

Monitoring of End-Tidal CO₂: Benefits to Critically Ill Neurological Patients

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Background: There have been few studies about the application of end-tidal CO₂ (PetCO₂) monitoring in neurologic disorders. The purpose of this study was to evaluate the correlation of PetCO₂ and arterial CO₂ (PaCO₂) in critically ill neurological patients. **Methods:** Patients with neurological disorders were monitored with sidestream capnometry while in the intensive care unit. Simultaneously, arterial blood gases were analyzed with a portable blood-gas analyzer. PetCO₂ levels correlated with PaCO₂ levels, based on neurologic diagnosis, presence of cardiopulmonary insufficiency, and ventilation state. **Results:** From 24 patients (12 female, mean age 60.5±14.0 years old), 208 PetCO₂ records were measured. The mean PetCO₂ was 30.63±7.34 mm Hg and the mean PaCO₂ was 38.20±8.84 mm Hg. There was a linear correlation between PetCO₂ and PaCO₂ (correlation coefficient=0.411, $P<0.001$). In both the central nervous system (CNS) and peripheral neuromuscular disease (PNS) groups, a linear correlation between PetCO₂ and PaCO₂ was also found, and the PNS group showed a higher correlation coefficient (0.648, $P<0.001$) than the CNS group (0.245, $P=0.006$). There was a correlation between PetCO₂ and PaCO₂ in the hypocapnia group, independent of cardiopulmonary insufficiency. However, no correlation between PetCO₂ and PaCO₂ was found in the hypercapnia group. **Conclusion:** PetCO₂ correlated with PaCO₂ in critically ill neurological patients. Despite of some limitation, PetCO₂ monitoring could be used to assess ventilation and pulmonary perfusion in the diagnosis and management of neurological disorders.

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KEY WORDS: Capnometry · Neurology · Critical care.

Introduction

Capnometry is a non-invasive technology used for the continuous measurement of the exhaled CO₂ throughout the respiratory cycle that is commonly referred to as end-tidal carbon dioxide (PetCO₂).¹ After van Weerden² reported on the clinical application of capnometry, it has been used to assess the correct placement of the endotracheal tube, to monitor the integrity of mechanical ventilation equipment, to detect pulmonary embolisms, and to wean from the mechanical ventilator.³⁻⁵ Recently, capnometry and pulse oximetry monitoring have been standard in the operating room setting, and this combination is becoming more routinely used in anesthesia, emergency and intensive care.⁶⁻¹⁰ However, the application of capnometry in clinical practice was formerly limited to critically ill patients, based on controversies surrounding the accuracy of PetCO₂ in predicting arterial CO₂. Ka-

lenda¹¹ used PetCO₂ monitoring during cardiopulmonary resuscitation to assess blood flow. Since PetCO₂ increased with chest compression strength, PetCO₂ monitoring was important for assessing pulmonary perfusion. Levine et al.¹² found that PetCO₂ levels lower than 10 mm Hg, 20 minutes after cardiopulmonary resuscitation, were a predictor of death in patients that suffered an out-of-hospital cardiac arrest.

There have been few studies about the application of PetCO₂ monitoring in neurologic disorders. PetCO₂ monitoring was used to screen patients with acute stroke for sleep apnea syndrome.¹³ Capnography and pulse oximetry can detect respiratory insufficiency in neuromuscular patients.¹⁴ For patients with traumatic brain injury, the correlation between PetCO₂ and arterial carbon dioxide (PaCO₂) was low and the usefulness of PetCO₂ monitoring was greeted with skepticism.¹⁵ However, despite the disagreement about the importance of PetCO₂ monitoring for neurological patients, studies were limited to a specific disease category of neurological disorders. Furthermore, the feasibility of respiratory monitoring by continuously measuring PetCO₂ levels has not been studied in critically ill neurological patients. The purpose of

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this study was to evaluate the validity of PetCO₂ monitoring in critically ill neurological patients, compared with PaCO₂ levels in arterial gas. Furthermore, we studied whether PetCO₂ monitoring was a more reliable measure for specific categories of neurological diseases.

Materials and Methods

We recruited patients with neurologic disorders who required intensive care from a single, tertiary medical center from March to December 2008. Patients who were under 18 years, or were admitted due to a non-neurologic disorder with any etiology of shock or immediate resuscitation, were excluded. Details of demographic data and clinical characteristics such as neurologic diagnosis, presence of cardiopulmonary insufficiency, and methods of respiration support were obtained from medical records. The following parameters were recorded for the analyses: respiratory rate, oxygen saturation (SaO₂), PetCO₂, arterial O₂ (PaO₂), PaCO₂.

