Arteriovenous carbon dioxide and pH gradients during cardiac arrest

WILLIAM GRUNDLER, M.D., MAX HARRY WEIL, M.D., PH.D., AND ERIC C. RACKOW, M.D.

ABSTRACT In a porcine preparation of cardiac arrest, we demonstrated that there is a marked paradox of venous acidemia and arterial alkalemia. This paradox is related to decreased clearance of CO₂ from the lungs when pulmonary blood flow is critically reduced. Accordingly, increased venous Pco₂ rather than metabolic acidosis due to lactic acidosis predominates during the initial 8 min of cardiopulmonary resuscitation. Arterial blood gases fail as indicators of systemic acid-base status and therefore as indicators of tissue acidosis. Circulation 74, No. 5, 1071-1074, 1986.

THE ACIDEMIA and consequent cellular acidosis that result from cardiopulmonary resuscitation (CPR) have been attributed to critical reduction of oxygen transport function with consequent anaerobic metabolism and metabolic lactic acidosis due to increases in the concentration of blood lactic acid. However, Fillmore et al.¹ and subsequently Bishop et al.² observed alkalosis in arterial blood during the initial 10 min of CPR. This was due to hypocapnea and therefore respiratory alkalosis. During this initial period, only minor increases in blood lactate concentrations were observed.¹ This is of importance because sodium bicarbonate is routinely administered in the clinical setting of cardiac arrest and this intervention both augments alkalosis and carries the added risk of fatal hyperosmolality.³ These observations prompted the clinical recommendation of the American Heart Association that the decision of whether to administer bicarbonate therapy be based on measurements of arterial blood gases.⁴

During CPR in a porcine preparation of cardiac arrest, we observed a remarkable paradox between the pH and Pco₂ conditions in arterial and central venous blood. Decreased arterial Pco₂ and elevated arterial pH were accompanied by an elevated venous Pco₂ and depressed venous pH. This paradox was reversed after restoration of spontaneous circulation. These observations indicate that earlier concepts relating to acid-base changes during CPR and the presumed benefits of bicarbonate treatment are invalid.

Methods

Twelve healthy immature minipigs weighing 17 to 25 kg were anesthetized by ear vein injection of 25 mg/kg pentobarbital and neuromuscular block was induced by administration of 0.09 mg/kg pancuronium bromide. The trachea was intubated and ventilation was maintained with a pressure-cycled ventilator. The ventilator was adjusted to deliver a fractional inspired oxygen concentration (Fio₂) of 0.4, 12 breaths/min, and a tidal volume adjusted so as to maintain Paco₂ at 40 ± 5 mm Hg. Expired gas volume and the carbon dioxide concentration were continuously measured with a Fleisch pneumotachometer (C. J. Enterprises, Tarzana, CA) and an infrared CO₂ analyzer (ETCO₂ meter, Instrumentation Laboratories, Lexington, MA).

A balloon-tipped, triple-lumen, thermodilution pulmonary arterial catheter (Swan-Ganz catheter 93A-131-7F, American Edwards, Santa Ana, CA) was surgically inserted via the right femoral vein into the pulmonary artery. A No. 8F Cordis Ducov catheter was advanced from the right femoral artery into the thoracic aorta. A specially designed catheter sheath was advanced from the internal jugular vein into the right ventricle. A flexible guidewire advanced through the sheath was impacted against the right ventricular wall such that an electrocardiographic current indicating subendocardial injury was observed. Ventricular fibrillation was then induced by an alternating current of 100 mA delivered to the right ventricular wire and to an indifferent electrode in the subcutaneous tissue of the anterior chest. After 210 sec of ventricular fibrillation, external counter-shocks were administered with a direct-current defibrillator (Lifeport 911 Physio-Control, Redmond, WA) at progressive energy levels of 40, 80, 200, and 300 J until a viable rhythm was restored. In each instance, electromechanical dissociation (EMD) was induced. EMD was defined as a viable electrical rhythm with systolic aortic pressure of less than 30 mm Hg, a pulse pressure less than 5 mm Hg, and a narrow QRS complex at a rate greater than 40/min.

