

spinning a 40  $\mu$ l sample was injected on to the liquid chromatography column, and detected at 273 nm.

Differences between methods were analysed using a paired *t* test.

## Results

The mean difference between the theophylline concentrations obtained from the alternative assays of the individual patient samples was 0.38 mg/l. There was no significant difference between the two assay methods ( $t=1.65$ ).

The coefficient of variation of repeated measurements for the Acculevel stick at 9 mg/l was 5.36%.

## Discussion

There are various ways of measuring methylxanthines, including reverse phase HPLC,<sup>4</sup> gas liquid chromatography, and high pressure cation exchange chromatography, but these methods require considerable expertise. Homogenous enzyme immunoassay is simpler but still requires specific machinery which must be carefully used to obtain reliable results.<sup>5</sup> Theophylline stick assays are simple, reliable, and can be used by clinicians after limited training. An alternative theophylline stick assay requires the separation of plasma and a specific machine for measurement.<sup>6</sup>

This whole blood theophylline stick assay requires neither separation of plasma, nor expensive technology. It is particularly suitable for use outside normal

working hours, casualty departments, and in small hospitals that do not have access to a therapeutic drug monitoring service. It is highly acceptable, particularly to children, as it requires only 12  $\mu$ l of whole blood obtained by finger prick. As with all stick assays, care must be taken to follow the correct procedure, or inaccuracies will result.

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Correspondence to Dr A C Elias-Jones, Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

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## Monitoring of end tidal CO<sub>2</sub> in neonatal intensive care

A M C WATKINS AND A M WEINDLING

*Regional Neonatal Intensive Care Unit, Liverpool Maternity Hospital, Liverpool*

**SUMMARY** The use of monitoring end tidal carbon dioxide pressure (PetCO<sub>2</sub>) in neonatal intensive care was studied in 19 infants with respiratory disease. PetCO<sub>2</sub> correlated poorly with arterial pCO<sub>2</sub>, the relation being principally determined by the severity of pulmonary disease. Monitoring end tidal CO<sub>2</sub> cannot be recommended for neonates with pulmonary disease.

important. End tidal pCO<sub>2</sub> monitors, suitable for use with neonates, have recently been developed and have been proposed as alternatives to transcutaneous pCO<sub>2</sub> monitors for non-invasive monitoring of CO<sub>2</sub> content in ill premature infants. We therefore examined the accuracy and clinical usefulness of measuring the end tidal partial pressure of CO<sub>2</sub> (PetCO<sub>2</sub>) in such a group of infants.

## Method

In modern neonatal intensive care units the continuous monitoring of arterial carbon dioxide partial pressure (PaCO<sub>2</sub>) has become increasingly

The monitor used was an Engstroem Eliza infrared capnometer. This was connected to the patient's respiratory circuit by a 15 mm endotracheal tube

adapter, incorporating a standard Luer connection at right angles to the body (Respiratory Support Products), and a length of Engstroem Aridus reinforced tubing two metres long. This system permitted sampling without increasing respiratory dead space. The capnometer took samples from the airway at a constant 50 ml/min and analysed the gas continuously; it displayed PetCO<sub>2</sub> breath by breath on the monitor, together with the mean PetCO<sub>2</sub> every 30 seconds and 15 minutes, and the maximum PetCO<sub>2</sub> over a 15 minute period. The response time of the machine was 150 msec. Samples were taken from babies who were not intubated using a fine catheter inserted into the anterior nares or nasopharynx.

Infants were selected for the study if they were clinically stable and had indwelling arterial catheters. PetCO<sub>2</sub> measurements were compared with simultaneous PaCO<sub>2</sub> measurements. Infants were studied for four hours during which between one and five measurements were taken. Five infants were studied on more than one occasion at different stages of their illness.

Nineteen infants were studied, 15 while intubated (62 readings), and four while receiving oxygen or breathing air (seven readings). Their gestational ages ranged from 25 to 35 weeks (median 29 weeks), and birth weights from 744 g to 2385 g (median 1280 g). Sixteen had hyaline membrane disease of varying degrees of severity, two had transient tachypnoea of the newborn, and one had pneumonia. The severity of disease varied widely, alveolar arterial oxygen gradients (AADO) ranging from 18 to 660 mm Hg. Three of the intubated infants were having continuous positive airway pressure only, and 59 were receiving intermittent positive pressure ventilation.

