Physiologic Dead Space, Venous Admixture, and the Arterial to End-tidal Carbon Dioxide Difference in Infants and Children Undergoing Cardiac Surgery

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End-tidal CO₂ (PETCO₂), arterial CO₂ (PACO₂), mixed expired CO₂ (PECO₂), arterial and mixed venous oxygen contents were measured and the PACO₂ to PETCO₂ difference (ΔPACO₂) physiologic dead space to tidal volume ratio (V₁/V₉) and venous admixture (Q₁/Q₉) were calculated in 41 anesthetized infants and children undergoing repair of congenital cardiac lesions. Eighteen were cyanotic; 9 with normal pulmonary blood flow (PBF) and normal intracardiac anatomy (normal group); and 9 with increased PBF (cyanotic group). Twenty-three were cyanotic; 14 with right to left intracardiac shunts and decreased PBF (cyanotic (D) group); and 9 with mixing lesions with normal or increased PBF (cyanotic (I) group). Correlations between PACO₂ and PETCO₂ in the four groups of children were carried out and the relationship of ΔPACO₂ to V₁/V₉ and Q₁/Q₉ was determined. PETCO₂ correlated closely with the PACO₂ in the normal and cyanotic groups (r = 0.97 and 0.91, respectively) and the lines of regression for the relationship between PACO₂ and PETCO₂ for both groups did not differ from the line of identity (P > 0.05). Mean ± SD V₁/V₉ for the normal and cyanotic groups were 0.35 ± 0.17 and 0.39 ± 0.19, respectively (NS). Corresponding values for the cyanotic (D) group and cyanotic (I) group were 0.35 ± 0.16 and 0.55 ± 0.16, respectively (NS), and were significantly greater than those from the normal and cyanotic groups (P < 0.05). The relationship of ΔPACO₂ to V₁/V₉ and Q₁/Q₉ demonstrated that V₁/V₉ was the most important determinant of ΔPACO₂, but in instances where Q₁/Q₉ were large (e.g., cyanotic congenital heart disease) the percentage contribution of Q₁/Q₉ to the ΔPACO₂ can be considerable. It is concluded that PETCO₂ is an acceptable estimate of PACO₂ in subjects with cyanotic congenital heart disease but underestimated the PACO₂ in subjects with cyanotic congenital heart disease. (Key words: Anesthesia: cardiac; children. Heart: cyanotic heart disease; congenital heart disease; cyanotic heart disease. Lung: end-tidal to arterial P₉CO₂ difference; physiologic dead space; venous admixture.)

THE CARBON DIOXIDE tension difference between blood (pulmonary capillary) and alveolar gas in children without cardiopulmonary disease is usually small and end-tidal carbon dioxide tension (PETCO₂) accurately approximates arterial carbon dioxide tension (PACO₂). However, the arterial to end-tidal carbon dioxide tension difference (ΔPACO₂) can be increased in patients with cardiopulmonary disease. This increase has been attributed to two possible causes: an abnormality of the physiologic dead space to tidal volume ratio (V₁/V₉) and an increase in venous admixture (Q₁/Q₉).* Physiologic dead space is composed of the sum of anatomic dead space, alveolar dead space, and dead space-like ventilation produced by alveoli with high ventilation to perfusion ratios. Venous admixture is a measure of the theoretical fraction of the cardiac output that passes through the cardiopulmonary system without absorbing oxygen. It is a convenient index of shunt but does not define the anatomic pathway of shunt. V₁/V₉ and Q₁/Q₉ is the primary determinant of the ΔPACO₂ in individuals with normal cardiopulmonary systems because Q₁/Q₉ is quantitatively less important due to the small difference in the mixed venous and arterial CO₂ tension and the small size of the shunt. Patients with congenital heart disease (CHD) have altered ventilation–perfusion ratios producing abnormalities of both V₁/V₉ and Q₁/Q₉, which may affect the ΔPACO₂, but the relative contribution of V₁/V₉ and Q₁/Q₉ to the ΔPACO₂ have not been fully examined in patients with CHD. The purpose of this study was to evaluate the accuracy of PETCO₂ to assess the PACO₂ in children with various forms of CHD and to determine the contribution of V₁/V₉ and Q₁/Q₉ to the ΔPACO₂.

Methods

After approval from the Human Experimentation Committee, 41 infants and children, ASA physical status 2–3 scheduled for corrective cardiac surgery were studied. Patients diagnosed as having pulmonary disease or congestive heart failure were excluded from the study. Patients with existing arterial to pulmonary palliative shunts or clinically significant aorto-pulmonary collaterals and those in whom a mixed venous blood sample could not be obtained from the main pulmonary artery were also excluded. The patients were divided into four groups according to their cardiopulmonary diagnosis as determined from physical, laboratory, radiologic, echocardiographic, and/or angiographic examinations. Eighteen patients presented with cyanotic congenital heart disease (ACHD). Nine of these patients demonstrated no intracardiac abnormality and presented for surgical treatment.