After onset of EMD, chest compression was initiated with a
TABLE 1
Nonresuscitated animals (seven trials, seven animals)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Time (min)</th>
<th>Site</th>
<th>pH (units)</th>
<th>ΔpH (units)</th>
<th>PCO₂ (mm Hg)</th>
<th>ΔPCO₂ (mm Hg)</th>
<th>Lactate (mmol/liter)</th>
<th>SAP (mm Hg)</th>
<th>DAP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>-5</td>
<td>A</td>
<td>7.45 ± 0.03</td>
<td>0.03 ± 0.01</td>
<td>39.9 ± 1.1</td>
<td>5.0 ± 1.0</td>
<td>2.1 ± 0.5</td>
<td>137 ± 9</td>
<td>107 ± 7</td>
</tr>
<tr>
<td>B</td>
<td>-5</td>
<td>V</td>
<td>7.42 ± 0.03</td>
<td></td>
<td>44.9 ± 1.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMD</td>
<td>+2</td>
<td>A</td>
<td>7.63 ± 0.04</td>
<td>0.30 ± 0.05B</td>
<td>20.2 ± 2.6B</td>
<td>34.2 ± 4.1B</td>
<td>3.2 ± 0.5</td>
<td>55 ± 6A</td>
<td>17 ± 3A</td>
</tr>
<tr>
<td>EMD</td>
<td>+2</td>
<td>V</td>
<td>7.33 ± 0.03</td>
<td></td>
<td>54.3 ± 3.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMD</td>
<td>+4</td>
<td>A</td>
<td>7.56 ± 0.03C</td>
<td>0.26 ± 0.04B</td>
<td>22.9 ± 2.4B</td>
<td>35.0 ± 5.0B</td>
<td>3.9 ± 0.4C</td>
<td>54 ± 6A</td>
<td>20 ± 4A</td>
</tr>
<tr>
<td>EMD</td>
<td>+4</td>
<td>V</td>
<td>7.29 ± 0.03</td>
<td></td>
<td>57.9 ± 3.9C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMD</td>
<td>+8</td>
<td>A</td>
<td>7.50 ± 0.02</td>
<td>0.27 ± 0.05B</td>
<td>22.9 ± 2.6B</td>
<td>39.4 ± 5.0B</td>
<td>4.9 ± 0.4C</td>
<td>51 ± 6A</td>
<td>18 ± 2A</td>
</tr>
<tr>
<td>EMD</td>
<td>+8</td>
<td>V</td>
<td>7.23 ± 0.03B</td>
<td></td>
<td>62.4 ± 3.8C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMD</td>
<td>+16</td>
<td>A</td>
<td>7.38 ± 0.04</td>
<td>0.22 ± 0.06C</td>
<td>30.5 ± 6.1</td>
<td>36.9 ± 8.2C</td>
<td>6.4 ± 0.4B</td>
<td>41 ± 6A</td>
<td>12 ± 3A</td>
</tr>
<tr>
<td>EMD</td>
<td>+16</td>
<td>V</td>
<td>7.16 ± 0.03B</td>
<td></td>
<td>67.4 ± 5.3C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B = baseline; A = arterial; V = venous; ΔpH = arterial minus venous pH; ΔPCO₂ = venous minus arterial PCO₂; SAP = systolic arterial pressure; DAP = diastolic arterial pressure.

*p < .001; *p < .01; *p < .05; all p values indicate differences from baseline values.

