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Alveolar partial pressures of carbon dioxide and oxygen measured by a helium washout technique

J Jordanoglou, G Tatsis, J Danos, S Gougoulakis, D Orfanidou, M Gaga

Abstract

A non-invasive technique was developed for measuring alveolar carbon dioxide and oxygen tension during tidal breathing. This was achieved by solving the Bohr equations for mean alveolar carbon dioxide and oxygen tensions ($\bar{P}ACO_2$, $\bar{P}AO_2$) from known values of the deadspace:tidal volume ratio measured by helium washout, and from the mixed expired partial pressure of carbon dioxide and oxygen. The derived values of w$\bar{P}ACO_2$ and w$\bar{P}AO_2$ were compared with $PaCO_2$ obtained from arterial gas analysis and $\bar{P}AO_2$ calculated from the ideal air equation. Four normal subjects and 58 patients were studied. Calculated and measured PCO_2 values agreed closely with a difference in mean values (w$\bar{P}ACO_2$ − $PaCO_2$) of 0·01 kPa; the SD of the differences was 0·7 kPa. The difference in mean values between w$\bar{P}AO_2$ and $\bar{P}AO_2$ was 0·02 kPa; the SD of the differences was 0·93 kPa. The method is simple and not time consuming, and requires no special cooperation from the patients. It can be applied in the laboratory or at the bedside to any subject breathing tidally. Physiological deadspace:tidal volume ratio, $\bar{P}AO_2$ and $\bar{P}ACO_2$, static lung volumes, respiratory exchange ratio, carbon dioxide production, oxygen uptake, tidal volume, and total ventilation can be measured with acceptable accuracy and reproducibility in one test. An arterial blood sample is needed initially to provide an independent measure of $PaCO_2$ and for measurement of the alveolar-arterial PO_2 difference. Subsequently, $PaCO_2$ can be estimated from w$\bar{P}ACO_2$ sufficiently well for clinical purposes and PaO_2 or SaO_2 can be monitored by non-invasive methods.

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There are several indirect methods for measuring alveolar oxygen and carbon dioxide tensions in normal subjects.[1–6] The results obtained by these techniques are of uncertain value in patients with maldistribution of the inspired air within the lungs.[3 4 7]

The aim of this paper is to describe a non-invasive method for estimating alveolar carbon dioxide and oxygen tensons ($\bar{P}ACO_2$, $\bar{P}AO_2$) during quiet breathing in normal subjects and in patients. The method is based on the helium washout technique for measuring the physiological deadspace:tidal volume ratio.[8]

Methods

PROTOCOL

We studied 62 subjects, 52 men and 10 women, aged 30–75 years. The subjects consisted of four normal subjects (doctors working in the unit) and 58 patients with chronic bronchitis and emphysema, asthma, or lung fibrosis of different causes. The patients were investigated as part of their routine assessment before and after treatment. The procedure can be divided into three stages (fig 1).

A Helium equilibration between lungs and spirometer

For helium equilibration between lungs and spirometer[8] the subject first rebreathed helium in a closed circuit, as for measurement of functional residual capacity (FRC). Rebreathing was discontinued when the helium fractional concentration measured at the mouth had remained stable in both respiratory phases for about one minute (Fo).

B Helium washout from the lungs

The patient breathed ambient air quietly through the valve system (A and B, fig 1) until the fractional concentration of helium in the last expirate (n—that is, FEn) was 1–2%. The mean helium fractional concentration ($\bar{F}E$) in mixed expired air was measured in bag 1.

C Expired helium free air collection

One to two minutes after stage B subjects were asked to breathe quietly through valves A and B as previously but expired air was now collected in bag 2. The mean fractional concentrations of carbon dioxide ($\bar{F}ECO_2$) and oxygen ($\bar{F}EO_2$) were then measured in bag 2. Arterial blood was sampled in the middle of the expired air collection for measurement of $PaCO_2$ and PaO_2.

The method can also be applied with the subject breathing oxygen enriched inspired air, provided that the inspired concentration of oxygen remains stable during the entire procedure.

