A simple breathing circuit minimizing changes in alveolar ventilation during hyperpnoea

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ABSTRACT: Many clinical and research situations require maintenance of isocapnia, which occurs when alveolar ventilation ($V'A$) is matched to CO_2 production.

A simple, passive circuit that minimizes changes in $V'A$ during hyperpnoea was devised. It is comprised of a manifold, with two gas inlets, attached to the intake port of a nonbreathing circuit or ventilator. The first inlet receives a flow of fresh gas ($CO_2=0\%$) equal to the subject's minute ventilation ($V'E$). During hyperpnoea, the balance of $V'E$ is drawn (inlet 2) from a reservoir containing gas, the carbon dioxide tension (PCO_2) approximates that of mixed venous blood and therefore contributes minimally to $V'A$.

Nine normal subjects breathed through the circuit for 4 min at 15–31 times resting levels. End-tidal PCO_2 (P_{et,CO_2}) at rest, 0, 1.5 and 3.0 min were (mean $\pm$ SE) 5.1 $\pm$ 0.1 kPa (38.1 $\pm$ 1.1 mmHg), 4.9 $\pm$ 0.1 kPa (36.4 $\pm$ 1.1 mmHg), 5.0 $\pm$ 0.2 kPa (37.8 $\pm$ 1.6 mmHg) and 5.0 $\pm$ 0.2 kPa (37.6 $\pm$ 1.4 mmHg) ($p=0.53$, analysis of variance (ANOVA)), respectively; without the circuit, P_{et,CO_2} would be expected to have decreased by at least 2.7 kPa (20 mmHg). Six anaesthetized, intubated dogs were first ventilated at control levels and then hyperventilated by stepwise increases in either respiratory frequency (f_R) from 10 to 24 min $^{-1}$ or tidal volume (V_T) from 400 to 1,200 mL. Increases in f_R did not significantly affect arterial CO_2 tension (P_{a,CO_2}) ($p=0.28$, ANOVA). Only the highest V_T decreased P_{a,CO_2} from control (-0.5 ± 0.3 kPa (-3.4 ± 2.3 mmHg), $p<0.05$).

In conclusion, this circuit effectively minimizes changes in alveolar ventilation and therefore arterial carbon dioxide tension during hyperpnoea.

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Several clinical conditions [1–3] and research protocols [4–7] require increases in minute ventilation ($V'E$) at constant (or nearly constant) arterial carbon dioxide tension (P_{a,CO_2}). At a constant CO_2 production, P_{a,CO_2} is inversely related to alveolar ventilation ($V'A$), which is a function of $V'E$. When $V'E$ increases, P_{a,CO_2} falls unless CO_2 is added to the inspired gas. Maintaining a constant P_{a,CO_2} despite an irregular breathing pattern requires continuous and proportional adjustment of the fractional concentration of inspired CO_2 (F_{I,CO_2}). Manual adjustments of F_{I,CO_2} may be adequate if changes in $V'E$ are slow or if wide variations in $V'A$ are acceptable. Automated feedback systems provide finer control of $V'A$ but can result in phase delays, unstable responses or overdamping, despite the use of expensive equipment and complex algorithms. A simple breathing circuit was developed and tested that minimizes the effect of $V'E$ on $V'A$ by passively and continuously matching the inspired CO_2 to $V'E$ regardless of the extent or pattern of breathing.

Methods

The basic concept underlying this approach is that the flow of fresh gas ($F_{I,CO_2}=0$) contributing to alveolar CO_2

exchange is kept constant. When $V'E$ is less than or equal to the fresh gas flow (FGF), the subject inhales only fresh gas. Therefore:

$$V'A = FGF \quad (1)$$

When $V'E$ exceeds FGF, the balance of inhaled gas is drawn from a reservoir containing a reserve gas with a carbon dioxide tension (PCO_2) equal to that of mixed venous blood and thus does not participate in CO_2 exchange, ensuring that $V'A$ is limited by FGF, as indicated by the following equation:

$$V'A = FGF + (V'E - FGF) \times ((P_{v,CO_2} - \text{reserve gas } PCO_2) / P_{v,CO_2}) \quad (2)$$

where P_{v,CO_2} is the oxygenated mixed venous PCO_2 . When the PCO_2 of the mixed venous and reserve gas are not equal, the $V'A$ depends on both this difference and the difference between $V'E$ and FGF.

