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A simple and portable breathing circuit designed for ventilatory muscle endurance training (VMET)

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Summary
Background: Ventilatory muscle endurance training (VMET) involves increasing minute ventilation ($\dot{V}_E$) against a low flow resistance at rest to simulate the hyperpnea of exercise. Ideally, VMET must maintain normocapnia over a wide range of $\dot{V}_E$. This can be achieved by providing a constant fresh gas flow to a sequential rebreathing circuit. The challenge to make VMET suitable for home use is to provide a source of constant fresh gas flow to the circuit without resorting to compressed gas.
Methods: Our VMET circuit was based on a commercial sequential gas delivery breathing circuit (Pulmanex Hi-Ox, Viasys Healthcare, Yorba Linda, CA USA). Airflow was provided either by a small battery-driven aquarium air pump or by the entrainment of air down a pressure gradient created by the recoil of a hanging bellows that was charged during each inhalation. In each case, fresh gas flow was adjusted to be just less than resting $\dot{V}_E$. Eight subjects then breathed from the circuit for three 10 min periods consisting of relaxed breathing, breathing at 20 and then at 40 L/min. We monitored $\dot{V}_E$, end-tidal PCO_2 ($P_{ET}CO_2$) and hemoglobin O_2 saturation (SpO_2).
Results: During hyperpnea at 20 and 40 L/min, $P_{ET}CO_2$ did not differ significantly from resting levels with either method of supplying fresh gas. SpO_2 remained greater than 96% during all tests.

Abbreviations: VMET, ventilatory muscle endurance training; $\dot{V}_E$, minute ventilation (L/min); $\dot{V}_A$, alveolar ventilation (L/min); PCO_2, partial pressure of CO_2 (mmHg); $P_{ET}CO_2$, end-tidal partial pressure of CO_2 (mmHg); $P_{ET}O_2$, end-tidal partial pressure of O_2 (mmHg); FGF, fresh gas flow (L/min); SpO_2, hemoglobin oxygen saturation measured via pulse oximetry.

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Conclusion: Isocapnic VMET can be reliably accomplished with a simple self-regulating, sequential rebreathing circuit without the use of compressed gas.

Introduction

For endurance exercise training, breathing does for chest muscles what running does for leg muscles.[1] By analogy then, ventilatory muscle endurance training (VMET) requires periods of prolonged, sustained increases in minute ventilation ($\dot{V}_E$). This differs from training by inhaling against a resistance, which is analogous to weight training. Indeed, VMET improves both ventilatory and exercise endurance in healthy runners,[2] swimmers,[3] cyclists,[4] sedentary volunteers,[5,6] and wheelchair-bound athletes.[7,8] It can also increase endurance in the elderly,[9] individuals with restrictive lung disease,[10] cystic fibrosis,[11] myasthenia gravis,[12] and patients recovering from spinal cord injury.[13] In patients with chronic obstructive pulmonary disease (COPD), VMET improves exercise tolerance as well as the perception of dyspnea; it even improves quality of life.[14–16]

With exercise, $\dot{V}_E$ is matched to O_2 consumption and CO_2 production so that O_2 requirements are met, and end-tidal partial pressure of CO_2 ($P_{ET}CO_2$) changes little from that at rest. VMET ideally exercises only respiratory muscles, potentially resulting in a low steady state arterial partial pressure of CO_2 ($PaCO_2$). Breathing circuits used for VMET must therefore reduce the efficiency with which ventilation eliminates CO_2. This is commonly done by replacing some fixed portion of the inhaled air with previously exhaled gas (i.e., partial rebreathing), leaving only the atmospheric air portion of inspired gas (i.e., fresh gas) to contribute to CO_2 elimination.[17] To maintain isocapnia, however, the flow of this fresh gas (FGF) — not that of rebreathed gas — must remain constant despite increases in $\dot{V}_E$.[18] Thus, with devices that use a constant volume of rebreathed gas to reduce CO_2 elimination, one must either accept some variations in $P_{ET}CO_2$ as $\dot{V}_E$ varies[15] or, attempt to restrain tidal volume and breathing frequency[14] to fixed levels.

