Monitoring of end tidal carbon dioxide and transcutaneous carbon dioxide during neonatal transport

D G Tingay, M J Stewart, C J Morley

Objective: To assess the accuracy of measurements of end tidal carbon dioxide (CO₂) during neonatal transport compared with arterial and transcutaneous measurements.

Design: Paired end tidal and transcutaneous CO₂ recordings were taken frequently during road transport of 21 ventilated neonates. The first paired CO₂ values were compared with an arterial blood gas. The differences between arterial CO₂ (PaCO₂), transcutaneous CO₂ (TcPCO₂), and end tidal CO₂ (PetCO₂) were analysed. The Bland-Altman method was used to assess bias and repeatability.

Results: PetCO₂ correlated strongly with PaCO₂ and TcPCO₂. However, PetCO₂ underestimated PaCO₂ at a clinically unacceptable level (mean (SD) 1.1 (0.70) kPa) and did not trend reliably over time within individual subjects. The PetCO₂ bias was independent of PaCO₂ and severity of lung disease.

Conclusions: PetCO₂ had an unacceptable under-recording bias. TcPCO₂ should currently be considered the preferred method of non-invasive CO₂ monitoring for neonatal transport.

Arterial blood gases and TcPCO₂ are commonly used to monitor ventilation. The aim of this study was to assess the accuracy and reliability of PetCO₂ monitoring during neonatal transport.

METHODS

Ventilated infants requiring road transport to a level 3 neonatal intensive care unit during March to August 2002 were recruited if the paediatrician involved in the transport was specifically trained to use both PetCO₂ and TcPCO₂ monitors, an arterial catheter was being used, endotracheal tube position could be confirmed by chest radiograph before transport, and both TcPCO₂ and PetCO₂ monitoring could be started before the first arterial blood gas was measured by the NETS team. Because of the effects of barometric pressure on PetCO₂, infants transported by air were not studied. Informed parental consent was obtained for each infant before transport.

Infants were not studied if they were older than 28 days, had a capillary refill time of greater than two seconds, or PaCO₂, PetCO₂, or TcPCO₂ readings could not be made or were lost during transport.

PetCO₂ was measured using the Microgas 7650 system (weight 5.6 kg) with Combi.M sensor 82 (Linde, Basel, Switzerland) applied to the skin of the anterior chest or abdomen. The manufacturers report that the Combi.M sensor 82, once calibrated, will remain accurate for up to four hours on site. PetCO₂ was measured using a side stream end tidal analyser specifically designed for neonatal use (the Agilent Microstream system; Agilent Technologies, Andover, Massachusetts, USA); a result was the highest of five consecutive measurements. Arterial blood gases were analysed with the i-STAT portable clinical analyser (i-STAT Corporation, East Windsor, New Jersey, USA). Infants were ventilated using the Hoekloos Infant ventilator Mark 3.

Abbreviations: PaCO₂, arterial partial pressure of carbon dioxide; TcPCO₂, transcutaneous partial pressure of carbon dioxide; PetCO₂, end tidal partial pressure of carbon dioxide; NETS, Newborn Emergency Transport Service (Victoria); PaO₂/PaCO₂ ratio, alveolar-arterial oxygen tension ratio
The Australian Therapeutics Goods Administration has approved both devices for use in newborn infants. A specialist neonatal transport nurse and neonatal paediatrician escorted all infants.

After calibration of the TcPCO2 and PetCO2 monitors, paired CO2 measurements were recorded every 20 minutes, starting at stabilisation and continuing throughout the transport. The initial recordings were calibrated with a simultaneous PaCO2. The NETS team was not blinded to the TcPCO2 or PaCO2 values; any ventilator changes were based on the TcPCO2 or PaCO2 values.

The severity of each baby’s lung disease was determined by calculating the alveolar to arterial oxygen tension ratio (PAO2/PaO2 ratio) where PaO2 = (Barometric pressure − 47) × (FiO2 − PaO2). Severe lung disease was defined as a PAO2/PaO2 ratio <0.3. A PAO2/PaO2 ratio of <0.3 has been associated with less precision of PetCO2 measurements to estimate PaCO2.

