Trending peripheral venous PCO₂ in patients with respiratory failure using mathematically arterialised venous blood gas samples

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ABSTRACT

Background Trending venous blood gases (VBGs) has been suggested as an alternative to arterial blood gases (ABGs) in patients with respiratory failure, but there are limits to its utility. The aim of this study was to compare the trend of venous carbon dioxide partial pressure (PCO₂) (pCO₂v) with mathematically arterialised PCO₂ (pCO₂ca) and to further evaluate whether pCO₂ca follows change in arterial pCO₂ (pCO₂a) more accurately.

Methods We analysed two data sets. The first was a retrospective study of patients with respiratory failure admitted to the intensive care unit. Venous samples were mathematically arterialised using the vTAC method. The change in pCO₂ between two consecutive samples (ΔpCO₂) for pCO₂v was compared with the change in calculated pCO₂ca values. In the second data set taken from previously published work, we analysed 82 trend points (difference between consecutive samples) for change in pCO₂. There were pCO₂v, pCO₂a and pCO₂ca values for each trend point. The primary outcome measures were the 95% limits of agreement (LOAs) between different sampling methods for ΔpCO₂.

Results In the first data set, 46 patients had 203 VBG results giving 157 trend points for ΔpCO₂ analysis. The 95% LOAs for ΔpCO₂ca and ΔpCO₂v were −9.28 to 11.12 mm Hg.

In the second data set, 95% LOAs for ΔpCO₂ were −9.46 to 9.48 mm Hg for ΔpCO₂a and ΔpCO₂v, −8.94 to 8.58 mm Hg for ΔpCO₂ca and ΔpCO₂v, and −4.54 to 4.91 mm Hg for ΔpCO₂a and ΔpCO₂ca.

Conclusion This study suggests that trending pCO₂v is not an accurate way to trend pCO₂a in patients with respiratory failure. ΔpCO₂ca via vTAC trended differently to ΔpCO₂v. Our data suggest pCO₂ca more accurately trends pCO₂a.

BACKGROUND

Blood gas analysis with measurement of carbon dioxide partial pressure (pCO₂) is essential in the assessment of a critically ill patient with respiratory failure. Arterial blood gases (ABGs) are the accepted reference technique for the assessment of pCO₂; however, they are painful, technically challenging and require expertise to obtain. Venous blood gases (VBGs) are often obtained with any initial venous puncture and in our experience are often used alone in the initial assessment of ventilatory status.

There is agreement in the literature for the use of VBG instead of ABG for the assessment of pH, lactate, and bicarbonate for both central and peripheral VBGs. VBGs are a useful screening tool for respiratory function with pCO₂ >45 mm Hg being 100% sensitive for detecting the presence of hypercarbia and a pCO₂ <30 mm Hg being 100% predictive to rule out the presence of hypercarbia. However, venous (pCO₂v) and arterial pCO₂ (pCO₂a) are not interchangeable for further assessment as the limits of agreement (LOAs) are unacceptably wide ranging from −17.4 to +26 mm Hg (although some authors suggest closer agreement).

In addition, pCO₂v and pCO₂a do not have a consistent relationship to permit a simple conversion factor.

Several authors have suggested that pH or pCO₂ may be useful for trending change in respiratory status, although reliance on pCO₂ instead of ABG is likely to lead to unnecessary ventilator adjustment in intubated patients. One study looking at trending suggested that

Key messages

- Does mathematically arterialised venous carbon dioxide partial pressure (pCO₂) trend pCO₂ differently to venous pCO₂ alone, and if so, which follows arterial pCO₂ more accurately?
- Limits of agreement for change in pCO₂ between venous samples and arterial samples/mathematically arterialised venous blood were wide. The change in pCO₂ with mathematical arterialisation more closely followed arterial blood than venous sampling.
- Previous work has established that mathematical arterialisation of venous blood improves correlation with arterial blood. This is the first work to examine whether this improvement translates into improved ability to trend pCO₂.
the agreement for absolute change was reasonable for venous pH, but not for pCO₂v due to the wide LOAs. Recently, a method has been developed that allows the estimation of ABG values from venous samples based on mathematical modelling of oxygen utilisation and thus carbon dioxide production in the tissues based on haemoglobin, peripheral oxygen saturations and venous oxygen saturations. Using an estimate of the respiratory quotient and oxygen extraction, the pCO₂a is then estimated from the pCO₂v. Mathematically arterialised or calculated VBG can be calculated to within clinically acceptable criteria of the arterial blood gas values for pH and pCO₂. The remaining variability is similar to that seen within serial arterial blood sampling and within laboratory acceptable performance criteria. Calculated arterial values from peripheral venous blood have been found to be more accurate than those taken from central venous blood and caution is recommended when transforming central venous blood samples.

