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Neonatal Transcutaneous Carbon Dioxide Monitoring—Effect on Clinical Management and Outcomes

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BACKGROUND: This work aimed to compare frequency of blood gas measurements per day of mechanical ventilation, occurrence of extreme blood gas CO_2 values, and clinical outcomes among ventilated neonates managed with and without transcutaneous carbon dioxide (P_{tcCO_2}) monitors. This work also measures agreement between simultaneous P_{tcCO_2} and blood gas CO_2 measurements and ascertains factors that affect agreement. METHODS: This is a cohort study with retrospective analysis comparing 5,726 blood gas measurements and clinical outcomes for 123 neonates intubated for >48 h before and after the introduction of transcutaneous carbon-di-oxide monitoring devices in a single tertiary care unit. RESULTS: Median (interquartile range) blood gas frequency per mechanical ventilation day was 3.9 (2.6–5.3) and 2.9 (2.1–4.0) before and after P_{tcCO_2} monitoring ($P = .002$) without differences in clinical outcomes at discharge. After adjusting for confounders using Poisson regression, this difference remained significant. The mean ± 2SD blood gas-P_{tcCO_2} difference was −5.2 ± 17.3 mm Hg. 64% of simultaneous blood gas-P_{tcCO_2} measurements per subject were within ±7 mm Hg. Greater bias was noted with arterial sample and during the use of high-frequency ventilation. CONCLUSION: Despite only moderate agreement between simultaneous P_{tcCO_2} and blood gas measurements, P_{tcCO_2} monitoring statistically decreased blood gas frequency among ventilated neonates without affecting the duration of mechanical ventilation or clinical outcomes at discharge. The clinical impact of this technology appears to be minimal. *Key words: capnometry; neonatal; transcutaneous monitoring; outcomes.* [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Infants admitted to the neonatal ICU (NICU) frequently require respiratory support in the form of mechanical ventilation. Arterial, venous and capillary blood gas measurements allow clinicians to gauge the effect of mechanical ventilation on the infant's gas exchange. Samples for blood gas measurement are obtained by invasive techniques resulting in blood loss and only depict the physiologic state of the infant at the point in time when the sample was obtained.[1] Noninvasive methods to estimate P_{CO_2} offer a means of continuous assessment of ventilation without accompanying blood loss and infant manipulation. Transcutaneous carbon-dioxide monitors use heated skin sensors that increase blood flow through the cutaneous capillary system. The locally produced P_{CO_2} is then measured electrochemically and adjusted to provide an output reflective

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of the arterial blood P_{CO_2}. This transcutaneously measure carbon-di-oxide (P_{tcCO_2}) has been studied in selected groups of infants for short periods of time, demonstrating good agreement with arterial blood P_{CO_2}.[2-6] P_{tcCO_2} monitors are increasingly used in NICUs and are anticipated to improve respiratory and overall care of the neonates.[7,8] However, there are reasons to be concerned about the impact of P_{tcCO_2} monitoring in the course of standard NICU clinical care. Wide agreement between P_{tcCO_2} and arterial blood gas has been reported in the preterm population.[2] Many NICU infants remain intubated for long duration with evolving physiological states of cardiac output and fluctuating P_{CO_2} values that may alter P_{tcCO_2} agreement.[9,10] Further, many blood gas samples used in the NICU are capillary samples, and reports to date have correlated P_{tcCO_2} with arterial or venous samples.[2,7,11]

Although the American Association for Respiratory Care recognized the use of P_{tcCO_2} values in specific clinical situations, their statement noted that a hazard of P_{tcCO_2} use is "misinterpretation of falsely elevated or decreased values leading to inappropriate treatment of the patient."[12] Such false alarms could potentially lead to increased blood draws instead of reducing them or cause unnecessary ventilator manipulation and negatively affect outcomes. There is little published data on these issues. In this study, we aimed to determine whether the use of P_{tcCO_2} monitoring in everyday clinical practice among mechanically ventilated neonates over their entire course of intubation altered respiratory management, specifically blood draws and occurrence of extreme blood gas P_{CO_2} values, or impacted neonatal morbidities. We also aimed to measure agreement of simultaneously measured P_{tcCO_2} and blood gas CO_2 values and identify factors associated with discordance.

