Mainstream end-tidal carbon dioxide monitoring in ventilated neonates

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ABSTRACT

Introduction: Continuous noninvasive monitoring of the partial pressure of arterial carbon dioxide ($PaCO_2$) in ventilated neonates would help clinicians to reduce arterial blood sampling. Our objective was to determine the correlation and agreement between end-tidal carbon dioxide ($EtCO_2$) and $PaCO_2$ in newborns ventilated for various clinical situations.

Methods: This prospective study was undertaken over 15 months in a teaching hospital. Simultaneous end-tidal and arterial CO_2 pairs were obtained from ventilated neonates who were monitored by mainstream capnography and had indwelling arterial catheter. The correlation coefficient and degree of bias between $EtCO_2$ and $PaCO_2$ were assessed for various clinical situations.

Results: A total of 133 end-tidal and arterial CO_2 pairs were analysed from 32 ventilated newborns. The mean gestational age was 34.6 +/- 3.8 weeks and birth weight was 2,200 +/- 780 g. The overall coefficient of correlation (r) was 0.73 (p-value is less than 0.001). The $EtCO_2$ value was lower than the corresponding $PaCO_2$ value in 86.5 percent pairs, with a mean bias of -6.65 +/- 7.54 mmHg (95 percent CI, - 7.9 to - 5.35). The r-value was more than or equal to 0.92 in neonates ventilated for sepsis, asphyxia and apnoea of prematurity, 0.67 in hyaline membrane disease (HMD) and 0.69 in meconium-aspiration syndrome. In HMD, neonates who received surfactant had a better r-value than those who did not (0.76 vs. 0.6).

Conclusion: The correlation between mainstream $EtCO_2$ and $PaCO_2$ is good. Neonates with pulmonary disease will have a lower correlation. Surfactant therapy improves the correlation. $EtCO_2$ monitoring is helpful in trending or screening for abnormal $PaCO_2$ values.

Keywords: arterial carbon dioxide monitoring, end-tidal carbon dioxide monitoring, mainstream capnography, mechanical ventilation, neonate ventilation

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INTRODUCTION

Neonates on mechanical ventilation require monitoring for the adequacy of ventilation and oxygenation. Though arterial blood gas analysis is the gold standard of monitoring, it is expensive, leads to blood loss and iatrogenic anaemia, and each sample is only a snapshot view of the sampling moment. Pulse oximetry provides a noninvasive method of assessing the oxygenation and continuous surveillance of the partial pressure of arterial oxygen (PaO_2).[1] It is also essential to monitor the partial pressure of arterial carbon dioxide ($PaCO_2$) levels in the blood, because both low and high $PaCO_2$ levels may give rise to complications in neonates.[2-4] End-tidal carbon dioxide ($EtCO_2$) measurement is a continuous and non-invasive measurement of blood carbon dioxide tensions with fast response time to changes in blood CO_2 levels and internal calibrating ability. It will also reduce the blood loss associated with repeated arterial blood gas sampling.[5,6] There are few reports that showed a poor correlation in neonates with pulmonary disease.[7,8] However, recent studies have reported mainstream $EtCO_2$ monitoring as useful and accurate.[9-11] The present study was undertaken to assess the reliability of $EtCO_2$ as a function of $PaCO_2$ in various clinical situations by mainstream technique.

METHODS

The study was carried out prospectively over 15 months (July 2005 to September 2006) on ventilated neonates, who were monitored by mainstream capnography and indwelling arterial lines. Newborns with congenital heart diseases were excluded. Neonates were ventilated using pressure limited, time-cycled ventilators in either assist-control mode or synchronous intermittent mandatory ventilation mode. Vital parameters and the percentage of oxygen saturation in blood (SpO_2) were continuously monitored. Exhaled CO_2 was continuously monitored using a mainstream capnometer (Capnostat Mainstream CO_2 Module, Novametrix Medical Systems Inc, CA, USA) Endotracheal tube position was determined by chest radiograph, which also ensured bilateral equal air entry. The

Table I. List of patient characteristics (n=32).

Characteristics	No. (%)
Gender	
Male	22 (68.7)
Female	10 (31.3)
Place of birth	
Inborn	14 (43.8)
Out born	18 (56.3)
Indications for ventilation (primary disease)	
HMD	18 (56.3)
MAS	9 (28.1)
Sepsis	2 (6.3)
SBA	2 (6.3)
AOP	1 (3.1)
Gestational age (weeks)	
Range	27–40
Mean ± SD	34.6 ± 3.8
Birth weight (g)	
Range	840–3,500
Mean ± SD	2,200 ± 780

HMD: hyaline membrane disease; MAS: meconium-aspiration syndrome; SBA: severe birth asphyxia; AOP: apnoea of prematurity; SD: standard deviation

Table II. Disease-wise distribution of $EtCO_2$-$PaCO_2$ pairs (n = 133).