Arterial PaCO₂ measurements were performed by radial arterial puncture. Initial arterial sampling was taken on arrival at the intensive care unit and follow-up sampling was performed if clinically necessary. Arterial blood gases were analyzed with a portable blood-gas analyzer (GEM premier 3000, Instrumentation Laboratory, Werfen Group, Lexington, MA, USA). This portable blood-gas analyzer was calibrated every morning. The patients were under continuous PetCO₂ monitoring with sidestream capnometry, which utilized Microstream sampling technology connected to a patient-monitoring system (MP50, Philips medical system, Boeblingen, Germany). We recorded the respiratory rate, SaO₂ and PetCO₂ at the time of arterial sampling. PetCO₂ records were classified into two groups by ventilation status. Hypocapnia was defined PaCO₂ ≤40 mm Hg and hypercapnia was defined PaCO₂ >40 mm Hg.

We divided neurologic diagnosis into central nervous system (CNS) and peripheral neuromuscular disease (PNS) groups. Central nervous system diseases included stroke and other central nervous system diseases, while peripheral and neuromuscular system diseases included peripheral neuropathy, neuromuscular junction disorder, myopathy and motor neuron disease. Arterial to alveolar CO₂ difference [P(a-A) CO₂=arterial-alveolar CO₂ difference] was calculated at each sampling. The study was approved by the local hospital's ethics committee.

Statistical analysis

All data were analyzed using SPSS 10.0 software (SPSS, Chicago, IL, USA). Measurements were expressed as the mean±SD, and enumerated data were expressed as rates (%).

All provided *P*-values represent the results of two-tailed tests. *P*-values of <0.05 were considered statistically significant.

Differences between groups were tested using the Mann-Whitney U test or chi-squared test, depending on the distribution of the variables. We determined the correlation of PetCO₂ and PaCO₂ for each group according to neurologic diagnosis, anatomical location of the disease, presence of cardiopulmonary insufficiency, and ventilation status using Pearson correlation tests. We used a linear regression model to test the relationship between PaCO₂ and PetCO₂ for each group.

Results

From 24 patients (12 female, mean age 60.5±14.0 years old), 208 measurements of simultaneous PetCO₂ and arterial PaCO₂ were collected for analyses. The values of PetCO₂ ranged from 12-48 mm Hg (Table 1). The simultaneous measurement of PetCO₂ and PaCO₂, in addition to arterial blood gas analysis, was performed from one to thirty times for each patient. The neurological diagnosis included stroke in four-

TABLE 1. Characteristics of patients

	Patients	Samples
Age (years)	60.5±14.0	208
Male gender	12	96
Respiratory rate (breaths/minute)	19.8±5.8	
SaO ₂	97.65±2.36	

Values are mean±standard deviation. SaO₂: oxygen saturation

TABLE 2. Neurologic/Medical diagnosis of patients

	Patients (%)	Samples (%)
Neurologic diagnosis		
Stroke	14 (58.3)	83 (39.9)
Peripheral disease	1 (4.2)	12 (5.8)
NMJ disorder	2 (8.3)	51 (24.5)
Other CNS disease	5 (20.8)	40 (19.2)
Myopathy	1 (4.2)	10 (4.8)
Motor neuron disease	1 (4.2)	12 (5.8)
CNS vs. PNS		
CNS	19 (79.2)	123 (59.1)
PNS	5 (20.8)	85 (40.9)
Cardiopulmonary insufficiency		
Yes	9 (37.5)	84 (40.4)
No	15 (62.5)	124 (59.6)
All	24	208

Other central nervous system disease group included Parkinson hyperpyrexia syndrome, CNS malignancy, seizure, traumatic brain injury. NMJ: neuromuscular junction, CNS: central nervous system disease group, PNS: peripheral and neuromuscular system disease group

TABLE 3. Relationship between end-tidal carbon dioxide (PetCO₂) and arterial carbon dioxide (PaCO₂)

