The relationship of CO2 metabolism to tissue perfusion, microcirculation, and
treatment response in shock and sepsis
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END-TIDAL CO$_2$ PRESSURE IN THE
MONITORING OF CARDIAC OUTPUT
DURING CANINE HEMORRHAGIC SHOCK
ABSTRACT

The value of end-tidal CO₂ pressure (PETCO₂) in monitoring circulatory status has been recently established in cardiac arrest. In an effort to extend its usefulness to other low-flow states, we studied the changes of PETCO₂ during progressive hemorrhage in anesthetized, mechanically ventilated dogs. PETCO₂ correlated with cardiac index (CI) in a logarithmic way \( r = .95, P < .001 \), not only in the whole group but in any individual experiment as well. Venoarterial and arterial-end-tidal CO₂ gradients also correlated with CI \( r = .85, P < .001 \) and \( R = .63, P < .001 \), respectively. These results suggest that cardiac output reductions are followed by increments in respiratory dead space, so CO₂ accumulates in venous blood and its pulmonary excretion is decreased. In this way, sequential changes in PETCO₂ during mechanical ventilation could noninvasively contribute to hemodynamic evaluation in hemorrhagic shock.

Keywords. Intramucosal pH - Tonometry - Shock - Oxygen consumption - Oxygen delivery - Lactate

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INTRODUCTION

In the last few years, there has been a growing body of evidence that the end-tidal CO\(_2\) pressure (PETCO\(_2\)) may be a simple and useful measurement in the monitoring of blood flow during cardiopulmonary resuscitation [1-3]. Experimental and clinical data link changes in PETCO\(_2\) with parallel changes in cardiac output (CO). The venoarterial PCO\(_2\) gradient [P(v-a) CO\(_2\)] increases with decrements in PETCO\(_2\) as the pulmonary blood flow decreases. However, to our knowledge, the usefulness of PETCO\(_2\) as a noninvasive monitor of circulatory status in other states of low cardiac output like hemorrhagic shock has not been tested. Our aim is to study the behavior of PETCO\(_2\) during progressive bleeding in mechanically ventilated dogs.

MATERIALS AND METHODS

Eight adult mongrel dogs weighing 21 ± 5 kg were anesthetized with intravenous injection of 30 mg/kg of pentobarbital sodium. Then they were endotracheally intubated with a cuffed tube and they were ventilated with a Harvard ventilator at a frequency necessary to maintain a PETCO\(_2\) of 35 ± 1 mm Hg, a tidal volume of 15 mL/kg, FiO\(_2\) of 0.21 and an inspiratory/expiratory ratio of 0.35. This ventilatory setting was held constant throughout the experiment. Neuromuscular blockage was induced with intravenous injection of 0.06 mg/kg of pancuronium bromide. Supplementary doses were given as needed. Anaesthesia was maintained by hourly administration of 1 to 2 mg/kg of pentobarbital sodium. A flow-directed thermodilution catheter was surgically inserted via the right internal jugular vein into the pulmonary artery. A second catheter was advanced from the right femoral artery into the thoracic aorta. Cardiac output was measured by the thermodilution technique (Cardiac Output Computer model 9520-American Edwards Laboratories, Santa Ana, CA) using an average of at least three injections of 3 mL of iced 5% dextrose. Arterial and mixed venous blood gases were measured with standard electrodes (BMS 3 MK 2, Radiometer, Copenhagen). End-tidal CO\(_2\) pressure was continuously measured at the tip of endotracheal tube with an infrared absorption CO\(_2\) analyzer (Datex monitor and recorder, Puritan-Bennett Corp, Los Angeles, CA). The CO\(_2\) analyzer was calibrated using precision-analyzed gases. The blood temperature was monitored with the thermodilution catheter. It was maintained constant in each experiment (±0.3° C) in order to avoid changes in CO\(_2\) production. After basal measurements were taken, progressive bleeding was allowed through the arterial catheter in a stepwise fashion. During each step, 6 mL/kg of blood was removed. After this, we waited for the stabilization of PETCO\(_2\) and then measurements were repeated. The experiment was conducted in this way until the dog was in cardiac arrest. Cardiac index (CI) was calculated by dividing CO by body weight. The venoarterial CO\(_2\) gradient [P(v-a) CO\(_2\)] and the arterial end-tidal
CO₂ gradient [P(a-ET) CO₂] were calculated by simple subtraction. Least square error method was used to determinate regression equation between PETCO₂ and CI, P(v-a)CO₂ and CI and P(a-ET)CO₂. The correlation between PETCO₂ and CI was also studied in each individual experiment. In the analysis of the correlations, we chose the equation that showed the best fit (the highest R²).