The parents of all infants enrolled in the study provided written and signed informed consent for their infants to be transported by NETS and this involved specific consent to the use of all devices used in the study. This study was discussed with the Royal Women’s Hospital Ethics in Human Research Committee. It was decided that formal ethics approval was not required as the above written informed consent adequately informed the parents and addressed the ethical issues of the study.

### Statistical analysis

The differences between PaCO2, TcPCO2, and PetCO2 (expressed as P(a-Tc)CO2, P(a-Et)CO2, and P(Tc-Et)CO2 respectively) were analysed using a Student’s paired t test, and their correlations were calculated. The Bland-Altman technique was used to assess agreement and repeatability. A bias of less than ±0.7 kPa was considered clinically acceptable.

### RESULTS

Twenty six infants were enrolled, but five were excluded because the PetCO2 could not be continuously measured in three, both TcPCO2 and PetCO2 could not be measured in another, and in the fifth infant the initial blood gas was venous. Table 1 summarises the characteristics of the 21 infants. A total of 21 P(a-Tc)CO2 and P(a-Et)CO2 differences and 82 P(Tc-Et)CO2 differences (median recordings per subject 4.0 (range 2–10)) were calculated.

![Figure 1](http://fn.bmj.com/) Bland-Altman plot of the difference between PaCO2 and PetCO2 (P(a-Et)CO2) against average CO2.

![Figure 2](http://fn.bmj.com/) Bland-Altman plot of the difference between PaCO2 and TcPCO2 (P(a-Tc)CO2) against average CO2.

![Table 1](http://fn.bmj.com/) Characteristics of the 21 subjects enrolled in study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (weeks)</td>
<td>35</td>
<td>26–40</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2260</td>
<td>930–4600</td>
</tr>
<tr>
<td>Age at enrolment (hours)</td>
<td>4.8</td>
<td>1.8–61.2</td>
</tr>
<tr>
<td>Transportation time (minutes)</td>
<td>65</td>
<td>20–180</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.32 (0.12)</td>
</tr>
<tr>
<td>FiO2</td>
<td>0.52 (0.24)</td>
</tr>
<tr>
<td>PAO2/PaO2</td>
<td>0.85 (1.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory failure</td>
<td>15</td>
</tr>
<tr>
<td>Cyanotic heart disease</td>
<td>2</td>
</tr>
<tr>
<td>Persistent pulmonary hypertension of the newborn</td>
<td>1</td>
</tr>
<tr>
<td>Severe anaemia</td>
<td>1</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>1</td>
</tr>
<tr>
<td>Multiple congenital abnormalities</td>
<td>1</td>
</tr>
</tbody>
</table>

FiO2, Inspired oxygen fraction; PAO2/PaO2 ratio, alveolar-arterial oxygen tension ratio.

![Table 2](http://fn.bmj.com/) A comparison of CO2 (kPa) measured in three different ways

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean (SD)</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(a-Tc)CO2</td>
<td>21</td>
<td>−0.13 (0.71)</td>
<td>−0.46 to 0.19</td>
<td>0.4</td>
</tr>
<tr>
<td>P(a-Et)CO2</td>
<td>21</td>
<td>1.04 (0.98)</td>
<td>0.59 to 1.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P(Tc-Et)CO2</td>
<td>82</td>
<td>−0.07 (0.84)</td>
<td>−0.26 to 0.11</td>
<td>0.43</td>
</tr>
</tbody>
</table>
DISCUSSION
This study shows that, in neonates requiring ventilation during transport, TcPCO₂ monitoring more accurately reflected PaCO₂ than PetCO₂ monitoring. Furthermore, PetCO₂ monitoring should be used with caution. Both PetCO₂ and TcPCO₂ were linearly related to PaCO₂ and each other. However, a linear relation alone (or correlation coefficients—the method used in many of the previous reports) does not adequately describe the agreement between two clinical measurement techniques.2 10 11 Assessing agreement between two methods of clinical measurement is complex. The method described by Bland and Altman is a more informative technique for assessing agreement, reliability, and repeatability, and allows interpretation within a clinical context.10 12 With the use of this technique, PetCO₂ was neither as precise nor reliable a method of assessing PaCO₂ during the transport of ventilated neonates, whereas TcPCO₂ provided a more reliable method. The degree of bias demonstrated between PetCO₂ and PaCO₂ (1.04 kPa) is clinically unacceptable.

