving one measurement at each time point for each pig.

Spearman’s rank-order correlation, a nonparametric measure of correlation, was used to assess the relationship of potassium levels with pH, glucose, and calcium levels at each time point. The Wilcoxon signed rank test was used to test for a change in the measures from rewarming to the final post-CPB measurement.
RESULTS

Spearman’s rank-order correlation was used to assess the relationship of potassium levels with pH, glucose, and calcium at four time points, CPB, rewarming, weaning, and post-CPB. Arterial potassium levels were poorly correlated with arterial pH, glucose, and calcium at all time points. Venous potassium levels were highly correlated with venous pH during the rewarming period ($r = -0.975, p = .005$), and the post-CPB period ($r = -0.900, p = .037$). Venous potassium levels were also highly correlated with venous glucose levels during the rewarming period ($r = -0.900, p = .037$). The venous potassium levels were poorly correlated with venous pH at CPB and weaning periods, glucose at CPB, rewarming and weaning periods, and calcium at all time periods. The means and standard deviations for the measures are given in Tables 1 and 2. The correlations and $p$ values of potassium with pH, glucose, and calcium are found in Tables 3 and 4.

Wilcoxon signed rank test showed no significant change in measured potassium, pH, glucose, or calcium levels from the rewarming period to the final post-CPB measurement.

DISCUSSION

Disruptions in the excitation–contraction-coupling leading to arrhythmias during the perioperative period may occur for several reasons. Early indicators of these arrhythmias could possibly enable clinicians to treat or correct the underlying problem before weaning from CPB. In our study, we created a hyperkalemic state that resulted in severe arrhythmias seen in all five subjects. A number of factors influence potassium-shifting leading to hyperkalemia, which include acid-base balance, insulin, epinephrine, aldosterone, catechoamines, plasma osmolality, and drugs (12,13,19,21). During CPB not all of these variables are routinely measured. In this study, the variables observed other than potassium were glucose levels, calcium concentration, and pH for both arterial and mixed venous samples.

During the immediate prewean period, there was a significant correlation between venous [K+] and pH ($p < .01, r^2 = 0.891$). Arterial pH did not change during the weaning or post-CPB period, while venous pH declined significantly throughout the same period ($7.35 \pm 0.75$ to $7.20 \pm 0.17, p < .05$). During the weaning process, previously flow-deprived areas will be washed out carrying lactate and cardioplegic solution high in [K+]. In addition, glycolytic activity is enhanced, leading to the accumulation of lactic acid (21,22). To maintain acid-base balance, hydrogen ions are exchanged for potassium ions across the cell membrane adding to the already high [K+] thus increasing the potential for arrhythmias (21,22). During the study, no other measured variables correlated with hyperkalemia.

In summary, hyperkalemia caused a significant decline in venous pH evidenced in the early separation period of the subjects, but had no effect on other variables. Therefore, measurement of venous pH may be an early marker indicating myocardial dysfunction and dysrhythmia. Unfortunately, intraoperative electrophysiologic identification in study groups can be highly complex and expensive. Consequently, this leads to limitations within this study. In addition, we would have liked to have measured CK-MB, lactate levels, and intracellular [K+] and also included a larger study population with treatment and nontreatment groups.

### Table 1. Arterial means and standard deviations.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Potassium Mean</th>
<th>SD</th>
<th>pH Mean</th>
<th>SD</th>
<th>Glucose Mean</th>
<th>SD</th>
<th>Calcium Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB</td>
<td>4.7</td>
<td>1.24</td>
<td>7.4</td>
<td>0.04</td>
<td>134</td>
<td>75.7</td>
<td>1.1</td>
<td>0.08</td>
</tr>
<tr>
<td>Rewarm</td>
<td>6.3</td>
<td>0.25</td>
<td>7.5</td>
<td>0.01</td>
<td>109</td>
<td>61.7</td>
<td>1.2</td>
<td>0.17</td>
</tr>
<tr>
<td>Wean</td>
<td>6.5</td>
<td>0.23</td>
<td>7.3</td>
<td>0.34</td>
<td>115</td>
<td>71.2</td>
<td>1.3</td>
<td>0.09</td>
</tr>
<tr>
<td>Post CPB</td>
<td>6.9</td>
<td>0.72</td>
<td>7.4</td>
<td>0.11</td>
<td>101</td>
<td>65.5</td>
<td>1.3</td>
<td>0.13</td>
</tr>
</tbody>
</table>

### Table 2. Venous means and standard deviations.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Potassium Mean</th>
<th>SD</th>
<th>pH Mean</th>
<th>SD</th>
<th>Glucose Mean</th>
<th>SD</th>
<th>Calcium Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB</td>
<td>4.8</td>
<td>1.47</td>
<td>7.4</td>
<td>0.09</td>
<td>140</td>
<td>64.6</td>
<td>1.1</td>
<td>0.06</td>
</tr>
<tr>
<td>Rewarm</td>
<td>6.1</td>
<td>0.42</td>
<td>7.4</td>
<td>0.04</td>
<td>113</td>
<td>57.0</td>
<td>1.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Wean</td>
<td>6.7</td>
<td>0.79</td>
<td>7.4</td>
<td>0.06</td>
<td>113</td>
<td>64.1</td>
<td>1.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Post CPB</td>
<td>7.3</td>
<td>0.92</td>
<td>7.2</td>
<td>0.09</td>
<td>100</td>
<td>55.5</td>
<td>1.4</td>
<td>0.08</td>
</tr>
</tbody>
</table>

### Table 3. Arterial correlations with potassium.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>pH</th>
<th>Glucose</th>
<th>Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB</td>
<td>$r = -0.891$</td>
<td>$p = .01$</td>
<td>$r = -0.800$</td>
</tr>
<tr>
<td>Rewarm</td>
<td>$r = 0.316$</td>
<td>$p = .62$</td>
<td>$r = 0.400$</td>
</tr>
<tr>
<td>Wean</td>
<td>$r = 0.300$</td>
<td>$p = .62$</td>
<td>$r = 0.700$</td>
</tr>
<tr>
<td>Post CPB</td>
<td>$r = 0.300$</td>
<td>$p = .62$</td>
<td>$r = 0.700$</td>
</tr>
</tbody>
</table>

### Table 4. Venous correlations with potassium.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>pH</th>
<th>Glucose</th>
<th>Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB</td>
<td>$r = -0.600$</td>
<td>$p = 0.28$</td>
<td>$r = -0.600$</td>
</tr>
<tr>
<td>Rewarm</td>
<td>$r = -0.975$</td>
<td>$p = 0.005$</td>
<td>$r = -0.900$</td>
</tr>
<tr>
<td>Wean</td>
<td>$r = -0.500$</td>
<td>$p = 0.39$</td>
<td>$r = -0.500$</td>
</tr>
<tr>
<td>Post CPB</td>
<td>$r = -0.900$</td>
<td>$p = 0.037$</td>
<td>$r = -0.800$</td>
</tr>
</tbody>
</table>

$r = $ Spearman’s correlation coefficient.
$p = $ probability value.
$n = $ sample size.
REFERENCES