TABLE 2
Resuscitated animals (10 trials, seven animals)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Time (min)</th>
<th>Site</th>
<th>pH (units)</th>
<th>ΔpH (units)</th>
<th>PCO₂ (mm Hg)</th>
<th>ΔPCO₂ (mm Hg)</th>
<th>Lactate (mmol/liter)</th>
<th>SAP (mm Hg)</th>
<th>DAP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>-5</td>
<td>A</td>
<td>7.46 ± 0.02</td>
<td>0.06 ± 0.01</td>
<td>37.4 ± 0.9</td>
<td>7.8 ± 1.2</td>
<td>2.8 ± 0.7</td>
<td>120 ± 6</td>
<td>95 ± 5</td>
</tr>
<tr>
<td>B</td>
<td>-5</td>
<td>V</td>
<td>7.41 ± 0.02</td>
<td></td>
<td>45.2 ± 1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMD</td>
<td>+2</td>
<td>A</td>
<td>7.54 ± 0.05</td>
<td>0.23 ± 0.06C</td>
<td>20.1 ± 1.8A</td>
<td>34.2 ± 3.6A</td>
<td>3.9 ± 0.7</td>
<td>53 ± 5A</td>
<td>19 ± 3A</td>
</tr>
<tr>
<td>EMD</td>
<td>+2</td>
<td>V</td>
<td>7.31 ± 0.02B</td>
<td></td>
<td>54.2 ± 2.6B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>+2</td>
<td>A</td>
<td>7.24 ± 0.02A</td>
<td>0.05 ± 0.01</td>
<td>50.9 ± 3.1A</td>
<td>10.3 ± 2.0</td>
<td>6.1 ± 0.8C</td>
<td>119 ± 11</td>
<td>72 ± 10</td>
</tr>
<tr>
<td>RES</td>
<td>+2</td>
<td>V</td>
<td>7.19 ± 0.02A</td>
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<td>61.2 ± 2.1A</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>+4</td>
<td>A</td>
<td>7.25 ± 0.03A</td>
<td>0.04 ± 0.01</td>
<td>49.4 ± 3.2B</td>
<td>7.8 ± 1.4</td>
<td>5.9 ± 0.8C</td>
<td>125 ± 10</td>
<td>75 ± 8</td>
</tr>
<tr>
<td>RES</td>
<td>+4</td>
<td>V</td>
<td>7.21 ± 0.03A</td>
<td></td>
<td>57.2 ± 3.1B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>+8</td>
<td>A</td>
<td>7.26 ± 0.03A</td>
<td>0.04 ± 0.01</td>
<td>50.0 ± 2.7B</td>
<td>7.5 ± 1.4</td>
<td>5.6 ± 0.8C</td>
<td>118 ± 8</td>
<td>77 ± 9</td>
</tr>
<tr>
<td>RES</td>
<td>+8</td>
<td>V</td>
<td>7.22 ± 0.03A</td>
<td></td>
<td>57.5 ± 2.6B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RES</td>
<td>+16</td>
<td>A</td>
<td>7.32 ± 0.03B</td>
<td>0.06 ± 0.01</td>
<td>42.5 ± 2.6</td>
<td>11.2 ± 1.2</td>
<td>5.1 ± 0.8</td>
<td>114 ± 9</td>
<td>82 ± 8</td>
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<tr>
<td>RES</td>
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<td>V</td>
<td>7.27 ± 0.03B</td>
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<td>53.7 ± 2.7C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RES = resuscitated; other abbreviations are as in table 1.

*p < .001; *p < .01; *p < .05; all p values indicate differences from baseline.

Results

A total of 17 trials were completed on 12 animals. Seven of the animals were successfully resuscitated. Before the onset of ventricular fibrillation, there were normal differences between arterial and mixed venous PCO₂ and pH in both nonresuscitated and resuscitated animals (tables 1 and 2).

In the animals that were ultimately resuscitated, the arterial PCO₂ had declined from the baseline value of 37.4 to 20.1 mm Hg 2 min after the onset of EMD. Simultaneously, the venous PCO₂ was increased from 45.2 to 54.2 mm Hg. Consequently, there was a marked widening in the normal venoarterial PCO₂ gradient from 7.8 to 34.2 mm Hg. In the resuscitated...
animals, a normal venous arterial P<sub>CO<sub>2</sub></sub> gradient was restored (figure 1). The venoarterial P<sub>CO<sub>2</sub></sub> gradient persisted during the subsequent period of observation in nonresuscitated animals.

These changes in P<sub>CO<sub>2</sub></sub> were accompanied by reciprocal changes in pH so that at 2 min of EMD and CPR, the arterial pH was increased from 7.46 to 7.54. At the same time, the venous pH decreased from 7.41 to 7.31. Accordingly, the normal arterial venous pH gradient was increased from 0.06 to 0.23. After successful resuscitation, the pH gradient was promptly restored to 0.05 (figure 1). The venoarterial pH gradient persisted in the nonresuscitated animals.