Most of the infants in this study had mechanical ventilation instigated by the transport team; knowledge of any changes in the CO₂ is essential for safe delivery of ventilation. Frequent PaCO₂ measurements are not practical during neonatal transport; a reliable non-invasive indicator of PaCO₂ is essential. Calibrated TcPCO₂ is an acceptable surrogate for PaCO₂ trends over time. Transcutaneous gas monitoring is an established and validated practice in neonatology.1 Newborn infants are particularly suited to transcutaneous monitoring because of their thin skin. Although proper use is dependent on appropriate training and placement, the only practical limitations are skin perfusion (which may be altered by vasoconstrictive agents, hypovolaemia, and oedema) and the temperature produced by the device. The response time of TcPCO₂ is too slow (30–50 seconds) to allow monitoring of the respiratory pattern.19 TcPCO₂ monitoring in neonatal transport has previously been evaluated and shown to result in improved ventilation on arrival at the receiving institution.1 20

Many authors have reported a good correlation between PetCO₂, TcPCO₂, and PaCO₂ in newborn infants, but in only three studies that evaluated PetCO₂ was the relation assessed using the Bland-Altman technique.14 15 21 Rozycki et al14 described a mean (SD) P(a-Et)CO₂ bias of 0.92 (0.92) kPa in 45 newborn infants receiving mechanical ventilation, with only 36.9% of PetCO₂ values falling within 0.67 kPa of the PaCO₂. The authors concluded that the significant bias, PetCO₂ provided a reliable estimate of PaCO₂ trends. A similar mean P(a-Et)CO₂ difference of 0.91 (0.68) kPa was reported by Tobias and Meyer21 in 25 infants and toddlers (up to 48 months of age) receiving mechanical ventilation for respiratory failure; the P(a-Tc)CO₂ difference in this study was 0.31 (0.18) kPa. Sivan et al15 obtained a clinically acceptable P(a-Et)CO₂ result, with a mean difference of 0.45 (0.88) kPa in a study involving 134 children (aged 2 days to 16 years) receiving mechanical ventilation. The mean P(a-Tc)CO₂ in this group was 0.17 (0.96) kPa. The P(a-Tc)CO₂ bias was related to skin perfusion but remained clinically acceptable. Primary diagnosis was not described in this study, nor was the proportion of the population who were newborn infants, making inference to the neonatal population difficult. Sivan and colleagues concluded that the degree of the P(a-Et)CO₂ bias was reduced in children with mild lung disease, as defined by a PAO₂/PAO ratio of >0.3. In the cohort with severe lung disease, the mean P(a-Et)CO₂ 1.04 (0.97) kPa was similar to our study.

Parenchymal lung disease with ventilation perfusion (V/Q) mismatching and a PaO₂/PaO ratio <0.3 is a feature of most causes of neonatal respiratory failure. During our study, only two infants did not require oxygen, and nearly all had parenchymal lung disease. Our study was not designed to assess the relation between degree of lung disease and PetCO₂ accuracy.

PetCO₂ monitoring has been validated in adult ventilated patients and healthy anaesthetised infants, but the infants in

---

**What is already known on this topic**

- TcPCO₂ has been shown to be an accurate and reliable method of indicating PaCO₂ in neonates receiving intensive care.
- Although measurement of PetCO₂ can also indicate endotracheal tube position, in previous studies the ability to accurately reflect PaCO₂ has been variable.

