APPROXIMATE SIMULATION OF ACUTE HYPOBARIC HYPOXIA WITH NORMOBARIC HYPOXIA

J. Conkin[1], J.H. Wessel, III[2]. Universities Space Research Association[1], 3600 Bay Area Boulevard, Houston, TX 77058-3696, Wyle Integrated Science and Engineering Group[2], 1290 Hercules Drive, Suite 120, Houston, TX 77058-2769.

INTRODUCTION. Some manufacturers of reduced oxygen (O_2) breathing devices claim a comparable hypobaric hypoxia (HH) training experience by providing $F_IO_2 < 0.209$ at or near sea level pressure to match the ambient O_2 partial pressure (iso-pO_2) of the target altitude. **METHODS.** Literature from investigators and manufacturers indicate that these devices may not properly account for the 47 mmHg of water vapor partial pressure that reduces the inspired partial pressure of O_2 (P_IO_2). Nor do they account for the complex reality of alveolar gas composition as defined by the Alveolar Gas Equation. In essence, by providing iso-pO_2 conditions for normobaric hypoxia (NH) as for HH exposures the devices ignore P_AO_2 and P_ACO_2 as more direct agents to induce signs and symptoms of hypoxia during acute training exposures. **RESULTS.** There is not a sufficient integrated physiological understanding of the determinants of P_AO_2 and P_ACO_2 under acute NH and HH given the same hypoxic pO_2 to claim a device that provides isohypoxia. Isohypoxia is defined as the same distribution of hypoxia signs and symptoms under any circumstances of equivalent hypoxic dose, and hypoxic pO_2 is an incomplete hypoxic dose. Some devices that claim an equivalent HH experience under NH conditions significantly overestimate the HH condition, especially when simulating altitudes above 10,000 feet (3,048 m). **CONCLUSIONS.** At best, the claim should be that the devices provide an *approximate* HH experience since they only duplicate the ambient pO_2 at sea level as at altitude (iso-pO_2 machines). An approach to reduce the overestimation is to at least provide machines that create the same P_IO_2 (iso-P_IO_2 machines) conditions at sea level as at the target altitude, a simple software upgrade.

Learning Objectives:

1. Applying basic principles of respiratory physiology to the design of reduced oxygen breathing devices.
2. Working toward a better understanding of hypoxia.

APPROXIMATE SIMULATION OF ACUTE HYPOBARIC HYPOXIA WITH NORMOBARIC HYPOXIA

J Conkin[1] and JH. Wessel[2], III. Universities Space Research Association[1], Wyle Integrated Science & Engineering Group[2], Houston, Texas, USA 77058.

ABSTRACT

INTRODUCTION. Some manufacturers of reduced oxygen (O_2) breathing devices claim a comparable hypobaric hypoxia (HH) training experience by providing F_IO_2 < 0.209 at or near sea level pressure to match the ambient O_2 partial pressure (iso-pO_2) of the target altitude. METHODS. Literature from investigators and manufacturers indicate that these devices may not properly account for the 47 mmHg of water vapor partial pressure that reduces the inspired partial pressure of O_2 (P_IO_2). Nor do they account for the complex reality of alveolar gas composition as defined by the Alveolar Gas Equation. In essence, by providing iso-pO_2 conditions for normobaric hypoxia (NH) as for HH exposures the devices ignore P_AO_2 and P_ACO_2 as more direct agents to induce signs and symptoms of hypoxia during acute training exposures. RESULTS. There is not a sufficient integrated physiological understanding of the determinants of P_AO_2 and P_ACO_2 under acute NH and HH given the same hypoxic pO_2 to claim a device that provides isohypoxia. Isohypoxia is defined as the same distribution of hypoxia signs and symptoms under any circumstances of equivalent hypoxic dose, and hypoxic pO_2 is an incomplete hypoxic dose. Some devices that claim an equivalent HH experience under NH conditions significantly overestimate the HH condition, especially when simulating altitudes above 10,000 feet (3,048 m). CONCLUSIONS. At best, the claim should be that the devices provide an *approximate* HH experience since they only duplicate the ambient pO_2 at sea level as at altitude (iso-pO_2 machines). An approach to reduce the overestimation is to at least provide machines that create the same P_IO_2 (iso-P_IO_2 machines) conditions at sea level as at the target altitude, a simple software upgrade.

INTRODUCTION

Reduced O_2 breathing devices create a normobaric hypoxic (NH) exposure by providing an F_IO_2 < 0.209, breathed either through a mask or within a "hypoxia tent".