QUICK LOOK

Current knowledge

P_{tcCO_2} monitoring uses heated skin sensors that increase blood flow to the cutaneous tissue. The locally produced P_{CO_2} is then measured electrochemically and adjusted to provide an output reflective of the arterial blood P_{CO_2}. The relationship of P_{tcCO_2} to P_{aCO_2} is variable, depending on perfusion, temperature, and a number of other variables.

What this paper contributes to our knowledge

There was a moderate agreement between simultaneous P_{tcCO_2} and P_{aCO_2} measurements. The use of P_{tcCO_2} monitoring statistically decreased blood gas frequency among ventilated neonates without impacting the duration of mechanical ventilation or clinical outcomes.

Methods

Study Population and Design

This study was approved by the Partners Healthcare Human Research Committee. P_{tcCO_2} monitors (SenTec AG, Therwil, Switzerland) were introduced for clinical practice to our level III NICU in October 2010. This is a cohort study with retrospective analysis of data spanning 12 months before the introduction of the P_{tcCO_2} monitors, designated pre-P_{tcCO_2} (October 1, 2009 to September 30, 2010), compared with 14 months following their introduction, designated post-P_{tcCO_2} (December 1, 2010 to January 31, 2012). October and November of 2010 were considered a washout period (Fig. 1). All infants admitted to the NICU and mechanically ventilated for >48 h were included. In the post-P_{tcCO_2} cohort, inclusion criteria required P_{tcCO_2} monitor use for ≥50% of the ventilated time because we sought to measure only infants with consistent exposure to the P_{tcCO_2} monitor during their care. To detect a difference of 1 blood gas/day of mechanical ventilation with a power of 0.8, we needed at least 52 subjects in each period (PS version 3.1.2). Because we were interested in either an increase or a decrease in blood gas frequency and any increase would be of clinical relevance, this difference was chosen. The post-P_{tcCO_2} period was longer to capture this sample size. Infants with major congenital anomalies as defined by the Vermont Oxford Network or those transferred before extubation were excluded. End-tidal CO_2 monitoring was not practiced in the NICU during the study period.

Laboratory and Respiratory Data

Blood gas analyses were performed on a Siemens (Rapid Lab 1240) analyzer, and results were obtained from an electronic laboratory data repository. P_{tcCO_2} monitors were applied by respiratory therapists on physician order. Per policy, all ventilated infants were eligible for its use. It was calibrated every 8–12 h, initially with a blood gas drawn 30 min after P_{tcCO_2} monitor application. Respiratory data were abstracted from the flow sheets where respiratory therapists make date and time stamped entries for P_{tcCO_2} measurements, simultaneously drawn blood gas results (when performed), and hourly ventilator settings.

Outcome Measurements

Respiratory outcomes included total blood gas per infant adjusted for mechanical ventilation duration, percentage of extreme blood gas measurements/infant, bias between simultaneous P_{tcCO_2} and blood gas P_{CO_2} values, and

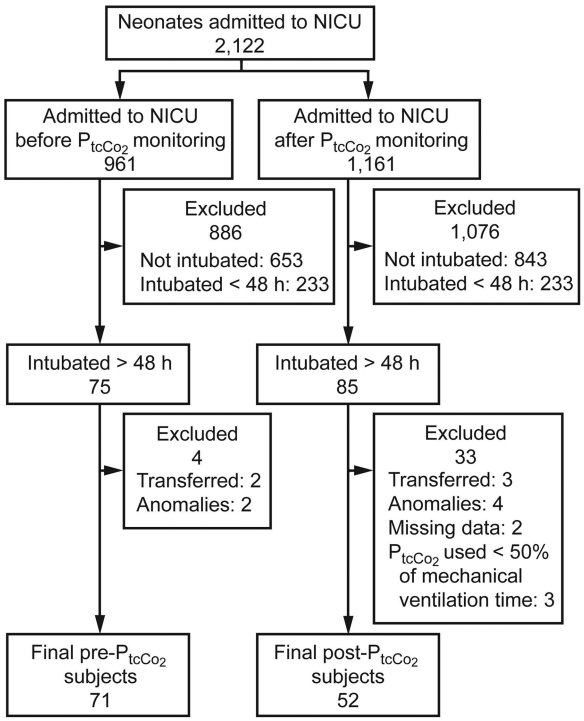

Fig. 1. Flow chart. NICU = neonatal ICU.