Data were analysed using the Statistical Package for the Social Sciences on an IBM 3083 computer.

The alveolar-arterial oxygen gradient was estimated by the following method:  $AADO = ((FiO_2 \cdot 7760) - (PaCO_2 \cdot 0.8)) - PaO_2$ .<sup>1</sup>

## Results

The capnometer recorded respiratory rate reliably whether the baby was intubated or not. It functioned well as an apnoea monitor. The nasal catheters used in non-intubated patients were poorly tolerated by the infants with respiratory distress and gave variable readings, which were affected by the position of the catheter and movement of the subject. Because of this detailed analysis has been presented only for the 62 measurements on intubated patients.

Fig. 1 is a plot of PaCO<sub>2</sub> against PetCO<sub>2</sub> showing

a poor overall correlation ( $r=0.387$   $p<0.01$ ). In 11 infants (32 readings) there was a useful correlation between end tidal and arterial PCO<sub>2</sub>; these infants were those with mild or moderate lung disease (maximum AADO 264). This was shown by excluding all readings at an AADO of greater than 300, which considerably improved the regression ( $r=0.749$   $p<0.0001$   $n=39$ ). Fig. 2 shows that the difference between PetCO<sub>2</sub> and PaCO<sub>2</sub> (PetCO<sub>2</sub>-PaCO<sub>2</sub>) correlated strongly with AADO ( $r=0.77$   $p<0.0001$ ).

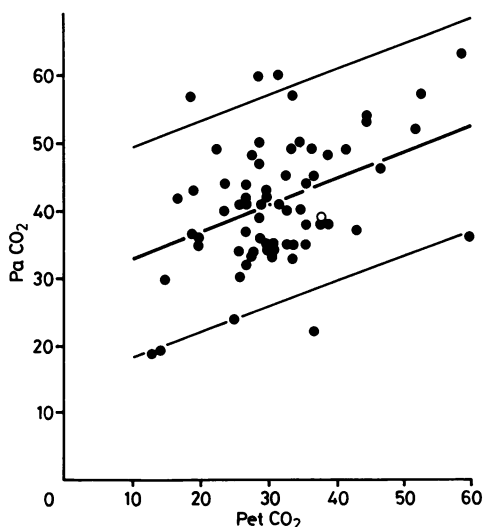


Fig. 1 Plot of PaCO<sub>2</sub> with simultaneously obtained PetCO<sub>2</sub> showing 95% confidence limits. ( $x=2$  values). ( $r=0.388$   $p<0.01$   $n=62$ ).

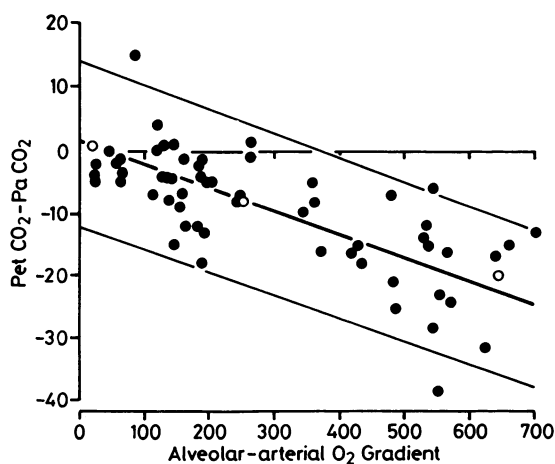


Fig. 2 Plot of (PetCO<sub>2</sub>-PaCO<sub>2</sub>) with AADO, showing 95% confidence limits. ( $x=2$  values) ( $r=-0.772$   $p<0.0000$   $n=62$ ).

Multiple regression analysis was undertaken to explore further the relative importance of the factors affecting the relation between PetCO<sub>2</sub> and PaCO<sub>2</sub>. The relation between PetCO<sub>2</sub> and PaCO<sub>2</sub> could be calculated satisfactorily if PetCO<sub>2</sub> and AADO were known; in particular, the addition of respiratory rate did not significantly ( $p < 0.1$ ) improve the accuracy of the prediction.  $\text{PaCO}_2 = 6.44 + (0.803 \cdot \text{PetCO}_2) + (0.032 \cdot \text{AADO})$ . ( $r = 0.725$ ,  $\text{SE} = 6$ ,  $12 \text{ F} = 32$ ,  $12 \text{ sig F} < 0.0001$   $n = 60$ ).

