A CONTINUOUS METHOD FOR MEASURING ACETYLENE IN EXPIRED GAS USING GLOW DISCHARGE AND ITS APPLICATION TO ASSESSMENT OF PULMONARY BLOOD FLOW*

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Summary In order to measure a rapid change in pulmonary blood flow the suitability of a glow discharge gas analyser for the continuous analysis of C_2H_2 was examined. The analyser was originally designed for continuous analyses of O_2 and CO_2 in expired air. However, we found that it responded specifically to C_2H_2 , when a gas mixture containing 5% O_2 , 40% CO_2 with a balance of N_2 was used as a carrier gas and a negative voltage of 20 V was applied to the proximal collector electrode against the distal. Under these conditions the C_2H_2 current was reproducible within 0.1 mmHg, the base line drift was smaller than 1 mmHg/hr and the 90% response time was about 0.6 sec. This method was applied to analysis of C_2H_2 in expired air in combination with a constant rate expiration technique. When a C_2H_2 gas mixture was inhaled and expired at a constant rate, the observed C_2H_2 curves agreed with the theoretical ones calculated at the pulmonary blood flow rates obtained separately with the conventional breath-holding method. The decay rate of the C_2H_2 curve showed a rapid change within 1.5 sec when exercise and a Valsalva-like maneuver were made during continuous expiration, suggesting a quick alternation in pulmonary blood flow.

During the analyses of O_2 and CO_2 in expired air using the glow discharge analyser elaborated by Mochizuki and co-workers (MOCHIZUKI and KAWAKAMI, 1965; MOCHIZUKI and NITTA, 1967; NITTA and MOCHIZUKI, 1969; MOCHIZUKI *et al.*, 1969; MOCHIZUKI and KAKIUCHI, 1973) we found that the analyser showed a signal current proportional to acetylene concentration in expired gas. It has often been thought that the continuous analysis of C_2H_2 would be of great value in respiratory physiology because such a technique would make possible the

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instantaneous measurement of the pulmonary blood flow. Hitherto C_2H_2 has been analysed by using a Haldane gas analyser or a gas chromatograph, both of which require more than 10 min for one analysis. If acetylene in expired gas can be analysed rapidly, it may permit the estimation of the change of C_2H_2 concentration in the alveolar air precisely during an entire course of exhalation. Since the alveolar C_2H_2 concentration during expiration depends on both the expiration rate and its uptake rate by the pulmonary blood, the pulmonary blood flow can be estimated from the expired C_2H_2 fraction if the expiration rate is maintained constant.

In the present study the optimal conditions of the glow discharge gas analyser for a rapid and continuous analysis of C_2H_2 were first investigated. Then this method was applied to observation of the pulmonary blood flow under conditions where the expiration rate was maintained constant.

METHODS

Analysis of acetylene. The glow discharge analyser is illustrated schematically in Fig. 1. The main part of this analyser is a glow discharge tube which is connected to a vacuum pump at one end and with a thin metal tube (internal diameter of 0.3 mm and length of 200 mm) at the other as the inlet of the carrier gas. Through this thin tube a C_2H_2 free carrier gas is sucked into the discharge tube. Since the thin tube acts as a resistance against the gas inflow, a gas pressure as low as 4 to 5 mmHg can be maintained in the discharge tube. The discharge electrodes were located facing each other on the side wall of the tube. Between these electrodes a high frequency discharge voltage (1 MHz, 1.3 kV) is applied from an oscillator. When a glow discharge takes place inside the tube, metastable ions can be detected as a current flowing through two collector electrodes placed in the discharge tube at a part distal to the glow discharge field. The proximal collector electrode *CE1* is grounded through a potentiometer *P* by which the potential difference between two collector electrodes (collector voltage) is varied. The distal collector *CE2*, connected to ground through a resistance of 1,000 Mohms, was led directly to an IC amplifier for detecting the ionic current. Since the C_2H_2 current was much affected by the collector voltage, it was varied from 170 to -25 V for finding out the optimal value. When used for measurements of expired C_2H_2 concentration -20 V was usually applied to the electrode. The discharge tube is connected to another thin metal tube *MT* (internal diameter of 0.18 mm and length of 200 mm) through which a small amount of gas to be analysed is sampled at a constant rate (14 ml/min). The sample gas is mixed with carrier gas at a constant ratio (14: 100) and then brought into the discharge field.