bias outside ±7 mm Hg. Blood gas P_{CO_2} values of ≤35 and ≥70 mm Hg were defined as extreme values because values outside of these ranges would generally result in intervention at our institution, irrespective of the infant's pH or clinical status. Based on previous literature we chose ±7 mm Hg as a clinically acceptable bias.[5,13-15] Clinical outcomes were culture-proven sepsis before (early onset) and after (late onset) 3 days of life; ≥Grade III intraventricular hemorrhage; bronchopulmonary dysplasia, defined as respiratory support or oxygen requirement at 36 weeks gestation (for neonates born <32 weeks) or at 28 days of life (for infants ≥32 weeks gestation at birth); necrotizing enterocolitis classified as ≥Bells stage II, including spontaneous intestinal perforation; patent ductus arteriosus diagnosed by echocardiogram or clinically and treated; and type 1 retinopathy of prematurity by ETROP (Early Treatment for Retinopathy of Prematurity) criteria.[16]

Analysis

Demographic and clinical outcomes of the 2 cohorts were compared using the Fisher exact test, chi-square test, Student *t* test, and Mann-Whitney test as appropriate. Infants requiring high-frequency ventilation were identified for subgroup analysis a priori. Poisson regression with overdispersion correction and offsetting for duration of mechanical ventilation was used to analyze the effect of P_{tcCO_2} monitor use on blood gas frequency when adjusting for confounders determined on bivariate analysis. We calculated the fraction of extreme values for individual subjects and averaged those values to give us proportions for the entire cohort to account for repeated measurements. After removing P_{tcCO_2} values of <15 or >100 as outliers (n = 23 observations), we analyzed 1,338 simultaneous P_{tcCO_2} and blood gas P_{CO_2} values. Bias was calculated as the mm Hg difference between simultaneous P_{tcCO_2} and blood gas P_{CO_2} measurements. The agreement between simultaneous P_{tcCO_2} and blood gas P_{CO_2} values was analyzed using a Bland-Altman plot for repeated measurements per subject with varying true values for each observation, and MedCalc 12.7.5 (MedCalc Software, Ostend, Belgium) was used to generate the plot. To account for repeated measurements in the same subject, we calculated the fraction of values for individual subjects within each bias range (±5, ±7, ±10, and ±15 mm Hg) and averaged those values to give us proportions for the entire cohort. Bivariate analysis of clinical factors associated with a bias outside ±7 mm Hg was explored, and a generalized estimating equations model was used to generate an adjusted model. All analysis other than specified was done using SAS 9.3 (SAS Institute, Cary, North Carolina).

Results

Frequency and Range of Blood Gas Measurements

Derivation of the study population is outlined in Figure 1. There were no significant differences in the admission characteristics and initial management between the 2 cohorts (Table 1). Median blood gas frequency per day of mechanical ventilation per infant was significantly lower in the post-P_{tcCO_2} period. The decrease in blood gas frequency was greater among the subset of infants who required high-frequency ventilation (jet or oscillatory ventilation) at any time (Table 2). Birthweight, gestational age, low admission temperature <36°C, use of P_{tcCO_2} monitoring, and high-frequency ventilation were significantly related to total number of blood gases for a subject in the bivariate analysis using Poisson regression when offsetting for duration of mechanical ventilation. In the multivariate model, adjusting for these variables and offsetting for mechanical ventilation duration, use of P_{tcCO_2} monitors remained significantly associated with reduced blood gases along with the use of high-frequency ventilation (Table 3). The post-P_{tcCO_2} cohort on average had a lower percentage of extreme values at 17.8 ± 8.4% than the pre-P_{tcCO_2} cohort with 19.4 ± 8.7%, but this difference was not significant (Table 2).

Clinical Outcomes

There were no significant differences in the duration of mechanical ventilation or use of rescue high-frequency

Table 1. Clinical Characteristics of Infants in the Pre-P_{tcCO_2} and Post-P_{tcCO_2} Periods