	PetCO ₂	PaCO ₂	Correlation	
			C	P
All (n=208)	30.63±7.34	38.20±8.84	0.411	<0.001
CNS vs. PNS				
CNS (n=123)	29.41±6.76	38.19±8.96	0.245	0.006
PNS (n=85)	32.39±7.81	38.22±8.71	0.648	<0.001
Cardiopulmonary insufficiency				
Yes (n=84)	31.40±6.71	41.64±7.61	0.351	0.001
No (n=124)	30.10±7.71	35.87±8.88	0.434	<0.001
Respiration method				
Mechanical ventilation (n=41)	28.24±5.56	40.07±10.73	0.366	0.019
Intubated (n=96)	32.31±6.04	36.78±6.49	0.572	<0.001
Non-intubated (n=71)	29.73±7.25	39.04±8.84	0.467	<0.001
Ventilation pattern				
PaCO ₂ ≤40 mm Hg (n=128)	28.42±6.11	32.52±5.07	0.446	<0.001
PaCO ₂ >40 mm Hg (n=80)	34.16±7.78	47.30±5.21	-0.129	0.253

Values are mean±standard deviation. CNS: central nervous system disease group, PNS: peripheral and neuromuscular system disease group

TABLE 4. Arterial-alveolar carbon dioxide difference [P(a-A)CO₂]

	P(a-A)CO ₂	P
All	7.57±8.87	
Cardiopulmonary insufficiency		<0.001
Yes	10.24±8.19	
No	5.77±8.88	
CNS vs. PNS		0.012
CNS	8.77±9.81	
PNS	5.84±6.98	
Respiration method		<0.001
Mechanical ventilation	11.83±11.32	
Intubated	4.47±5.81	
Non-intubated	9.31±9.31	
Ventilation pattern		<0.001
PaCO ₂ ≤40 mm Hg	4.09±5.95	
PaCO ₂ >40 mm Hg	13.14±9.91	

*values are mean±standard deviation. Mann-Whitney U test was used to compare among the groups. P(a-A)CO₂: arterial-alveolar CO₂ difference, CNS: central nervous system disease group, PNS: peripheral and neuromuscular disease group, PaCO₂: arterial carbon dioxide

teen patients, peripheral neuropathy in one, neuromuscular junction disorder in two, other central nervous system disease in five, myopathy in one, and motor neuron disease in one (Table 2). Other central nervous system diseases included Parkinsonism-hyperpyrexia syndrome, brain tumor, seizure, and traumatic brain injury. The CNS and PNS groups were composed of 19 (79.2%) and 5 (20.8%) patients, respectively. Cardiopulmonary insufficiency was diagnosed in nine patients including pneumonia in five, pneumothorax in one, pulmonary congestion in one, pulmonary embolism in one, and heart failure in one.

The mean PetCO₂ was 30.63±7.34 mm Hg and the mean PaCO₂ was 38.20±8.84 mm Hg. The mean respiratory rate was 19.8±5.8 breaths per minute and the mean SaO₂ was 97.65±2.36%. The correlation between PetCO₂ and PaCO₂ was linear, with a correlation coefficient of 0.411 ($P<0.001$) (Table 3).

The correlation coefficient between PetCO₂ and PaCO₂ was relatively higher in patients with stroke (correlation coefficient 0.686, $P<0.001$) and neuromuscular junction disorder (correlation coefficient 0.766, $P<0.001$) than the patients with the other diagnostic categories. With respect to the anatomical location, the PetCO₂ and PaCO₂ were significantly correlated with each other in the CNS and PNS groups (Fig. 1). However, the PNS group had a much higher correlation coefficient (0.648, $P<0.001$) than the CNS group (0.245, $P=0.006$). The correlation between PetCO₂ and PaCO₂ was significant in patients, independent of cardiopulmonary insufficiency. Although the correlation between PetCO₂ and PaCO₂ was significant regardless of the respiratory route, the correlation coefficient of the patients who had endotracheal tube placement (0.572, $P<0.001$) was higher than for patients needing mechanical ventilation (0.366, $P=0.019$) or those that did not require respiratory aids (0.467, $P<0.001$). There was a correlation between PetCO₂ and PaCO₂ in the hypoventilation group (correlation coefficient of 0.446; $P<0.001$), but no correlation in the hypoventilation group.

The P(a-A)CO₂ was calculated for all samples (Table 4). The mean P(a-A)CO₂ was 7.57±8.87 mm Hg. P(a-A)CO₂ was the largest for patients with other central nervous system diseases, cardiopulmonary insufficiency, mechanical ventilation problems and members of the hypoventilation group.

The P(a-A)CO₂ of the CNS group (8.77 ± 9.81) was significantly higher than that of the PNS group (5.84 ± 6.98 ; $P=0.012$). According to the ventilation pattern, the P(a-A) CO₂ was 4.09 ± 5.95 in the hypocapnia group and 13.14 ± 9.91 in the hypercapnia group, as expected.

