Respiratory Muscle Training and Exercise Endurance at Altitude

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BACKGROUND: Climbing and trekking at altitude are common recreational and military activities. Physiological effects of altitude are hypoxia and hyperventilation. The hyperventilatory response to altitude may cause respiratory muscle fatigue and reduce sustained submaximal exercise. Voluntary isocapnic hyperpnea respiratory muscle training (VIHT) improves exercise endurance at sea level and at depth. The purpose of this study was to test the hypothesis that VIHT would improve exercise time at altitude [3600 m (11,811 ft)] compared to control and placebo groups.

METHODS: Subjects pedaled an ergometer until exhaustion at simulated altitude in a hypobaric chamber while noninvasive arterial saturation (S_aO_2), ventilation ($\dot{V}_E$), and oxygen consumption ($\dot{V}O_2$) were measured.

RESULTS: As expected, S_aO_2 decreased to 88 $\pm$ 4% saturation at rest and to 81 $\pm$ 2% during exercise, and was not affected by VIHT. VIHT resulted in a 40% increase in maximal training $\dot{V}_E$ compared to pre-VIHT. Exercise endurance significantly increased 44% after VIHT ($P = <0.001$). $\dot{V}O_2$ (30 $\pm$ 3 ml $\cdot$ kg^{-1} $\cdot$ min^{-1}) and heart rate (177 $\pm$ 10 bpm) did not change during exercise and were not affected by VIHT ($P = 0.531$). Pre-VIHT $\dot{V}_E$ increased 21–27% during the initial 12 min of exercise, after which it decreased 17% at 17.7 $\pm$ 6.0 min. $\dot{V}_E$ at altitude post-VIHT increased more (49%) for longer (21 min) and decreased less (11% at 25.4 $\pm$ 6.7 min).

DISCUSSION: VIHT improved exercise time at altitude and sustained $\dot{V}_E$. This suggests that VIHT reduced respiratory muscle fatigue and would be useful to trekkers and military personnel working at altitude.

KEYWORDS: altitude, exercise, respiration, arterial CO_2, brain blood flow.

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Climbing and trekking at altitude are common recreational activities and are also, sometimes with short notice, required in military operations. A practical limitation for physical activity in unacclimatized individuals is at about 3658 m (12,000 ft) since, at that altitude, the P_{O_2} of atmospheric air humidified at body temperature is about 60 mmHg, which places the arterial P_{O_2} well into the steep down slope of the oxygen binding curve of the blood as objectively reflected by a depressed maximal oxygen consumption ($\dot{V}O_{2max}$).[6] Another practical limitation is that the operational ceiling in nonpressurized aircraft is limited to 3658 m (12,000 ft) by Federal Aviation Administration regulations (www.faa.gov, regulation 91.211). At higher altitudes individual physical effort and endurance are required. Although most high-altitude hypoxia is well tolerated, some persons may manifest maladaptive responses, leading to acute altitude illness.[24]

A well-known effect of altitude hypoxia is the chemoreflex initiated increase in pulmonary ventilation ($\dot{V}_E$).[7,28] This hyperventilation results in an increase in the work of breathing[2] and, thus, the energy cost of ventilation.[27] Respiratory muscle fatigue during sustained exercise also may lead to an additional, paradoxical hyper-ventilatory drive, leading to further respiratory muscle fatigue[17,26] and secondarily to locomotor muscle fatigue.[14,15] $\dot{V}O_{2max}$ is reduced at altitude[11] due to the low arterial oxygen saturation (S_aO_2) in addition to the low maximal cardiac output (CO).[11] These altitude-induced changes would also likely affect submaximal exercise capacity.

Respiratory muscle fatigue has been shown to limit submaximal and maximal exercise performance in healthy individuals

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at 1 ATA.[16] While respiratory muscles account for about 4% of the total oxygen consumption during exercise at 1 ATA, that percentage increases to 10–15% during maximal exercise when there is hyperventilation and when there is airflow limitation.[1] This suggests that respiratory muscle fatigue would occur at altitude and limit exercise capacity.