	Pre-P_{tcCO_2} (n = 71)	Post-P_{tcCO_2} (n = 52)	P
Female, n (%)	37 (52.1)	25 (48.1)	.72
Gestational weeks at birth, mean ± SD	28.6 ± 4.3	27.7 ± 3.9	.24
Birth gestation <37 weeks, n (%)	67 (94.4)	49 (94.2)	>.99
Birth weight, mean ± SD g	1,228 ± 854	1,062 ± 730	.26
Birth weight <1,500 g, n (%)	56 (78.9)	46 (88.5)	.23
Race, n (%)			.22
White	42 (59.2)	25 (48.1)	
Black	14 (19.7)	14 (26.9)	
Hispanic	13 (18.3)	8 (15.4)	
Others	2 (2.8)	5 (9.62)	
Steroid-eligible, n (%)	60 (84.5)	48 (92.3)	.27
Received any dose, n (%)	57 (95)	44 (91.7)	.70
Multiple gestation, n (%)	20 (28.2)	24 (46.2)	.057
C-section, n (%)	55 (77.5)	42 (80.8)	.82
Apgar score <5 at 5 min, n (%)	7 (9.9)	6 (11.5)	.67
Admission temperature, mean ± SD °C	36.3 ± 0.7	36.5 ± 0.4	.12
Ionotroph use during mechanical ventilation, n (%)	36 (50.7)	23 (44.2)	.58
Surfactant use, n (%)	70 (98.6)	52 (100)	>.99
Arterial line at any time during mechanical ventilation, n (%)	55 (77.5)	42 (80.8)	.82
Indication for intubation, n (%)			.82
RDS	51 (71.8)	41 (78.9)	
Neurologic abnormality	2 (2.8)	1 (1.9)	
MAS and/or PPHN	2 (2.8)	2 (3.9)	
Evolving lung disease*	10 (14.1)	6 (11.5)	
Others†	6 (8.5)	2 (3.8)	

* Evolving lung disease was defined as infants who were intubated or re-intubated after the first 3 d of life. Respiratory distress syndrome was defined as diagnosed in the medical record with intubation within the first 3 d of life.
† Others included airway issues, culture-positive sepsis, or necrotizing enterocolitis stage ≥2.
RDS = respiratory distress syndrome
MAS = meconium aspiration syndrome
PPHN = persistent pulmonary hypertension

ventilation in the 2 cohorts. The clinical outcomes measured at the time for hospital discharge between the 2 cohorts were also not significantly different (Table 2).

Blood Gas CO_2 and P_{tcCO2} Measure Agreement

We analyzed 1,338 simultaneous P_{tcCO_2} and blood gas measurements from 52 subjects in the post-P_{tcCO_2} cohort. Using a Bland-Altman plot for multiple measurements, we found mean ± 2SD bias of −5.2 ± 17.3 (Fig. 2). Subgroup analysis using only arterial blood gas values included 774 paired samples and found a mean bias ± 2SD of −7.2 ± 16. An average of 51.4 ± 21.5% of paired measurements had bias within ±5 mm Hg; 64 ± 20.6% within ±7 mm Hg; 78 ± 17.6% within ±10 mm Hg; and 92 ± 10.3% within ±15 mm Hg. On bivariate analysis, increasing birthweight, increasing blood gas measurements, high-frequency ventilation at the time of blood gas measure, and arterial sample were significant predictors of a bias outside ±7 mm Hg (Table 4). In the multivariable model, when adjusting for birthweight and blood gas number, being on high-frequency ventilation at the time of the blood gas measurement and having an arterial sample continued to significantly increase the odds of a bias ±7 mm Hg (Table 4). There was no significant relationship of sex, gestational age at birth, or chronological age of the infant at the time of the blood gas measurement.

Excluded Population

Of the 76 eligible infants in the post-P_{tcCO_2} period, 24 were excluded, per study criteria, due to <50% use of P_{tcCO_2} monitoring for the duration of mechanical ventilation. To account for selection bias, we compared the demographics and clinical characteristics of neonates excluded with those of neonates included and found that P_{tcCO_2} monitor use <50% of mechanical ventilation time was associated with shorter median mechanical ventilation time (5.4 [interquartile range 3.7–14.3] days vs 8.7 [interquartile range 5.6–22.1] days, P = .027), lower surfactant

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Table 2. Neonatal Blood Gas Comparison and Clinical Outcome of the 2 Cohorts (N = 123; Blood Gas Measurements = 5,726)