The test requires the subjects to breathe tidally at their own rate for about 10 minutes through a mouthpiece while in a sitting or semirecumbent posture. The method can be applied by a technician in the laboratory or at the bedside, and in total takes 20–30 minutes.

The following indices were calculated from the results of the helium washout test: functional residual capacity (FRC), the physiological deadspace:tidal volume ratio measured by the classical carbon dioxide method (VD/VT) and by the helium washout

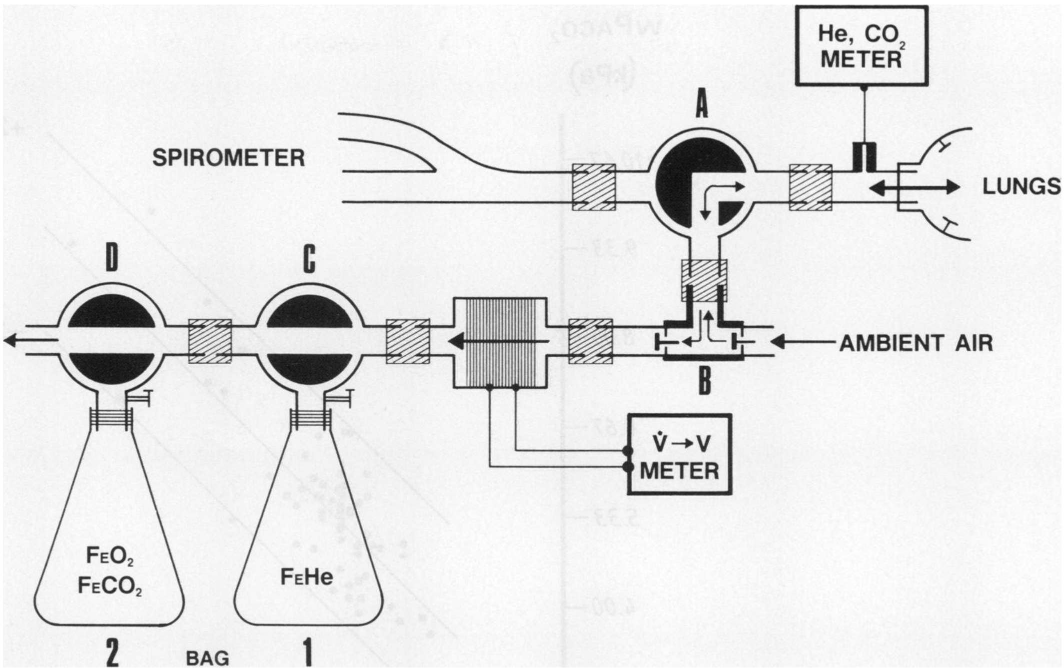

Figure 1 Diagram of the mechanical system used for the helium washout technique.

technique (wVD/VT), alveolar carbon dioxide and oxygen tensions measured by the helium washout technique (w$\bar{P}ACO_2$, w$\bar{P}AO_2$), the respiratory exchange ratio (RE), carbon dioxide production ($\dot{V}CO_2$), oxygen uptake ($\dot{V}O_2$), minute ventilation ($\dot{V}E$), and tidal volume (VT).

Alveolar carbon dioxide and oxygen tensions (w$\bar{P}ACO_2$, w$\bar{P}AO_2$) were calculated according to equations 1 and 2 (appendix). Alveolar oxygen tension was also calculated from the ideal air equation ($\bar{P}AO_2$).

Subjects underwent the helium washout test on two consecutive occasions; a mean value of w$\bar{P}AO_2$ and w$\bar{P}ACO_2$ was then used. $PaCO_2$ was measured once.

