Use of Maximum End-Tidal CO_2 Values to Improve End-Tidal CO_2 Monitoring Accuracy

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BACKGROUND: The arterial partial pressure of CO_2 (P_{aCO_2}) can be grossly estimated by the end-tidal partial pressure of CO_2 (P_{ETCO_2}). This principle is used in SmartCare (Dräger, Lübeck, Germany), which is an automated closed-loop system that uses P_{ETCO_2} to estimate alveolar ventilation during mechanical ventilation. OBJECTIVE: To assess whether the maximum P_{ETCO_2} value (instead of the averaged P_{ETCO_2} value) over 2-min or 5-min periods improves P_{aCO_2} estimation, and determine the consequences for the SmartCare system. METHODS: We continuously monitored breath-by-breath P_{ETCO_2} during ventilation with SmartCare in 36 patients mechanically ventilated for various disorders, including 14 patients with COPD. Data were collected simultaneously from SmartCare recordings, every 2 min or 5 min, and through a dedicated software that recorded ventilation data every 10 s. We compared the maximum and averaged P_{ETCO_2} values over 2-min and 5-min periods to the P_{aCO_2} measured from 80 arterial blood samples clinically indicated in 26 patients. We also compared SmartCare's classifications of patient ventilatory status based on averaged P_{ETCO_2} values to what the classifications would have been with the maximum P_{ETCO_2} values. RESULTS: Mean P_{aCO_2} was 44 ± 11 mm Hg. P_{aCO_2} was higher than averaged P_{ETCO_2} by 10 ± 6 mm Hg, and this difference was reduced to 6 ± 6 mm Hg with maximum P_{ETCO_2}. The results were similar whether patients had COPD or not. Very few aberrant values (< 0.01%) needed to be discarded. Among the 3,137 classifications made by the SmartCare system, 1.6% were changed by using the maximum P_{ETCO_2} value instead of the averaged P_{ETCO_2} value. CONCLUSIONS: Use of maximum P_{ETCO_2} reduces the difference between P_{aCO_2} and P_{ETCO_2} and improves SmartCare's classification of patient ventilatory status. *Key words: alveolar ventilation; capnometry; monitoring; mechanical ventilation; closed loop systems; weaning.* [Respir Care 2011;56(3):278–283.

Introduction

Monitoring of end-tidal partial pressure of CO_2 (P_{ETCO_2}) has applications in emergency medicine, anesthesia, and intensive care.[1,2] Although P_{ETCO_2} does not perfectly reflect arterial CO_2 measured from an arterial blood sample (P_{aCO_2}),[3,4] capnometry allows continuous monitoring of alveolar ventilation in intubated patients. The SmartCare automated ventilation and weaning system (Dräger, Lübeck, Germany) uses P_{ETCO_2} as a safety parameter, in addition to respiratory rate and tidal volume (V_T), to automatically control the pressure-support level.[5,6] SmartCare averages P_{ETCO_2}, respiratory rate, and V_T over 2-min or 5-min periods, classifies the patient's ventilatory status, and adjusts the pressure-support level accordingly. P_{ETCO_2} is not a main control parameter in SmartCare, but can be used in situations such as a low respiratory rate to help differentiate between, for instance, central hypoventilation leading to hypercapnia versus hyperventilation with hypocapnia. P_{ETCO_2} is known to frequently underestimate P_{aCO_2} because of ventilation-perfusion mismatching and dead-space effect.[7,8] A spontaneously breathing patient may intermittently have higher P_{ETCO_2} values than the averaged value during prolonged exhalations.[9] Such a value may better reflect alveolar P_{CO_2} and may thus be closer to P_{aCO_2}. We assessed the use of the maximum P_{ETCO_2} value instead of the averaged P_{ETCO_2} value over 2 min or 5 min. On the one hand, this could improve the

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accuracy of P_{ETCO_2} as a proxy for P_{aCO_2}, and on the other hand it could improve SmartCare's classifications of the patient's ventilatory status by using a more reliable P_{ETCO_2} value.

Methods

This study was purely observational, and the protocol was approved by the ethics committee of Erasme Hospital, Brussels, Belgium. The study was performed in the Erasme Hospital and Henri Mondor Hospital intensive care units.

