Attempts at estimating mixed venous carbon dioxide tension by the single-breath method

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ABSTRACT: The single-breath method was originally proposed by Kim et al. [1] for estimating the blood carbon dioxide tension and cardiac output. Its reliability has not been proven. The present study was undertaken, using dogs, to compare the mixed venous carbon dioxide tension (PvCO₂) calculated by the single-breath method with the PVCO₂ measured in mixed venous blood, and to evaluate the influence of variations in the exhalation duration and the volume of expired air usually discarded from computations as the deadspace. Among the exhalation durations of 15, 30 and 45 s tested, the 15 s duration was found to be too short to obtain an analyzable O₂-CO₂ curve, but at either 30 or 45 s, the calculated values of PVCO₂ were comparable to the measured PVCO₂. A significant agreement between calculated and measured PVCO₂ was obtained when the expired gas with PcO₂ less than 22 Torr was considered as deadspace gas.

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The single-breath method was developed by Kim et al [1], originally for the purpose of estimating the mixed venous and arterial carbon dioxide tension and cardiac output. The procedures described by them are as follows: take aliquots of expired gas during a prolonged single exhalation, and measure their carbon dioxide tension (PcO₂) and oxygen tension (Po₂). Plot the PCO₂ against the Po₂ for each sample, and draw a smooth curve through these points. Put the slope of the curve at a given point into the alveolar equation with corresponding values of Po₂ and PCO₂ to calculate instantaneous R (Rinst). Then plot the alveolar carbon dioxide tension (PA CO₂) against the Rinst, connect the points with a straight line, and read the values of mixed venous carbon dioxide tension (PvCO₂) and (PA CO₂) at appropriate Rinst values.

Many investigators have assessed this method, and some have demonstrated a good agreement between the PcO₂ values calculated by the single-breath method and those obtained by blood gas analyses [2-4]. Others have failed to show such an agreement [5]. In practising the single-breath method, there have been differences in e.g. duration of exhalation, choice of series deadspace volumes and the volume of expire. No standard procedure has been established.

In this study, we used the mixed venous carbon dioxide tension as a standard for a comparison purpose and studied the effects of variations in the exhalation duration and the choice of series deadspace on the results of the single-breath method. We used dogs as an experimental model.

Methods

The experimental set-up is illustrated in figure I. Five mongrel dogs (mean weight 12 kg) were anaesthetized with pentobarbital sodium (30 mg·kg⁻¹, i.v.). A tracheal cannula was inserted and pancuronium bromide (0.08 mg·kg⁻¹, i.v.) was administered. The dogs were artificially ventilated with air using an animal ventilator.
The gas in the tracheal cannula was continuously analysed by a mass spectrometer (Centronic 200MGA, time lag 500 ms) which was calibrated with standard gas mixture before and after the sample analysis. Blood gas tension was determined using a blood gas analyser (IL813). A Swan-Ganz catheter was passed through a femoral vein and its tip was positioned in the pulmonary artery to sample mixed venous blood.

The procedure used to obtain prolonged exhalation was similar to that of Mohammed and Hainsworth [3]; when the end-tidal Pco2 and heart rate became constant, the dog was disconnected from the respirator, and the lungs were deflated passively and then inflated manually, using a 2 l syringe, with an air volume twice the tidal volume. The plunger was then withdrawn immediately, but as slowly and continuously as possible, to the initial resting end-expiratory lung volume. Since the expiratory flow rates were not fixed between the procedures, the different exhalation durations corresponded to differing expiratory flow rates.

The concentrations of O2 and CO2 measured by the mass spectrometer were recorded on a X-Y recorder (Riken Denshi, F-42CP) giving the original O2-CO2 curve. From this curve, 50 points were read manually and, after eliminating the points which corresponded to the deadspace, a smooth curve, expressed as a quadratic regression, was drawn through these points using the least-squares technique. This regression curve was used for subsequent analysis. The first derivative, which is equivalent to the slope (s) of the tangent of the curve, was determined at various given portions of the curve. Using these s-values, the Rinst was obtained by the following equation [1]:

\[ Rinst = \frac{(s-Fo_2-s-Pco_2)}{(1-Fo_2-s-Pco_2)} \]

where Fo2 and Fco2 represent the expired gas fraction. The Pco2 was then plotted against the Rinst, and a straight line was drawn through the plotted points. The Pco2 at Rinst=0.32 was assumed to be the P\(_{\text{VCO2}}\) (calculated P\(_{\text{VCO2}}\)).

Mixed venous blood was withdrawn just before the single-breath exhalation, and the Pco2 of the blood was determined with the blood gas analyser (measured P\(_{\text{VCO2}}\)) to compare with the calculated P\(_{\text{VCO2}}\).

The tidal volume and respiratory frequency of the respirator were varied between each single-breath exhalation in order to obtain various values of P\(_{\text{VCO2}}\). The exhalation durations used were 15, 30 and 45 s.