The ionic current is mainly affected by O_2 and CO_2 coexisting in the expired gas. Therefore, in order to obtain a signal current responding specifically to C_2H_2 it is necessary to suppress the O_2 and CO_2 effects on the ionic current. One method of achieving this is to employ gas mixtures of O_2 and CO_2 of various

compositions as the carrier gas and examine the signals for O_2 , CO_2 and C_2H_2 in the sample gas. Thus, the mixtures with CO_2 fractions of 0, 15.7, 29.2 and 48.6% were prepared for the carrier gas with the O_2 fractions of 5.0 to 5.2% and N_2 as a balance. The following two test gases were prepared for the sample gas: 1) 0% C_2H_2 , 5.56% CO_2 , 15.08% O_2 and 79.36% N_2 and 2) 4.62% C_2H_2 , 17.70% O_2 and 77.68% N_2 . As a result of the measurement of this series it was found that a gas mixture containing 39.50% CO_2 , 6.12% O_2 and 54.38% N_2 was used as the carrier gas in both the methodological survey and the measurement of C_2H_2 concentration in the expired gas.

Measuring procedure of the pulmonary blood flow. For the blood flow measurement the subject inhaled a gas mixture with C_2H_2 as fast as possible (in 1.3 to 2.0 sec) from a spirometer and then began to exhale the alveolar gas at a constant flow rate of 80 to 90 ml/sec. The flow rate was controlled by a constant flow valve (OSBORN *et al.*, 1968) placed between the mouth and a pneumotachograph. A thin polyethylene tube was inserted into the tubing connecting the constant flow valve and pneumotachograph. Through the thin polyethylene tube a small fraction of the expired gas (3 ml/sec) was drawn by the suction pump and at the joint space *JS* a small fraction was led through the thin metal tube *MT* into the glow discharge tube. Water vapour in the expired gas was removed by the use of a semiconductor cooling unit inserted between the constant flow valve and the glow discharge analyser. Condensed water in the cooling unit was trapped in a glass bottle attached to the cooling unit. Moreover, in order to eliminate the occasional inflow of the water drop into the joint space *SJ* and further into the glow discharge field, the joint space was made conical as shown in Fig. 1.

The measurements were made in two normal adult subjects 1) at rest in an upright position, 2) at a transition stage from rest to exercise, 3) during steady exercise and 4) when the intrathoracic pressure was abruptly increased. Exercise was performed by the subjects running on a treadmill. At stage 2) the subjects first started at a standing rest state and then began running on the treadmill, keeping their expiration at a constant rate. At the Valsalva-like manoeuvre of the fourth stage the mouth pressure was measured using an electric manometer, assuming that the mouth pressure represented the intrathoracic pressure. The subjects began expiration at the mouth pressure of 4 or 5 mmHg and in 10 sec they made the forced exhalation, causing a large increase of the mouth pressure to 40 mmHg. The forced expiration usually lasted for 10 sec, and then, the pressure was lowered. The flow rate through the Osborn's valve was constant independently of the mouth pressure.

Calculation of the theoretical C_2H_2 curve during expiration. Since the mixed venous blood contains no C_2H_2 , the uptake rate of C_2H_2 by pulmonary blood flow $\dot{Q}$ (ml/sec) should be given by $a_b/760 \cdot P \cdot \dot{Q}$, where a_b is the solubility of C_2H_2 in the blood at 1 atm and the body temperature (0.740 ml C_2H_2 STPD/ml blood)

Fig. 1. Schematic illustration of the apparatus. DE: discharge electrodes, CE₁ and CE₂: the proximal and distal collector electrodes. JS: joint space for sampling of small fraction of sample gas, MT: thin metal tube for sample inlet and P: potentiometer.