Categories	EtCO2-PaCO2 pairs No. (%)
HMD	72 (54.1)
MAS	44 (33.1)
Sepsis	7 (5.3)
SBA	6 (4.5)
AOP	4 (3.0)

HMD: hyaline membrane disease; MAS: meconium-aspiration syndrome; SBA: severe birth asphyxia; AOP: apnoea of prematurity

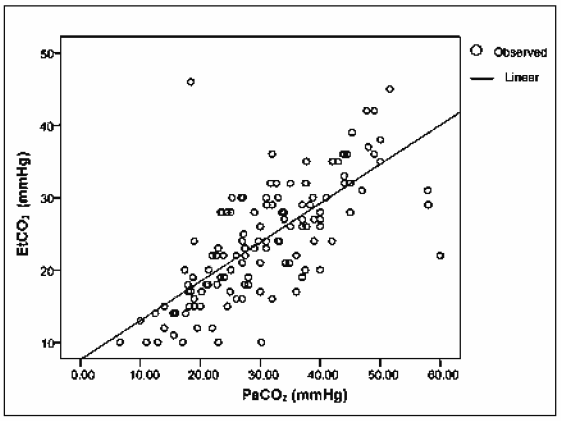

Fig. 1 Scattergram plot shows the relationship between end-tidal versus arterial carbon dioxide.
n = 133; r = 0.73; p < 0.001

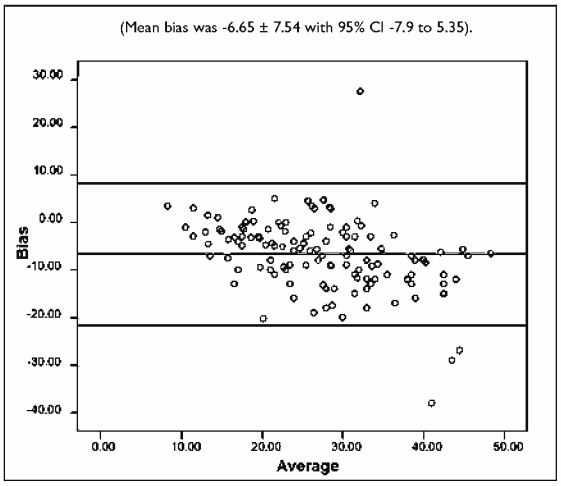

Fig. 2 Bland-Altman plot shows bias against average values of $EtCO_2$ and $PaCO_2$.

mainstream capnometer adaptor was placed just proximal to the endotracheal tube. Calibration was performed according to the manufacturer's recommendations. CO_2 monitoring resumed immediately after calibration. The ventilators used flow probes which alarmed if the exhaled volume was significantly less than the inhaled volume, ensuring that air leaks around the endotracheal tube would not be a confounding problem.

The sampling for arterial blood gas (ABG) was done after the baby had been stabilised and was subsequently ordered at the discretion of the treating physician. ABG measurement was done on ABL-TM5 blood gas system. During blood sampling, the value of $EtCO_2$ as shown on the LED display of the monitor was noted. Simultaneous $EtCO_2$ and $PaCO_2$ measurements were recorded on the proforma along with additional data including the ventilator settings and demographical details. The primary indication for ventilation was considered as the primary diagnosis. Correlation between $EtCO_2$ and $PaCO_2$ was assessed in various clinical situations based on the indication of ventilation. Correlation was also assessed in hyaline membrane disease (HMD) with respect to surfactant therapy. The data of simultaneously-recorded $EtCO_2$ and $PaCO_2$ values was analysed statistically using correlation analysis and a correlation coefficient (r). The differences between $EtCO_2$ and $PaCO_2$ (bias) were analysed using a Student's paired *t*-test, and the Bland-Altman technique was used to show the agreement and bias ($EtCO_2$-$PaCO_2$). A p-value of < 0.05 was considered as significant.

RESULTS

A total of 133 $EtCO_2$-$PaCO_2$ pairs were analysed from 32 newborns who required ventilation for various indications, like HMD, meconim-aspiration syndrome (MAS), sepsis, severe birth asphyxia (SBA) and apnoea of prematurity (AOP). Each ventilated newborn provided a median of four pairs (range 1–11). The mean gestational age was 34.6 ± 3.8 weeks, and mean birth weight, 2,200 ± 780 g. The commonest indication for ventilation was HMD

Table III. Correlation between $EtCO_2$ and $PaCO_2$ based on indication for ventilation (n = 133 pairs).