Patients

The main inclusion criteria were hemodynamic stability, acceptable neurological status (Glasgow coma score $\geq$ 8), PEEP not higher than 10 cm H_2O, and pressure-support ventilation with pressure support of $\leq$ 20 cm H_2O. Patients were excluded if a clinical procedure was going to be performed within the next few hours.

Data Collection

Arterial blood samples were drawn for clinical indications and analyzed (ABL700, Radiometer, Copenhagen, Denmark, and GEM Premier 4000, Instrumentation Laboratory, Lexington, Kentucky) within a few minutes. Patients were ventilated with an Evita XL ventilator (Dräger, Lübeck, Germany) provided with the SmartCare system and an infrared P_{ETCO_2} mainstream sensor (product number 6871500, Dräger, Lübeck, Germany) connected to a CO_2 cuvette for measurement. During pressure-support ventilation with SmartCare, a dedicated software (VentView, Dräger, Lübeck, Germany) recorded ventilatory data, including P_{ETCO_2}, every 10 s. SmartCare averages P_{ETCO_2} values over 2 min or 5 min to classify the patient's ventilatory status, and we downloaded these data from the ventilator to the computer.

Procedure

SmartCare averages respiratory rate, V_T, and P_{ETCO_2} over 2 min or 5 min, from values taken at a sampling period of 10 s. The VentView software records the respiratory data at the same sampling period. Recorded data correspond to the last breath of each 10-s data period. In a preliminary study, we compared VentView's P_{ETCO_2} data averaged along SmartCare periods to SmartCare's own data, and the difference between VentView and SmartCare's averaged data was always less than 0.5 mm Hg. For each considered period, the averaged and maximum P_{ETCO_2} were thus determined from the VentView data. Our study of P_{aCO_2}, P_{ETCO_2}, and SmartCare concerned 80 SmartCare periods of 2 min or 5 min, during which we took arterial blood samples. We compared SmartCare's classifications to the maximum P_{ETCO_2} values instead of the averaged P_{ETCO_2} values.

Statistics

We analyzed the relationship between P_{aCO_2} and the averaged and maximum P_{ETCO_2} with linear regression. We used the Pearson test to evaluate the correlation. Quantitative data are expressed as mean $\pm$ SD or median and interquartile range.

Results

The sample consisted of 36 mechanically ventilated patients, between March 2006 and July 2007. There were 14 females and 22 males, with a mean age of 63 $\pm$ 14 y. The patients' respiratory mechanics, as determined by the ventilator, were: dynamic compliance 44 mL/cm H_2O (IQR 31–63 mL/cm H_2O) and resistance 10 cm H_2O/L/s (IQR 7–13 cm H_2O/L/s). At inclusion, the mean PEEP was 5 (IQR 5–8) cm H_2O, the mean pressure-support level was 14 cm H_2O (IQR 12–16 cm H_2O), and the mean F_{IO_2} was 0.40 (IQR 0.31–0.4). Fourteen patients had COPD. Three patients were tracheotomized; the others were orotracheally intubated. All ventilation was with a heated humidifier.

The mean duration of ventilation recordings with SmartCare was 3 hours 36 min per patient (IQR 3 hours 9 min to 4 hours 57 min). Of the 36 subjects, 26 had arterial blood gas measurements contemporaneous with the VentView and SmartCare data.

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Table 1. Difference Between Averaged and Maximum P_{ETCO_2} and P_{aCO_2} During Ventilation With SmartCare*

	Difference (mm Hg) mean ± SD
P_{aCO_2}–averaged P_{ETCO_2}	10 ± 6
P_{aCO_2}–maximum P_{ETCO_2}	6 ± 6
Maximum P_{ETCO_2}–averaged P_{ETCO_2}	4 ± 3

* 26 patients. 80 pairs of values. P_{aCO_2} = 43 ± 10 mm Hg. Averaged end-tidal partial pressure of CO2 (P_{ETCO_2}) = 33 ± 7 mm Hg. Maximum P_{ETCO_2} = 37 ± 8 mm Hg.