The systolic arterial pressure decreased from 120 to 53 mm Hg during CPR in the animals that were successfully resuscitated and from 137 to 55 mm Hg in the nonresuscitated animals. No significant differences in arterial pressure or venoarterial gradients were observed between resuscitated and nonresuscitated animals during EMD.

A progressive decline in both arterial and venous pH of 0.02 pH units/min was accompanied by a progressive increase in arterial blood lactate from 2.1 to 3.2 mmol/liter at 2 min and to 6.4 mmol/liter at 16 min during CPR in the nonresuscitated animals. In eight animals, seven of which were successfully resuscitated, the expired CO<sub>2</sub> declined from a baseline level of 3.65 ± 0.15% to 0.24 ± 0.04% during ventricular fibrillation (p < .001 by paired t test). It increased to 0.10 ± 0.17% with chest compression and to 3.62 ± 0.27% after successful resuscitation (figure 2).

The gradients between arterial and mixed venous gases were solely due to an increase in venous P<sub>CO<sub>2</sub></sub>. This increase in venous P<sub>CO<sub>2</sub></sub> was related to a concurrent decrease in the volume of expired CO<sub>2</sub>. In figure 2, the reduction in end-tidal CO<sub>2</sub> at constant tidal volumes is demonstrated.

Discussion

The amount of CO<sub>2</sub> eliminated by alveolar ventilation is related to venous CO<sub>2</sub> content and pulmonary blood flow. Since pulmonary blood flow is severely reduced during CPR, even a 50% increase in venous P<sub>CO<sub>2</sub></sub> fails to maintain CO<sub>2</sub> delivery to the lungs. Consequently, it is a critical reduction in CO<sub>2</sub> delivery that accounts for decreased alveolar-capillary clearance of CO<sub>2</sub>. However, there is an increase in the ventilation-perfusion ratio accounting for decreased arterial P<sub>CO<sub>2</sub></sub>.

Unlike HCO<sub>3</sub> and H<sup>+</sup>, increases in dissolved CO<sub>2</sub> are accompanied by almost instantaneous decreases in intracellular pH. Since venous rather than arterial blood more closely approximates tissue acid-base conditions, the venous acidemia accompanying cardiac
arrest is likely to be associated with intracellular acidosis. It is cellular acidosis of myocardium that is implicated as the cause of impaired myocardial contractility, as it is in the clinical setting of EMD during CPR.11

We have recently demonstrated in humans undergoing CPR selective hypercapnea and marked acidemia in central venous but not in arterial blood, together with decreases in expired CO₂ comparable to those observed in our porcine preparation.12 The administration of sodium bicarbonate has been observed to produce a striking increase in both mixed venous P₅₀₂ and expired CO₂.* Accordingly, bicarbonate increases the CO₂ load. Resuscitation with restoration of cardiac output and pulmonary blood flow promptly increases the volume of expired CO₂ and decreases the mixed venous P₅₀₂. This reverses the abnormal venoarterial gradient of pH and P₅₀₂, even though there is a delay in the elimination of the accumulated CO₂ load with significant increases in both venous and arterial P₅₀₂ above those observed before cardiac arrest.

These observations suggest that, during CPR, increases in venous carbon dioxide in vital organs may produce profound cellular acidosis. In particular, increases in coronary venous CO₂, which have recently been observed in our laboratory, would most likely be associated with myocardial cellular acidosis.13 Improved techniques of CPR would enhance pulmonary blood flow and clearance of CO₂, thereby helping to reverse venous respiratory acidosis. Administration of base buffers that do not generate CO₂ loads, such as sodium carbonate (Na₂CO₃) or tromethamine, might also prove to be appropriate interventions during CPR in an effort to reverse critical tissue acidosis.

We conclude that arterial blood gases fail to reflect the acid-base status of systemic tissues during CPR and therefore should not be used as a guide for the administration of sodium bicarbonate. Since bicarbonate therapy increases the CO₂ load, its routine use during CPR is no longer advised.14

References
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14. Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC). JAMA 255: 2841, 1986
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