This study aims to answer the questions: does mathematical arterialised pCO₂v (pCO₂ca) trend pCO₂ differently to pCO₂v alone, and if so, which follows pCO₂a more accurately?

METHOD

Data set 1

We retrospectively collected venous blood gases to compare trends between pCO₂v and pCO₂ca. Adult patients admitted to the intensive care unit between July 2018 and June 2020 at Hawke’s Bay Hospital with chronic obstructive pulmonary disease (COPD) or respiratory failure were eligible for admission. Hawke’s Bay Hospital is a regional New Zealand hospital serving a population of 165,000. Approval for audit was obtained and as these results were retrospectively collected then de-identified prior to analysis, patient consent was not required. Data collection included age, sex, presence of cardiac failure and concern for shock. In the event of repeat presentations for a single patient during the admission period for the study, only data from the first admission were extracted. Patients were excluded if there were less than two VBG samples available (no trend) or peripheral SpO₂ near the time of VBG collection was not available. Twenty patients were recorded as being on non-invasive ventilation (NIV), two were intubated and data were unavailable regarding NIV use for 12. Our laboratory uses an ABL85 FLEX blood gas machine (Radiometer Medical ApS, Bronshøj, Denmark).

Venous to arterial conversion of pCO₂ was performed using vTAC software (OBI Medical, Jacob Møllers Gade 4, Hadsund, Denmark). In the absence of literature defining an acceptable limit for the difference in ΔpCO₂ between measurement methods, we defined the acceptable ΔpCO₂ as 5 mm Hg. One small study suggested a difference of 6.6 mm Hg being the upper limit of clinical acceptability for difference in point estimate of pCO₂. The primary outcome of interest was 95% LOAs between ΔpCO₂v and ΔpCO₂ca, displayed graphically on Bland-Altman plots.

Data set 2

Data were provided by the authors of a previous study in which multiple data points in individual patients were measured. These data were further analysed for ΔpCO₂a, ΔpCO₂v and ΔpCO₂ca. Patients with previously diagnosed COPD admitted to the Department of Respiratory Diseases at Aalborg Hospital, Denmark due to exacerbation, were included in the study. Informed oral and written consent was obtained from patients in all cases. Patients were only studied on weekdays over a single week and were therefore recruited on Monday–Wednesday to maximise the number of study days, making this a convenience sample. On each day during this period, if an arterial blood sample was ordered as part of routine clinical practice on the ward round in a recruited patient, the on-duty biotechnician responsible for taking the arterial sample would then take an additional peripheral venous sample. The corresponding venous and arterial samples were taken within a few minutes of each other. Pulse oximetry SpO₂ was performed as part of the usual routine by the biotechnician and noted. These samples were then evaluated for ΔpCO₂ comparison between ΔpCO₂a, ΔpCO₂v and ΔpCO₂ca. This data set used an ABL835 FLEX blood gas machine (Radiometer Medical ApS, Bronshøj, Denmark).

As we used previously collected data for this, there was no power calculation made for this arm of the study.

Statistical analysis

Bland-Altman plots of mean versus difference with 95% LOA for any two of ΔpCO₂a, ΔpCO₂v and ΔpCO₂ca are presented to compare agreement for ΔpCO₂ (figure 1). Adjustment for multiple comparisons was not made after finding essentially identical SDs for all data sets using the first observation only and all observations as discrete data points.

The number of patients in whom the difference between any two measures of ΔpCO₂ between ΔpCO₂a, ΔpCO₂v and ΔpCO₂ca was greater than 5, 7.5 and 10 mm Hg, respectively, is presented in table 1.

The analysis for the first data set was powered for a 95% CI around the upper and lower bounds of the LOA of 1.5 mm Hg with 100 changepoints analysed. Baseline descriptive statistics are presented as mean and 95% CIs unless otherwise indicated.