and P (mmHg) is the partial pressure of C_2H_2 in the alveolar air. The inspired C_2H_2 is dispersed not only in the gas phase of the lung but also into the lung tissue as clarified by CANDER and FORSTER (1959). The quantity dissolved in the lung tissue is proportional to the alveolar C_2H_2 tension, and is given by $P \cdot a_t / 760 \cdot V_t$, where V_t and a_t are the tissue volume and C_2H_2 solubility (0.768 ml C_2H_2 STPD/ml tissue) of lung tissue, respectively. On the other hand, the C_2H_2 fraction in the alveolar air F is given by $F = P / (P_b - 47)$, thus, the total amount of C_2H_2 ($V_{C_2H_2}$ ml STPD) in the lung is given by

$$V_{C_2H_2} = \frac{P}{P_b - 47} \cdot V_g + P \cdot \frac{a_t}{760} \cdot V_t \quad (1),$$

where V_g is the volume of lung gas phase (ml STPD). Putting $a'_t = a_t \cdot (P_b - 47) / 760$, $V_{C_2H_2}$ is expressed by

$$V_{C_2H_2} = F \cdot (V_g + a'_t \cdot V_t) \quad (2).$$

When the alveolar gas is expired at a constant rate of C_e (ml/sec STPD) from the initial lung gas volume V_{g_0} and the initial fraction F_0 , the quantity of C_2H_2 remaining in the total lung at time t after onset of expiration is given by

$$V_{C_2H_2} = F \cdot (V_g + a'_t \cdot V_t) = F_0 \cdot (V_{g_0} + a'_t \cdot V_t) - \int_0^t F \cdot \dot{Q} \cdot a'_b \cdot dt - \int_0^t C_e \cdot F \cdot dt \quad (3),$$

where a'_b is $a_b \cdot (P_b - 47) / 760$. By differentiating Eq. (3) and putting $V_g = V_{g_0} - C_e \cdot t$, the rate of the C_2H_2 fraction change in the alveolar gas is given by

$$dF/dt = -\alpha'_b \cdot F \cdot \dot{Q} / (Vg_o + \alpha'_t \cdot Vt - Ce \cdot t) \quad (4).$$

Since alveolar gas arrives at the glow discharge tube after flowing through the dead space of the airway, the initial alveolar F is measurable in actual analyses only at a transit time td after the onset of expiration. Therefore, for the purpose of a proper comparison of the theoretical curves with the actual records, Eq. (4) must be solved with the initial condition that F is F_o at time of td . If we abbreviate the volume of dead space as Vd , the transit time td is given by Vd/Ce . Therefore, by integrating Eq. (4) from time td to t , the time course of F/F_o is given by the following equation

$$F/F_o = \left[\frac{Vg_o + \alpha'_t \cdot Vt - Ce \cdot t}{Vg_o + \alpha'_t \cdot Vt - Vd} \right]^{\alpha'_b \cdot \dot{Q}/Ce} \quad (5).$$

The F_o was calculated by extrapolating the C_2H_2 curve to time td . The lung tissue volume was assumed invariably equal to 500 ml (FUKUI and MOCHIZUKI, 1972).

RESULTS

The relations between the fraction of CO_2 in the carrier gas and both the signal currents of C_2H_2 and CO_2 at a collector voltage of 0 V are shown in Fig. 2.

Fig. 2. Relationship between CO_2 content of the carrier gas and the electric signals of the rapid gas analyser for C_2H_2 and CO_2 at a collector voltage of 0 volt.

As the CO_2 content of the carrier gas increased there was a reduction in both of these signal currents. The CO_2 current was suppressed more than the C_2H_2 current. At a 40% CO_2 fraction of the carrier the C_2H_2 current corresponding to 4.62% C_2H_2 in the sample gas was 50 times greater than that due to 5.56% of CO_2 in the sample gas.

The effects of the collector voltage on the signal currents of CO_2 and C_2H_2 were examined when CO_2 fraction in the carrier gas was 40%. As shown in Fig. 3, the signal currents for both the gases became small in a negative voltage range,

Fig. 3. Effects of collector voltage on signal currents of C_2H_2 and CO_2 with a carrier gas consisting of 6.12% O_2 , 39.50% CO_2 and 54.38% N_2 .

but the CO_2 signal current became much smaller than that for C_2H_2 . At -20 V the CO_2 signal current was so small to be negligible in relation to that for C_2H_2 . The response time of the C_2H_2 current also depended on the collector voltage. The time required for 90% response is plotted against collector voltage in Fig. 4. In a negative voltage range the response time became shorter than in a positive and it was 0.6 sec at -20 V. For testing stability and reproducibility of the signal current the analyser was left in operation for more than 3 hours, and sample gases with 4 different C_2H_2 concentrations of 0.52, 1.37, 2.44, and 3.19% were given intermittently and repeatedly. A section from a long-term recording is shown in Fig. 5. It was concluded that the base and signal currents were fairly stable and reproducible when the collector voltage was -20 V and the CO_2 fraction in the carrier gas was 40%. The C_2H_2 signal current was reproducible with an error of 0.1 mmHg and the base line drift was less than 1 mmHg/hr. The calibration curve was not linear at concentrations close to 0%, while it was fairly linear above 1%.