**What this study adds**

- This study shows that TcPCO₂ accurately reflects PaCO₂ during neonatal transport, whereas PetCO₂ underestimates PaCO₂ by about 1.0 kPa, a clinically unacceptable difference.
- PetCO₂ was also unable to reliably reflect TcPCO₂ over time, therefore this study supports the use of TcPCO₂ as the preferred method of non-invasive CO₂ monitoring during neonatal transport.
our study had respiratory failure.\textsuperscript{10} Pet\textsubscript{CO2} is dependent on alveolar CO\textsubscript{2} (PACO\textsubscript{2}) and the site of sampling. Non-uniform alveoli CO\textsubscript{2} emptying patterns in patients with large ventilation perfusion mismatching result in PACO\textsubscript{2} underestimating \textsubscript{PaCO2}.\textsuperscript{2,22}

Technical limitations of end tidal analysis in patients with high rate, low tidal volume breathing would have contributed to the difference between Pet\textsubscript{CO2} and \textsubscript{PaCO2}. To account for the fresh inhaled gas admixture during proximal Pet\textsubscript{CO2} sampling, a minimum sampling flow rate of 150 ml/min is required.\textsuperscript{11} The end tidal analyser used in our study sampled at 50 ml/min. Despite manufacturer assurances, this may have had an impact on our results. The response time of end tidal analysers must be less than the respiratory cycle. The response time of the end tidal analyser used was 190 milliseconds, which is adequate for the ventilation rates used during the study, although at high respiratory rates with a short expiratory time, all exhaled alveolar gas would not have migrated to a proximal end tidal sampling site on completion of each respiratory cycle.\textsuperscript{11}

The relation between Tc\textsubscript{PCO2} and Pet\textsubscript{CO2} was not constant over time within individuals, even when both values were adjusted to \textsubscript{PaCO2}. In our opinion Pet\textsubscript{CO2} monitoring cannot be used to reliably monitor trends in \textsubscript{PaCO2} over time in newborn infants with lung disease.

Despite our findings, Pet\textsubscript{CO2} monitoring may offer some benefits over Tc\textsubscript{PCO2} monitoring. Primarily the ability to rapidly and reliably confirm endotracheal tube position within the trachea, with either a capnograph or colorimetric end tidal CO\textsubscript{2} indicator, is of great benefit within the noisy environment of neonatal transport.\textsuperscript{12} This study did not aim to assess the ability of Pet\textsubscript{CO2} or Tc\textsubscript{PCO2} to indicate endotracheal tube position. Inadvertent extubation is not a common occurrence in our transport population and did not occur in any of the neonates involved in this study. Further study is required to determine the role of Pet\textsubscript{CO2} in ensuring the endotracheal tube position during transport.

CONCLUSIONS

Owing to the bias of about \(-1\) kPa and lack of consistency in measuring \textsubscript{PaCO2} over time, Pet\textsubscript{CO2} cannot be recommended during neonatal transport to monitor ventilation. Tc\textsubscript{PCO2} monitoring was generally more precise, reliable, and agreed with \textsubscript{PaCO2}. Tc\textsubscript{PCO2} monitoring is the preferred method of non-invasive CO\textsubscript{2} monitoring during neonatal transport.

\begin{table}
\centering
\caption{Relation between Pet\textsubscript{CO2} values and severity of lung disease}
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
 & \multicolumn{3}{|c|}{Severe (n = 12)} & \multicolumn{3}{|c|}{Mild-moderate (n = 8)} \\
\hline
 & Mean (SD) & 95\% CI & p Value & Mean (SD) & 95\% CI & p Value \\
\hline
P_{et-ti}CO2 & 1.21 (0.76) & 0.87 to 1.88 & \(<0.001\) & 0.99 (1.16) & 0.61 to 1.37 & 0.013 \\
\hline
All CO\text sub{2} values in kPa. Severe lung disease, PACO\textsubscript{2}/PaO\textsubscript{2} ratio \(<0.3\); mild-moderate lung disease, PACO\textsubscript{2}/PaO\textsubscript{2} ratio \(\geq 0.3\).
\end{tabular}
\end{table}

\begin{thebibliography}
\bibitem{12} Rich GF, Saccoz JM. Continuous end-tidal \textsubscript{CO2} sampling within the proximal endotracheal tube estimates arterial \textsubscript{CO2} tension in infants. Can J Anaesth 1991;3:201–3.
\bibitem{13} Agilent M3015A Microstream \textsubscript{CO2} measurement server extension data sheet. Andover, MA: Agilent Technologies Inc, 2000.
\end{thebibliography}