	Pre-P_{tcCO_2} (n = 71)	Post-P_{tcCO_2} (n = 52)	P
Mechanical ventilation, median (IQR) d	7.8 (4.1–33.3)	8.7 (5.6–22)	.57
Use of any HFV, *n* (%)	32 (45.1)	29 (55.8)	.28
HFV, median (IQR) d	4.3 (2.4–7.8)	3.5 (3–7)	.66
BGs drawn/d of mechanical ventilation, median (IQR)	3.9 (2.6–5.3)	2.9 (2.1–4.0)	.002
BGs drawn/d of HFV, median (IQR)	6.6 (5.5–8)	4.7 (3.3–5.2)	<.001
% of BG P_{CO_2} values outside 35–70 mm Hg range, mean ± SD	19.4 ± 8.7	17.8 ± 8.4	.48
% of arterial BG/patient, mean ± SD	62.6 ± 33.8	64.9 ± 28.8	.71
% of capillary BG/patient, mean ± SD	47.1 ± 31.5	45.7 ± 31.8	.82
% of venous BG/patient, mean ± SD	7.7 ± 13.3	5.1 ± 3.0	.45
Postnatal steroid use, *n* (%)	3 (4.2)	1 (1.9)	.64
Bronchopulmonary dysplasia, *n* (%)	25 (35.2)	24 (46.2)	.27
Retinopathy of prematurity, *n* (%)	5 (7)	3 (5.8)	.66
Necrotizing enterocolitis, *n* (%)	10 (14.1)	5 (9.6)	.58
Surgical necrotizing enterocolitis, *n* (%)	6 (8.5)	3 (5.8)	>.99
Intraventricular hemorrhage, *n* (%)	15 (21.1)	14 (26.9)	.52
Patent ductus arteriosus, *n* (%)	53 (74.7)	42 (80.7)	.52
Early onset sepsis, *n* (%)	2 (2.8)	1 (1.9)	>.99
Late onset sepsis, *n* (%)	12 (16.9)	6 (11.5)	.37
Failed hearing screen, *n* (%)	5 (7.0)	2 (3.9)	.38
No. of blood transfusions, mean ± SD	6.1 ± 5.4	5.8 ± 3.8	.68
Disposition, *n* (%)			.43
Home	52 (73.2)	42 (80.8)	
Died	9 (12.7)	3 (5.8)	
Transferred	10 (14.1)	7 (13.5)	
Mortality, *n* (%)	9 (12.7)	3 (5.8)	.24
Median d of hospital stay (IQR)*	89 (49–107)	95 (81–105)	.21

* Reported for neonates going home.
IQR = interquartile range
HFV = high-frequency ventilation
BG = blood gas

use (87.5% vs 100%, P = .028) and high-frequency ventilation use (16.7% vs 55.8%, P = .002), suggesting a healthier group. Other clinical characteristics were comparable (see Supplementary Table 1 at http://www.rcjournal.com).

Discussion

In this study, we found that use of P_{tcCO_2} monitors in the NICU did not increase and in fact reduced the frequency of blood gas sampling despite only moderate agreement (Tables 2 and 3). P_{tcCO_2} monitor use could have had no impact on the frequency of blood gas sampling if clinicians did not trust the P_{tcCO_2} output; conversely, the continuous display of (potentially abnormal) P_{tcCO_2} output could have prompted more sampling if clinicians felt obliged to obtain confirmatory blood gases. However, we found that among the infants for whom P_{tcCO_2} monitoring was used ≥50% of the mechanical ventilation time, the addition of P_{tcCO_2} monitoring technology *reduced* blood gases. This finding was robust when controlling for demographic characteristics and markers of severity of respiratory illness over 2 time periods and within the subgroup of infants requiring high-frequency ventilation (Tables 2 and 3). The clinical impact of this reduction in terms of blood loss is possibly minor, and the absence of a larger difference is possibly related to the wide agreement. We found no difference in frequency of arterial line insertion, type of arterial line (umbilical vs peripheral), or blood transfusions in the 2 cohorts (Tables 1 and 2). Transcutaneous devices, which reduce the need for needle sticks, have been cited as a mode for decreasing pain in the care of newborns.[17] In the current study, we were unable to obtain frequency of needle sticks in the cohorts. The impact of reduced blood gas frequency on acute and chronic pain scores when considering manipulation needed to apply P_{tcCO_2} monitors remains to be explored.

