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Transcutaneous Pco_2 Monitoring in Newborn Infants During General Anesthesia Is Technically Feasible

Victoria Karlsson, RN, MMSc,* Bengt Sporre, MD,† and Johan Ågren, MD, PhD*

BACKGROUND: Transcutaneous (TC) measurement of Pco_2 (TC Pco_2) is a well-established method to monitor assisted ventilation in neonatal intensive care, but its use in the operating room is limited, and the data regarding its performance during general anesthesia of the newborn are lacking. The aim of this study is to evaluate the performance of continuous TC Pco_2 monitoring during general anesthesia in newborn infants.
METHODS: Infants (n = 25) with a gestational age of 23 to 41 weeks and a birth weight of 548 to 4114 g were prospectively enrolled. During general anesthesia and surgery, TC Pco_2 was measured continuously and recorded at 1-minute intervals. Five-minute mean values were compared with simultaneously obtained blood gas (BG) analyses of Pco_2. Only the first paired TC and BG samples were used in this analysis. We defined precision as 2.1 times the standard deviation of the difference of the 2 samples. $P < .01$ was considered statistically significant.
RESULTS: We obtained samples from 25 infants. The difference between TC and BG was 0.3 ± 0.7 kPa (mean ± standard deviation) giving a precision of 1.47 kPa. Nineteen of twenty-five (76%) sample pairs displayed a difference of <1 kPa (99% confidence interval, 48%–92%, P = .016). The difference in paired samples was similar for different gestational and postnatal ages and did not appear to be affected by electrocautery.
CONCLUSIONS: In this small study, we did not demonstrate that TC CO_2 monitoring was accurate at $P < .01$. This partly reflects the small size of the study, resulting in wide 99% confidence bounds. (Anesth Analg 2016;123:1004–7)

Monitoring of assisted ventilation is of vital importance in the operating room (OR). In the newborn, several factors contribute to the unique challenge of providing appropriate gas exchange during general anesthesia. These include (but are not limited to) the process of postnatal cardiorespiratory adaptation with persistence of fetal shunting, the neonate's propensity for atelectasis formation, and the use of anesthesia delivery systems primarily designed for use in larger patients. Also, in abdominal surgery, either changes in abdominal pressure or surgical manipulation might cause rapid changes in minute ventilation and ventilation-perfusion mismatch and impact on gas exchange. Carbon dioxide is a potent vasoactive substance, and there is a clear relation between the partial pressure of carbon dioxide and cerebral perfusion.[1] Both hypo- and hypercapnia are related to adverse neurologic outcome.[2] Most importantly, induced hypocapnia in the neonate is associated with cerebral artery vasospasm, reduced cerebral perfusion, and an increased risk of ischemic periventricular white matter injury.[3,4]

From the *Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; and †Unit for Pediatric Anesthesia, University Hospital, Uppsala, Sweden.

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Address correspondence to Victoria Karlsson, RN, MMSc, Department of Women's and Children's Health, Uppsala University, COP2, Barnoperation, Akademiska sjukhuset, 75185 Uppsala, Sweden. Address e-mail to victoria.karlsson@kbh.uu.se.

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Because the magnitude of CO_2 changes are not easily anticipated or estimated during assisted ventilation, Pco_2 needs to be continuously monitored to ensure proper management. During anesthesia and surgery, this is most commonly performed by continuous measurement of end-tidal (ET) Pco_2 and complemented by intermittent analysis of Pco_2 in arterial or capillary blood. The ET method is well established for use in adults and older children,[5,6] but many of the factors that contribute to the complex respiratory physiology of the newborn and the presence of pulmonary immaturity and/or disease also impact on the accuracy of ET Pco_2 monitoring.[7] Consequently, in the neonatal intensive care unit (NICU), continuous Pco_2 is almost exclusively obtained by transcutaneous (TC) measurements. In the NICU, TC monitoring of Pco_2 is considered to be the standard of care both for absolute measurement and trend analysis, and TC readings have been found to correlate well with blood Pco_2.[8–10] However, the use of TC Pco_2 monitoring in intraoperative care of neonates is limited, and to our knowledge, its accuracy has not been established in this population. We hypothesized that TC Pco_2 monitoring would be a relevant method in the operating room as well. To assess the accuracy of TC measurements, we compared TC Pco_2 and blood gas (BG) analyses obtained during general anesthesia in newborn infants.

METHODS

The investigation was approved of by the regional ethical review board, and in all cases, written parental consent was obtained before study inclusion. The study was not registered because patients were not assigned to treatment groups.