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of conduction disturbances (normal group) and nine demonstrated left-to-right intracardiac shunting of blood with increased pulmonary blood flow (PBF) (cyanotic group). Twenty-three patients were classified as cyanotic. Fourteen of these patients demonstrated right-to-left intracardiac shunting with decreased PBF (cyanotic [D] group) and nine demonstrated mixing-type lesions with normal or increased PBF (cyanotic [I] group).

**PREMEDICATION**

Patients younger than 1 yr were premedicated with atropine 0.02 mg/kg im 30 min prior to induction of anesthesia. Patients older than 1 yr received pentobarbital 2.0 mg/kg orally or rectally 1 h prior to induction and atropine 0.02 mg/kg (maximum 0.6 mg) with morphine 0.2 mg/kg im 30 min prior to induction of anesthesia.

**ANESTHESIA**

Anesthesia was induced with fentanyl (50 μg/kg iv) and diazepam (0.4 mg/kg) and paralysis was achieved with pancuronium (0.15 mg/kg). The trachea was intubated with an endotracheal tube of adequate diameter so that there was no audible air leak below 35 cmH₂O peak inspiratory pressure. The tip of the endotracheal tube was positioned approximately midway between the vocal cords and the carina. Ventilation was controlled with an Air-Shields Ventimeter (ASV) ventilator and an Ayre's t-piece breathing circuit (Mapleson B). Fresh gas flow (nonrebreathing), tidal volume, peak inspiratory pressure, and respiratory rate were adjusted to maintain the Paco₂ within the range of 30–40 mmHg. PEEP was 3 cmH₂O. Anesthesia was maintained with 100% oxygen, fentanyl (6 μg·kg⁻¹·h⁻¹) by constant iv infusion with pancuronium given for muscle relaxation.

**STUDY METHODS**

End-tidal Pco₂ was sampled continuously at a flow rate of 150 ml/min, using a Puritan-Bennett Model 253 infrared analyzer (response time of 200 ms) calibrated with dry 5.17% CO₂ prior to each study. End-tidal Pco₂ data were recorded with a Datex Recorder (Puritan-Bennett Corporation, Los Angeles, California). Inspired Pco₂ (PiCO₂) and PETCO₂ were obtained by sampling gas through a number 16 or 19 Deseret Intracath (number 19 was used for endotracheal tubes ≤3.0 mm OD), which was inserted through the elbow (#12800, Dryden Corporation, Indianapolis, Indiana) of the anesthetic circuit to within 5 mm of the distal end of the endotracheal tube. The hub of the Intracath was secured to the Luer-Lock connector of a 1.5 meter sampling tube (#126671, Dryden Corporation) attached to the analyzer. All end-tidal CO₂ measurements were corrected for water vapor pressure, barometric pressure, and oxygen concentration. Mixed expired partial pressure of carbon dioxide (PEco₂) was measured by collecting the expired gas over 5 min in a Douglas bag using a nonmixing three-way directional valve inserted between the Ayres t-piece and the elbow connector. During the collection period end-tidal monitoring was discontinued to prevent loss of sampled gas.

All subjects were studied while in the supine horizontal position. The study commenced after the chest was opened (sternotomy) with sternal retractors placed to allow access to the main pulmonary artery and completed before cardiopulmonary bypass was instituted. Each patient was hemodynamically stable and ventilation of the lungs was unchanged for no less than 15 min at the desired ventilator settings prior to beginning the study.

**CALCULATIONS**

Physiological dead space to tidal volume ratios were calculated using the equation:

\[ V_D/V_T = (P_{CO}_2 - P_{Eco}_2)/(P_{CO}_2 - P_{iCO}_2) \]

where PiCO₂ = the inspired partial pressure of carbon dioxide. V_D/V_T calculations were corrected for equipment dead space (measured by water displacement).

To calculate venous admixture, arterial (right radial artery), and mixed venous (main pulmonary artery by direct puncture) blood samples were obtained simultaneously and were analyzed with a Nova Biomedical Stat Profile 1 gas analyzer, which was calibrated prior to each study. Pulmonary end capillary Po₂ was assumed equal to calculated alveolar Po₂ (PAO₂). PAO₂ was calculated using the alveolar air equation applicable for patients breathing an inspired oxygen fraction (FiO₂) of 1.0:¹⁵

\[ PAO₂ = FiO₂(Pb - 47) - Paco₂ \]

where Pb = barometric pressure, and 47 = the partial pressure of water vapor at 37°C.¹⁵ Paco₂ rather than PETCO₂ was chosen because PETCO₂ may underestimate the partial pressure of CO₂ in the alveoli (PAO₂).¹⁷,²⁰ Within the range of PAO₂ in this study, errors in PAO₂...
as large as 10 mmHg would produce insignificant changes in the capillary oxygen content.