The availability of a continuous display of CO_2 levels could have hastened corrective changes to ventilator parameters before the values drifted to extreme levels. However, the percentage of extreme values in the 2 cohorts was not significantly different. Using blood gas P_{CO_2} as a marker

Table 3. Incidence Rate Ratios for Total Number of Gases by Bivariate and Multivariate Poisson Regression When Offsetting for Duration of Mechanical Ventilation

Predictor	Bivariate IRR (95% CI)	*P*	Adjusted IRR (95% CI)	*P*
Gestational age, wks	1.04 (1.01–1.06)	.003	1.02 (0.97–1.07)	.41
Birth weight, g	1.00 (1.00–1.00)	.001	1.00 (0.99–1.00)	.34
P_{tcCO_2} monitor used	0.82 (0.69–0.97)	.02	0.80 (0.7–0.93)	.003
Use of any HFV	1.56 (1.34–1.82)	<.001	1.59 (1.38–1.82)	<.001
Admission temperature <36°C	1.24 (1.03–1.49)	.02	0.88 (0.76–1.03)	.11
Male sex	1.10 (0.93–1.29)	.28	NA	NA
White race	1.00 (0.85–1.18)	.98	NA	NA
Vaginal delivery	0.97 (0.79–1.19)	.74	NA	NA
No antenatal steroids	1.15 (0.97–1.38)	.11	NA	NA
Multiple gestation	0.85 (0.71–1.02)	.08	NA	NA
Apgar score ≥5 at 5 min	0.81 (0.64–1.03)	.08	NA	NA
No inotrope use	0.90 (0.76–1.07)	.24	NA	NA

IRR = incidence rate ratio
HFV = high frequency ventilation
NA = not applicable

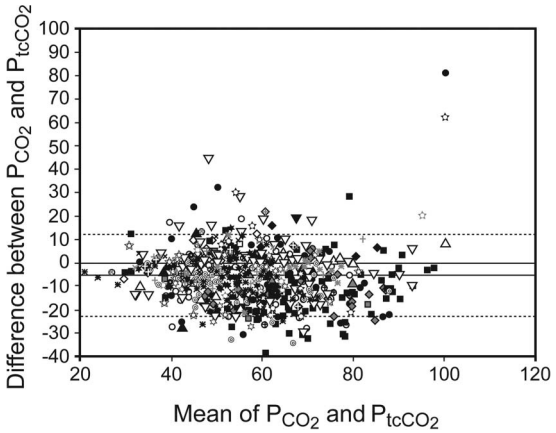

Fig. 2. Bland-Altman plot for multiple measurements of 52 subjects with 1,338 simultaneous blood gas P_{tcCO_2} measurements. Multiple measurements for each subjects are depicted by a unique shape. The center horizontal line depicts the mean, and outside dotted lines show ±SD.

of P_{CO_2} fluctuations is biased by the fact that blood gas P_{CO_2} values in the abnormal range trigger more blood gases, whereas the absence of out-of-range values in another subject may merely reflect fewer tests. We partly adjusted for this by dividing the number of extreme values by the total blood gas number per infant. Our small sample size may also be insufficient to detect a statistically significant difference. Prospective timed sampling of infants with and without P_{tcCO_2} monitoring would be needed to demonstrate variability with more precision.

Our study demonstrates that P_{tcCO_2} monitoring is a reliable source of clinical information in most, but not all, critically ill neonates. 64% of values had a bias within ±7 mm Hg. We also found wider agreement limits of 12.2 to −22.5 compared with some prior studies.[4,5,13,14] Our study, however, evaluates a large blood gas-P_{tcCO_2} sample over the entire span of an infant's ventilated course, making fluctuation in agreement more likely. Further, >80% of our population is constituted by very low birthweight infants, in whom a lower correlation has been reported, compared with pediatric and adult studies.[2] Of note, it is likely that despite the moderate agreement, the reduction in blood gas frequency was due to the use of the P_{tcCO_2} values as a trend rather than as a point in time measure.

We investigated variables associated with wide blood gas-P_{tcCO_2} agreement. Most studies previously reporting agreement have used arterial blood gases, which is the accepted standard.[2,4,14] Recently, good correlation was also reported between P_{tcCO_2} measurements and venous samples among pediatric subjects.[11] In our study, 41% of simultaneous P_{tcCO_2} and blood gas values were capillary samples. A survey of 39 NICUs in Europe reported that 49% of units used capillary gases to calibrate P_{tcCO_2} measurements.[7] There is no information on the agreement of P_{tcCO_2} with capillary gases, which, although not the accepted standard, are frequently used in practice. We found that P_{tcCO_2} values agree better with capillary blood samples than arterial (Table 4). This is perhaps not surprising, given that the P_{tcCO_2} monitor senses CO_2 diffusion from heated capillary beds and possibly conveys the same difference that capillary gases demonstrate from simultaneous arterial gases. We adjusted for the infant's age (because arterial samples are likely to be obtained earlier in the infant's care when umbilical arterial lines are present and respiratory status is evolving) and mode of ventilation. Arterial blood gases remained associated with greater bias than capillary samples. We also found significant associations with the use of high-frequency ventilation and bias

