Relationship between Arterial and End-Tidal Carbon Dioxide Pressure during Controlled Ventilation in Porcine Neonates

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Abstract: To investigate the validity of ETCO₂ in porcine neonates, which have been frequently used as an experimental model for human neonates, the relationship between arterial (PaCO₂) and end-tidal PCO₂ (ETCO₂) in porcine neonates was examined under different respiratory conditions by regulating both inspiratory flow and positive end expiratory pressure (PEEP). The difference between PaCO₂ and ETCO₂ widened significantly, according to the significant decrease in tidal volume/body weight ratio (TV/BW) caused by the increase of PEEP. A lower correlation between PaCO₂ and ETCO₂ was observed in <6 ml/kg than in ≥6 ml/kg TV/BW. It therefore seems reasonable to conclude that, in porcine neonates, the valid ETCO₂ measurements corresponding to PaCO₂ would be obtained at ≥6 ml/kg TV/BW.

Key words: ETCO₂, neonates, porcine

Since end-tidal PCO₂ (ETCO₂) was proposed as an index of arterial PCO₂ (PaCO₂), continuous monitoring of airway PCO₂ was in wide practical use [1, 3, 8, 9, 11]. But, ETCO₂ measurements may be influenced by various respiratory factors [2, 4–6, 10], as it was suggested that a significant determinant of the difference between PaCO₂ and ETCO₂ (P (a–pc) CO₂) is the presence or absence of lung disease [11]. In man, it was recommended that ETCO₂ values be calibrated for an individual patient by making an initial measurement of PaCO₂ [11], because ETCO₂ may substantially underestimate PaCO₂. In experimental animals, likewise, measurement of ETCO₂ has been availed as a parameter representing cardiopulmonary function [7]. But in laboratory animals and particularly their neonates, which have been used as an experimental model for human neonates, the validity of using ETCO₂ measurements must be questioned, since they have little respiratory or circulatory reserve. We therefore examined the relationship between ETCO₂ and PaCO₂ in different artificial respiratory conditions in porcine neonates. This study is intended as an investigation of the validity of ETCO₂ in porcine neonates, which have frequently been used as the animal model to study human neonatal pneumonia.

Studies were carried out on nine trihybrid LWD
([Landrace * Large White] * Duroc) porcine neonates (aged 10–14 days, weighing 2.6–4.0 kg), which had their general health evaluated in a pre-operative examination.

The operation was performed under general anesthesia with sodium pentobarbital (30 mg/kg body weight, i.v.) following premedication with atropine sulfate (0.05 mg/kg, s.c.). Immediately after the induction of anesthesia, the animals were intubated, and placed on a pressure-limited time-cycled neonatal ventilator (BP200 Infant Ventilator, Borns Co.). Prior to ventilation, they were immobilized with pancuronium bromide (0.4 mg/kg, i.v.). The initial settings were a peak inspiratory pressure of 18 cm H2O, fraction inspired oxygen (FiO2) of 0.3, respiratory rate of 30 breaths/min, and an inspiratory/expiratory ratio of 1:2. Nine separate respiratory conditions were then artificially created with different permutations of inspiratory flow (8, 10, 12 l/min) and positive end expiratory pressure (PEEP) (0, 3, 5 cm H2O), and the respiratory parameters described below were monitored.

Expired gases for measurement of ETCO2 were sampled from the T-connector site through an attached tube (outer diameter 1.8 mm, length 90 cm) at the rate of 150 ml/min, and ETCO2 was analyzed with a capnometer (Multicap, Datex Co.). PaCO2 was measured in a blood sample taken through a polyethylene catheter (PE160, Intramedic, Clay Adams) inserted into the femoral artery. Tidal volume (TV) was measured simultaneously, and the TV/body weight ratio (TV/BW) was calculated. Under fluoroscopic guidance, a 5Fr flow-directed thermodilution catheter (Swan-Ganz) was positioned in the pulmonary artery via the external jugular vein for measurement of cardiac output (CO). CO was then converted to the cardiac index (CI; CO/BW).

All data obtained in this study were expressed as the mean ± SD. Statistical differences in the various parameters were analyzed by repeated measures ANOVA or factorial ANOVA, and Scheffé’s method was used for simultaneous multiple comparisons. P < 0.05 was considered significant. The correlation between ETCO2 and PaCO2 was examined by simple regression analysis.

The changes in PaCO2, ETCO2, P (a-pe) CO2, CI, and TV/BW caused by regulation of inspiratory flow and PEEP are shown in Table 1. P (a-pe) CO2 and TV/BW changed significantly. The increase in P (a-pe) CO2 and the decrease in TV/BW tended to correspond to the increase in PEEP rather than inspiratory flow.