The contents of oxygen were calculated using the coefficient of 1.54 ml O2/gm Hb and 0.003 ml O2/100 ml blood/mmHg for the physical solution of oxygen in blood. All values were corrected for temperature, pH, and base excess. 21, 22

Venous admixture was calculated using the shunt equation

\[ Q_v/Q_t = (C_{CO_2} - C_{AO_2})/(C_{CO_2} - C_{VO_2}) \]

where \( C_{CO_2} \) = end capillary oxygen content, \( C_{AO_2} \) = arterial oxygen content and \( C_{VO_2} \) = mixed venous oxygen content. 18

**STATISTICS**

The demographic data were compared using Student’s t test with Bonferroni correction for multiple comparisons. The relationships between PETCO\(_2\), \( \Delta P_{CO_2} \), Qv/Qt, \( \Delta P_{CO_2} \), and the \( Q_v/Q_t \), \( \Delta P_{CO_2} \), and \( V_D/V_T \); and \( Q_v/Q_t \) and \( V_D/V_T \) were determined by least squares linear regression analysis and the coefficient of determination (r²). The slopes and intercepts of the regression lines between PETCO\(_2\) and \( \Delta P_{CO_2} \), PaCO\(_2\), were compared with the line of identity using Student’s t test. 25 The relationship between \( \Delta P_{CO_2} \), Qv/Qt, and \( V_D/V_T \) was determined by multiple linear regression analysis. All data are presented as mean ± SD. Statistical significance was accepted at \( P \leq 0.05 \).

**Results**

The patient demographic data (table 1) demonstrate no statistical difference in age or weight of the patients among patients in the four groups. There was no significant difference in hematocrit between patients in the two acyanotic groups nor between those in the two cyanotic groups; however the hematocrits of the cyanotic groups were significantly greater than those in the acyanotic groups.

PETCO\(_2\) underestimated PaCO\(_2\) in all patients studied. The \( \Delta P_{CO_2} \) for the individual groups of patients are presented in table 2. There was no statistical difference in the \( \Delta P_{CO_2} \) between the acyanotic and normal groups (\( P \)

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**Table 2. Mean Values (±SD) for \( \Delta P_{CO_2} \), \( V_D/V_T \) and \( Q_v/Q_t \) in the Four Groups of Patients**

<table>
<thead>
<tr>
<th></th>
<th>( \Delta P_{CO_2} ) (mmHg)</th>
<th>( V_D/V_T )</th>
<th>( Q_v/Q_t )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>2.7 ± 1.8</td>
<td>0.35 ± 0.11</td>
<td>0.06 ± 0.08</td>
</tr>
<tr>
<td>Acyanotic</td>
<td>2.9 ± 2.0</td>
<td>0.39 ± 0.19</td>
<td>0.13 ± 0.11</td>
</tr>
<tr>
<td>Cyanotic (D)</td>
<td>9.4 ± 4.1*</td>
<td>0.57 ± 0.17*</td>
<td>0.38 ± 0.16*</td>
</tr>
<tr>
<td>Cyanotic (I)</td>
<td>12.1 ± 2.8*</td>
<td>0.63 ± 0.16*</td>
<td>0.55 ± 0.16*</td>
</tr>
</tbody>
</table>

* \( P \leq 0.05 \) different from the normal and acyanotic group.

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**Fig. 1.** The regression line for the correlation between PETCO\(_2\) and PaCO\(_2\) for each group is represented by the continuous line (- - -). The regression lines for the four groups are described by the equations: normal group \( y = 2.51 + 0.88X \) (r\(^2 \) = 0.97), acyanotic group \( y = 0.61 + 91X \) (r\(^2 \) = 0.91), cyanotic (D) group \( y = 7.28 + 0.47X \) (r\(^2 \) = 0.28), and cyanotic (I) group \( y = 14.20 + 1.06X \) (r\(^2 \) = 0.83). The line of identity in each case is represented by the broken line (---).
≤ 0.05) nor between the two cyanotic groups (P ≤ 0.05), but there was a significant difference between patients in the acyanotic and normal groups and those in the two cyanotic groups (P ≤ 0.05).

The relationship between PETCO₂ and PaCO₂ for the four groups are presented in figure 1. There was no significant difference between the slope and intercept of the lines of regression for the normal and acyanotic groups as compared with the line of identity. The slope of the line of regression for the cyanotic (D) group was statistically different from the line of identity (P ≤ 0.05). There was no difference between the slope of the line of regression for patients of the cyanotic (I) group and the line of identity, but the intercept of the line of regression was significantly different than the line of identity (P ≤ 0.05).

