

Transcutaneous PCO₂ monitoring in infants hospitalized with viral bronchiolitis

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Received: 18 May 2014 / Revised: 24 July 2014 / Accepted: 19 August 2014 / Published online: 28 August 2014
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Abstract Our objective was to assess within a feasibility study the correlation and agreement of transcutaneous carbon dioxide (PtcCO₂) monitoring with venous carbon dioxide (PvCO₂) in infants with bronchiolitis in the emergency room (ER) and pediatric department. Sixty infants (aged 3.6±3.3 months) admitted to our ER with bronchiolitis were included. PtcCO₂ measurements (SenTec Digital Monitoring System) collected prospectively were compared with simultaneous PvCO₂ drawn for patient care. Analysis included 100 measurements. The correlation of PtcCO₂ and PvCO₂ ($r=0.71, p<0.001$) was good, and the agreement (mean difference±standard deviation

of the differences 1.9±7.0 mmHg) was adequate; average PtcCO₂ was slightly lower than PvCO₂. Changes in PtcCO₂ and PvCO₂ for consecutive measurements within each patient correlated ($r=0.41, p<0.01$). The level of PtcCO₂ correlated with disease severity clinical score ($p<0.001$).

Conclusions: PtcCO₂ monitoring was feasible in the ER and pediatric department and was found to have a good correlation and adequate agreement with PvCO₂ in infants with bronchiolitis. Because the standard deviation of the differences was relatively high, though comparable to the literature, we suggest that PtcCO₂ should not replace blood gas but rather serve as a complementary tool for trending and for real-time continuous assessment of the CO₂ levels.

Communicated by Peter de Winter

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Keywords Bronchiolitis · Noninvasive monitoring ·
Transcutaneous carbon dioxide

Abbreviations

ABG Arterial blood gas
PtcCO₂ Transcutaneous carbon dioxide
VBG Venous blood gas

Introduction

Bronchiolitis is one of the most common respiratory viral infections among children younger than 2 years [16] and one of the most common causes of hospital admission during the winter months. Approximately 3 % of otherwise healthy infants are hospitalized annually due to viral bronchiolitis for respiratory monitoring and supportive care [2].

Continuous noninvasive monitoring in the pediatric ward is important because the respiratory condition of infants with bronchiolitis may deteriorate [17]. This will be even more important and even crucial if high-flow nasal cannula will become an optional mode of treatment for bronchiolitis in

the emergency room (ER) and the pediatric ward [5, 12, 20]. The medical team treating sicker infants, needing nasal support within the pediatric ward, will need objective continuous noninvasive measures that will predict the need for endotracheal intubation and timely transport to the intensive care unit [1, 12, 13]. Currently, these infants are followed by pulse oximetry oxygen saturation and repeated blood gases to assess carbon dioxide retention as a warning sign for impending respiratory failure.

Arterial blood gas (ABG) sampling represents the gold standard for acquiring blood gases and acid-base status [28], but repeated ABGs are not feasible in the pediatric wards, where the use of venous blood gases (VBG) is more prevalent. Adequate correlation between venous CO₂ (PvCO₂) and arterial CO₂ was shown by several studies [8, 10, 28]. However, venous gas sampling may cause discomfort and pain and may not be accurate if the infants cry (hyperventilation) or hold their breath (apnea) during the puncture. Furthermore, it does not allow continuous monitoring, an important tool, that may help early recognition of impending respiratory failure and timely transfer to a Pediatric Intensive Care Unit (PICU).

Transcutaneous PCO₂ (PtcCO₂) measurement represents a simple and noninvasive technique for continuous monitoring of ventilation [6, 7, 21, 22, 27]. Holmgren and Sixt evaluated children with asthmatic symptoms and concluded that the transcutaneous technique can be used for monitoring acute bronchial obstruction and for evaluating the effects of treatment in children of different ages [11]. Measuring PtcCO₂ with a new device that does not cause thermal injuries to the skin may enable adequate continuous noninvasive monitoring [21, 24]. To the best of our knowledge, no study was performed previously on noninvasive monitoring of PtcCO₂ in infants with bronchiolitis in the ER or the pediatric ward.