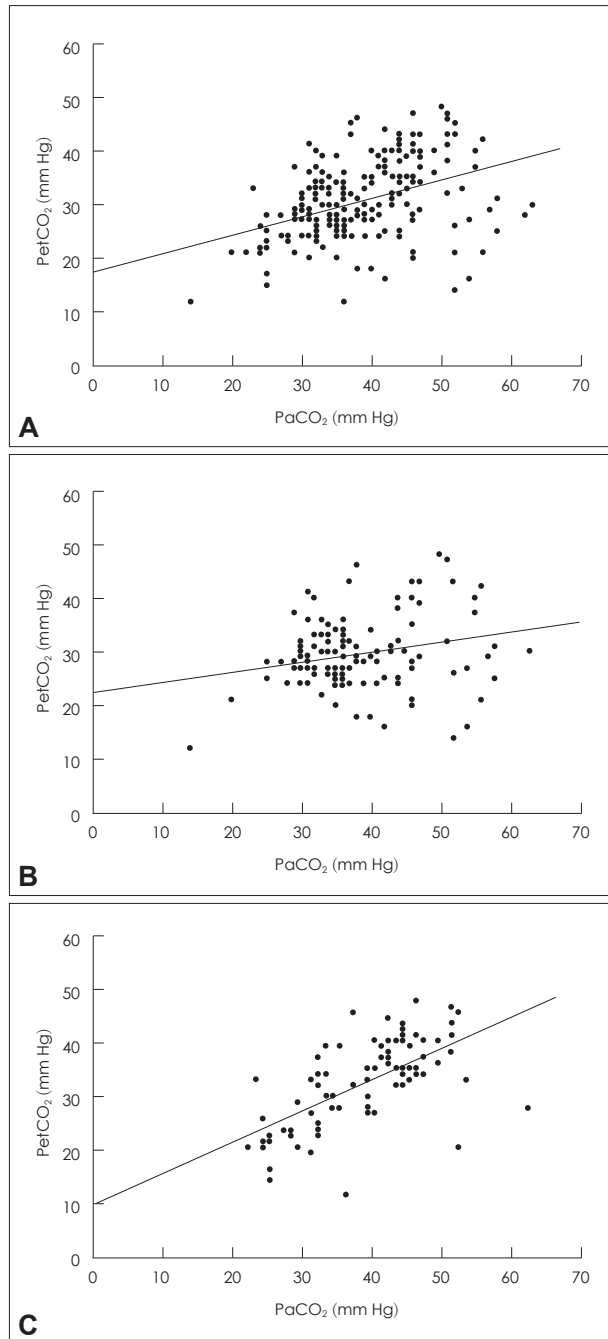


FIGURE 1. Linear correlation curve of end-tidal carbon dioxide (PetCO₂) and arterial carbon dioxide (PaCO₂). A: Total patients (n=208, correlation coefficient=0.411, $P<0.001$). B: Central nervous system disease group (n=123, correlation coefficient=0.245, $P=0.006$). C: Peripheral and neuromuscular disease group (n=85, correlation coefficient=0.648, $P<0.001$).

Discussion

The main purpose of this study was to evaluate the correlation of PetCO₂ and PaCO₂ in critically ill neurological patients. We found that there was a relatively good correlation between PetCO₂ and PaCO₂ in patients with neurological disorders. However, the correlation coefficients were not uniform for each disease group. Patients with stroke and neuromuscular junction disorder showed a good correlation between PetCO₂ and PaCO₂, whereas the patients with other diagnoses showed no significant correlation. The correlation between PetCO₂ and PaCO₂ was more prominent in the PNS disease, hypocapnia, and no cardiopulmonary insufficiency groups.

The differences in correlation coefficient between CNS and PNS groups with respect to the clinical situation, may be due to the involvement of a different mechanism that could lead to the respiratory problem.