Patient and public involvement

Ours is a retrospective cohort study involving the mining of de-identified laboratory data. Neither patients nor the public were involved in the recruitment or conduct of the study, nor are there plans to disseminate results to patients.
Figure 1  Bland-Altman plots for the change (delta) in pCO₂ between compared measurements. pCO₂, carbon dioxide partial pressure.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Proportion of samples where difference in ΔpCO₂ was greater than 5, 7.5 and 10 mm Hg, respectively, for two different sampling methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference in ΔpCO₂</td>
<td>Calculated arterial/venous ΔpCO₂</td>
</tr>
<tr>
<td>Data set</td>
<td>1st data set</td>
</tr>
<tr>
<td>&gt;5 mm Hg</td>
<td>34/156 (21.8%)</td>
</tr>
<tr>
<td>&gt;7.5 mm Hg</td>
<td>14/156 (9.0%)</td>
</tr>
<tr>
<td>&gt;10 mm Hg</td>
<td>5/156 (3.2%)</td>
</tr>
</tbody>
</table>

pCO₂, carbon dioxide partial pressure.
RESULTS

Baseline variables for parameters on the first blood gases taken as well as bias for ΔpCO$_2$ between groups are shown in table 2.

Data set 1

In our retrospective data set, 46 patients were eligible for study admission with a total of 203 VBG samples collected resulting in 157 trend points (ΔpCO$_2$) being available for analysis. For example, a patient with three VBG samples had two trend points available for analysis with values calculated between the first and second sample and the second trend point between the second and third sample. This data set included patients on high-flow nasal cannula and NIV. The most common diagnoses were COPD, right heart failure, obesity-related hypoventilation and pneumonia. Only three patients had any potential concern for shock—defined as blood pressure <90 mm Hg systolic or vasopressor requirement at time of sampling. The change in pCO$_2$ between two consecutive samples for pCO$_2v$ was compared with the change in calculated pCO$_2ca$ values.

The 95% LOAs for ΔpCO$_2ca$ and ΔpCO$_2a$ were −9.46 to 9.48 mm Hg for ΔpCO$_2a$ and ΔpCO$_2v$, and −8.94 to 8.58 mm Hg for ΔpCO$_2ca$ and ΔpCO$_2v$. The ΔpCO$_2a$ had a strong linear correlation with both ΔpCO$_2ca$ and ΔpCO$_2v$ (R$^2=0.946$ and 0.823, respectively).

When compared with the change in pCO$_2$ of arterial samples, two of the mathematically calculated (ΔpCO$_2ca$) samples were greater than 5 mm Hg different to the arterial samples vs 22 of the venous pCO$_2$ samples. Similarly, when comparing ΔpCO$_2v$ with ΔpCO$_2ca$, there were 17 samples in the venous group that were outside the 5 mm Hg range (table 1).

Data set 2

In this data set, 54 patients were studied over the period June 2010–June 2011 in normal working hours (08:00–15:00). Forty-four patients received nasal oxygen, in 20 patients this was delivered by a high-flow humidification device (Optiflow, Fisher and Paykel). The remaining 10 patients received NIV support including oxygen delivery (Vivo30, Breas). Two patients switched between oxygen delivery methods during the study. As the protocol was such that each patient was studied over a single week then a varying number of days were studied for each patient with 13 patients studied on a single occasion, 13 on 2 days, 17 on 3 days, 9 on 4 days, and a single patient on both 5 and 6 days.

From these data, 136 paired samples resulting in 82 trend points (ΔpCO$_2$) were available for analysis for change in pCO$_2$ for pCO$_2a$, pCO$_2v$ and pCO$_2ca$. The 95% LOAs were −4.54 to 4.91 mm Hg for ΔpCO$_2a$ and ΔpCO$_2ca$, −9.46 to 9.48 mm Hg for ΔpCO$_2a$ and ΔpCO$_2v$, and −8.94 to 8.58 mm Hg for ΔpCO$_2ca$ and ΔpCO$_2v$. The ΔpCO$_2a$ had a strong linear correlation with both ΔpCO$_2ca$ and ΔpCO$_2v$ (R$^2=0.946$ and 0.823, respectively).

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DISCUSSION

While pCO$_2v$ is known to have unacceptably wide LOAs for the estimation of pCO$_2a$ levels in patients with respiratory failure, it has been suggested that pCO$_2v$ could be used for trending. This suggestion is not supported by either our data or the limited available literature.$^{12}$ In both data sets, pCO$_2ca$ and pCO$_2v$ measured ΔpCO$_2$
differently with moderately wide LOA. Similarly, wide LOAs between ΔpCO2v and ΔpCO2a were seen in the second data set. In this second data set, pCO2ca trended pCO2a within limits that may be clinically acceptable.