The aim of the current study was to assess within a feasibility study the correlation and agreement of PtcCO₂ monitoring with PvCO₂ in infants with viral bronchiolitis in the ER and pediatric department.

Material and methods

Study design

This was a prospective, observational study, conducted at Bnai Zion Medical Center, Haifa, Israel, between January 2011 and March 2013. Infants aged 0–18 months with viral bronchiolitis were connected to a PtcCO₂ monitoring device, and these measurements were compared to PvCO₂ sampling drawn for patient care. The study was approved by the institutional review board in our center, and parents of all infants signed an informed consent prior to participation in the study.

Our primary outcome measure was the correlation and agreement between PtcCO₂ and PvCO₂. Our secondary outcomes were to assess the trending ability of PtcCO₂ measurements and to evaluate the correlation of PtcCO₂ with disease severity.

Study population

Included in the study were infants admitted to the ER and hospitalized with the clinical diagnosis of viral bronchiolitis in the pediatric ward, and whose parents signed an informed consent. A disease severity clinical score, based on a validated score [2, 18], but simplified for practical daily clinical practice using the following parameters was performed for each patient: (1) respiratory rate >60 breaths/min, (2) clinical signs of respiratory distress (retractions, nasal flaring), (3) oxygen saturation <92 % on room air, (4) oxygen requirement (if SpO₂<90 % or respiratory distress), (5) heart rate >160 beats/min, (6) findings of fine crackles, and (7) wheezing on physical examination. Each clinical parameter constitutes an equal value (0 if none and 1 if present) in the clinical score to a sum between 0 and 7 points. Excluded were infants with skin rash or eruption.

Study procedure

Monitoring of the infants, using the SenTec Digital Monitoring System (SenTec Inc. Therwil, Switzerland), was performed and recorded by a physician or a nurse who was instructed on the methodology of using the device prior to the study. The sensor was warmed to a constant surface temperature of 42 °C to improve local arterialization of the measurement site. The use of lower temperatures (42 °C as opposed to 45–47 °C used before) was shown to decrease dramatically the risk for skin burning in infants [24]. Prior to application of the sensor to the patient, the sensor was prepared and calibrated as per the manufacturer recommendations. The sensor was then applied to the patient's chest or upper abdomen for 15 min, allowing a correct stabilization of the PtcCO₂ values. We evaluated the recordings, and PtcCO₂ values obtained under inadequate conditions (not enough time for calibration or when the system alarmed) were excluded from analysis.

After the stabilization period, a VBG was obtained as required by the patient's clinical condition, while documenting the PtcCO₂ value at the same time. Clinical decisions were made only according to the VBG, and PtcCO₂ values were recorded for study purpose only. Patients who were hospitalized and needed further blood gases sampling for clinical assessment were either continuously monitored by the PtcCO₂ device or reconnected to the device before obtaining a repeat venous sample according to the working load in the pediatric ward.

Statistical analysis

We evaluated the correlation of PtcCO₂ and PvCO₂ by linear regression analysis and assessed the agreement between these measurements (bias [mean difference] and precision [standard deviation of the differences]) by the Bland-Altman technique [4]. A mean difference <5 mmHg was considered acceptable and >5 mmHg unacceptable as for end-tidal CO₂ (ETCO₂) values [9, 14, 23]. We evaluated the correlation between the changes in PvCO₂, and the simultaneous changes in PtcCO₂ for consecutive measurements within each patient by linear regression analysis. We performed multiple linear stepwise regression analysis to assess the correlation of PtcCO₂ and clinical disease parameters. Level of significance was set at $p < 0.05$. Data are presented as mean ± SD or median (range). Statistical analysis was performed using SigmaStat version 2.03 (Chicago, IL) software.