There are several ways to define the deadspace. We adopted the method in which the deadspace was defined by the values of Pco2 in expired air, since this method had been employed by many other investigators [2, 6, 7] and is easy to perform. The cut-off values for Pco2, chosen were 10, 15, 20, 25, and 30 Torr. Figure 2 shows an example of the O2-CO2 curve and cut-off CO2 levels which define the deadspace. Within 50 points, read manually, there were almost no points which precisely corresponded to the cut-off values of deadspace, so we adopted the point which was nearest to the cut-off values of deadspace.

At exhalation durations of 30 and 45 s, scattergrams of measured P\(_{\text{VCO2}}\) vs calculated P\(_{\text{VCO2}}\) were constructed for the five different deadspaces defined by various Pco2 in expired air as mentioned above. A regression line was drawn on each scattergram, providing five regression lines at each exhalation duration. We assumed that a slope closer to 1.0 and an intercept on the Y-axis closer to zero indicated the closer agreement between the calculated P\(_{\text{VCO2}}\) and the measured P\(_{\text{VCO2}}\). Using the values of the slopes and intercepts of these regression lines, the best condition for estimating P\(_{\text{VCO2}}\) was found by regression analysis. In this study we selected the data by use of the Smirnov test.

![Fig. 2](image-url)  
An example of the O2-CO2 curve in which duration of exhalation is 30 s. Each value of Pco2 means the level of assumed deadspace volume.

**Results**

Since observed O2-CO2 curves were nearly straight at an exhalation duration of 15 s and analyisable O2-CO2 curves could hardly be obtained, the results achieved at this exhalation duration were not included in further analysis.

Figure 3 shows the results obtained at a constant exhalation duration of 30 s and various deadspaces. For each deadspace volume defined by a Pco2 level of 10, 15, 20, 25 or 30 Torr, there was a significant (r=0.87-0.93, p<0.01) positive correlation between the measured and the calculated P\(_{\text{VCO2}}\) values.

The results obtained at an exhalation duration of 45 s are shown in figure 4. Here again, measured and calculated P\(_{\text{VCO2}}\) values were significantly (r=0.87-0.94, p<0.01) correlated with each other.

The relationship between the slope of the regression line and the Pco2 level of presumed deadspace air for the 30 s duration is shown in figure 5A, and the relationship between the Y-intercept of the regression line and the Pco2 level in figure 5B. Regression analysis indicated that both relationships were first-order regression (p<0.05) and the best approximation was obtained when the cut-off Pco2 for the deadspace was assumed to be 22 Torr, namely at the slope and the intercept being close to 1 and 0, respectively.

The relationship between the slope and the Pco2 level and that between the intercept and the Pco2, at the 45 s exhalation duration, are shown in figure 6A and
Fig. 3. - Relationship between measured $P_{\text{vco}_2}$ and calculated $P_{\text{vco}_2}$ at exhalation duration 30 s. A: $P_{\text{co}}_2$ of deadspace gas is assumed $<10$ Torr; B: $P_{\text{co}}_2 <15$ Torr; C: $P_{\text{co}}_2 <20$ Torr; D: $P_{\text{co}}_2 <25$ Torr; E: $P_{\text{co}}_2 <30$ Torr. Each case shows significant correlation ($p<0.01$).

Fig. 4. - Relationship between measured $P_{\text{vco}_2}$ and calculated $P_{\text{vco}_2}$ at exhalation duration 45 s. A: $P_{\text{co}}_2$ of deadspace gas is assumed $<10$ Torr; B: $P_{\text{co}}_2 <15$ Torr; C: $P_{\text{co}}_2 <20$ Torr; D: $P_{\text{co}}_2 <25$ Torr; E: $P_{\text{co}}_2 <30$ Torr. Each case shows significant correlation ($p<0.01$).
Fig. 5. - Relationship between $P_{\text{CO}_2}$ level of deadspace gas and slope and intercept of regression line (represented in fig. 2). Exhalation duration is 30 s. A: Relationship between $P_{\text{CO}_2}$ level of deadspace and slope of regression line. B: Relationship between $P_{\text{CO}_2}$ level of deadspace and intercept of regression line.

Fig. 6. - Relationship between $P_{\text{CO}_2}$ level of deadspace gas and slope and intercept of regression line (represented in fig. 3). Exhalation duration is 45 s. A: Relationship between $P_{\text{CO}_2}$ level of deadspace and slope of regression line. B: Relationship between $P_{\text{CO}_2}$ level of deadspace and intercept of regression line.