The ideal VMET system for home use would have two important properties. The first is that it should maintain normocapnia over a wide range of $\dot{V}_E$. Isocapnia can be maintained independently of $\dot{V}_E$ if the FGF remains constant and the balance of $\dot{V}_E$ is made up with previously exhaled gas (partial rebreathing).[17,19] Banzett et al.[19] have pointed out that the sequential gas delivery circuit is one such self-regulating system. However, its source of fresh gas traditionally comes from a cylinder of compressed gas, which is impractical to install outside of large institutions. This leads to the second desirable property of a home system: it should operate without compressed gas.

Our aim was to test the concept of a ''home-use'' VMET circuit based on sequential gas delivery for maintaining normocapnia. To provide constant FGF without compressed gas, we tested two systems: a commercial battery-driven aquarium aeration pump and a custom, self-charging bellows that needs no external power. We did so by assessing their ability to maintain normocapnia and peripheral oxygen saturation (SpO_2) over a wide range of$\dot{V}_E$.

Methods

After approval from our institutional ethics review board, eight healthy, non-smoking subjects gave written informed consent to participate in this study. Anthropometric data are shown in Table 1.

Breathing circuit

The breathing circuit consisted of a commercially available sequential gas delivery breathing manifold (Pulmanex Hi-Ox, Viasys Healthcare, Yorba Linda, CA USA) modified by adding a gas reservoir to the expiratory limb[17] (Fig. 1). When $\dot{V}_E$ exceeds the FGF, previously exhaled gas is inhaled from the expiratory reservoir via the bypass limb.

FGF sources

For the first source of fresh gas, we used a battery-driven aquarium air pump (2.4 W, A.1F21N2.C12VDC, Hargraves, Mooresville, NC USA) (Fig. 1b). A mass gas flow meter (AWM700, Honeywell, Morristown, NJ USA) was used to

Table 1 Anthropometric and ventilation data for all subjects.

Subject #	Age (y)	Sex	Ht (cm)	Wt (kg)	$\dot{V}_A$ Control (L/min)	$P_{ET}CO_2$ control (mmHg)	SpO_2 control (%)
1	22	F	150	42.3	3.7	39.6	97.4
2	24	F	173	68.2	6.9	40.6	97.7
3	34	M	168	63.6	5.7	40.4	97.6
4	23	M	170	59.1	6.8	35.4	97.9
5	25	M	173	59.1	4.3	41.3	97.7
6	30	M	185	86.4	6.3	41.7	97.1
7	36	F	179	84.1	6.7	39.2	97.5
8	59	M	183	77.7	4.6	36.7	97.4
Mean	31.6		67.9	67.6	5.6	39.4	97.5
SD	12.2		4.3	14.8	1.3	2.2	0.2