~~The~~ Some manufacturers claim an equivalent acute hypobaric hypoxic (HH) experience but under NH conditions. This eliminates the need for an expensive hypobaric chamber and the risk of decompression sickness associated with hypobaric exposure, creating ~~. So a~~ a cost-effective hypoxia training niche ~~is created with these devices, if they~~ these devices deliver ~~what they~~ as promised.

METHODS

~~We reviewed~~ Literature was reviewed to understand the operations of three reduced O_2 breathing devices: ROBD® (1), PROTE® (8), and GO_2Altitude® (http://www.hypoxic-training.com).

The devices seem to duplicate the ambient partial pressure of O_2 (iso-pO_2) at sea level as exists at the target altitude~~, or something else besides P_IO_2~~-(7).

The method to convert feet altitude to ambient pressure was never specified, a necessary detail to understand the operation of these devices. ~~But~~ Through analysis, it appears that Eq. 1 is used.

Eq. 1 defines a "Standard Atmosphere - 1976" where distance in kilometers is converted to the equivalent ambient pressure as mmHg.

$$PB_{hypo}\ (mmHg) = 760 * [288.15 / (288.15 - 6.5 * altitude\ (km))]^{-5.25588} \qquad Eq.\ 1$$

Eq. 2 is an alternative to Eq. 1 (10).

$$PB_{hypo}\ (mmHg) = \exp[6.63268 - 0.1112 * altitude\ (km) - 0.00149 * altitude^2\ (km)] \qquad Eq.\ 2$$

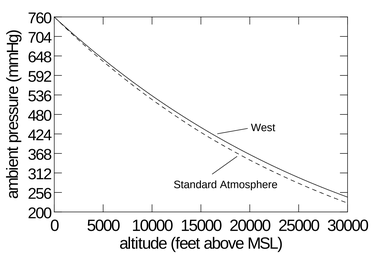

Fig. 1: The relationship between pressure and altitude as feet above mean sea level (MSL) diverges given two equations.

Eq. 3 converts the y-axis in Fig. 1 to F_IO_{2normo} under normobaric pressure (F_IO_{2normo}) that represents the pO_2 while breathing air at these pressures for the iso-pO_2 machines (Fig. 2).

$$F_IO_{2normo} = PB_{hypo} * F_IO_{2hypo} / PB_{normo} \qquad Eq.\ 3$$

where PB_{normo} is most often 760 mmHg, but could be different if the training is done at a location other than sea level, F_IO_{2hypo} is most often 0.209 but could be different if you are breathing an O_2 mixture that is not "air", and PB_{hypo} comes from either Eq. 1 or 2 that computes the ambient pressure for a particular altitude.

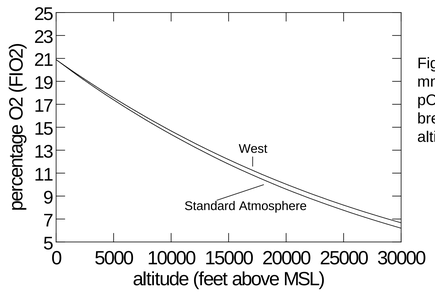

Fig. 2: F_IO_2 needed at 760 mmHg to provide the equivalent pO_2 you would breathe while breathing air at the given altitude.

Eq. 4 computes the F_IO_2 under normobaric conditions (F_IO_{2normo}) to provide for iso-P_IO_2.

$$F_IO_{2normo} = (PB_{hypo} - 47) * F_IO_{2hypo} / (PB_{normo} - 47) \qquad Eq.\ 4$$

This simple improvement would provide a device that delivers a simulation of HH while under NH conditions accounting for 47 mmHg of water vapor pressure, as seen in Fig. 3.

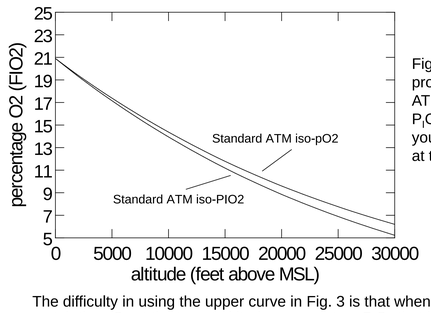

Fig. 3: F_IO_2 needed at 760 mmHg to provide the equivalent pO_2 (Standard ATM iso-pO_2 curve) or the equivalent P_IO_2 (Standard ATM iso-P_IO_2 curve) you would breathe while breathing air at the given altitude.

The difficulty in using the upper curve in Fig. 3 is that when you provide a F_IO_2 at sea level to match the pO_2 at the target altitude you create a P_IO_2 that is greater than the P_IO_2 at the target altitude, a consequence of ignoring pH_2O.