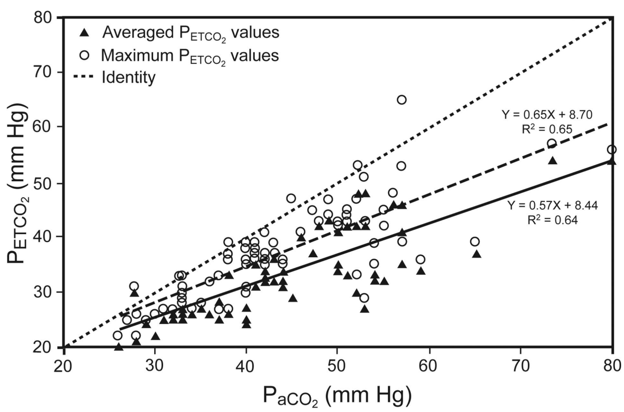

Fig. 1. Linear regression analysis of 80 pairs of maximum (dashed line) and averaged (solid line) end-tidal partial pressure of carbon dioxide (P_{ETCO_2}) and P_{aCO_2} values, from 26 patients.

Relationship Between P_{ETCO_2} and P_{aCO_2}

We analyzed 80 pairs of P_{ETCO_2} and P_{aCO_2} values from 26 patients. The mean ± SD number of arterial blood gas measurements was 3 ± 1 per patient. Mean P_{aCO_2} was 44 ± 11 mm Hg.

Table 1 shows the differences between the averaged and maximum P_{ETCO_2} and P_{aCO_2} values. The pairs of values were obtained during 49 2-min SmartCare periods and 31 5-min SmartCare periods. P_{aCO_2} was higher than averaged P_{ETCO_2} by 10 ± 6 mm Hg. Taking the maximum instead of the averaged P_{ETCO_2} value reduced the difference with P_{aCO_2} by 4 mm Hg. Figure 1 shows the linear regression of the averaged and the maximum P_{ETCO_2} against the P_{aCO_2} values. The coefficient of regression was closer to identity with the maximum P_{ETCO_2} values. Figure 2 plots the maximum P_{ETCO_2} against the averaged P_{ETCO_2}.

Relationship Between P_{ETCO_2} and P_{aCO_2} Relative to COPD

There were 44 values from the 14 COPD patients and 36 values from 12 the non-COPD patients (Table 2). The results were similar whether patients had COPD or not.

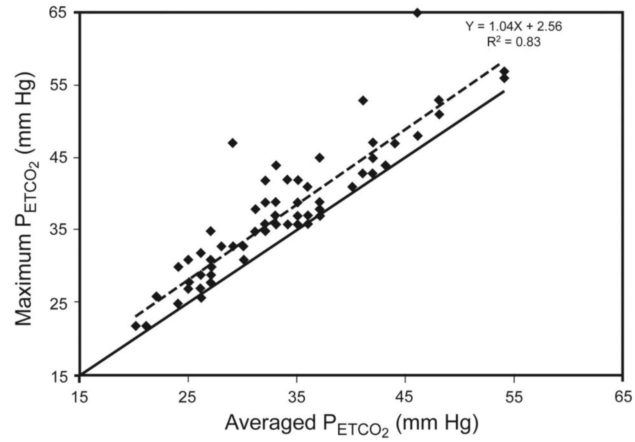

Fig. 2. Linear regression analysis of maximum end-tidal partial pressure of carbon dioxide (P_{ETCO_2}) versus averaged P_{ETCO_2}. The solid line is the identity line. The dashed line is the regression line.

Exclusion of P_{ETCO_2} Aberrant Values

We defined an aberrant value as a contextually non-physiologic high P_{ETCO_2} value. Aberrant values, measured via CO_2 infrared sensor, may be due to moisture, water, or dirt on the sensor. Because using one single maximum P_{ETCO_2} value instead of averaged P_{ETCO_2} values ran the risk of using aberrant values, when the difference between 2 consecutive values (separated by 10 s) was more than 40 mm Hg, the latter value was considered aberrant. We found 32 aberrant values (in the 74,777 total measurements), which came from 6 patients. Four patients had only one aberrant value, one patient had 21 aberrant values, and one patient had 7 aberrant values. The rate of aberrant values was 0.04%. We discarded all aberrant values.