Results

During the study period, a total of 100 PvCO₂ and PtcCO₂ simultaneous samplings were obtained from 60 patients who presented with viral bronchiolitis. The median number of sampling per patient was 1 (range 1–4). In 28 patients, we performed more than one sampling. The first sample for each patient was obtained in the ER, while the sequential measurements were made in the ER or the pediatric department. Two samples were excluded due to technical problems. One was due to manufacturer warning (inadequate probe adhesion), and in the second case, there was not enough time for stabilization before obtaining the reading. No problems related to skin warming or sensor placement were observed after removing the sensor.

Patient characteristics and clinical conditions at study entry are presented in Tables 1 and 2, respectively.

Figure 1 shows the agreement between PvCO₂ and PtcCO₂ by a Bland-Altman plot. The agreement was adequate, with a mean difference of 1.9 mmHg and a standard deviation of the differences of 7.0 mmHg. Figure 2 shows the positive linear correlation between PvCO₂ and PtcCO₂. The correlation coefficient was good ($r = 0.71$, $p < 0.001$).

We evaluated the correlation of changes in PvCO₂ and the simultaneous changes in PtcCO₂ for consecutive measurements within each patient ($n = 28$) and found an adequate correlation ($r = 0.41$, $p < 0.01$).

We also found positive linear correlation between PtcCO₂ and the disease severity clinical score at study entry ($p < 0.001$). We tested whether this correlation would remain significant when the two other variables (PvCO₂ [positive correlation as discussed above] and weight [found to have negative correlation, i.e., larger weight was associated with lower PtcCO₂, $p < 0.001$]) that correlated with PtcCO₂ on

Table 1 Patient's characteristics ($N = 60$ patients)

Column	Mean	SD	Median	Min.	Max.
Age (months)	3.6	3.3	2.5	0.5	18.0
Weight (kg)	5.8	2.1	5.5	2.8	13.0
Length of hospitalization (days)	3.1	3.0	2.0	0.5	15.0
No readings	1.6	0.8	1.0	1.0	4.0
Medical history					
No primary diagnosis	47				
Congenital heart disease	5				
Pulmonary hypertension in neonatal period	3				
Prematurity	6				
Respiratory distress syndrome	1				
Gastroesophageal reflux	2				
Hyper-reactive airway disease	2				
Down syndrome	1				

univariate analysis were entered into a model of multiple linear stepwise regression. The disease severity clinical score remained independently associated with PtcCO₂ ($p < 0.05$). By replacing the disease severity clinical score with its components in this multiple regression model, we found that the need for oxygen ($p < 0.005$), heart rate ($p < 0.05$), and the respiratory rate ($p < 0.05$) were all correlated with PtcCO₂.

Infant weight was found to have a negative correlation with PtcCO₂ ($p < 0.001$) and with PvCO₂ ($p < 0.001$). PtcCO₂ and PvCO₂ in infants above the median weight ($n = 30$) in our cohort were significantly lower compared to those of infants below the median weight ($n = 29$) (36.9 ± 6.0 vs. 49.4 ± 8.8 mmHg and 41.0 ± 4.8 vs. 49.9 ± 8.1 mmHg, respectively; $p < 0.001$). The mean difference in infants above the median weight compared with infants below the median weight was significantly larger (4.0 vs 0.4 mmHg, $p < 0.005$), but the standard deviation of the differences was smaller (5.2 vs. 7.7 mmHg). PtcCO₂ and PvCO₂ correlated in infants above and below the median weight ($r = 0.70$ and 0.64 , respectively; both $p < 0.001$).

Table 2 Clinical condition at study entry ($n = 60$ patients)

Column	Mean	SD
Respiratory rate (breaths/min)	57	11.3
Heart rate (beats/min)	165	22.3
SpO ₂ [%]	95	4.9
Clinical score	3.0	1.6
Clinical parameters (number of patients)		
Crepitations	32	
Wheezing	30	
Retraction	34	
Feeding problems	15	
Oxygen requirement	35	