INSTRUMENTATION

A water spirometer (Mijnhardt Volutest) was used. Valves A, C, and D were two way valves and valve B a one way Rudolph valve (1400) (deadspace 50 ml). The total deadspace of the system, including mouthpiece, tubing, and valves A and B, was 100 ml. Expired volume was measured by a screen (Fleisch No II) connected to a pneumotachograph (Godart) attached to a pen recorder or oscilloscope. The helium fractional concentration in the spirometer, bag 1, and each expiration was measured by a helium-carbon dioxide meter (Mijnhardt; linear response up to 90%, response time <100 ms) connected to a pen recorder. The same instrument was used to measure carbon dioxide concentration in each expiration in stage C. The concentration of oxygen and carbon dioxide in bag 2 ($\bar{F}EO_2$, $\bar{F}ECO_2$) was measured by an oxygen-carbon dioxide analyser (Fenyves and Gut). Arterial PO_2 and PCO_2 were measured by oxygen and carbon dioxide electrodes (ABL 2, Radiometer). The results were calculated on the Hewlett-Packard 85 computer.

STATISTICAL ANALYSIS

The relations between the derived and measured blood gas pressures were explored by the method of Bland and Altman.[9] The limits of agreement for the two measurements were calculated from the mean ($\bar{x}$) of the differences ((w$\bar{P}ACO_2$ − $PaCO_2$) or (w$\bar{P}AO_2$ − $\bar{P}AO_2$)) and from the standard deviation of the differences (SD) (limits of agreement = $\bar{x} \pm 2$ SD). The 95% confidence intervals (CI) for the bias was calculated as $\bar{x} \pm 2 \times SE_m$.

Results

ALVEOLAR PCO_2

$PaCO_2$ ranged from 4 to 9·3 kPa. The mean difference between w$\bar{P}ACO_2$ and $PaCO_2$ was 0·01 kPa (95% CI = 0·19 to −0·17 kPa; table). The SD of the differences was 0·7 kPa.

Alveolar carbon dioxide tension estimated

Analysis of the results according to the method of Bland and Altman[9] showing the degree of agreement between the values for alveolar carbon dioxide tension obtained by the helium washout technique (w$\bar{P}ACO_2$) and arterial carbon dioxide tension ($PaCO_2$) and between the helium washout alveolar oxygen tension (w$\bar{P}AO_2$) and alveolar oxygen tension estimated from the ideal air equation

Measuring agreement	w$\bar{P}ACO_2$ (eqn 1) related to $PaCO_2$	w$\bar{P}AO_2$ (eqn 2) related to $\bar{P}AO_2$ (ideal air eqn)
Mean of the differences (kPa)	0·01	0·02
Standard deviation of the differences (kPa)	0·70	0·93
Limits of agreement (kPa)		
Upper	1·41	1·87
Lower	−1·39	−1·83
95% confidence interval for the bias (kPa)	0·19 to −0·17	0·26 to −0·22