SmartCare Classification

The classification of ventilation made by SmartCare for every recording using the averaged P_{ETCO_2} and the maximum P_{ETCO_2} values among the 3,137 SmartCare classifications for the 36 patients differed only for 49 classifications (1.6%), in 9 patients. For the pairs of data related to these classifications, the difference between maximum and averaged P_{ETCO_2} was 16 ± 9 mm Hg, with a median of 13 mm Hg (IQR 13–20 mm Hg).

Discussion

The maximum P_{ETCO_2} value was on average 4 mm Hg closer to P_{aCO_2} than the averaged P_{ETCO_2}. Linear regression between P_{ETCO_2} and P_{aCO_2} was closer to the identity line with maximum P_{ETCO_2}. The use of maximum P_{ETCO_2} in-

Table 2. P_{ETCO_2} and P_{aCO_2} in COPD Versus Non-COPD Patients During Ventilation With SmartCare

Patients	P_{aCO_2} (mm Hg)	Averaged P_{ETCO_2} (mm Hg)	Maximum P_{ETCO_2} (mm Hg)	Comparison	Difference (mm Hg) mean ± SD	Pearson Correlation (r)
Without COPD (36 paired values, 12 patients)	40 ± 10	31 ± 7	35 ± 9	P_{aCO_2} – averaged P_{ETCO_2}	9 ± 6	0.773
				P_{aCO_2} – maximum P_{ETCO_2}	5 ± 6	0.813
				Maximum P_{ETCO_2} – averaged P_{ETCO_2}	4 ± 4	0.936
With COPD (44 paired values, 14 patients)	46 ± 10	35 ± 8	39 ± 7	P_{aCO_2} – averaged P_{ETCO_2}	11 ± 6	0.799
				P_{aCO_2} – maximum P_{ETCO_2}	7 ± 6	0.795
				Maximum P_{ETCO_2} – averaged P_{ETCO_2}	4 ± 3	0.903

P_{ETCO_2} = end-tidal partial pressure of CO_2

frequently changed the classification determined by SmartCare.

Relationship Between P_{ETCO_2} and P_{aCO_2}

P_{ETCO_2} is supposed to represent alveolar P_{CO_2} (P_{ACO_2}), which is determined by the speeds at which CO_2 is filling alveoli and being emptied from alveoli. The P_{ACO_2} depends on CO_2 production by tissues and venous blood flow content. CO_2 exhalation from alveoli depends on alveolar ventilation. If the alveolar ventilation-perfusion ratio ($\dot{V}_A/\dot{Q}$) is low, the P_{ACO_2} will be close to venous pressure. If this ratio is normal, the P_{ACO_2} will be close to P_{aCO_2}. If $\dot{V}_A/\dot{Q}$ is high, the P_{ACO_2} will be closer to the inspired CO_2.[7] So P_{aCO_2} tends to be higher than P_{ACO_2}, mainly because of ventilation-perfusion discrepancies. P_{ACO_2} and P_{ETCO_2} can thus be different, owing to the patient's ventilation and pulmonary condition (eg, restrictive or obstructive lung disease). Allowing a prolonged or complete exhalation (compared to a normal breath) could increase P_{ETCO_2}.[10] A longer exhalation may therefore better reflect P_{ACO_2} among spontaneous breaths. We inferred that the use of maximum P_{ETCO_2} during periods of 2 min or 5 min, as determined by the SmartCare system for averaging its parameters, could be a better indicator of alveolar ventilation than the averaged P_{ETCO_2} during the same period.

We measured averaged P_{ETCO_2}, maximum P_{ETCO_2}, and P_{aCO_2} contemporaneously. Table 1 shows that the difference between averaged P_{ETCO_2} and P_{aCO_2} was around 10 mm Hg, a value reported in several previous studies.[11-14] Our maximum P_{ETCO_2} values were closer to P_{aCO_2} by about 4 mm Hg, compared to the averaged P_{ETCO_2}. The maximum P_{ETCO_2} had a higher correlation coefficient ($r = 0.65$ vs 0.57) in all periods (see Fig. 1), which indicates that maximum P_{ETCO_2} better approximates P_{aCO_2} than does averaged P_{ETCO_2}.