RESULTS

End-tidal CO₂ pressure strongly correlated with CI in each individual experiment. In all cases, the best fit was logarithmic. The correlation coefficients ranged from 0.93 to 1 (Table 1). A typical experiment is shown in Fig. 1. The mean fit of the individual data (r = .97, P < .001, y = 44.62 * x ^0.16) was not different from the fit of the pooled data (r=.95 ,P<.001, y = 48 * x ^0.21, (Fig. 2, P = NS). Venoarterial

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>r</th>
<th>p</th>
<th>Regression Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>.99</td>
<td>&lt;.02</td>
<td>PETCO₂ = 40.25•CI^0.14</td>
</tr>
<tr>
<td>2</td>
<td>.93</td>
<td>&lt;.05</td>
<td>PETCO₂ = 44.69•CI^0.13</td>
</tr>
<tr>
<td>3</td>
<td>.97</td>
<td>&lt;.02</td>
<td>PETCO₂ = 40.59•CI^0.13</td>
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<tr>
<td>4</td>
<td>.97</td>
<td>&lt;.02</td>
<td>PETCO₂ = 41.18•CI^0.17</td>
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<tr>
<td>5</td>
<td>.97</td>
<td>&lt;.02</td>
<td>PETCO₂ = 50.23•CI^0.21</td>
</tr>
<tr>
<td>6</td>
<td>1.00</td>
<td>&lt;.01</td>
<td>PETCO₂ = 44.62•CI^0.21</td>
</tr>
<tr>
<td>7</td>
<td>.94</td>
<td>&lt;.01</td>
<td>PETCO₂ = 45.35•CI^0.18</td>
</tr>
<tr>
<td>8</td>
<td>.96</td>
<td>&lt;.02</td>
<td>PETCO₂ = 40.94•CI^0.15</td>
</tr>
<tr>
<td>Mean</td>
<td>.97</td>
<td>&lt;.001</td>
<td>PETCO₂ = 44.62•CI^0.16</td>
</tr>
</tbody>
</table>

Figure 1. Correlation between PETCO2 and CI in an individual experiment.
CO₂ gradient correlated with CI, and the best fit was hyperbolic ($r = .85$, $P < .001$, Fig. 3). Arterial-end-tidal CO₂ gradient correlated linearly with CI ($r = .63$, $P < .001$, Fig. 4).

**Figure 2.** Correlation between PETCO₂ and CI in the whole group.

**Figure 3.** Correlation between P(v-a)CO₂ and CI in the whole group.

**DISCUSSION**

According to Fick’s principle applied to CO₂, changes in CO should induce modifications in the arterial and mixed-venous CO₂ contents. As CO is reduced, CO₂ accumulates proximal to pulmonary capillaries. In this way, reductions in CO are followed by widening of P(v-a)CO₂ as was shown in different circumstances. Recently, there has been a great interest in widening of P(v-a) CO₂ during cardiac arrest [3-12]. This results in a difference in acid-base state between mixed-venous
and arterial blood, which is characterized by the paradox of mixed-venous respiratory acidosis and arterial respiratory alkalosis. However, these changes are also observed in patients with low flow states [13], canine hemorrhagic shock [14], canine endotoxemia [15], and oleic acid pulmonary injury treated with positive end-expiratory pressure [16]. The reductions in pulmonary blood flow also curtail CO₂ excretion by the lungs. Accordingly, PETCO₂ correlates with CO during cardiopulmonary resuscitation [1-3]. Our results are in agreement with these descriptions. The reductions in CO were followed by increments in P(v-a)CO₂. The underlying mechanism might be an alteration in pulmonary V/Q distribution, with increments in dead space, as was described in hypovolemia [17-20]. As evidence of the role of this mechanism, P(a-ET)CO₂ increased with reductions in CI, and has previously been shown to correlate with Vd/Vt [21]. As a consequence, PETCO₂ was strongly correlated with CI. The behavior of each individual experiment was similar to that of the pooled data. The best-fitting equation was logarithmic in all cases. Previous reports have characterized this relationship as linear [1-3], which could be due to different analyses of the data. Another cause of disagreement might be that previous investigations have focused on the steeper portion of the curve because the investigator’s study goal was cardiopulmonary resuscitation, and thus a very low CO. Our description appears to be more physiologic and emphasizes that the more significant changes in PETCO₂ will occur at lower CO values. Limiting the usefulness of PETCO₂ value as a monitor of CO is the fact that PETCO₂ is also determined by alveolar ventilation and CO₂ production [22]. The former confounding problem is of minor importance during controlled mechanical ventilations but may be significant if ventilatory changes or pulmonary pathology do occur. Changes in CO₂ generation could explain changes in PETCO₂ when HCO₃Na is infused. These difficulties could be overcome by a new approach using a partial rebreathing technique [23].

Fig. 4. Correlation between P(a-ET)CO₂ and CI in the whole group.
In this study we evaluated the usefulness of PETCO₂ in canine hemorrhagic shock. Hemorrhagic shock is a life-threatening condition that is frequently present in the intensive care unit setting. The adequacy of tissue perfusion and its response to treatment depends mainly on the clinical assessment of peripheral perfusion such as the state of consciousness, skin, temperature, pulse, urine output and nail beds. However, associated injuries to brain, extremities and kidney could complicate these evaluations. Cuffed measurements of blood pressure may not reflect the aortic pressure because of generalized vasoconstriction [24]. In this setting, the monitoring of sequential changes of PETCO₂ could be a useful adjunct in the management of mechanically ventilated patients. In addition, it lacks the morbidity rate and mortality rate of the thermodilution technique. Nevertheless, careful clinical trials are required to translate these results to clinical grounds.

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