It is best to provide a F_IO_2 at sea level as defined by the lower curve in Fig. 3 that at least produces the equivalent P_IO_2 at sea level as at the target altitude, ~~a consequence of not ignoring~~ which would account for pH_2O.

Example: 9.0% F_IO_2 at 1 ATA on the display of an iso-pO_2 machine would indicate that you are at about 21,500 feet altitude with a pO_2 of 68.5 mmHg (Eq. 3). But P_IO_2 at 1 ATA is 64.1 mmHg, equivalent to breathing air at 19,700 feet, so an iso-pO_2 machine overestimates the simulated altitude by 1,800 feet. This is a consequence of ignoring the contribution of pH_2O.

RESULTS

Even accounting for pH_2O is not sufficient to account for P_AO_2 and P_ACO_2 as more direct agents to induce signs and symptoms of hypoxia during acute training exposures (2).

Fenn et al., as early as 1946, provided the theoretical foundation on why alveolar gas composition would *never be identical* under NH and HH conditions given the same hypoxic P_IO_2, a consequence captured in the derivation of the Alveolar Gas Equation.

Fig. 4 is an example of how NH and HH given the same P_IO_2 of 57.3 mmHg (22,000 ft) would not produce identical P_AO_2 and P_ACO_2.

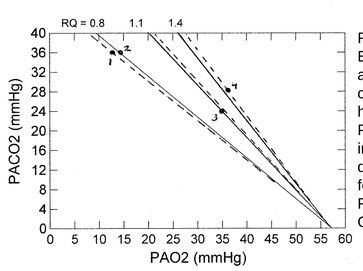

Fig. 4. Application of the Alveolar Gas Equation to demonstrate the inability to accurately reproduce HH under NH conditions given an example of an acute hypobaric training exposure to 22,000 ft. P_IO_2 is 57.3 mmHg in both conditions, the intercept for all respiratory quotient (RQ) diagonals when P_ACO_2 is zero. Diagonals for HH are solid lines and those for NH (8% F_IO_2) are dashed lines, all from the Alveolar Gas Equation (Eq. 5).

$$P_AO_2 = P_IO_2 - P_ACO_2 * [F_IO_2 + ((1 - F_IO_2) / RQ)]. \qquad Eq.\ 5$$

Point 1: NH trainee dons mask at 760 mmHg with F_IO_2 of 8% and RQ of 0.8, and P_AO_2 quickly drops to 13 mmHg – a stimulus to hyperventilate.

Point 2: HH trainee rapidly ascends on air to 22,000 feet with same RQ of 0.8, and P_AO_2 quickly drops to about 14 mmHg – a slightly less stimulus to hyperventilate than NH.

Point 3: Hyperventilation of *rarified air* in this example acutely places HH trainee on the 1.1 RQ diagonal given the conditions in Table 1, column 2.

TABLE 1. Reasonable Response to Acute HH and NH Exposures

parameter	HH Example P_IO_2 57 mmHg	NH Example P_IO_2 57 mmHg
PB (mmHg)	321	760
F_IO_2	0.21	0.08
V_E (l_{BTPS}/min)	14.3	16.5 ↑
V_A (l_{BTPS}/min)	10.4	12.0 ↑
VCO_2(ml_{STPD}/min)	289	389 ↑
VO_2 (ml_{STPD}/min)	262	278 ↑
RQ	1.1	1.4 ↑
V_A/VCO_2	0.036	0.031 ↓
P_AO_2 mmHg	35	37 ↑
P_ACO_2 mmHg	24	28 ↑
P_AN_2 (mmHg)	215	648 ↑

Point 4: Hyperventilation of *dense air* in this example acutely places NH trainee on the 1.4 RQ diagonal given the conditions in Table 1, column 3.

Loeppky et al. 1997 (and others) shows a greater increase in the rate and depth of breathing in NH relative to HH. In the above example the increase in minute ventilation (V_E) and alveolar ventilation (V_A) in NH relative to HH results is a greater P_AO_2 and P_ACO_2 as a result of increased VCO_2 from breathing the relatively dense gas during NH.

It follows from Loeppky and our example in Fig. 4 that physiological responses would be different after peripheral and central chemoreceptor responses are integrated within the central nervous system.

Even if the Alveolar Gas Equation was used in reduced O_2 breathing devices one must account for the complex time-dependent role that P_AN_2 has in modifying P_AO_2 and P_ACO_2 under a particular hypoxic P_IO_2.