It has been suggested that pH may be used as a surrogate marker to trend respiratory function in patients with respiratory failure combined with clinical assessment.12,22 We have chosen not to analyse pH in this study for two reasons. The 95% CIs for pH when used in assessing respiratory function have been reported as ±0.3.4,6 Via the Henderson-Hasselbalch equation (pH=6.1+log (HCO3-/ (0.03×PCO2))), a change in pCO2 in the range of ±10 mm Hg from a pCO2 of 40 mm Hg (without metabolic abnormality) would be required to cause this change in pH without concurrent metabolic abnormality. Additionally, the logarithmic basis of pH calculation and greater acute proportional change in pCO2 than bicarbonate23 make acute change in pH in hypercapnoeic respiratory failure driven largely by proportional change in pCO2 (online supplemental appendix 1). Given the choice to define adequacy of agreement in terms of absolute rather than relative change in pCO2, we have not further analysed pH.

This work along with current evidence suggests that the change in pCO2ca is a more accurate marker of the trend in pCO2a than venous pH or pCO2v. It is of interest that analysis incorporating the peripheral pCO2 may potentially be a more accurate representation of the patient’s ‘true’ physiology than arterial samples in the setting of acute change in ventilation. Transient changes in ventilation as might occur with sampling anxiety-related hyperventilation appear to be reflected within seconds in pCO2a, while this effect is mitigated in venous blood.24 As a method where this mitigating effect is maintained and which also corrects for variability in tissue oxygen metabolism, pCO2ca via vTAC holds theoretical advantages.

There are limitations to this study. The two groups analysed were different, data set 1 appearing to have more acute and severe respiratory failure with higher baseline pCO2 and lower pH. This may reflect the different time of sampling with samples in data set 1 being taken in the emergency department and intensive care unit versus patients established in the ward in data set 2. Without arterial samples, the LOA for ΔpCO2 from data set 1 can only demonstrate that in this population pCO2ca and pCO2v gas tracked CO2 differently. Data set 2, with concurrent VBG and ABG samples, allowed direct comparison of all three values - arterial, venous and calculated. The narrower LOAs between ΔpCO2ca and ΔpCO2a suggest that ΔpCO2ca tracks change in pCO2a better than ΔpCO2v in this population. Correlation of ΔpCO2 for VBG/ABG and vTAC (calculated arterial) values in the most acute phase of respiratory failure represents an opportunity for future research. Of note, other studies of critically ill patients with wide ranges of diagnoses admitted to intensive care, pulmonary medicine or emergency departments retain small LOAs <5 mm Hg when comparing single timepoint pCO2ca with pCO2a.13–19,25

Peripheral saturations obtained were as close to the time of documented sampling as possible. Given the first set of data is retrospective, it is possible the actual saturation at the time of sampling may be different to that recorded. Previous assessments of an adequately ‘well perfused limb’ for the measurement of peripheral saturations for the purpose of calculating arteriovenous differences from venous samples required a clearly recognisable pulse and a normal capillary response.15 We cannot confirm this retrospectively, but few patients had any concern for shock described in their clinical notes. Another study of pCO2ca using routinely available blood samples found results in line with experimentally controlled conditions, despite no attempt to ensure reasonable peripheral perfusion beyond routine clinical practice.16

We did not correct for the use of multiple data points from individual patients but do not believe there was any difference in the within and between patient variance that altered the LOA. Data using the first observation from each patient only had essentially identical SDs to those used for the presented LOA, and there was no significant within/between groups difference in variance on one-way analysis of variance. A non-parametric presentation of results is also included in table 1.

Central venous saturations were unlikely to have featured significantly in this patient population. Delay in time from VBG sampling to blood gas analysis may well have occurred, but up to 15 min delay has shown no significant change in calculated values.17 While bubbles in VBG sampling tubes can affect values, there is no reason to believe our sample does not represent everyday clinical practice.

CONCLUSION

This study suggests that trending pCO2v is not an accurate way to trend pCO2a in patients with respiratory failure. ΔpCO2ca via vTAC trended differently to ΔpCO2v. Our data suggest pCO2ca more accurately trends pCO2a. Further research on this aspect of mathematical arterio-venous difference of VBGs is warranted.

Contributors GC and MW conceived the study. MW collected data, assisted with data analysis, wrote the first draft and led the writing of subsequent drafts. GC analysed data and provided oversight.

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Patient consent for publication Not required.

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Provenance and peer review Not commissioned; externally peer reviewed.

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