Infants with shorter expiratory times tended to have less accurate readings, reflected in a bigger difference between end tidal and arterial pCO<sub>2</sub> (PetCO<sub>2</sub> - PaCO<sub>2</sub>). There was a poor correlation between expiratory time and this score ( $r = 0.265$   $p < 0.05$   $n = 62$ ).

Infants with short expiratory times were those with more severe respiratory disease, characterised by high respiratory rate and AADO. Because of this multiple analysis of variance and covariance for the error score (PetCO<sub>2</sub> - PaCO<sub>2</sub>) with AADO, respiratory rate, expiratory time, and PaCO<sub>2</sub> was performed. AADO correlated strongly ( $p < 0.0001$ ) with this score, as did PaCO<sub>2</sub> ( $p < 0.0001$ ). Expiratory time ( $p < 0.05$ ) and respiratory rate ( $p < 0.05$ ) correlated weakly with this score once AADO was controlled for.

The capnometer created little extra work for nurses, requiring only the temporary disconnection of the sampling catheter during lavage and suction of the endotracheal tube. If this was neglected water was aspirated into the machine, making it temporarily useless. Calibration, taking 60 seconds, is required every three to four weeks.

## Discussion

PetCO<sub>2</sub> may be a good approximation to PaCO<sub>2</sub> but it is not identical, as it varies depending on the ventilation pattern and lung function of the subject at the time.<sup>2-4,6</sup> PetCO<sub>2</sub> measurements have been shown to correlate well with PaCO<sub>2</sub> in subjects without lung disease.<sup>5,6</sup> PetCO<sub>2</sub> is most likely to equal or exceed PaCO<sub>2</sub> at high tidal volumes, high CO<sub>2</sub> outputs (as in exercise), and at low respiratory rates.<sup>3,5</sup> PetCO<sub>2</sub> measurements considerably underestimate PaCO<sub>2</sub> in adults with lung disease or pulmonary embolism, which cause ventilation-perfusion inequality.<sup>5</sup>

Infants with respiratory disease generally have a high respiratory rate, low tidal volume, and considerable ventilation-perfusion imbalance. It was, therefore, hardly surprising that the relation between PetCO<sub>2</sub> and PaCO<sub>2</sub> was variable and association frequently poor in this group. We have shown that AADO is the major determinant of the relation

between PetCO<sub>2</sub> and PaCO<sub>2</sub>, and that respiratory rate and expiratory time have a definite but less important effect.

We consider that the capnometer was accurately measuring the PetCO<sub>2</sub>, as in all infants the expiratory time was greater than the response time of the machine (150 msec), and in all but one was at least twice this time. PetCO<sub>2</sub> is not necessarily a good index of PaCO<sub>2</sub> in infants with severe lung disease, as in these infants alveolar ventilation is poor and may show wide regional variation, and definite ventilation-perfusion imbalance. This, coupled with the short expiratory time and high respiratory rate of these infants, may account for the large differences between these two indices.

In premature infants with respiratory distress AADO characteristically changes rapidly as the respiratory illness runs its course. The use of PetCO<sub>2</sub> is, therefore, unlikely to be helpful even as a trend monitor. Changes in the PetCO<sub>2</sub> may be due either to a change in PaCO<sub>2</sub>, or to a change in the relation between PetCO<sub>2</sub> and PaCO<sub>2</sub> as the AADO changes in the course of the respiratory illness or as the ventilation pattern of the infant is changed therapeutically.

There may well be a place for PetCO<sub>2</sub> measurement in the management of premature infants with normal lung function, for example, in the detection and analysis of obstructive apnoea or during anaesthesia. For most premature infants with respiratory illness, however, this technique cannot be recommended.

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Correspondence to Dr A M C Watkins, Regional Neonatal Intensive Care Unit, Department of Child Health, University of Liverpool, Liverpool Maternity Hospital, Liverpool L7 7BN.

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