Condition	HMD	MAS	SBA	Sepsis	AOP
Sample size (%)	72 (54.14)	44 (33.08)	7 (5.26)	6 (4.51)	4 (3.00)
$EtCO_2$ (mmHg)					
Range	10–46	10–36	19–45	12–29	10–17
Mean ± SD	26.1 ± 8.2	22.2 ± 7.0	27.9 ± 10.83	22.0 ± 6.38	14.5 ± 3.31
$PaCO_2$ (mmHg)					
Range	10–60	11–44	23–51	14–37	6.6–20
Mean ± SD	33.7 ± 12.1	27.8 ± 7.2	35.4 ± 11.3	28.7 ± 8.2	14.4 ± 6.2
r-value	0.67	0.69	0.92	0.98	0.98

HMD: hyaline membrane disease; MAS: meconium-aspiration syndrome; SBA: severe birth asphyxia; AOP: apnoea of prematurity; SD: standard deviation; r: correlation coefficient
All figures are rounded to two decimal places

Table IV. $EtCO_2$-$PaCO_2$ correlation in hyaline membrane disease (n = 72 pairs).

Condition (No. of newborns)	Overall (18)	Surfactant (7)	No surfactant (11)
Sample size (%)	72 (54.13)	31 (23.31)	41 (30.83)
$EtCO_2$ (mmHg)			
Range	10–46	10–39	13–46
Mean ± SD	26.1 ± 8.2	27.3 ± 8.3	25.2 ± 8.2
$PaCO_2$ (mmHg)			
Range	10–60	12.9–58	10–60
Mean ± SD	33.7 ± 12.1	36.6 ± 10.9	31.4 ± 12.6
r-value	0.67	0.76	0.6

SD: standard deviation; r: correlation coefficient

(56.25%). The non-pulmonary indications represented 15.63% (5/32) of the neonates (Table 1). Table II shows the disease-wise distribution of $EtCO_2$ and $PaCO_2$ pairs. HMD, the commonest indication for ventilation, provided a sample size of 54.14% (72/133 pairs), followed by MAS with 33.08% (44/133 pairs).

The scattergram plot of the $EtCO_2$-$PaCO_2$ relationship is shown in Fig. 1. We found variability in the relationship between the two measures of CO_2 monitoring. However, the overall correlation between $EtCO_2$-$PaCO_2$ was good, with an r-value of 0.73 ($p < 0.001$). The $EtCO_2$ value was lower than the corresponding $PaCO_2$ value in 86.47% (115/133) pairs with a mean bias of -6.65 ± 7.54 mmHg ($EtCO_2 = 24.3 \pm 8$ vs. $PaCO_2 = 31 \pm 11$ mmHg). The 95% confidence interval for the bias was - 7.9 to - 5.35 mmHg. In 13.5% (18/133) pairs the $EtCO_2$ value was higher than the corresponding $PaCO_2$ values. The bias in the relationship between the $EtCO_2$ and $PaCO_2$ is illustrated in Fig. 2, where the difference is plotted against the average of the values.[12] The $EtCO_2$ values were within 5 mmHg of the corresponding $PaCO_2$ in 30.08% (40/133) pairs.

The correlation between $EtCO_2$ and $PaCO_2$ in neonates ventilated for various clinical situations is shown in Table III. The r-value was different for pulmonary and other than pulmonary conditions. An r-value of ≥ 0.92 was observed in neonates ventilated for sepsis, SBA and AOP. The r-value was 0.67 and 0.69 in HMD and MAS, respectively. Among the 18 neonates with HMD, 11 could not be treated with surfactant, as the parents could not afford it. We analysed the r-values for neonates ventilated for HMD, in those who received surfactant and those who did not (Table IV). The overall r-value was 0.67 in the HMD group. The correlation was better in the surfactant group (r = 0.76), compared to the non-surfactant group (r = 0.6). Further, during the initial hours of ventilation, the correlation between $EtCO_2$ and $PaCO_2$ was good in the surfactant group (r = 0.72), compared with the non-surfactant group (r = 0.57). The correlation improved in both the groups later during the course of ventilation.

DISCUSSION

Treating respiratory problems, especially with ventilator support, is a critical part of the neonatal intensive care. In ventilated neonates, continuous monitoring of both O_2 as well as CO_2 are essential. Determining the $PaCO_2$ has become more critical with the increased recognition that both low and high $PaCO_2$ levels are associated with long-term morbidity.[2-6] Although ABG analysis remains the most accurate method of monitoring blood CO_2 tensions, alternative methods are desirable in neonates

to minimise blood loss. Transcutaneous CO_2 monitoring is an alternative, but has limitations such as sensor-associated burns, damage to the skin by adhesive, erratic behaviour in the presence of acidosis, long calibration and stabilisation intervals and the need to change the sensors every four hours.[13,14] Capnography, on the other hand, provides continuous surveillance of arterial CO_2 tensions without any of the deleterious effects of the transcutaneous monitoring.