The calculated V₅/V₇ for each of the four groups of patients is presented in table 2. There was no statistical difference between the acyanotic and normal groups nor between the two cyanotic groups. The two cyanotic groups demonstrated a significantly greater V₅/V₇ than the acyanotic and normal groups (P ≤ 0.05). The relationship between the ΔPCO₂ and V₅/V₇ for the four groups of patients is shown in figure 2. The V₅/V₇ shows a direct and linear correlation with the ΔPCO₂.

The Q₆/Q₇ for each of the four groups of patients is presented in table 2. The Q₆/Q₇ did not differ significantly between the acyanotic and normal groups nor between the two cyanotic groups. The two cyanotic groups demonstrated a significantly greater Q₆/Q₇ than the acyanotic and normal groups. The Q₆/Q₇ correlated directly and linearly with the ΔPCO₂ (fig. 3).

The linear relationship between V₅/V₇ and Q₆/Q₇ was poor (r² = 0.32). Because the two independent variables were not closely related, multiple linear regression was used to determine the dependency of ΔPCO₂ on both Q₆/Q₇ and V₅/V₇. The derived equation describing this relationship is:

\[ \Delta P_{CO_2} = -1.55 + 0.91Q_6/Q_7 + 13.38V_5/V_7 \]

The r² value for these data was 0.69.

**Discussion**

This study demonstrates that PETCO₂ significantly underestimates PaCO₂ of children with cyanotic congenital heart disease but is an acceptable estimate of PaCO₂ in children with acyanotic heart disease. These data agree with previous studies in children with healthy and intact cardiopulmonary systems and with studies in patients with cardiopulmonary disease including congenital heart disease with right-to-left intracardiac shunting of blood. Although the ΔPCO₂ values of the cyanotic (I) group are greater (P ≤ 0.05) than the values obtained by Fletcher in his study of children with mixed shunts,
FIG. 3. The regression line for the correlation between ΔF CO₂ and Q̇L/Q̇T for each group is represented by the continuous line (---). The regression lines for the four groups are described by the equations: normal group y = 0.41 + 17.67X (r² = 0.19), cyanotic group y = 1.02 + 15.28X (r² = 0.76), cyanotic (D) group y = 1.85 + 19.86X (r² = 0.61), and cyanotic (I) group y = -6.05 + 30.77X (r² = 0.69).

The contrasting results of the two studies are in agreement. Both groups of patients demonstrated mixing type lesions, but the patients in the current study were all cyanotic whereas several of the patients in Fletcher’s study were acyanotic. The greater mean ΔP CO₂ demonstrated in the current study is due to the effect of the larger Q̇L/Q̇T of the cyanotic patients on the ΔP CO₂ as discussed below. The ΔP CO₂ of the cyanotic patients in Fletcher’s study are of the same magnitude as those obtained in the current study.

The relationship between V D/V T and ΔP CO₂ is in agreement with previously published studies. The effect of physiologic dead space on ΔP CO₂ was determined because both anatomic and alveolar dead spaces contribute to ΔP CO₂. Consequently, Pac CO₂ was used to calculate dead space rather than PET CO₂, which may underestimate the true V D/V T.

The values of V D/V T determined in the cyanotic (D) patients postinduction are significantly greater than reported values obtained preoperatively in cyanotic patients with decreased pulmonary blood flow and are similar to but still greater than alveolar V D/V T values obtained from other anesthetized cyanotic patients. The increase in V D/V T in anesthetized patients may be attributed to the introduction of muscle paralysis and positive pressure ventilation producing a decrease in pulmonary blood flow. This would be exacerbated in the current study by the presence of an open mediastinum. Also, dead space calculations are affected, not only by the underlying disorder but also by the apparatus dead space. Intubation bypasses much of the upper airway and measured physiologic dead space in an intubated adult may underestimate true physiologic dead space. However, in smaller children apparatus dead space assumes a relatively greater importance than in adults because the absolute volume of physiologic dead space is less. In the current study the effect of apparatus was minimized by placing the nonmixing three-way directional valve between the Ayre’s t-piece and the elbow connector and corrected by measuring apparatus dead space by water displacement. Studies of unanesthetized pediatric patients following complete repair of their cardiac lesions demonstrate the return of V D/V T to lower values.

Q̇L/Q̇T is a mathematically determined estimate of the amount of blood that passes through the cardiopulmonary system without absorbing oxygen. Differences between the predicted and measured Q̇L/Q̇T may be attributed to pulmonary arterial blood that perfuses alveoli with low V/Q ratios and to the admixture of bronchial and venticular venous blood. The Q̇L/Q̇T ratio increases ΔP CO₂ by shunting venous blood with a greater P CO₂ tension than that in the alveoli and end-capillary blood, to the left side of the heart. This increases the Pac CO₂ compared with the alveolar or end capillary P CO₂.