Respiratory muscle training (RMT) can markedly enhance exercise endurance at ground level by 30 to 69%[5,22] and is particularly effective in environmental conditions, such as diving, that a priori challenge lung function where it has been reported to be increased by 86%.[26,32] Voluntary isocapnic hyperpnea training (VIHT) improves respiratory muscle endurance[23,25] and exercise endurance at 1 ATA.[5,22,25] The weight of the evidence at 1 ATA suggests that VIHT makes the ventilatory system more resistant to muscular fatigue during exercise[30] and prevents a decline in tidal volume (VT).[5,22,26]

Based on previous studies, the purpose of the current study was to test the hypothesis that VIHT would improve exercise performance at simulated altitude up to 3600 m (11,811 ft). Additionally, we hypothesized that improved exercise capacity of the respiratory muscles would allow hypoxia-induced hyperventilation to be sustained for a longer time.

METHODS

The study was approved by the Institutional Review Board. After recruitment the subjects read the informed consent form, were encouraged to ask questions, and then signed the form if willing to participate. A health history was obtained and a physical exam, including a chest X-ray, was administered prior to participation.

The study was a controlled repeated measures design with the subjects acting as their own controls. Two groups ($N = 5$ each) were recruited separately and both completed 4 wk of VIHT; one group was tested at 3000 m (9843 ft) and the other group at 3600 m (11,811 ft). The subjects tested at 3658 m (12,000 ft) were retested 3 mo after completing VIHT when their respiratory muscles were detrained,[31] at which time this group served as a control group (when compared to the respective pre-VIHT data). For this part of the study they are referred to as the post-VIHT inactivity group (Pst-$VIHT_{inact}$) group. A third group was a placebo control (VIHTp), which performed a placebo VIHT (described below) that involved five subjects undergoing the endurance exercise test at 3658 m (12,000 ft).

Subjects

Recruited from the local university community were 15 male subjects. Only men were studied due to a requirement from the study sponsor, whose personnel are currently only men, and to avoid effects of hypoxia on potential pregnancies in women. The subjects were familiarized with the protocol and procedures, including a training flight in the altitude chamber, and then they performed a short trial period of VIHT. The subjects were participating in exercise training at least 3 d/wk, but were not athletes. The subjects were nonsmokers and were given an aviation physical, including chest X-ray, to eliminate comorbid conditions. There were no significant differences in the characteristics of the subjects among the three groups. On average they were 23.7 ± 2.2 yr of age, 178 ± 2 cm in height, 74.8 ± 3.1 kg in weight, and had a cycling $\dot{V}O_{2max}$ of 40 ± 3 $ml \cdot kg^{-1} \cdot min^{-1}$.

Procedures

Due to the complexity and cost of performing these experiments and the potential for acute high-altitude illness during exercise,[24] one group was studied at 3000 m (9843 ft) first. As the results were positive and there were no limitations observed in the first group, a second group was studied at 3600 m (11,811 ft). As there was a beneficial effect of VIHT on exercise endurance and the experiments at 3600 m were successful, the Pst-$VIHT_{inact.}$ and the VIHTp groups were studied at 3600 m. The subjects were not randomized as they often encountered each other during testing and training and it was undesirable that individuals in the Pst-$VIHT_{inact}$ group and VIHTp group would recognize that they were following different protocols than the VIHT group.

The subjects initially underwent a maximum oxygen uptake test on an electrically braked cycle ergometer (Collins Pedal Mate, Warren E. Collins, Braintree, MA) at sea level pressure inside the altitude chamber. The work rate was started at 50 W for 3 min and increased by 50 W every 2 min until voluntary exhaustion. A week later they completed an exercise endurance test to voluntary exhaustion while at altitude. Based on previous work, subjects exercised at 75% of sea level pretraining $\dot{V}O_{2max}$ at 3000 m (9843 ft) and 70% of sea level per-training $\dot{V}O_{2max}$ at 3600 m (11,811 ft) to have the same exercise time at the two different altitudes and be comparable to previous experiments at 1 ATA that used 80% of sea level $\dot{V}O_{2max}$. After these pre-VIHT tests the subjects completed 4 wk of VIHT or placebo VIHT (VIHTp). A week after completion of the VIHT or VIHTp, their exercise endurance capacity at altitude was again tested. To optimize the protocol and compare to the VIHT group, the VIHTp and $VIHT_{inactive}$ groups were tested at 3600 m.

The altitude tests were performed at simulated altitudes of 3000 m (9843 ft) and 3600 m (11,811 ft) with the subjects seated erect on a cycle ergometer in air. They breathed chamber air during ascent and decent, but breathed hypobaric hypoxic gas from a bag-in-box system via a two-way mouthpiece at chamber pressure during exercise. VIHT was performed 3 d/wk for 30 min/d for 4 wk. Each subject was provided a computer-supported training device built in-house on which he performed the assigned VIHT or placebo VIHT training. Each week two sessions were performed off campus and one in the laboratory.