Maximum P_{ETCO_2} was also found more accurate by Weinger et al.[9] They recorded P_{aCO_2} and P_{ETCO_2} in 25 patients after cardiotomy and being weaned with intermittent mandatory ventilation. P_{ETCO_2} varied widely from breath to breath, and two thirds of the time the P_{ETCO_2} of spontaneous breaths was greater than that of ventilator breaths. Maximum P_{ETCO_2} was the most accurate indicator of P_{aCO_2} ($r = 0.77$, $P < .001$), and the arterial-to-end-tidal difference was 4 ± 4 mm Hg ($P < .01$).

Chopin et al[10] also found a larger difference between maximum P_{ETCO_2} and P_{aCO_2} in patients with pulmonary embolism (12 mm Hg) versus patients without (1 mm Hg). They used a prolonged passive exhalation until maximum P_{ETCO_2} was reached and found those values much closer to P_{aCO_2}.

Lujan et al[14] studied 120 non-ventilated patients and control subjects, classified in 4 equal groups according to COPD severity. With each subject, arterial blood was sampled, then the subject was asked to breath normally through a mouthpiece attached to a sidestream capnograph, and then to produce 3 maximal exhalations of at least 5 s each. For the entire cohort they found a better Pearson correlation between P_{aCO_2} and P_{ETCO_2} with maximal exhalation ($r = 0.88$, $P < .001$) than with P_{ETCO_2} during normal tidal breathing ($r = 0.72$, $P < .01$). However, they also found that P_{ETCO_2} during maximal expiration tended to overestimate P_{aCO_2}. In our study we found a similar alveolar-versus-end-tidal CO_2 difference (−2 mm Hg, interquartile range–3 to −1 mm Hg) in only 6 of the 80 pairs of maximum P_{ETCO_2} and P_{aCO_2} values. However, for the whole data the mean difference was positive (6 ± 6 mm Hg). The difference with Lujan's study,[14] which often found an overestimation of P_{aCO_2}, may be due to the long duration of maximal exhalation maneuvers (at least 5 s), while it was only spontaneous exhalations in our study.

P_{ETCO_2} and P_{aCO_2} Relative to COPD

P_{ETCO_2} can be a poor proxy for P_{aCO_2} in patients with parenchymal lung disease or emphysema undergoing weaning from mechanical ventilation.[15] In our clinical study we observed (see Table 2) a similar difference (4 mm Hg) between the maximum and averaged P_{ETCO_2} in COPD and

Table 3. SmartCare's Classification of Ventilation Periods*

Condition	Spontaneous Respiratory Rate Condition (f)	V_T Condition	P_{ETCO_2} Condition	Change in Pressure Support
Hypoventilation	f < f low	V_T low ≤ V_T	P_{ETCO_2} high ≤ P_{ETCO_2}	Increase
Acute tachypnea	f max ≤ f	V_T low ≤ V_T	20 mm Hg ≤ P_{ETCO_2}	Increase
Insufficient ventilation	f low ≤ f < f max	NA	P_{ETCO_2} high ≤ P_{ETCO_2}	Increase
	f low ≤ f	V_T < V_T low	NA	Increase
Tachypnea	f high ≤ f < f max	V_T low ≤ V_T	20 mm Hg ≤ P_{ETCO_2} < P_{ETCO_2} high	Increase
Central hypoventilation	f < f low	V_T < V_T low	P_{ETCO_2} high ≤ P_{ETCO_2}	No change
Unexplained hyperventilation	f high ≤ f	V_T low ≤ V_T	P_{ETCO_2} < 20 mm Hg	No change
Normal ventilation	f low ≤ f < f high	V_T low ≤ V_T	P_{ETCO_2} < P_{ETCO_2} high	Decrease (weaning)
Hyperventilation	f < f low	NA	P_{ETCO_2} < P_{ETCO_2} high	Decrease