Circuit description

The circuit (fig. 1) consists of a nonbreathing valve connected distally to two ports. The first port is connected

Fig. 1. — Schematic diagram of breathing circuit used for human subjects. For studies in dogs, the demand regulator was replaced with a positive end-expiratory pressure valve and the reserve gas cylinder was replaced by a Douglas bag prefilled with different concentrations of CO_2 .

to a source of fresh gas, a small (<1 L) reservoir (to collect fresh gas during exhalation) and a one-way pop-off valve (to allow venting of excess fresh gas). For the studies in human subjects, the second port was connected *via* an adjustable demand valve (Scubapro 150; Scubapro, Sturtevant, WI, USA) to a cylinder of reserve gas containing 5.5% CO_2 . The demand valve was adjusted to an opening pressure of $\sim 1.5 \text{ cmH}_2\text{O}$. For the studies in dogs, the second port was connected to a 300 L Douglas bag containing reserve gas with different concentrations of CO_2 (see below).

Human subjects

After obtaining approval from the institutional ethics board and informed consent from the subjects, nine healthy subjects aged 19–25 yrs and ranging in weight from 55–95 kg breathed through the circuit by means of a mouthpiece and a low-resistance heat-moisture exchanger while wearing noseclips. During normal breathing, the FGF was set equal to $\dot{V}'_E$ by adjusting the flowmeter until the fresh gas reservoir just emptied at the end of each inspiration. Subjects were then instructed to breathe maximally ("breathe as hard as you can") for 3 min. Flows were recorded by means of a Pitot tube (Voltek Enterprises, Willowdale, Canada) and the signal was integrated to obtain volume. CO_2 was sampled continuously at the mouthpiece (Medical Gas Analyzer LB-2; Sormedics Corp., Anaheim, CA, USA). Analogue signals were digitized at a rate of 60 samples $\cdot \text{s}^{-1}$ and recorded using data-acquisition software (WINDAQ/200, DATAQ Instruments, Akron, OH, USA).

Studies in dogs

Following approval from the institutional ethics board, six mongrel dogs of either sex weighing 20–25 kg were anaesthetized with methohexital ($5\text{--}7 \text{ mg}\cdot\text{kg}^{-1}$ for induction followed by an infusion of $0.15\text{--}0.30 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) and intubated. Adequacy of anaesthetic depth was deduced from the eyelash reflex, lack of spontaneous movements and stable cardiac frequency and blood pressure. A catheter was placed in the femoral artery for monitoring blood pressure and periodic sampling of blood for gas analysis.

The dogs were ventilated with a conventional piston ventilator (Harvard Apparatus model 618, South Natick, MA, USA). For each dog, tidal volume (V_T) of 400 mL and a respiratory frequency (f_R) of 10 min^{-1} (duty cycle 0.5) were used. All dogs were ventilated to just below their apnoeic thresholds (by adjusting V_T by 50 mL increments) so that they made no respiratory efforts. Tidal CO_2 was sampled continuously (Ametek, Thermox Instruments Division, Pittsburgh, PA, USA) at the proximal end of the endotracheal tube. Flow was measured with a pneumotachograph (Vertek series 47303A; Hewlett-Packard, Palo Alto, CA, USA) and the signal integrated to obtain volume. Analogue signals were digitized at a rate of 17 samples $\cdot \text{s}^{-1}$ and recorded using the same data-acquisition software as that used in studies on human subjects.

Because of differences in initial P_{a,CO_2} among dogs (reflecting individual V_T /body weight ratios and/or anaesthetic levels), the CO_2 concentration in the reserve gas was arbitrarily adjusted for each dog to approximate the P_{v,CO_2} . To facilitate setting the concentration of CO_2 in the reserve gas for each dog, the demand valve was replaced with a one-way positive end-expiratory pressure (PEEP) valve and the cylinder with a bag containing premixed gas. This circuit is functionally identical to that used in studies on humans. The circuit was connected to the intake port of the ventilator. Under control conditions, FGF was adjusted so that the fresh gas reservoir just emptied during each ventilator cycle; this was confirmed by a slight rise in F_{I,CO_2} above zero.

After attaining a steady state (difference $<0.2 \text{ kPa}$ (1.5 mmHg) in two successive P_{a,CO_2} taken 5 min apart), V_T was increased at 5 min intervals from 400 to 600 to 900 to 1,200 mL. In a second trial at a fixed V_T (approximately 400 mL), f_R was increased at 5 min intervals from 10 to 14 to 18 to 22 min^{-1} . An arterial blood sample for the determination of blood gases was drawn at the beginning and end of each interval.