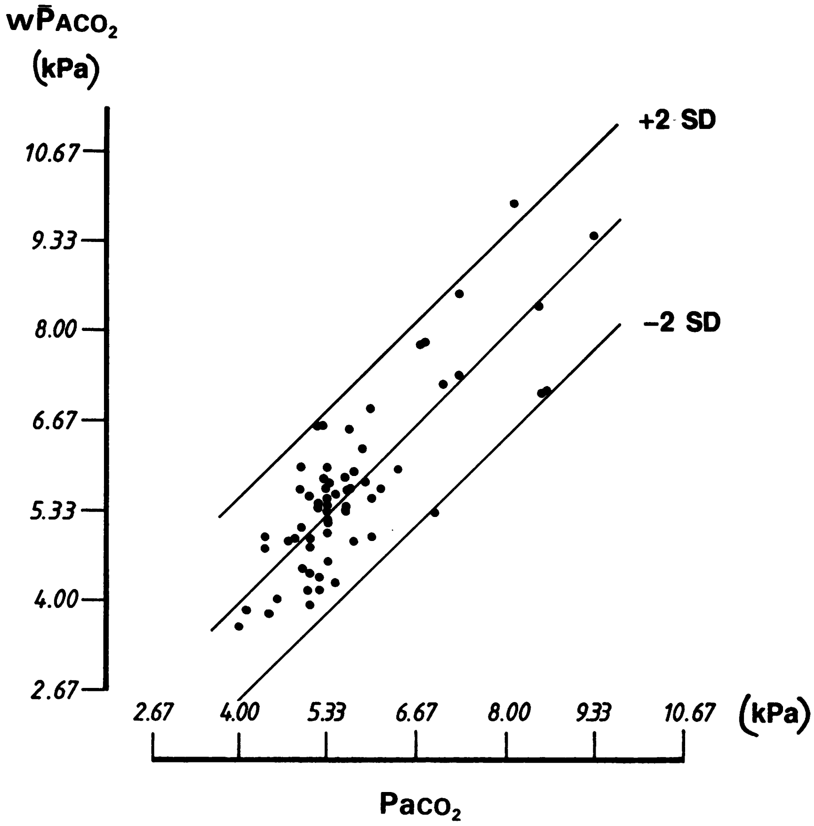

Figure 2 Relation between the individual values of the helium washout alveolar carbon dioxide tension ($w\bar{P}ACO_2$), estimated from equation 1, and those of the arterial carbon dioxide tension ($PaCO_2$). The line is the regression line.

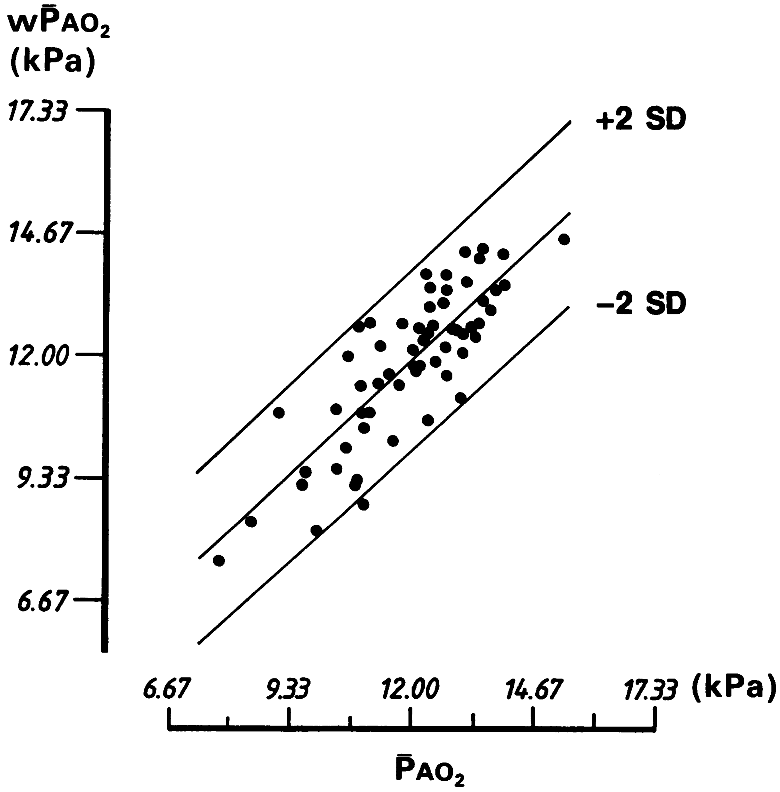

Figure 3 Individual values of the helium washout alveolar oxygen tension ($w\bar{P}AO_2$), estimated from equation 2, in relation to those of alveolar oxygen tension estimated from the ideal air equation. The line is the regression line.

from equation 1 ($w\bar{P}ACO_2$) was related to $PaCO_2$ according to equation *a*:

$$w\bar{P}ACO_2 = 0{\cdot}1610 + 0{\cdot}9763 \times PaCO_2 \text{ kPa} \quad (a)$$

(in traditional units $wPACO_2 = 1{\cdot}2078 + 0{\cdot}9763 \times PaCO_2$ mm Hg) (fig 2).

ALVEOLAR PO_2

$\bar{P}AO_2$, derived from the ideal air equation, ranged from 8 to 14·7 kPa. The mean difference between $w\bar{P}AO_2$ and $\bar{P}AO_2$ was 0·02 (95% CI 0·26 to −0·22) kPa; (table). The SD of the differences was 0·93 kPa.