An accurate application of the Alveolar Gas Equation requires that the inspired N_2 volume be equal to the expired N_2 volume:

$$VN_2 = V_I * F_IN_2 - V_E * F_EN_2 = 0. \qquad Eq.\ 6$$

Eq. 6 is applicable in maneuvers such as breath holding, voluntary hyperventilation, or exercise. But Eq. 6 is invalid to greater or lesser degree when ambient pressure changes or $F_IO_2 \neq 0.209$, or some combination of both *until* a new P_AN_2 equilibrium is established.

NH necessarily requires N_2 molecules to move from the lungs into the tissues while HH requires N_2 molecules to move from the tissues into the lungs, each moving under different concentration gradients and possibly different time constants until a new dynamic equilibrium is achieved during a chronic NH or HH exposure.

The transient movement of N_2 changes P_AN_2 at constant PB, so changes the O_2-CO_2 point between NH and HH until the differences eventually become small and constant as each O_2-CO_2 point migrates onto its appropriate RQ diagonal near 0.8.

CONCLUSIONS

TABLE 2. Unresolved Issues Given Same Hypoxic P_IO_2

parameter	HH	NH	acute➔*time*➔chronic
f_v	↓	↑	?
V_T	↓	↑	?
V_E	↓	↑	?
V_A	↓	↑	?
VCO_2	↓	↑	?
VO_2	↓	↑	?
RQ	↓	↑	?
V_A/VCO_2	↑	↓	?
P_AO_2	↓	↑	?
P_ACO_2	↓	↑	?
F_EN_2/F_IN_2	↑	↓	?
V_D/V_T	?	?	?
Q	?	?	?
V_A/Q	↑ (5)	?	?
pH_{CSF}	?	?	?
% AMS	↑	↓	?

There is not an adequate integrated physiological understanding of the determinants of P_AO_2 and P_ACO_2 under NH and HH given the same hypoxic pO_2 to claim a device that provides TRUE isohypoxia.

Isohypoxia is defined as the same distribution of hypoxia signs and symptoms under any circumstances of equivalent hypoxic dose, and hypoxic pO_2 or even P_IO_2 are incomplete doses (3).

Both time-dependent P_AO_2 and P_ACO_2 should be considered in a calculation of hypoxic dose.

We *hypothesize* that the integrated hypoxic dose over the same exposure time is less in NH than HH for the same hypoxic P_IO_2.

Some devices that claim an equivalent HH experience under NH conditions significantly overestimate the HH condition, especially when simulating altitudes above 10,000 feet (3,048 m).

At best, the claim should be that the devices provide an *approximate* HH experience since they only duplicate the ambient pO_2 at sea level as at altitude (iso-pO_2 machines).

A first step ~~a~~ approach to reduce the overestimation is to at least provide machines that create the same P_IO_2 (iso-P_IO_2 machines) conditions at sea level as at the target altitude, a simple software upgrade from Eq. 3 to Eq. 4.

REFERENCES

1. Artino Jr AR, Folga RV, Vacchiano C. Normobaric hypoxia training: the effects of breathing-gas flow rate on symptoms. Aviat Space Environ Med 2009; 80:547-52.
2. Conkin J. pH_2O and simulated hypobaric hypoxia. Aviat Space Environ Med (in press).
3. Conkin J, Wessel JH, III. Critique of the equivalent air altitude model. Aviat Space Environ Med 2008; 79:975-82.
4. Fenn WO, Rahn H, Otis AB. A theoretical study of the composition of the alveolar air at altitude. Amer J Physiol 1946; 146:637-53.
5. Haab P, et al. Ventilation-perfusion relationships during high-altitude adaptation. J Appl Physiol 1969; 26:77-81.
6. Loeppky JA, et al. Ventilation during simulated altitude, normobaric hypoxia, and normoxic hypobaria. Respir Physiol 1997; 107:231-9.
7. Moniaga NC, Griswold CA. Loss of consciousness and seizure during normobaric hypoxia training. Aviat Space Environ Med 2009; 80:485-8.
8. Self DA, et al. Physiological equivalence of normobaric and hypobaric exposures of humans to 25,000 feet (7620 m). Aviat Space Environ Med 2011; 82:97-103.
9. U.S. Standard Atmosphere – 1976. US Committee on Extension to the Standard Atmosphere. NOAA, Washington D.C. (NOAA-S/T 76-15672: Superintendent of Documents, U.S. Government Printing Office (Stock No. 003-017-00323-0), 1976.
10. West JB. Safe upper limits for oxygen enrichment of room air at high altitude. High Alt Med and Biol 2001; 2:47-51.