Tests for significant differences were performed using one- or two-way analysis of variance (ANOVA) with *post hoc* analysis where appropriate. A p -value <0.05 was considered significant.

Results

Human subjects

There was considerable variability in $\dot{V}'_E$ and breathing patterns between subjects but individual subjects tended to sustain a particular breathing pattern throughout the run. When $\dot{V}'_E$ was high in relation to FGF, both were inhaled simultaneously and subjects did not perceive any transition from fresh to reserve gas. Figure 2 presents the end tidal P_{CO_2} ($P_{\text{Et},\text{CO}_2}$) of subject 1, as well as the variation in V_T and f_R during 3 min of maximal ventilatory effort. Results for all subjects are summarized in table 1. Average $P_{\text{Et},\text{CO}_2}$ for 10 breaths at control, the first 10 s of hyperventilation ("0" min) and 1.5 and 3 min were (mean $\pm$ SE) $5.1 \pm 0.1 \text{ kPa}$ ($38.1 \pm 1.1 \text{ mmHg}$), $4.9 \pm 0.1 \text{ kPa}$ ($36.4 \pm 1.1 \text{ mmHg}$), $5.0 \pm 0.2 \text{ kPa}$ ($37.8 \pm 1.6 \text{ mmHg}$) and $5.0 \pm 0.2 \text{ kPa}$ ($37.6 \pm 1.4 \text{ mmHg}$) ($p=0.53$, ANOVA), respectively.

Fig. 2. – Breath-by-breath airway carbon dioxide tension (PCO_2), respiratory frequency (f_R) and tidal volume (V_T) for subject 1 during maximum voluntary ventilation for 3 min. After an initial small decline (due to the delayed appearance of CO_2 produced by the increased work of breathing), PCO_2 varied <0.4 kPa (<3 mmHg) from onset despite large variations in V_T and f_R . (1 mmHg=0.133 kPa.)

Dogs

Figure 3 presents traces of airway PCO_2 and V_T for dog 5 during changes in f_R or V_T . Figure 4 shows the changes in P_a,CO_2 in all dogs during changes in f_R or V_T . The maximum increase in f_R did not affect mean P_a,CO_2 (-0.3 ± 0.2 kPa (-2.2 ± 1.8 mmHg), range 0.1 to -0.6 kPa (0.4 to -4.8 mmHg), $p=0.28$). Increases in V_T decreased mean P_a,CO_2 only at a V_T of 1200 mL (by -0.5 ± 0.3 kPa (-3.4 ± 2.3 mmHg), range 0.1 to -0.7 kPa (0.4 to -5.6 mmHg), $p<0.05$).

Discussion

The circuit maintained P_a,CO_2 at control values in humans despite a wide range of ventilatory patterns and up to a

Table 1. – Minute ventilation ($V'E$) and end-tidal carbon dioxide tension (P_{Et,CO_2}) during maximal ventilatory efforts in human subjects

Subject	Control	Time min		
		0	1.5	3
V'E				
1		131	124	118
2		75	63	56
3		80	78	68
4		117	80	76
5		153	109	93
6		83	93	79
7		120	82	84
8		74	53	57
9		150	104	90
P_{Et}CO₂				
1	40.3	33.6	34.9	35.6
2	36.6	30.9	28.1	28.0
3	42.0	42.5	43.2	42.7
4	41.0	34.5	38.8	38.8
5	35.6	37.3	41.9	41.2
6	41.5	39.1	39.1	38.9
7	36.6	36.7	36.5	36.4
8	32.8	37.6	35.6	36.3
9	36.5	35.6	42.1	40.4

Values represent averages of 10 breaths at control, onset (0 min), 1.5 and 3 min.