The current study has showed a good correlation and agreement between the end-tidal and arterial CO_2 tensions. The overall r-value was 0.73. In 1987, a poor r-value of 0.387 was reported by Watkins and Weindling in neonates with pulmonary disease.[8] Recently, higher r-values of 0.83 and 0.81 were reported by Rozycki et al[9] and Wu et al,[10] respectively. Amucho Singh and Singhal reported an r-value of 0.71,[11] which is closer to our study report. The mean bias observed in our study was -6.65 ± 7.54 mmHg. The consistent negative bias of $EtCO_2$ in our study agrees with previous reports of mainstream capnometry in neonates.[6,9,15] In 86.5% of pairs, the $EtCO_2$ was lower than the corresponding $PaCO_2$. Similar results have been reported in earlier studies.[9,11] $EtCO_2$ is usually 2–5 mmHg less than $PaCO_2$. The lower value for the end-tidal measurements may be attributable to gas mixing proximal to the endotracheal tube. Measurement of CO_2 from gas sampled distally to the endotracheal tube-ventilator connection more closely matches the arterial value. Measuring CO_2 in this manner would require side stream technology, which is not clinically useful in newborns.[15]

Decreased ventilation will increase $PaCO_2$ and $EtCO_2$ difference, as in HMD, MAS, atelectasis and pneumonia. In the pre-surfactant era, $EtCO_2$ monitoring was reported to be unreliable for estimating $PaCO_2$ in preterms with respiratory distress. While analysing the r-value for various clinical situations, we found that r was different for pulmonary, and other than pulmonary, conditions. The r-value ranged from 0.67 to 0.98, being lowest in the non-surfactant HMD group. The r-value of ≥ 0.92 was observed in neonates ventilated for sepsis, SBA and AOP. Though correlation was significant, r-values were lower in cases with HMD (0.67) and MAS (0.69). However, the number of newborns without primary lung disease was small. Previous studies by Watkins and Weindling reported a poor correlation in neonates with pulmonary disease.[8] Garcia Canto et al wrote in their conclusion that $EtCO_2$ does not maintain a good correlation with $PaCO_2$ in serious lung illnesses.[7] We also observed a significant but lower correlation in pulmonary disorders. In HMD, the overall correlation was 0.67. Nangia et al found a correlation of only 0.55 in the HMD group.[16] Similarly, in MAS, we found an r-value of 0.69, in contrast to that reported by Nangia et al (0.94).[16]

Early improvement in lung mechanics has been reported with exogenous surfactant treatment.[17] Hence, surfactant therapy is said to improve $EtCO_2$ and $PaCO_2$ correlation. Rozycki et al[9] and Amuchou Singh et al[11] respectively reported a correlation of 0.82 and 0.81, in those that received surfactant. We found a correlation of 0.76 in neonates who received surfactant. This correlation was better than that of neonates who did not receive the surfactant (r = 0.6). In 1997, a correlation of only 0.55 was noted by Nangia et al[16] in neonates with HMD and who were not treated with surfactants. Early improvement in the lung mechanics of the surfactant group was reflected by a better correlation of $EtCO_2$-$PaCO_2$ pairs, and early weaning of the ventilator. The continuous nature of noninvasive $EtCO_2$ monitoring is useful to follow trends and adjust ventilator settings. $EtCO_2$ monitoring also leads to less handling of the sick neonates, apart from reducing the number and total volume of blood samples.

The present study showed a good correlation and agreement between mainstream $EtCO_2$ and $PaCO_2$ in newborns ventilated for various clinical situations. Despite the overall variability in the $EtCO_2$ values throughout the entire range of $PaCO_2$, $EtCO_2$ was able to estimate trends in $PaCO_2$. The consistent negative bias of the $EtCO_2$ was similar to that reported in previous studies using mainstream capnometry in neonates. A higher correlation observed in babies ventilated for sepsis, asphyxia and AOP, compared to those with HMD and MAS, suggested that $EtCO_2$ monitoring is affected by the degree of pulmonary disorders. Surfactant therapy improved the accuracy of $EtCO_2$ measurements. $EtCO_2$ may guide us to adjust the ventilatory settings, allow minimal handling of sick neonates and minimise blood loss. However, periodic checks of blood gases are still needed to ensure that $PaCO_2$ is within the normal range.

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