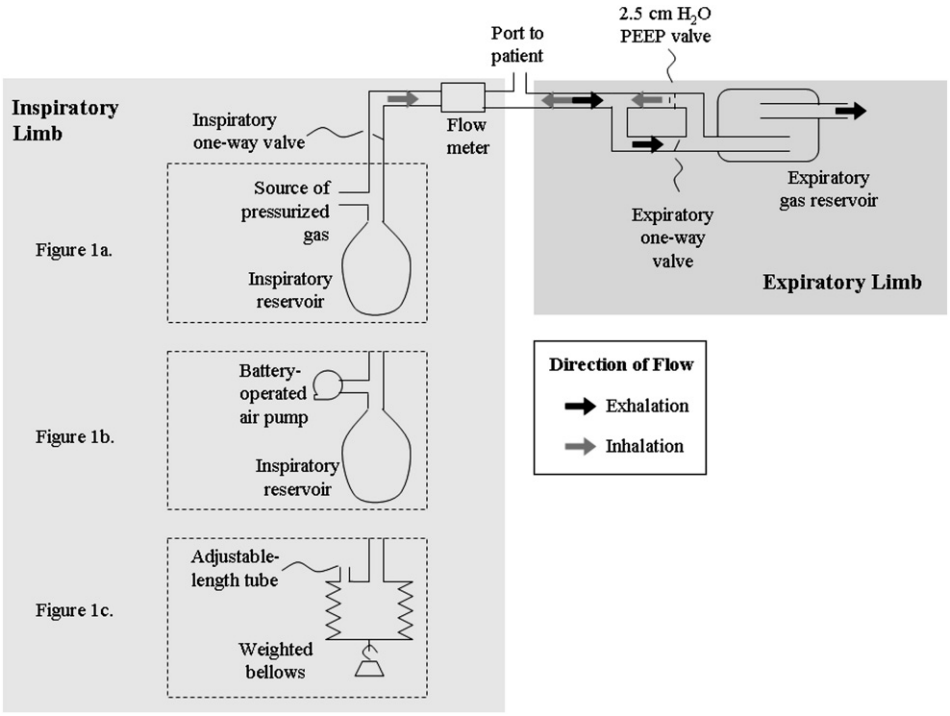

Figure 1 Schematics of VMET circuits. a: Generic sequential rebreathing circuit with fresh gas supplied by pressurized gas source. b: gas flow is supplied by a battery operated pump; c: schematic of a bellows system charged during inspiration to provide a pressure gradient for entrainment of air during exhalation and thereby provide a near constant flow of air (FGF) to the circuit throughout the respiratory cycle.

calibrate the pump dial settings between 2 and 10 L/min and monitor gas flow.

For the second source of FGF, we assembled a system designed to provide near constant FGF caused by the pressure gradient resulting from the recoil of a weighted bellows that collapsed with each inhalation (Fig. 1c). The weight on the bellows plate was calibrated such that the pressure differential across the weight was less than the 2.5 cmH_2O opening pressure of the valve on the cross-over limb of the breathing manifold. To control the FGF from the bellows to the inlet of the breathing manifold, we varied the length of the 0.32 mm i.d. inflow resistance tubing. An electronic flowmeter (4040E, TSI, Shoreview, MN USA) was used to determine the flow-length relation of the resistance tubing. A subject breathed at 20 L/min through the circuit to generate the pressure gradient for calibrating the tubing lengths. As the pressure gradient across the tubing is limited by the opening pressure of the cross-over valve, it varies within a small range during a breath at any $\dot{V}_E$ (Fig. 2). The resulting flow through the resistance tubing is therefore primarily a function of its length (L). L (in cm) was chosen according to the required FGF from the empirically derived relationship $L = 319.26e^{(-0.5022\ *FGF)}$ (Fig. 2).

$\dot{V}_E$ was monitored by a pneumotachograph (Vmax, Viasys HealthCare, Yorba Linda, CA USA) on the inspiratory limb of the breathing circuit, and displayed breath-by-breath on a screen visible to the subject. Tidal gas was sampled from inside the face mask and analyzed for $P_{ET}CO_2$ and $P_{ET}O_2$ (Vmax, Viasys HealthCare, Yorba Linda, CA USA). Blood oxygen saturation (SpO_2) was monitored continuously by pulse oximetry (AS/3 Datex-Ohmeda, Stockholm Sweden).

Protocol

Subjects were seated comfortably in a laboratory. They held the mask connected to the breathing circuit tightly to their faces to ensure an air-tight seal. The expiratory reservoir was only attached to the VMET circuit after the fresh gas source was confirmed to be operational; at all other times, the inspiratory limb of the circuit was open to room air.