Table 4. Adjusted Odds Ratios for Factors Contributing to Blood Gas-P_{tcCO_2} Bias Greater Than ±7 mm Hg

Predictor	Bivariate Odds Ratio (95% CI)	*P*	Adjusted Odds Ratio (95% CI)	*P*
Gestational age (per wk)	1.03 (0.97–1.08)	.27	NA	NA
Male sex	0.96 (0.62–1.48)	.84	NA	NA
Infant age at the time of the BG (per d)	0.98 (0.95–1.02)	.34	NA	NA
Birth weight (per 100 g)	1.03 (1–1.05)	.02	1.02 (0.99–1.05)	.15
HFV at the time of the BG	1.83 (1.3–2.6)	<.001	1.56 (1.06–2.27)	.02
Arterial sample	1.75 (1.27–2.44)	<.001	1.67 (1.22–2.28)	.001
No. of total gases (per 5 gases)	1.04 (1.01–1.07)	.003	1.05 (1.02–1.08)	.001

NA = not applicable
BG = blood gas
HFV = high frequency ventilation

greater than ±7 (Table 4). High-frequency ventilation is largely used as a rescue mode of ventilation in our center, and therefore blood P_{CO_2} levels tend to be higher before high-frequency ventilation is initiated, which can cause wider agreement limits. Sicker infants on high-frequency ventilation possibly have differences in peripheral perfusion that we could not quantify in this study.

Finally, we addressed the impact of P_{tcCO_2} monitoring on infant outcomes. More frequent ventilator changes could impact infants in a positive manner by better control of CO_2 or could simply lead to more interventions for inaccurate reads that negatively impacted outcomes. We found no difference in major clinical or respiratory outcomes (Table 2). Our findings are, however, limited by our sample size, which was not powered for the individual clinical outcomes. A prospective, randomized, and blinded study of infants clinically managed with and without P_{tcCO_2} monitoring would be needed to accurately assess whether the use of P_{tcCO_2} monitors influences ventilator control and clinical outcomes in neonates.

Our study is limited by its retrospective, observational design based on a single center experience. We focused on sick NICU infants requiring mechanical ventilation for >48 h, including a heterogeneous array of pathologies ranging from extreme prematurity to meconium aspiration in term infants. We selected this group to reflect a NICU population where the use of a P_{tcCO_2} monitor could have most impact. Our results are therefore best generalizable to this population. We excluded 24 infants in the post-P_{tcCO_2} period because they spent <50% of their mechanical ventilation time on P_{tcCO_2} monitors. This exclusion criterion was designed a priori to limit inclusion of infants where P_{tcCO_2} monitor use was insufficient to have a conceivable impact. We found no significant demographic differences when we compared these infants with those who did have P_{tcCO_2} monitor use ≥50% of the ventilated time, although significantly reduced surfactant need, mechanical ventilation duration, and high-frequency ventilation use suggest that the infants with <50% of ventilated time on P_{tcCO_2} monitors were less severely ill (see Supplementary Table 1). We could not completely ascertain why these infants spent <50% of ventilated time on P_{tcCO_2} monitors. Chart review suggests that in some cases, an initial lack of correlation led to early abandonment of the technology; in others, rapid clinical improvement may have led to the idea that it was not needed; but in many cases no reason could be determined. This exclusion criterion was designed to reflect real-life practice, and we recognize that it probably selected for infants in whom care providers identified P_{tcCO_2} monitors to correlate better. The pre-post cohort design limits our ability to account for secular trends. Although this limitation cannot be resolved completely, the proximity of the time periods studied, absence of any major NICU respiratory management policy changes during the time, and comparable demographics of the infants minimize the impact of this limitation on the results of the study.

Conclusions

P_{tcCO_2} monitoring is used in clinical practice with moderate correlation in most neonates over a range of gestational ages, disease pathology, and modes of ventilation. In clinical practice, when used consistently, P_{tcCO_2} monitors were associated with decreased blood gas sampling but no significant change in ventilatory control or major morbidities. Further study is needed to determine how to optimally employ this noninvasive monitoring technique, potentially to decrease phlebotomy-associated blood loss and increase the safety of mechanical ventilation.

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