Fig. 4. Effects of collector voltage on the response time of C_2H_2 signal current at a hypercapnic carrier gas containing 39.50% CO_2 .

Fig. 5. A section from a long term recording and the reproducibility of C_2H_2 signal. C_2H_2 gas mixtures were analysed repeatedly at the noted clock time.

Examples of continuous analysis of the expired gas are shown in Figs. 6, 8, and 9. The curves in Fig. 6A and B were obtained at rest and during a steady exercise of 5 km/hr respectively, while the expiration was maintained at a rate of 90 ml/sec. The upper and lower curves show the flow rate and C_2H_2 fraction respectively. The decrease of C_2H_2 became steeper during exercise than at rest. The ratio of instantaneous C_2H_2 value to the initial, F/F_0 , is plotted against the expiration time

Fig. 6. Examples of actual recordings. A; at rest and B; at mild exercise of treadmill running at 5 km/hr and 0% grade. The curves above and below show the airflow of prolonged expiration and C_2H_2 in the expired gas, respectively.

Fig. 7. Time course of F/F_0 . Circles show the actually observed values and the lines were calculated from Eq. (5) for various $\dot{Q}$'s.

with circles in Fig. 7. The thick lines depicted in the same figure show the theoretical curves calculated from Eq. (5) at 5 different $\dot{Q}$ values by putting $V_0=4,700$ ml according to the actual value measured by He analysis. The measured F/F_0 values both at rest and exercise agreed well with the theoretical curves calculated at $\dot{Q}$ of 4.7 and 10.6 liter/min within time range of 0 to 20 sec and 0 to 15 sec respectively. The $\dot{Q}$ values measured subsequently in the same subject by the conventional C_2H_2 breath-holding method (CANDER and FORSTER, 1959) were 4.8 and 11.4 liter/min at rest and during exercise, respectively, showing agreement with the $\dot{Q}$ values estimated by the present C_2H_2 gradient method.

The C_2H_2 curves obtained at the transition stage from rest to exercise are shown in Fig. 8. At the onset of exercise the gradient of the C_2H_2 curve became clearly steep as seen in Fig. 8B and C. In addition, the C_2H_2 uptake rate during

Fig. 8. Examples of actual recording of C_2H_2 decrease at transition from rest to exercise. A; at rest, B and C; treadmill walking at 3 km/hr with 0% grade and running at 6 km/hr with 10% grade were started at the arrow, respectively.

running at a speed of 6 km/hr and a grade of 10% shown in Fig. 8C was apparently larger than that obtained in the case of 8B when walking at a speed of 3 km/hr. As shown in those curves the increase of the C_2H_2 uptake occurred within 2.5 sec after the start of exercise. Since the transit time of the alveolar air through the dead space was estimated to be longer than 1 sec, the delay of appearance time of the current change from that of the alveolar C_2H_2 change would also be at least 1 sec. Thus, the increase in C_2H_2 uptake is estimated to have occurred within 1.5 sec following onset of exercise.

An example of the C_2H_2 curves obtained in the state No. 4 where the intrathoracic pressure was abruptly increased is shown in Fig. 9. The curves show from top to bottom the a) flow rate during expiration, b) C_2H_2 concent-

Fig. 9. Effects of intrathoracic pressure on the decay rate of C_2H_2 in the expired gas during a Valsalva-like manoeuvre. The mouth pressure was first 4 mmHg and then increased to 40 mmHg. 10 sec thereafter the pressure was lowered to 8 mmHg. The curves from top to bottom show the flow rate of expiration, $P_{C_2H_2}$ and the mouth pressure. The pressure curve was displayed on another recorder at a chart speed half of the other curves and was subsequently attached to this figure.

ration both recorded at a chart speed of 240 mm/min and c) the mouth pressure recorded on another recorder at a speed of 120 mm/min. The flow rate was kept constant by the Osborn's valve regardless of the change in the expiration effort. The C_2H_2 decrease was apparently slowed down by the elevation of the alveolar pressure and again accelerated by the reduction of the pressure.