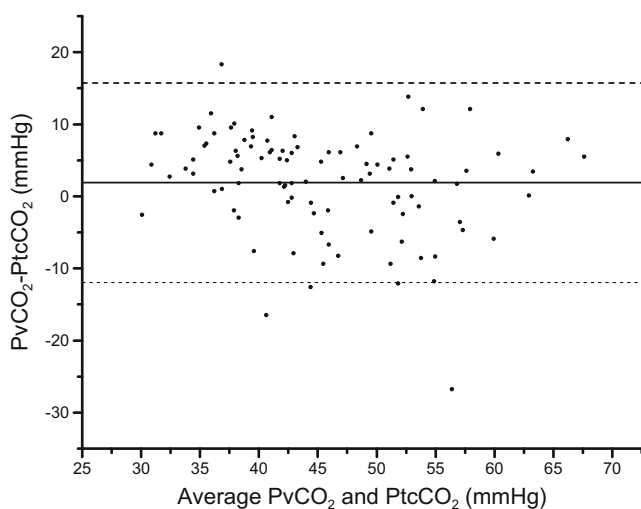


Fig. 1 Bland-Altman plot showing the agreement (bias±precision 1.9 ± 7.0 mmHg) between $PvCO_2$ and $PtcCO_2$ (dashed line represents ± 1.96 SD)

Five infants were transferred to the pediatric intensive care unit. All had relatively high levels of CO_2 on admission. One infant diagnosed with atrial septal defect who developed heart failure had $PvCO_2$ of 43 and $PtcCO_2$ of 51 mmHg and was supported with nasal continuous positive airway pressure. One infant had $PvCO_2$ of 44 and $PtcCO_2$ of 45 mmHg, developed pneumothorax, and before transfer, had $PvCO_2$ of 55 and $PtcCO_2$ of 60 mmHg and was supported with high-flow nasal cannula. One infant had $PvCO_2$ of 65 and $PtcCO_2$ of 62 mmHg; one infant had $PvCO_2$ of 51 and $PtcCO_2$ of 54 mmHg; and one infant had $PvCO_2$ of 60 and $PtcCO_2$ of 48 mmHg, and before transfer, had $PvCO_2$ of 70 and $PtcCO_2$ of 62 mmHg and was supported with high-flow nasal cannula. Yet, our study was not powered to evaluate the correlation of specific CO_2 levels and outcomes.

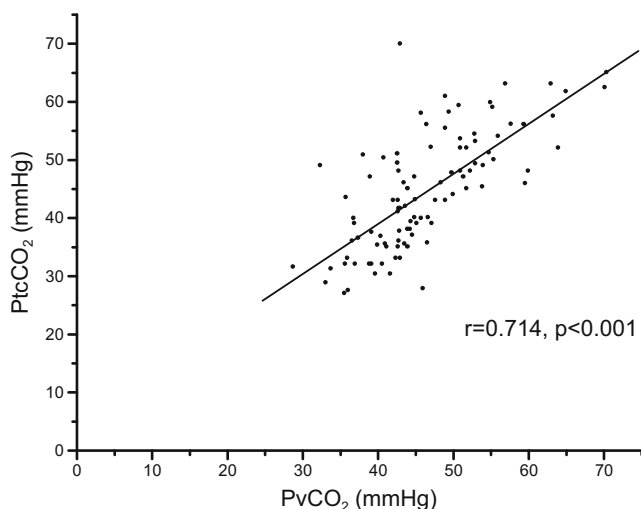


Fig. 2 Correlation between $PvCO_2$ and $PtcCO_2$ ($r=0.71$, $p<0.001$)

Discussion

We found that $PtcCO_2$ was a feasible noninvasive method for estimating $PvCO_2$ in patients with viral bronchiolitis in the ER and the pediatric department. $PtcCO_2$ had a good correlation and an adequate agreement with $PvCO_2$. We also encountered within-patient trending ability. The level of $PtcCO_2$ correlated with the disease severity clinical score, just showing its clinical implication as another estimate for disease severity.