Alveolar oxygen tension calculated from equation (2) ($w\bar{P}AO_2$) was related to $\bar{P}AO_2$ according to equation (*b*):

$$w\bar{P}AO_2 = 0{\cdot}7358 + 0{\cdot}9388 \times \bar{P}AO_2 \text{ kPa} \quad (b)$$

(in traditional units $w\bar{P}AO_2 = 5{\cdot}5186 + 0{\cdot}9388 \times \bar{P}AO_2$ mm Hg) (fig 3).

The mean value of $w\bar{P}AO_2$ was 11·96 (SD 1·68) kPa. The mean value of $\bar{P}AO_2$, calculated from the ideal air equation on the basis of $w\bar{P}ACO_2$ instead of $PaCO_2$, was 11·95 (SD 1·68) kPa.

The mean difference between duplicate measurements was 0·33 (range 0–0·87) kPa for $w\bar{P}AO_2$ and 0·23 (range 0–0·65) kPa for $w\bar{P}ACO_2$.

Discussion

The alveolar air composition is still a matter of debate, because $\bar{P}AO_2$ and $\bar{P}ACO_2$ cannot be measured accurately while a subject breathes quietly. A traditional approach to determining $\bar{F}ACO_2$ is to use the Bohr equation,

$$VD/VT = 1 - \bar{F}ECO_2/\bar{F}ACO_2,$$

given that the deadspace:tidal volume ratio for carbon dioxide (VD/VT) is known. In normal subjects and in patients with chronic bronchitis, asthma, and pulmonary fibrosis the VD/VT ratio for carbon dioxide is very similar to that obtained by the helium washout technique (wVD/VT).[8] The close relation between wVD/VT and VD/VT can be explained on theoretical grounds. In an ideal lung (VD = 0) the decay in helium concentration in the expired air during the washout procedure follows a power equation of the form $F_n = F_0 \, . \, x^{-n}$ (where $x = 1 + VA/FRC$); the mean value of this change is $\bar{F}IE$.[8] As there is no deadspace the mean fractional concentration of helium in the alveolar air ($\bar{F}IA$) is equal to $\bar{F}IE$. In real lungs ($VD \neq 0$) the mean fractional concentration of helium in mixed expired air ($\bar{F}E$) is smaller than $\bar{F}IE$. The terms in the above power equation have the same value in real and ideal lungs, so the difference ($\bar{F}IE - \bar{F}E$) is solely due to the decrease in helium concentration in the collecting bag resulting from the helium free volume of deadspace air [n × (VT − VA)]. As the volume of helium expired from real lungs during the multibreath washout procedure is equal to that from the ideal lungs, the ratio of the alveolar part of the tidal volume (VA) to tidal volume (VT) is equal to $\bar{F}E/\bar{F}IE$ ($\bar{F}IE = \bar{F}IA$).[8] The ratio VA/VT is also incorporated in the Bohr equation for carbon dioxide ($\bar{F}ECO_2/\bar{F}ACO_2$). If the mechanisms of intrapulmonary gas mixing responsible for the reduction in gas concentration from mean alveolar to mixed expired gas during quiet breathing are equally effective for helium and carbon dioxide, the ratio $\bar{F}E/\bar{F}IE$ must equal the ratio $\bar{F}ECO_2/\bar{F}ACO_2$. This has been shown for helium and sulphur hexafluoride, the washout curves of which are very close.[10] $\bar{F}ECO_2$ and $\bar{F}E$ represent the mean carbon dioxide and helium fractional concentrations respectively in the collection bag, obtained from all alveolar compartments whether slow or fast emptying. In these compartments the alveolar carbon dioxide fractional concentrations, which depend on the local $\dot{V}A/\dot{Q}c$ ratios, can be represented by a mean value, $\bar{F}ACO_2$, the term used in the Bohr equation to calculate the overall physiological deadspace:tidal volume ratio.[11] $PaCO_2$ is the perfusion weighted mean value of carbon dioxide partial pressures in blood from all perfused alveolar compartments, complete equilibration between alveolus and end capillary blood being assumed.[12] The wVD/VT ratio expresses only the gas distribution within the airspace of the lungs whereas VD/VT, calculated on the basis of $PaCO_2$ as an estimate of $\bar{P}ACO_2$, is affected by abnormalities in the pulmonary circulation and by diffusion defects in the alveolar membrane. In most instances, however, membrane diffusion defects and pulmonary right to left shunt (except when large) do not affect the VD/VT ratio for carbon dioxide. $w\bar{P}ACO_2$ therefore provides a good estimate of $PaCO_2$. There are certain conditions in which differences would be expected between wVD/VT and VD/VT and between $w\bar{P}ACO_2$ and $PaCO_2$. In non-steady state hyperventilation and in pulmonary embolism, for example, wVD/VT will be less than VD/VT and $w\bar{P}ACO_2$ lower than $PaCO_2$. This requires further investigation; no patient with pulmonary embolism was included in our study.