Subjects

We prospectively and consecutively enrolled neonates with a postconceptional age (PCA) of <44 weeks who were admitted to the NICU at Uppsala University Children's Hospital and scheduled for surgery. Enrollment was consecutive but

Table 1. Infant Data	
At birth	
Gestational age	32 + 1 wk (23–41)
Birth weight	1940 g (548–4110)
At day of study	
Postconceptional age	36 + 5 wk (25–41)
Weight	2530 g (670–4110)
Ventilator	*n* = 10
Nasal CPAP/cannula	*n* = 2
Room air/no support	*n* = 13

Values are median (range).
Abbreviations: CPAP, continuous positive airway pressure.

limited by the availability of the primary investigator (V.K.). Data on each infant's gestational age, birth weight, PCA, and weight at day of study are given in Table 1.

Transcutaneous Pco_2 Monitoring

TC partial pressure of carbon dioxide (TC Pco_2; kilopascal) was measured continuously by use of the TC technique using the E5280 probe (TCM 4/40, Radiometer, Denmark) with a probe temperature of 43°C according to manufacturer recommendations. Heating of the probe increases capillary blood flow as well as the diffusion of CO_2 and O_2 through the skin. Before probe placement and at 4-hour intervals, the electrode was calibrated against air and test gas. If calibration failed, the electrode membrane was replaced, and the electrode was recalibrated. The probe was placed on the upper chest, and the measurement site was changed at least every hour to minimize skin redness/thermal injury. After each probe placement, the electrode was allowed to stabilize for 15 minutes before recording TC Pco_2 values at 1-minute intervals.

Blood Gas CO_2 Analysis

BG analysis was performed using capillary blood samples (100 µL/sample) obtained from each infant's warmed foot and was immediately analyzed for Pco_2 (BG Pco_2; kilopascal) using an automated BG analyzer (ABL 800, Radiometer). By warming the foot, the capillary blood is considered arterialized and has been shown to correlate very well with arterial blood CO_2 in newborn infants.[11]

Measurement Procedure

In preparation for anesthesia, the TC probe was placed simultaneously with the application of electrocardiogram leads and pulse oximetry. Anesthesia was induced with thiopental (3 mg/kg), atropine (0.02 mg/kg), fentanyl (1–10 µg/kg), and neuromuscular block obtained with atracurium (0.5 mg/kg). Anesthesia was maintained with sevoflurane supplemented with intermittent dosing of fentanyl. All patients were intubated using uncuffed endotracheal tubes (2.5–3.0 mm) with pharyngeal pack and were managed using an anesthesia delivery system and ventilator (FLOW-i, Maquet, Sweden) in pressure control (infants weighing <2.8 kg) or pressure-regulated volume control mode (infants weighing >2.8 kg). Tidal volumes were set at 7 mL/kg body weight with a respiratory rate of 40–60/min and adjusted according to standard monitoring (ET Pco_2). Infants already on the ventilator before anesthesia were initially kept on their NICU ventilator settings.

The first blood sampling was performed after the anesthesia had been induced, the infant was intubated (including placement of a pharyngeal pack), maintained on the ventilator, and before the start of surgery. Additional blood sampling (1–2 per infant) was undertaken during the surgicy and recovery, but it was not included further in this analysis. All study data monitoring and collection were performed by the same person who had no role in taking care of the patient. The OR team was blinded to the TC Pco_2 data but it had access to the BG data.

Treatment of Data

Statistical analysis was performed using Statistical Package for Social Science, SPSS version 20 (IBM Corp, Armonk, NY). The TC Pco_2 value was calculated as the mean of the 5 TC Pco_2 values immediately before BG sampling. Limits of agreement were evaluated by the use of Bland–Altman analysis.[12] The analysis was based on the difference between paired measurements of TC and BG Pco_2 (ie, TC Pco_2 – BG Pco_2). Bias was calculated as the average difference. Precision was calculated as the standard deviation of the difference × 2.1 (calculated as the 2-sided *t*-inverse statistical for $P = .05$ and 24 degrees of freedom × square root (1 + 1/25). Differences were assessed by Student paired *t* test. Data are expressed as mean ± standard deviation or median (range). A *P* value of <.01 was considered statistically significant. A priori, we considered an accuracy ±1 kPa to be clinically acceptable based on previously reported results from older infants during anesthesia[13,14] and from the NICU environment.[8] The number of subjects was based on convenience. There was no power analysis before the study.

RESULTS

The analyzed data include BG and TC Pco_2 pairs from 25 infants (Figure 1). Bland–Altman analysis revealed a bias of 0.3 ± 0.7 kPa and a precision of ±1.47 kPa (Figure 2). The TC Pco_2 to BG Pco_2 difference was ≤1 kPa in 19 of 25 (76%) data pairs (99% confidence interval, 48%–92%, $P = .016$ versus random chance (ie, 50%).