* This table presents all SmartCare diagnosis or classifications functions of different parameters' values as compared to their threshold. It also presents the consequences on pressure support for each classification. The zone of respiratory comfort corresponds to normal values for the 3 parameters.
V_T = tidal volume (ml)
P_{ETCO_2} = end-tidal partial pressure of CO_2
f low = lower limit of spontaneous breathing frequency: 15 breaths/min
f high = upper limit of spontaneous breathing frequency: 30 breaths/min (34 breaths/min with neurological disorders)
f max = maximum limit of spontaneous breathing frequency: 36 breaths/min
V_T low = lower limit of V_T: 300 mL (250 ml, for body weight < 55 kg)
P_{ETCO_2} high = upper limit of P_{ETCO_2}: 55 mm Hg (65 mm Hg for patients with COPD)
NA = not applicable

non-COPD patients. In the non-COPD patients, however, there was a higher correlation coefficient between P_{aCO_2} and maximum P_{ETCO_2} (r = 0.77 versus r = 0.81), whereas the correlation coefficient was not different (r = 0.8) in the COPD patients. In both the COPD and non-COPD patients the difference between P_{ETCO_2} and P_{aCO_2} was similarly smaller with the maximum P_{ETCO_2}.

We did not measure intrinsic PEEP, which can influence the difference between P_{aCO_2} and P_{ETCO_2}. Blanch et al[16] addressed this issue in 24 paralyzed and sedated patients on volume-controlled ventilation. They partitioned their population into 2 groups, according to the presence of intrinsic PEEP (13 patients) or not (11 patients). They found a higher P_{aCO_2}-P_{ETCO_2} difference in the intrinsic PEEP group and a better correlation of P_{ETCO_2} with P_{aCO_2} in patients without intrinsic PEEP.

SmartCare and P_{ETCO_2}

SmartCare uses P_{ETCO_2} as a security threshold to delimit the zone of respiratory comfort (Table 3) and in the algorithm by which it classifies the patient's ventilatory status.[17-19] High P_{ETCO_2} (> 65 mm Hg for COPD, > 55 mm Hg for non-COPD), respiratory rate, and V_T cause SmartCare to classify the ventilation period into a diagnosis such as central hypoventilation, hyperventilation, or insufficient ventilation. Low P_{ETCO_2} (< 20 mm Hg) is also used to classify unexplained hyperventilation, defined by a high respiratory rate and normal V_T unresponsive to changes in pressure level.[19] In SmartCare the use of maximum P_{ETCO_2} would better classify the patient's ventilatory status in a very small but potentially important number of cases. Indeed, SmartCare uses different safety thresholds (depending on the presence of chronic CO_2 retention, as indicated by the user) to detect central hypoventilation, defined as a low respiratory rate and a high P_{ETCO_2}, or insufficient ventilation, as a low V_T and a high P_{ETCO_2}. These are rare situations but need to be recognized. If P_{ETCO_2} markedly underestimates P_{aCO_2}, the diagnosis will occur late (ie, with a very high P_{aCO_2} value). If at least one P_{ETCO_2} value during a 2-min or 5-min period is above a P_{ETCO_2} threshold, it would change SmartCare's ventilatory status classification. Using the maximum P_{ETCO_2} would make SmartCare more sensitive to higher CO_2 values, which might result in better classification. It could also offer more stability in situations where there is alternation between pathological and non-pathological classifications, because abnormal ventilation would be diagnosed earlier. The use of maximum P_{ETCO_2} would increase the classifications of hypoventilation and insufficient ventilation, leading SmartCare to increase pressure support or to alarm. The use of maximum P_{ETCO_2} would have changed 1.6% of the classifications in our patients. There were 28 changes from normal ventilation to insufficient ventilation, which represents 57% of the overall changes in classification. In this study, however, the classification changes were retrospective and did not affect our care decisions.

Conclusions

Currently, P_{ETCO_2} measurement via infrared sensor usually underestimates P_{aCO_2}. Maximum P_{ETCO_2} seems to be closer to alveolar CO_2 than averaged P_{ETCO_2}. Use of maximum P_{ETCO_2} could improve the accuracy and efficiency of SmartCare without being harmful to the patient.

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