The P (a-pe) CO2 data were divided into seven categories of TV/BW as follows: <2, 2–4, 4–6, 6–8, 8–10, 10–12 and ≥12 ml/kg. P (a-pe) CO2 showed significant changes at the boundary of 6 ml/kg (Fig. 1). For ≥6 ml/kg TV/BW, P (a-pe) CO2 values became significantly greater than those for <6 ml/kg. There were no differences in CI among the seven categories.

On the basis of these results, all data were classified by TV/BW as <6 ml/kg and ≥6 ml/kg, and the correlations between the ETCO2 and the PaCO2 were analyzed. Although ETCO2 values correlated significantly with PaCO2 in both ≥6 ml/kg and <6 ml/kg TV/BW, a higher correlation was observed in ≥6 ml/kg than in <6 ml/kg (Fig. 2-1).

Table 1. Changes in arterial blood CO2 (PaCO2), end-tidal CO2 (ETCO2), P (a-pe) CO2, cardiac index (CI) and tidal volume/body weight ratio (TV/BW), as increasing inspiratory flow and positive end expiratory pressure (PEEP)

<table>
<thead>
<tr>
<th>Inspiratory Flow (L/min)</th>
<th>0</th>
<th>3</th>
<th>5</th>
<th>10</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP (cm H2O)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>31.1 ±9.5</td>
<td>36.2 ±11.5</td>
<td>42.7 ±12.8</td>
<td>32.5 ±9.7</td>
<td>36.5 ±11.5</td>
</tr>
<tr>
<td>ETCO2 (mmHg)</td>
<td>27.8 ±7.8</td>
<td>14.4 ±8.4</td>
<td>15.4 ±12.9</td>
<td>30.7 ±9.8</td>
<td>21.1 ±8.1</td>
</tr>
<tr>
<td>P (a-pe) CO2 (mmHg)</td>
<td>3.4 ±4.06</td>
<td>21.7 ±13.86</td>
<td>27.3 ±4.46</td>
<td>1.8 ±3.16</td>
<td>15.4 ±8.56</td>
</tr>
<tr>
<td>CI (l/min/kg)</td>
<td>0.25 ±0.06</td>
<td>0.28 ±0.08</td>
<td>0.25 ±0.06</td>
<td>0.29 ±0.02</td>
<td>0.27 ±0.06</td>
</tr>
<tr>
<td>TV/BW (ml/kg)</td>
<td>7.6 ±2.16</td>
<td>4.1 ±1.66</td>
<td>3.0 ±1.06</td>
<td>8.5 ±2.46</td>
<td>5.0 ±1.96</td>
</tr>
</tbody>
</table>

* Values were calculated by using a standard formula for [PaCO2-ETCO2]. A, B, C, D: Values with different superscripts within the same row are significantly different (p<0.05). Data were analyzed statistically by using repeated measures ANOVA.
PaCO\(_2\) and ETCO\(_2\) values tended to increase and decrease, respectively, in accordance with the decrease in TV/BW caused by increasing PEEP. This result appeared to originate in the increase in functional residual capacity and the decrease in tidal volume resulting from the increase in PEEP. That is, it was suspected that, in spite of the increase in alveolar CO\(_2\) promoted by the increase in functional residual capacity, expired CO\(_2\) was lessened because of the decrease in tidal volume. It is generally believed that the increasing difference between ETCO\(_2\) and PaCO\(_2\) indicates a decrease in pulmonary blood flow [10]. In this study, however, it was indicated that the increasing PEEP had little effect on pulmonary circulation, since no significant variation in CI was observed.

It was suggested that ETCO\(_2\) measurements did not precisely reflect PaCO\(_2\) at <6 ml/kg TV/BW, because P (a-pe) CO\(_2\) values increased significantly at <6 ml/kg and the coefficient of correlation between PaCO\(_2\) and
ETCO₂ in <6 ml/kg was low. In addition, this suggestion was supported by the fact that flat expiratory plateau phases, which should be essential in order for ETCO₂ to reflect PaCO₂ [5, 9], were not shown in the capnogram for <6 ml/kg.

It therefore follows that tidal volume should be taken into account to obtain reliable ETCO₂ measurements in laboratory animals in evaluating human neonatal respiratory function during controlled ventilation with PEEP. It seems reasonable to conclude that, in porcine neonates, valid ETCO₂ measurements corresponding to PaCO₂ would be obtained at ≥6 ml/kg TV/BW.

References