During the training sessions, the VIHT groups breathed through a lightweight mouthpiece that had inspiratory and expiratory check valves and a rebreathing bag attached. This contrivance was designed to have a low breathing resistance that allowed for high levels of ventilation. Isocapnic blood levels were maintained during VIHT via the rebreathing bag, which was filled with part of the expiration and then inhaled during

the next inspiration. As the rebreathing bag emptied, fresh air entered through the lightly spring-loaded inspiration valve. The volume of fresh air inspired in each breath was regulated by the natural regulation of breathing, which was always adequate to maintain isocapnia as verified by measurements of expired air end-tidal CO_2 during training sessions in an earlier study in our laboratory using the same techniques and equipment.[32] The subject's breathing frequency during VIHT was monitored by an electronic pressure gauge in the mouthpiece so as to verify that breathing kept pace with synchronized visual and auditory signals from an electronic metronome. The volume of the rebreathing bag was initially set at a value representing approximately 55% of the subject's slow vital capacity (SVC). The breathing frequency (f_b) was selected by dividing 60% of the subject's earlier measured maximal voluntary ventilation (MVV) by the bag volume such that $f_b = MVV\ (0.60) / V_{bag}$. If needed, the bag volume was adjusted so that it corresponded with an f_b that the subject could maintain for approximately 30 min. In each successive daily session, the subject then had to increase the f_b by 1-2 breaths/min after 20 min of training. When possible, they then continued at this higher frequency for the last 10 min of training. The next training session began at the highest frequency achieved in the previous session and this was then maintained for 20 min followed by an increase of 1-2 breaths/min for the remaining 10 min. When the f_b reached 50 breaths/min, the bag volume was increased by 0.1 L and f_b was reduced to the value that would maintain the same level of ventilation, and the cycle was then repeated. A microprocessor in the training device stored every breath during training and the investigators reviewed the files during the weekly in-lab training to monitor and verify that VIHT was performed properly each week.

The VIHTp was performed on the same respiratory training devices as was VIHT except that the rebreathing bag had been removed. This training was similar to one previously successfully used in an earlier study.[32] Specifically, the subjects took a maximal inspiration, held the breath for 10 s, and then exhaled and resumed spontaneous breathing for the next 20 s. These maneuvers were repeated every 30 s for 30 min three times per week for 4 wk. The subjects had been informed that the purpose of this "training" was to see if it would modify breathing function. Unbeknownst to them it had been determined in the previous study it did not affect pulmonary or exercise performance.[32]

Before the VIHT started the subject's maximum oxygen uptake ($\dot{V}O_{2max}$) was determined using a progressive resistance test on an electrically braked (Collins Pedal Mate) cycle ergometer. Subjects pedaled at 60 rpm and the work rate was set initially at 50 W (3 min), and then increased in 50-W increments every 2 min until the subject reached voluntary exhaustion. Oxygen consumption was determined by standard open circuit methods (see below for description).

After the $\dot{V}O_{2max}$ test the subjects completed cycle endurance tests to voluntary exhaustion at a workload of 75% at 3000 m (9843 ft) or 70% at 3600 m (11,811 ft) of the predetermined sea level $\dot{V}O_{2max}$. In addition to exercise time, measures of ECG, noninvasive oxygen saturation (S_aO_2) (pulse-oximeter, Masimo, Irvine, CA), $\dot{V}O_2$, $\dot{V}_E$, and end-tidal CO_2 ($P_{ET}CO_2$) were measured throughout the test in all conditions.

The subject and two tenders participated inside the altitude chamber, a dedicated chamber operator controlled ascents to and descents from altitude and observed the subjects and tenders via a porthole and video monitor, and another technician monitored the data collection. An investigator and medical monitor supervised the experiments and, to ensure safety, continuously observed ECG and S_aO_2. The subject wore a harness to prevent him from falling from the bike in case of loss of consciousness due to hypoxia. In addition, a gurney-like platform was available inside the chamber to lay the subject supine in the event of loss of consciousness and an oxygen breathing mask was kept on stand-by.