Discussion

Although all previous investigations of this method were based on the same principle, described by Kim et al. [1], there are some differences in detailed procedures. The main causes that lead to various appraisals of this method are differences in the manner of smoothing the data sampled from the $O_2$-$CO_2$ curve, of determining the equation of the curve, and of defining the deadspace, and duration of exhalation. In data sampling from the $O_2$-$CO_2$ diagram Kim et al. [1] discarded any points which deviated from the curve by more than $\pm0.35$ Torr in either $O_2$ or $CO_2$, and if more than 3 out of 7 points were thus rejected the whole experiment was discarded. Gilbert and Auchincloss [8] discarded the curve if more than one point of $P_{\text{CO}_2}$ deviated by more than 0.2% from the curve. Chen et al. [2] rejected any points that deviated from regression curve by more than 0.7 Torr and computed the entire regression again. If more than 25% of
the points were rejected, they discarded the whole breath. On the other hand, HLASTALA et al. [5], BUDERER et al. [6] and MOHAMMED and co-workers [3,4] smoothed the curve without rejecting any points, as we also did in this study. With regard to the equation for the O₂-CO₂ curve, BUDERER et al. [6] and CHEN et al. [2] used quadratic regression, HLASTALA et al. [5] and GRONLUND [9] employed third-order polynomial equations, and INMAN et al. [7] used an exponential equation. GILBERT and AUCHINCLOSS [8], MOHAMMED and co-workers [3, 4] and BUDERER et al. [6] did not describe their method of approximation. GRONLUND [9] suggested, in his simulation study, that minute differences in the approximation curve led to large variations in the calculated results. We fitted the data by quadratic regression because this polynomial order resulted in the least residual sum of squares by the least-squares technique, indicating this regression to be the best fitted approximate polynomial.

A similar problem occurs in fitting a polynomial for the R-Pco₂ curve. CHEN et al. [2] used quadratic regression and obtained calculated results from the tangent line drawn at R=0.38. We fitted regression lines by the least-squares technique.

The manner of discarding the early portion of expired air which contains predominantly deadspace air varied with authors. According to KIM et al. [1], the first part of the expiration was delivered to a 500 ml bag, thus eliminating the deadspace gas from the sampling. GILBERT and AUCHINCLOSS [8] did not describe how the deadspace gas was treated. HLASTALA et al. [5] measured the deadspace during each tidal breath, which was equivalent to the anatomical deadspace, using CO₂ as an indicator. BUDERER et al. [6], CHEN et al. [2] and INMAN et al. [7] assumed the deadspace as the part of the O₂-CO₂ curve corresponding to the Pco₂ less than 30 Torr, whereas MOHAMMED and co-workers [3, 4] eliminated the first 2 s of the expiration. Although the manner of HLASTALA et al. [5] seems reasonable, their method can be performed only when tidal breathing is adopted and might be impossible for prolonged exhalation. In this study, we obtained the best calculated values with the deadspace defined as the part of the O₂-CO₂ curve corresponding to Pco₂ less than 22 Torr. The exact volume of the deadspace to be eliminated from the expiration has not been examined critically.

With regard to the duration of exhalation, a duration over 10 s was used by Kim et al. [1] and MOHAMMED and co-workers [3,4], whilst CHEN et al. [2] adopted precisely 10 s duration. HLASTALA et al. [5] and GRONLUND [9] demonstrated that the longer the duration, the smaller the deviation of values of cardiac output. In our study, the durations of exhalation of 15, 30 and 45 s were examined. With 15 s duration it was impossible to calculate the slope of the tangent. On the other hand, with 30 or 45 s duration, the O₂-CO₂ curve could be computed and similar results were obtained at either duration. This indicates, therefore, that the single-breath method requires appropriately prolonged exhalation. Such durations as 30 and 45 s are applicable only in experimental animals, but apparently cannot be applied directly to human subjects.

The duration of exhalation used in our study was extremely long compared with previous studies in dogs [3, 4]. This may be attributed to the fact that a tracheal tube inserted orally in a small dog may increase the deadspace. During exhalation longer than 20 s, recirculation occurs and this may affect the composition of expired air [10, 11]. Hence, the appropriate duration of exhalation should also be considered in order to attenuate the effect of recirculation.

Since the alveolar gas equation is used for analysis in the single-breath method, it is highly possible that diseased lungs with ventilation/perfusion (V/Q) unevenness may give erroneous results [12]. Compartment with a large V/Q may be attributed to the cause of errors in the single-breath method [13].

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References
Essai d'estimation de la PCO₂ du sang veineux mêlé par la méthode "single breath". H. Ōhta, O. Takatani, T. Matsuoka. La méthode "single breath" a été proposée par Kim, et al, pour estimer la tension sanguine en CO₂ et le débit cardiaque. Sa valeur n'a pas encore été prouvée. L'étude a été entreprise pour comparer, chez les chiens, la PVCO₂ calculée par la méthode "single breath" avec la PVCO₂ mesurée dans le sang veineux mêlé, et pour évaluer l'influence des variations de la durée d'expiration celle volume de gaz expiré, habituellement rejeté des calculs comme espace mort. Parmi les durées d'expiration de 15, 30 et 45 secondes, qui ont été testées, celle de 15 secondes s'avère trop brève pour obtenir une courbe O₂-CO₂ analysable, mais, que ce soit à 30 ou à 45 secondes, les valeurs calculées de PVCO₂ sont comparables aux valeurs mesurées. Une similitude significative entre les valeurs calculées et mesurées de PVCO₂ a donc été obtenue lorsque le gaz expiré ayant moins de 22 Torr de PCO₂ a été considéré comme espace mort. Eur Respir J., 1989, 2, 90-95.