The use of $PtcCO_2$ has already been evaluated in patients hospitalized in Neonatal ICU and PICU [3, 15]. In a relative recent study in the PICU [25], the SenTec device demonstrated a correlation coefficient of 0.93 and a mean difference of 4.3 ± 10.6 mmHg. Wilson et al [27] showed a mean difference of less than 2.0 ± 1.0 mmHg in patients during surgery for repair of cyanotic congenital heart disease. However, there are only a few studies in the settings of ER or in the pediatric department, and there are no previous reports, to our knowledge, in infants with bronchiolitis. In a study from 1986 comparing $PaCO_2$ and $PtcCO_2$ in children with acute asthmatic state who were admitted to the pediatric ward, the $PtcCO_2$ overestimated the arterial carbon dioxide on an average of 3.0 ± 3.4 mmHg, most probably due to metabolic CO_2 production in the epidermis cells [26]. Our results are consistent with previous results in other clinical conditions and settings. Although the mean difference of the $PtcCO_2$ was relatively small in our study, the 95 % CIs were relatively wide, as reported in other studies using $ETCO_2$ and $PtcCO_2$ [3, 9, 14, 15, 23, 25, 26]. Thus, $PtcCO_2$ like $ETCO_2$, should not replace blood gas but rather serve as a complementary tool for trending and for real-time continuous assessment of the CO_2 levels. We suggest correlating the $PtcCO_2$ and the $PvCO_2$ for monitoring in the individual patient.

While there is no definition for an adequate agreement for $PtcCO_2$, a mean difference of <5 mmHg was considered adequate for $ETCO_2$ [9, 14, 23]. Our results comply with that definition. Thus, as $PtcCO_2$ performed by the medical and nursing teams in the ER and the pediatric department revealed a good correlation and an adequate agreement with $PvCO_2$, it was found to be a feasible and reliable method for noninvasive estimation of PCO_2 in bronchiolitis.

In our study, we used $PvCO_2$ and not arterial carbon dioxide ($PaCO_2$) as reported in previous studies [3, 19, 26, 27]. The use of $PaCO_2$ sampling represents the gold standard method for acquiring patients' acid-base status [28]. Nevertheless, this method is less feasible in the ER and pediatric department as opposed to the intensive care units where infants and children may have an arterial line. The need for repeated sampling is crucial for recognizing deterioration in infants with bronchiolitis. We use venous sampling in our ER and pediatric department because it has less complications associated with arterial sampling, is more convenient, and requires less skill by the medical and nursing teams. A study

published in 2004 evaluated the agreement and correlation between capillary, venous, and arterial blood gases and found that the $PvCO_2$ is larger than the $PaCO_2$ by a mean of 5.7 mmHg and that the correlation was excellent ($r=0.97$) [28]. This study supports our clinical decision to use $PvCO_2$ as a practical medical tool to follow children with bronchiolitis and scientifically as an optional comparative standard for $PtcCO_2$. In our study, we found that the $PtcCO_2$ was lower than the $PvCO_2$ by a mean difference of 1.9 ± 7.0 mmHg, as opposed to other studies where it was higher than $PaCO_2$ [3, 19, 26, 27]. The use of $PvCO_2$ instead of $PaCO_2$ explains the different direction of the bias.

$PtcCO_2$ might be a better method for non-invasive assessment of CO_2 compared with $ETCO_2$ in bronchiolitis because nasal discharge and nasal oxygen flow (especially high-flow nasal cannula), common in bronchiolitis, might interrupt the latter. Yet, only two studies were published on the use of $ETCO_2$ in bronchiolitis [5, 16]. Lashkeri et al. [16] examined $ETCO_2$ by capnometry for admitted and discharged infants and found no correlation between the $ETCO_2$ reading and the infants' clinical score. Bressan et al [5] monitored infants with bronchiolitis treated with high-flow nasal cannula with $ETCO_2$, but had to shortly disconnect the nasal flow to allow measurement. Both studies did not validate the $ETCO_2$ results with blood gases. Thus, more studies and "head-to-head" comparison of the two methods is required before concluding which method is better for continuous noninvasive CO_2 assessment in infants with bronchiolitis.