DISCUSSION

The ionic current following glow discharge is affected by the gas species introduced into the discharge field by 1) the amount of ions produced from the introduced gas itself and 2) the recombination rate of the ionized gas molecules. In the present study C_2H_2 caused an increase of the ionic current, suggesting that C_2H_2 molecules are ionized by the glow discharge much more easily than the gas mixtures of N_2 , O_2 and CO_2 . However, between the signal currents of C_2H_2 and

the discharge field intensity no specific correlation was observed. Therefore, it was necessary to suppress the unwanted signals of other gas species than C_2H_2 . According to MOCHIZUKI and NITTA (1967), when a gas mixture consisting of CO_2 and N_2 was used as the carrier gas, the signal responding to O_2 became observable, and in a similar manner the signal current for CO_2 appeared when the carrier gas contained O_2 and N_2 . Following their finding, in our effort to find out the optimal conditions for continuous C_2H_2 analysis, we examined the effects of carrier gases containing both O_2 and CO_2 on the signal current for C_2H_2 . As a result it was found that the current specifically responded when a gas mixture consisting of 5% O_2 , 40% CO_2 and a balance of N_2 was used as the carrier gas. Moreover, the collector voltage showed a remarkable effect on both the C_2H_2 and CO_2 currents, and the latter current was almost eliminated, when -20 V was applied to the proximal collector electrode against the distal. In detail, however, the CO_2 signal current responding to 5.56% CO_2 in the sample gas caused a 1.2% relative error to the signal current responding to 4.62% C_2H_2 . In order to minimize the above error, gas mixtures with 4 to 5% CO_2 which corresponded to the CO_2 content in the expired gas were used for calibration of the C_2H_2 concentration of expired gas. Since water vapour also affected the ionic currents, a simple water elimination unit was designed and attached to the analyser as shown schematically in Fig. 1. Thus, the sample gas flows through a V-shaped passage bored in the aluminium block which was cooled at $0.5^\circ C$ by the use of a semiconductor cooling unit. A part of the sample gas was sucked out from the opening at the bottom of the passage and brought the condensed water into the trap bottle. Thus, the water content of the sample gas was kept sufficiently low for practical usage.

The present method is suited especially to the continuous analysis of C_2H_2 in the expired gas. To demonstrate this merit, it was used for observations on the expired C_2H_2 concentration during a constant rate expiration. For examining the validity of this method the change in C_2H_2 fraction in expired gas, F/F_0 , was compared with the theoretically calculated curves. As shown in Fig. 7 the F/F_0 values at rest and during exercise fell on the theoretical curves calculated from Eq. (5) by putting $\dot{Q}=4.7$ and 10.6 liter/min, which agreed closely with the $\dot{Q}$ values obtained subsequently in the same conditions by the breath-holding method. In 15 to 20 sec after the onset of expiration the observed points began to deviate from the theoretical curves probably because of recirculation of the pulmonary blood. The above agreement suggests that with this method it is possible to measure the pulmonary blood flow instantaneously from the C_2H_2 curves. Furthermore, the rapid changes appearing at the transition from rest to exercise or by the Valsalva-like manoeuvre clearly support the fidelity of the flow measurement. At the onset of exercise the increase of C_2H_2 uptake occurred within 1.5 sec, indicating a rapid reaction of the pulmonary blood flow to the exercise.

NINOMIYA and WILSON (1966) made a similar observation in dogs by the use of an implanted magnetic flow meter that heart rate was promptly increased at

the onset of exercise. The interval between the first and second heart beats immediately after the onset of exercise was markedly reduced. In 7 to 10 secs the cardiac output reached a level of 63.2% of the maximum value observed at the given work load. The present findings suggest that such a rapid reaction also occurs in human subjects.

The rapid decrease in $\dot{Q}$ caused by an elevation of intrathoracic pressure was observed by Fox *et al.* (1966) using a dye-dilution method. The results shown in Fig. 9 are in agreement with their findings. Above all it seems certain that the present continuous method, when combined with a constant flow expiration technique, offers a new possibility for making measurements of changes in pulmonary blood flow in man.

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