30-fold increase in $V'E$, which otherwise should have lowered PCO_2 by at least 2.7 kPa (20 mmHg). At constant CO_2 production and dead space, these maximal increases in ventilation tested to the limit the ability of the circuit to prevent changes in PCO_2 . In ventilated dogs, P_a,CO_2 decreased only at the highest V_T . The greater changes in P_a,CO_2 in the dogs were attributed to: 1) imprecise matching of the PCO_2 of the reserve gas to the dog's P_v,CO_2 ; 2) prolonged duration of the manoeuvre in dogs (>15 min *versus* 3 min for human subjects); 3) the extent of hyperventilation (see below); and 4) possible effects of mechanical ventilation on systemic and pulmonary blood flow (ventilation-perfusion mismatching, physiological and anatomical dead space) and, therefore, P_a,CO_2 and P_v,CO_2 . Nevertheless, the ranges over which P_{Et,CO_2} and P_a,CO_2 varied in these studies are similar to those reported in studies with less hyperventilation and utilizing more complex equipment [2, 3, 8].

Although conventional servocontrolled techniques designed to prevent changes in PCO_2 with hyperpnoea are less affected by changes in CO_2 production than the present circuit, they have limitations. Small changes in ventilatory pattern can uncouple P_{Et,CO_2} and P_a,CO_2 [7], resulting in P_{Et,CO_2} being an inappropriate variable for controlling P_a,CO_2 . For example, a smaller V_T decreases $V'A$ (which tends to increase P_a,CO_2) but will also decrease P_{Et,CO_2} , causing a servocontroller to respond with an inappropriate increase in F_i,CO_2 . If, in an attempt to obtain fine control, the gain in a servocontrol system is set too high, the response becomes unstable and may result in oscillation of the controlled variable [4]. Conversely, if the gain is set too low, compensation lags [8]. Overdamping of the signal results in the response never reaching the target. To address these problems, servocontrollers require complex algorithms [9] and expensive equipment.

Fig. 3. — Effect of sequential changes in respiratory frequency (f_R) and tidal volume (V_T) on airway carbon dioxide tension (P_{CO_2}) in dog 5. The circuit passively adjusted the inspiratory carbon dioxide fraction (F_{I,CO_2}) in response to changes in minute ventilation whether caused by changes in f_R or in V_T . Numbers above the graph indicate the level of ventilation at each stage. (1 mmHg=0.133 kPa.)

When CO_2 production is constant, this circuit is superior to servocontrolled systems in that it passively compensates for changes in $V'E$ minimizing changes in $V'A$ and pre-empting the need for subsequent compensation. Maintenance of a nearly constant $V'A$ occurs even during irregular breathing, including brief periods when $V'E$ is less than the FGF; excess FGF is stored in the fresh gas reservoir and contributes to $V'A$ when ventilation subsequently exceeds FGF.

When CO_2 production, and therefore P_{V,CO_2} , increases (e.g. with increased work of breathing or exercise), this method requires modification because FGF, if fixed, will no longer clear enough CO_2 to maintain normocapnia. To increase $V'A$, one must increase FGF or decrease the PCO_2 of the reserve gas below the P_{V,CO_2} (Equation 2). Compensating for increased CO_2 production by increasing FGF would have required constant adjustment of FGF in hyperpnoeic subjects with variable $V'E$. Therefore, it was decided to decrease the PCO_2 of the reserve gas. By trial and error, it was found that 5.5% CO_2 in the reserve gas (instead of 6.5% corresponding to a P_{V,CO_2} of 6.1 kPa (46 mmHg)) established a suitable gradient of CO_2 partial pressure to match closely CO_2 elimination to increases in CO_2 production resulting from increased work of breathing at higher $V'E$.

The circuit presented here bears a superficial resemblance to the Mapleson D anaesthetic circuit, which minimizes the effect of changes in total ventilation on $V'A$. However, with that circuit, $V'A$ remains less than FGF at all levels of ventilation but asymptotically approaches FGF at high ventilation [10]. In contrast, the present circuit limits the $V'A$ to FGF at any $V'E$ greater than FGF.

In summary, we describe a simple circuit that dissociates alveolar ventilation from minute ventilation. It passively minimizes increases in alveolar ventilation that would normally accompany hyperpnoea at constant or, by adjusting the carbon dioxide tension of the reserve gas, increased carbon dioxide production. The circuit may provide a simple and inexpensive alternative to servocontrolled systems for research and have therapeutic applications.

Fig. 4. — Arterial carbon dioxide tension (P_{a,CO_2}) resulting from: a) step changes in tidal volume (V_T) at constant respiratory frequency (f_R); and b) changes in f_R at constant V_T . *: $p<0.05$, significantly different from control. Each symbol represents an individual dog and bar is the mean of the dogs. (1 mmHg=0.133 kPa.)

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