As shown in figure 2, there was a reasonably close linear correlation between $w\bar{P}ACO_2$ and $PaCO_2$. The difference between $PaCO_2$ and $w\bar{P}ACO_2$ values in individual subjects was up to 1·4 kPa (mean difference with 2 SD) (table). This difference will to some extent represent the noise of the two methods but may also reflect a real difference between these two terms in the patients studied.

There was also a reasonably close linear relation between alveolar oxygen tension measured from the ideal air equation ($\bar{P}AO_2$) and $w\bar{P}AO_2$ (fig 3). The difference between $w\bar{P}AO_2$ and $\bar{P}AO_2$ was abolished when $w\bar{P}ACO_2$ was used instead of $PaCO_2$ in the ideal air equation, because both the Bohr equation for oxygen and the ideal air equation are derived from the equation of the respiratory exchange ratio.

The rebreathing method of Campbell and Howell for measuring alveolar carbon dioxide tension[2] takes less time and equipment than the method described here, but there is no accurate way of predicting arterial PCO_2 from the oxygenated mixed venous value. The procedure we describe requires no special cooperation from the patient, who has only to breathe tidally at his own rate, whether in the laboratory or in the ward. Static lung volumes, the physiological deadspace:tidal volume ratio, alveolar oxygen and carbon dioxide tension, the respiratory exchange ratio, carbon dioxide production and oxygen uptake, tidal volume, and minute ventilation can all be measured easily with acceptable accuracy and reproducibility. Patients with respiratory failure can be monitored non-invasively after an initial arterial sample has been taken for blood gas analysis. Measurement of alveolar carbon dioxide tension ($w\bar{P}ACO_2$), arterial oxygen saturation by ear or pulse oximetry, or tissue oxygen tension by the transcutaneous electrode (PTO_2) may reduce the need for an arterial puncture. Arterial blood sampling is needed only when alveolar gas tensions have to be related to arterial blood gas tensions, mainly to determine the alveolar-arterial oxygen gradient.

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Appendix

The alveolar carbon dioxide and oxygen fractional concentrations were calculated according to equations 1 and 2 respectively.*

$$w\bar{F}ACO_2 = \frac{\bar{F}ECO_2}{\frac{\bar{F}E}{\bar{F}iE} + VDV \times \left(\frac{1}{VT} - \frac{1}{V'T}\right)} \quad (1)$$

and $w\bar{P}ACO_2 = w\bar{F}ACO_2 \times (PB - 47)$

$$w\bar{F}AO_2 = \frac{\bar{F}EO_2 - FIO_2 \times \left[1 - \frac{\bar{F}E}{\bar{F}iE} - VDV \times \left(\frac{1}{VT} - \frac{1}{V'T}\right)\right]}{\frac{\bar{F}E}{\bar{F}iE} + VDV \times \left(\frac{1}{VT} - \frac{1}{V'T}\right)} \quad (2)$$

and $w\bar{P}AO_2 = w\bar{F}AO_2 \times (PB - 47)$,

where $\bar{F}iE$, derived from the washout curve, is the ideal mean concentration of helium in the expired air if there were no deadspace, VDV is the deadspace of the valve system (0·1 l), VT is the tidal volume during the helium washout from the lungs, and V'T is the tidal volume during the collection of expired air after complete washout of helium.

*The full formulae are available on request.