The TC to BG Pco_2 bias (Table 2) and data pairs are displayed further in subgroups depending on postnatal age (<1 week or >1 week; Figure 3) and gestational age (preterm or term; Figure 4).

DISCUSSION

The present relatively small investigation does not demonstrate that TC measurements accurately reflect Pco_2 in newborn infants during general anesthesia. The precision was 1.47 kPa, less than our accepted accuracy of 1 kPa. Although the TC Pco_2 determination in 76% of the subjects was within our acceptable range of ±1 kPa of the concurrent BG Pco_2, this did not reach statistical significance at $P < .01$, as demonstrated by the lower confidence bound of 48% (less than random sample).

The recognition that extremes of Pco_2, even for brief periods of time, are associated with long-term neonatal morbidity emphasizes the need for reliable and continuous monitoring of Pco_2 during general anesthesia. Arterial BG analysis from intermittent sampling from an indwelling

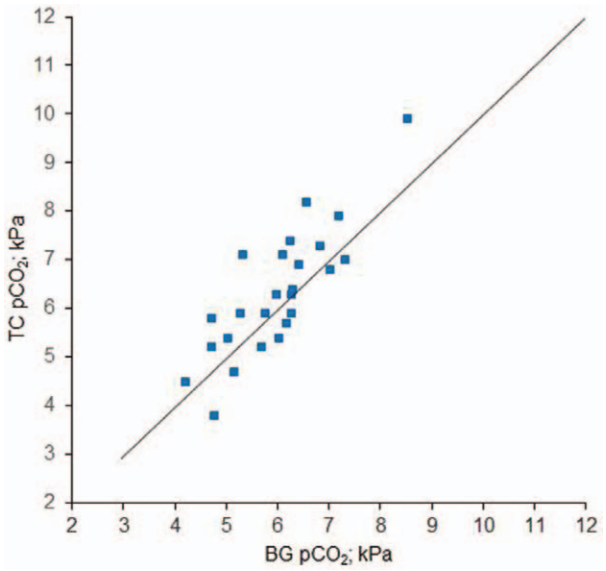

Figure 1. Correlation between transcutaneous (TC) and blood gas (BG) P_{CO_2} data pairs (n = 25). The diagonal line is the line of identity (X = Y).

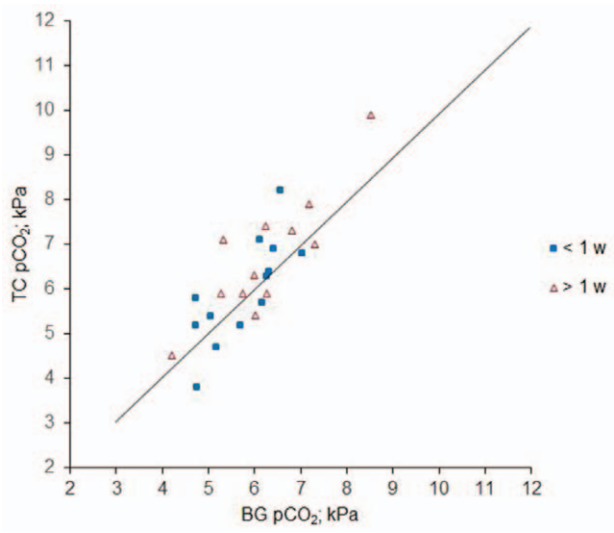

Figure 3. Transcutaneous (TC) and blood gas (BG) P_{CO_2} in infants with a postnatal age of <1 week or >1 week. The diagonal line is the line of identity (X = Y).

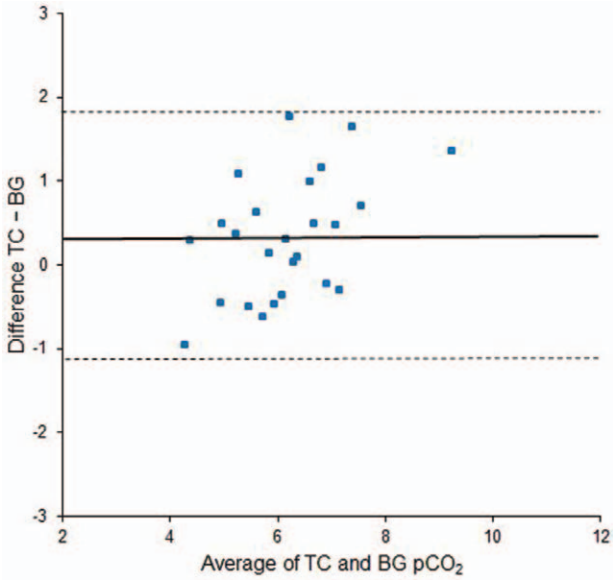

Figure 2. Bland–Altman plot of the difference between transcutaneous (TC) and blood gas (BG) P_{CO_2} (n = 25) versus the average of the 2. The lines represent the TC to BG bias (solid line) and the precision (±2.10 × SD; broken lines).