Continuous respiratory monitoring is important in infants hospitalized with bronchiolitis. Oxygen saturation is already a standard of care, but noninvasive monitoring of CO_2 is not performed routinely, and blood gas samples are used in certain infants to help in recognizing infant fatigue and impending respiratory failure [17]. The ability to predict ventilatory deterioration as early as possible is crucial, especially in centers with no PICU, to allow transport at a timely manner to a PICU. The level of CO_2 was shown to predict apnea and failure of high-flow nasal cannula and the need for endotracheal ventilation [1, 12, 13]. To our knowledge, no other study assessed the trending of $PtcCO_2$ in bronchiolitis. Wennergren et al [26] demonstrated increasing $PtcCO_2$ with increasing severity of asthma symptoms in infants. We found an adequate correlation within each patient, but not as good as we predicted. This could result from the small number of infants with more than one reading and the small number of readings within each patient. We had only one SenTec Digital Monitoring System used in few children, and the monitoring was not continuous; the monitor was connected just before blood gas sampling in some infants. This could affect the results. Another reason could rely on the fact that the infants admitted were transferred from the ER to the pediatric department and measurements were performed by a different team. On the other hand, a methodological bias in our data collection

could result from the fact that measurements were not completely independent in some infants in whom more than one measurement was included. As trending ability may be more important than obtaining a certain $PtcCO_2$ level, more studies evaluating the trending ability of $PtcCO_2$ in bronchiolitis are needed before relying on that method in clinical care.

Infants with bronchiolitis in the ER and pediatric department need mainly supportive care and monitoring for the general and the cardiorespiratory condition. Currently, we use for that purpose medical history, clinical parameters, and blood gases as needed. By using multiple linear stepwise regression model, we tried to determine whether there is a correlation between the clinical parameters and the infant's ventilation ability, using $PtcCO_2$ measurements. The level of $PtcCO_2$ correlated with disease severity clinical score ($p<0.001$), and its individual component: oxygen requirement, heart rate, and respiratory rate. This implies a potential role for $PtcCO_2$ as an assessment tool for disease severity in infants with bronchiolitis.

Infant weight was found to have a negative correlation with $PtcCO_2$ and with $PvCO_2$. Lower levels of $PtcCO_2$ and $PvCO_2$ in infants above the median weight in our cohort compared to the levels in infants below the median weight suggest better ventilation ability in larger infants with bronchiolitis. The mean difference in infants above compared to below the median weight was significantly larger, but the precision was smaller. In both groups, $PtcCO_2$ and $PvCO_2$ correlated. The possibility that a technical error is responsible for the inverse ratio between weight and $PtcCO_2$ is less plausible, but we cannot rule out that the infant weight affected the mean difference. The smaller mean difference in smaller infants makes $PtcCO_2$ suitable for the target population of hospitalized infants with bronchiolitis.

Our study is limited by the relative small number of participants with more than one measurement despite extended study duration of three winter periods. Technical constraints and the heavy workload in the ER and the pediatric department during the bronchiolitis season hampered our ability to obtain high-quality and steady measurements of continuous noninvasive $PtcCO_2$.

We conclude that $PtcCO_2$ is a feasible noninvasive method for estimating $PvCO_2$ in patients with viral bronchiolitis in the ER and pediatric department. It had a good correlation and an adequate agreement with $PvCO_2$ and possible trending ability, and it may serve as an additional tool for disease severity assessment. Because the standard deviation of the differences was relatively high, $PtcCO_2$ should not replace blood gas but rather serve as a complementary tool for trending and for real-time continuous assessment of the CO_2 levels. Larger prospective studies are warranted to evaluate the utility of continuous monitoring of $PtcCO_2$ in the settings of the ER and pediatric department and as a predictor of clinical deterioration or improvement in infants with viral bronchiolitis,

focusing on continuous monitoring, trending ability, and on the use in infants needing nasal respiratory support that does not allow the use of other noninvasive methods such as ETCO_2 .

Acknowledgments

Funding source No external funding was secured for this study.

Financial disclosure SenTec Inc. supported the study by supplying a SenTec monitor and supplies for the study.

Conflict of interest We have no conflicts of interest to disclose, and we had no financial relationship with the organization that sponsored the research.

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