First, the air pump (and the expiratory reservoir) was attached to the breathing circuit. The air pump was initially set to provide a FGF of air well in excess of $\dot{V}_E$ (as judged from sustained distension of the fresh gas reservoir). After 10 min, the pump flow was adjusted to just less than $\dot{V}_E$ as indicated by collapse of the inspiratory reservoir and an

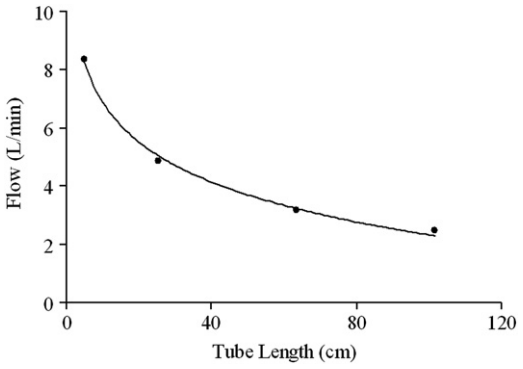

Figure 2 Relation between air flow and length of the resistance tubing. The pressure gradient was generated by a subject breathing on the circuit with the weighted bellows (see Methods).

increase in PCO_2 on the capnograph tracing during the latter part of inspiration. Subjects breathed at rest for at least an additional 2 min to ensure that $P_{ET}CO_2$ remained stable between 39 and 41 mmHg. The resulting airflow (i.e., FGF) was assumed to be equivalent to alveolar ventilation ($\dot{V}_A$).[17] Subjects were then asked to increase $\dot{V}_E$ to approximately 20 L/min for 10 min. $\dot{V}_E$ was controlled by using visual feedback from the values of $\dot{V}_E$ displayed on the screen of the metabolic cart.

The pump assembly was then detached and the self-inflating bellows was connected to the inspiratory limb of the breathing circuit (Fig. 1c). A length of resistance tubing was chosen to provide the same flow as that produced by the pump. Subjects were asked once again to increase $\dot{V}_E$ to approximately 20 L/min. This protocol was subsequently repeated at a $\dot{V}_E$ of 40 L/min using both the pump assembly and the self-inflating bellows. Subjects rested for at least 5 min between tests.

All analog data were digitized and recorded on customized data acquisition software (LabView 7.1, National Instruments, Austin, TX USA). Data during the last 3 min of each protocol were analyzed for average $P_{ET}CO_2$, SpO_2 and $\dot{V}_E$.

We evaluated the precision of FGF delivery by the two methods by comparing observed flow to target flow under each $\dot{V}_E$ condition. We evaluated the ability of the circuit to maintain arterial gas concentrations by comparing $P_{ET}CO_2$ and SpO_2 during each $\dot{V}_E$ condition to baseline levels. Comparisons were done using a two factor repeated measures ANOVA, with an alpha level of 0.05. All statistics were performed using SigmaStat (Aspire Software International, Ashburn, VA USA).

Results

All subjects were able to complete the protocol without any discomfort or symptoms indicative of hypocapnia, hypercapnia, or hypoxia. At no time did $P_{ET}CO_2$ fall below 35 mmHg or exceed 45 mmHg, or SpO_2 fall below 96%.

The $\dot{V}_E$ and $P_{ET}CO_2$ of a representative subject are shown in Fig. 3. $P_{ET}CO_2$ did not differ significantly from control levels when either the pump ($F = 0.41$, $p = 0.748$) or the tube assembly ($F = 1.99$, $p = 0.15$) was used. SpO_2 remained greater than 96% during all tests (Table 2). Increases in $\dot{V}_E$ tended to increase the flow of entrained

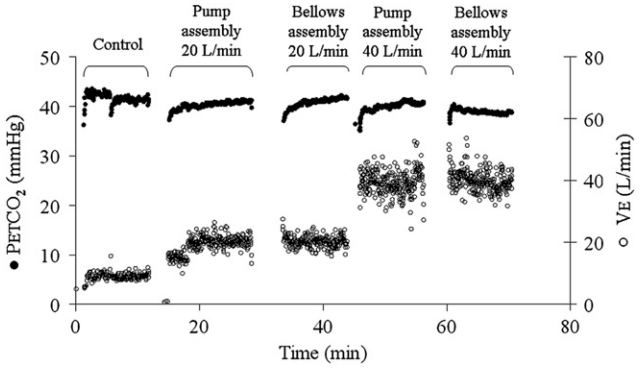

Figure 3 Breath-by-breath measurements of $P_{ET}CO_2$ and $\dot{V}_E$ from a representative subject. The circuit maintained normocapnia despite an approximate 6-fold increase in $\dot{V}_E$.