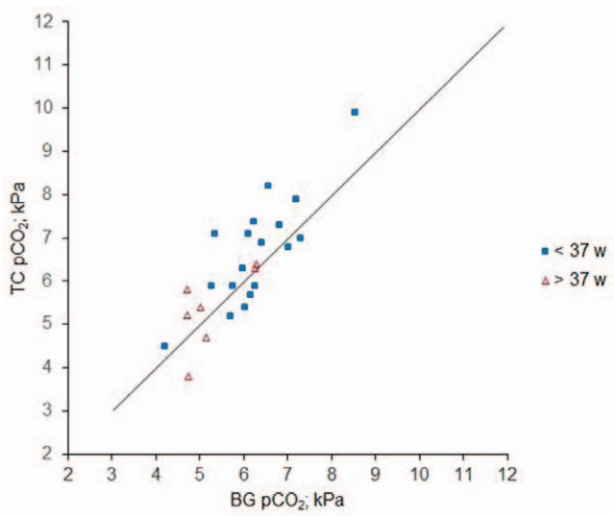

Figure 4. Transcutaneous (TC) and blood gas (BG) P_{CO_2} in preterm or term infants. The diagonal line is the line of identity (X = Y).

Table 2. Transcutaneous to Blood Gas P_{CO_2} Difference

Infant Group	n	TC-BG
All	25	0.3 ± 0.7
PNA		
<1 wk	12	0.1 ± 0.7
>1 wk	13	0.5 ± 0.7
GA		
<37 wk	18	0.4 ± 0.7
>37 wk	7	0.1 ± 0.7

Values are bias ± standard deviation (kilopascal).
Abbreviations: BG, blood gas; GA, gestational age; PNA, postnatal age; TC, transcutaneous.

catheter is considered the gold standard in measuring P_{CO_2}. However, the dynamics of neonatal anesthetic management mandate the use of continuous measurements. Also, placing arterial lines in the tiniest infants is often painful, cumbersome, resource consuming, and it carries a risk of vascular thrombosis.[15] The most commonly applied method in anesthesia, ET CO_2 monitoring, is known to be less accurate in infants with lung disease, high respiratory rate, and small tidal volumes,[16] and it is therefore of variable value at times.

TC monitoring of P_{CO_2} is well established in the NICU, and several studies have demonstrated a good correlation between TC and BG P_{CO_2} in this setting.[8] The method is independent of pulmonary disease, tidal volume, high respiratory rates, and ventilator mode (eg, small tidal volumes or high-frequency oscillatory ventilation), but it may be influenced by skin edema and hypoperfusion.[17]

Two previous studies have evaluated TC for intraoperative use in pediatric patients.[13,18] Both studies report a good agreement between TC and BG Pco_2, but those studies did not include any newborn infants. The authors of these studies recommend using TC as a complement to ET monitoring of Pco_2. In a review from the study by Molloy and Deakins[19] in 2006 conclude that TC is superior to ET and promote the use of TC for noninvasive trend monitoring of Pco_2, particularly in infants with pulmonary disease.

Arguably, management of a newborn in the NICU is distinct from that in the OR, where access to the small patient is limited by sterile draping and for the purpose of maintaining thermal stability. To measure TC Pco_2, the electrode needs to be calibrated, heated, and repositioned at regular intervals. These procedures did not create a barrier to the performance of the measurements in our study, suggesting that TC Pco_2 monitoring requires minimal staff training.

To conclude, because of the small size of our study, we were unable to demonstrate that TC monitoring of Pco_2 in the OR was sufficiently accurate for clinical use. A larger study is required to address this question.

DISCLOSURES

Name: Victoria Karlsson, RN, MMSc.
Contribution: This author helped design the study, collect the data, analyze the data, and prepare the manuscript.
Name: Bengt Sporre, MD.
Contribution: This author helped design the study, collect the data, and prepare the manuscript.
Name: Johan Ågren, MD, PhD.
Contribution: This author helped design the study, review the data, analyze the data, and prepare the manuscript.
This manuscript was handled by: James A. DiNardo, MD.

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