Neurological disorders could cause respiratory problems by several mechanisms.^{16,17} Diseases affecting the brainstem may manifest with impaired control of ventilation.^{18,19} Lesions affecting the pontine respiratory group may manifest with central alveolar hypercapnia, abnormal respiratory rhythm, or both. Brainstem tumors such as gangliogliomas, medulloblastomas and lymphomas may produce central neurogenic hypocapnia.^{20,21}

Diseases of the peripheral nervous system commonly affect the respiratory motor unit, resulting in reduced vital lung volume and restrictive hypercapnia.^{19,22} Since patients with respiratory muscle weakness take rapid shallow breaths, PaCO₂ may be reduced early in the disease.²³ However, hypercapnia is induced when respiratory muscle strength falls to 25% of normal strength.²⁴ In this study, the mean respiratory rate was 17.8 breaths/minute in the CNS group and 21.2 breaths per minute in PNS group with mild tachypnea. However, the mean PetCO₂ was lower in the CNS group (29.41 mm Hg) than in the PNS group (32.39 mm Hg). PetCO₂ measurements were affected by minute ventilation. Decreased respiratory drive and decreased minute ventilation could explain the lower PetCO₂ values in the CNS group, compared to the PNS group. The different respiratory pattern, based on anatomical location, could affect the correlation.

Another possible cause could be the presence of cardiopulmonary insufficiency; the ratio of cardiopulmonary insufficiency was much higher in the CNS group than the PNS group. Although the correlation between PetCO₂ and PaCO₂ was significant in patients with and without cardiopulmonary insufficiency, the correlation coefficient was higher in patients without cardiopulmonary insufficiency, as expected. The correlation between PetCO₂ and PaCO₂ was more evi-

dent in hemodynamically stable patients.²⁵ PetCO₂ was helpful for predicting PaCO₂ only in patients without significant parenchymal lung disease.⁴ It was also useful for adjusting ventilator parameters in patients without major cardiopulmonary damage.²⁶ The limited correlation between PetCO₂ and PaCO₂ was caused by major changes in the pulmonary ventilation/perfusion ratio (V/Q). Aspiration, pneumothorax and pleural effusion cause atelectasis and lead to hypercapnia with a V/Q ratio below 1.0. Pulmonary embolism and other causes of impaired pulmonary perfusion, such as low cardiac output, can raise the V/Q ratio above 1.0.²⁷⁻³² Neurological disorders can cause ventilator problems by involving the cardiac or respiratory muscle, myocardial ischemia, pulmonary embolism, or aspiration pneumonia. In this study, cardiopulmonary insufficiency was more common in the CNS group and a V/Q mismatch could be the cause of the low correlation coefficient in the CNS group.

Regarding the ventilation pattern, there was a relatively good correlation in the hypocapnia group, however, no correlation was found in the hypercapnia group. This result was expected because of decreased expiration of arterial CO₂.

Although there was a correlation between PetCO₂ and PaCO₂, a physiological gradient exists between PaCO₂ and alveolar PCO₂, reflecting the existence of physiological, pulmonary dead space. This gradient has been reported to range from 2 mm Hg (in a conscious patient) to 5 mm Hg (in an intubated and sedated patient), where the PaCO₂ exceeded the PetCO₂.^{9,26,33} The gradient may increase in patients with severe pulmonary or major systemic disease. In this study, this gradient was higher in the CNS, cardiopulmonary insufficiency, mechanical ventilator, and non-intubated groups, compared to the others. Thus, if this gradient was initially calculated during PetCO₂ monitoring, changes in the gradient could detect increases in the physiological dead space and hemodynamic changes.

The presence of several limitations in this study warrants further investigations. First, the small number of patients and samples limited our generalization of the results, especially in the PNS group. Second, in this study we used a sidestream capnometer. With this, a sampling of exhaled air was drawn through a sampling tube into an analyzer that was placed some distance away from the patient. Thus, the PetCO₂ levels may have been underestimated.^{34,35}

Despite the limitations, this study showed that capnometry could be a useful tool for assessing some clinical parameters in critically ill neurological patients. First, PetCO₂ monitoring allowed the detection of ventilation pattern changes in patients with respiratory problems due to neurologic disorders. Second, the reliability of PetCO₂ monitoring was greater for the diseases of peripheral neuromuscular origin. Third,

PetCO₂ monitoring enabled the efficient adjustment of the mechanical ventilator and other respiratory support equipment. Further investigation of the ventilation pattern should increase the ability to determine the localization of the lesion and understand the progression of the disease.

Conclusion

The results suggest that, despite of some limitation, PetCO₂ monitoring using capnometry can be used for assessment of ventilation and hemodynamic status in critically ill neurological patients. PetCO₂ monitoring is a valid measure for patients with peripheral and neuromuscular disease. However, we recommend that arterial blood-gas analysis be performed, at least once, to assess initial ventilation patterns and P(a-A)CO₂ values.

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