Table 2 $P_{ET}CO_2$ and SpO_2 at $\dot{V}_E$ of 20 and 40 L/min with two sources of air flow (* indicates difference from Control at $p < 0.05$ level).

PUMP	Control	20 L/min	40 L/min
$P_{ET}CO_2$ (mmHg)	39.4 ± 2.2	39.3 ± 1.2	40.2 ± 3.0
SpO_2 (%)	97.5 ± 0.2	97.5 ± 0.2	97.3 ± 0.4
$\dot{V}_E$ (L/min)	7.8 ± 1.0	20.1 ± 1.3	38.7 ± 2.5
FGF (L/min)	5.6 ± 1.3	5.6 ± 1.3	5.3 ± 1.3
Bellows	**Control**	**20 L/min**	**40 L/min**
$P_{ET}CO_2$ (mmHg)	39.4 ± 2.2	41.4 ± 2.0	39.1 ± 2.3
SpO_2 (%)	97.5 ± 0.2	97.2 ± 0.4*	97.5 ± 0.3
$\dot{V}_E$ (L/min)	7.8 ± 1.0	21.4 ± 2.0	39.5 ± 1.6
FGF (L/min)	5.6 ± 1.3	4.7 ± 1.2*	5.5 ± 1.5

fresh gas ($p < 0.01$) with both methods, but not sufficiently to affect $P_{ET}CO_2$.

Discussion

Our VMET circuits maintained $P_{ET}CO_2$ at resting levels (i.e., normocapnia) for all subjects even during a more than 6-fold increase in $\dot{V}_E$ above resting levels. This was achieved by providing a constant FGF to a sequential rebreathing circuit, enabling it to maintain normocapnia independent of $\dot{V}_E$. The aim of making the system independent of compressed gas is to improve its portability, reduce its cost, and thus increase its practicality for use outside the clinical setting.

In 1976, Leith and Bradley first demonstrated that sustained normocapnic hyperpnea is more effective for respiratory muscle endurance training (as indicated by ventilatory endurance during maximum voluntary ventilation) than resistance training.[1] Since then, multiple studies have shown that VMET increases ventilatory capacity, exercise tolerance, and reduces breathlessness during exercise.[2,4,6] In patients with cystic fibrosis, VMET for 25 minutes a day, 5 days per week for 4 weeks improved ventilatory muscle endurance as much as intense physical activity for 1.5 h per day.[11] Hyperpnea training also improves inspiratory muscle strength, peak oxygen consumption ($\dot{V}O_2max$), maximal work rate, and even quality of life in subjects with restrictive lung disease.[10] In patients with COPD, VMET improves maximal sustained ventilatory capacity, $\dot{V}O_2max$, and maximal $\dot{V}_E$ during exercise.[14–16] Similar results have been obtained in patients with neuromuscular disorders due to spinal cord injury [7,8,13] and myasthenia gravis.[12]

To be effective, VMET training generally requires about 20 min per day, 5 days a week for at least a month. Such intensive training precludes visits to a clinic and can only be managed if it can be performed at home. The available portable systems recommended for home use fix the extent of rebreathing rather than the rate of entrainment of air ($\dot{V}_A$), thus allowing $P_{ET}CO_2$ to vary with $\dot{V}_E$. Such systems require constant interventions to maintain normocapnia[1,2] but $P_{ET}CO_2$ may nevertheless vary widely (from 33[15] to >53 mmHg [5]) with $\dot{V}_E$. The advantage of a system based on sequential rebreathing is that, as long as the FGF entering the circuit is constant, $\dot{V}_A$, and hence $P_{ET}CO_2$, remain constant over a wide range of $\dot{V}_E$.[20] For portability and out-of-clinic use, a method of maintaining a constant FGF without the need for a cylinder

of compressed gas is necessary. One obvious method is to provide ambient air from a simple battery-powered electrical pump. Our 2.4 W aquarium pump can run for 8 h when powered by a single 12 volt lead acid battery.

How to maintain a constant FGF without external power is less obvious. The pressure across a partially expanded bellows is determined by the weight of the bellows plate and its surface area. During inspiration, the pressure should therefore remain constant (ignoring momentum of the weight). We selected a weight for the plate that would require a pressure of approximately -1.5 cmH_2O to lift it. The opening pressure of the cross-over valve is approximately -2.5 cmH_2O. Thus, during inspiration, as long as the pressure in the breathing circuit remains between -1.5 and -2.5 cmH_2O, the bellows will collapse (i.e., the plate will rise). Once the bellows collapses, continued inspiratory effort reduces the pressure in the bellows to less than the opening pressure of the cross-over valve. Opening of the cross-over valve allows previously exhaled gas to be inhaled from the expiratory reservoir. Throughout this phase of inhalation, the pressure inside the bellows remains constant at the opening pressure of the cross-over valve, i.e., -2.5 cmH_2O.

We used this same system to generate the pressure gradient used to calibrate the lengths of resistance tubing that determine the FGF into the bellows. Because the fluctuation of the pressure gradient across the tubing remained within approximately 1 cmH_2O throughout the respiratory cycle (i.e., between 1.5 and 2.5 cmH_2O), and the resistance to flow in the tubing was constant, the entrained flow of air (i.e., FGF) was essentially constant. And, as mentioned above, as long as the FGF is constant, $\dot{V}_A$ (and therefore $P_{ET}CO_2$) remains constant. Table 2 indicates that the small variations in the FGF entrained by the bellows assembly were too small to affect the $P_{ET}CO_2$.

One limitation of our approach is that the FGF must initially be set equal to $\dot{V}_A$. One can identify when FGF equals $\dot{V}_E$ because the volume of the inspiratory reservoir at the end of inspiration remains constant. $\dot{V}_A$ is then obtained by making a small, arbitrary reduction in FGF below $\dot{V}_E$. ''Small'' may be imprecise but, in practice, there is considerable leeway in the FGF reduction. In our study, to obtain a FGF ''equal to $\dot{V}_A$'', we reduced the FGF until $P_{ET}CO_2$ rose above resting values during the latter part of inspiration, indicating rebreathing. As previously argued,[17,18] this rebreathed gas flows into the anatomical deadspace and has no effect on $P_{ET}CO_2$. Assuming a 70 Kg male with tidal volume of 0.5 L and anatomical deadspace of 0.014 L, FGF can be reduced by nearly one third without resulting in an increase in $P_{ET}CO_2$ (see discussion in Somogyi et al.[17]). Once the FGF is set, the stability of the $P_{ET}CO_2$ depends on the constancy of CO_2 production.[17] Although $\dot{V}_A$ is constant, CO_2 production may increase with even small movements, such as changing body position or tensing muscles, or with increased work of breathing[21] that accompanies the increased $\dot{V}_E$. Conversely, CO_2 production may decrease if the subject relaxes tensed muscles. In our study, these uncontrolled variables did not seem to affect $P_{ET}CO_2$.

Conclusion

A sequential rebreathing circuit is self-regulating with respect to $P_{ET}CO_2$, providing the basis for a simple VMET system that maintains isocapnia over a wide range of $\dot{V}_E$. The additional requirement of a constant fresh gas flow can be met by using either of the two compact, inexpensive systems which we propose: a simple battery-driven aquarium pump, and a self-charging bellows system. Both eliminate the need for a cylinder of compressed gas. In our study each system maintained normocapnia and normal SpO_2 during VMET despite a 6-fold increase in $\dot{V}_E$.

Conflict of interest statement

Patent applications for the method and apparatus of maintaining constant PCO_2 have been filed according to the intellectual property guidelines of the University Health Network in Toronto, Canada. DP, JF, JD, MS and SI may benefit financially should this technology be successfully commercialized.

DYB, AM, JSH, RR, GDW have no conflicts of interest to disclose.

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