At the surface, noninvasive S_aO_2 and heart rate (HR) were measured. After sea level control readings, the chamber was evacuated to simulated altitude. At altitude, control readings were taken again at rest. Respiratory variables were measured with a bag-in-box system. The bag-in-box system had a linear displacement spirometer connected to the box for setting inspired bag volume and determining, VT, $\dot{V}_E$, and breathing frequency (b_f) and to calculate $\dot{V}O_2$ during the experiment. The subject breathed from a mouthpiece with one way inspiratory and expiratory valves mounted inside a facemask. Hoses for inspired and expired air running from the mouthpiece were connected to the two gas bags (meteorological balloons) inside the bag-in-box. The inspiratory bag had a near constant flow of fresh humidified air from a compressed–air tank. A mass spectrometer (Model II, Perkin Elmer, Pomona, CA) sampled the mixed expired gas composition as it was piped (see details below) through a dry gas meter on the outside of the chamber for measurement of $\dot{V}_E$. The necessary pressure head to force the gas out to the outside 1-atm pressure was obtained by temporarily raising the pressure in the box surrounding the breathing bags with compressed air. A separate mass spectrometer (Model II, Perkin Elmer) monitored air composition on the exhalation side of the mouthpiece for determination of $P_{ET}CO_2$.

After resting data collection, the subject began pedaling at 60–65 rpm with a workload of 70% or 75% [3000 m (9843 ft) and 3600 m (11,811 ft), respectively] of his predetermined sea level $\dot{V}O_{2max}$. Endurance exercise time was the time from the start of exercise until voluntary exhaustion, determined by the subject's inability to sustain the 60–65 rpm pedaling rate on the ergometer at the chosen work rate. When the subject had pedaled for 2 min, he was connected to the expiration bag in the bag-in-box for collection of the exhaled gas (typically 1 min) and during the same time recordings of S_aO_2, HR, and capillary blood flow velocity (CBFv) were made, after which the subject was switched back to the breathing bag providing air for inspiration. The process of collecting and dumping expired gas was repeated every 3 min until the subject indicated that he felt he could only do about 1 more minute of exercise, and then a final bag was collected. After completion of data collection, the chamber pressure was restored to 1 ATA.

Statistical Analysis

The data are represented as mean and standard deviation for the individual variables. As the main aim of this study was to determine the effect of VIHT on exercise performance and the absence of significant differences between measured variables, the data for the subjects tested at 3000 m (9843 ft) and 3600 m (11,811 ft) were combined for statistical analysis ($N = 10$). Increasing the number to 10 also increased the statistical power of the analysis. The VIHT, Pst-VIHT$_{inact}$ group, and the VIHTp group pre- and post-VIHT testing data were compared by repeated measures ANOVA. The data analysis for all tests passed the Normality and Equal Variance tests. All statistical comparisons were made using SigmaPlot (San Jose, CA). A level of significance of ≤ 0.05 was used for all comparisons.

RESULTS

The following abbreviations will be used in the result presentation below: For the point in time when a Pre-VIHT run is terminated due to exhaustion: Pre-VIHT-ExhstTm; for the point in time when a Post-VIHT run is terminated due to exhaustion: Pst-VIHT-ExhstTm; for the point in time during an ongoing Pst-VIHT run when the earlier recorded Pre-VIHT-ExhstTm is reached and data on physiological variables are collected: Pre-VIHT-EqStTm and Pst-VIHT-EqStTm (equal stop time).

All 15 subjects completed their respective VIHT or VIHTp and pre- and post-testing. The 10 subjects that completed VIHT performed 12 training sessions. The mean ($\pm$ SD) of the training ventilations are shown as functions of the number of training sessions for the VIHT group in **Fig. 1**. There were increases in training ventilation levels amounting to about a 40% increase over the 12 wk (Fig. 1) [$F(8,11) = 26.5$, $P = <0.001$]. The VIHTp group breathing procedure was held constant over the 4 wk of training; thus, there was no increase in training ventilation.

The voluntary exercise time to exhaustion at altitude for all groups are shown in **Fig. 2**. The 44% increase in exercise endurance comparing Post-VIHT to Pre-VIHT was significant [Fig. 2, $F(9,1) = 56.67$, $P = <0.001$]. Overall 9 out of the 10 subjects in the training group improved their exercise time to exhaustion. There were no significant differences in pre- compared to post-testing for the Pst-VIHT$_{inact}$ and the VIHTp [Fig. 2, $F(9,1) = 0.074$, $P = 0.872$; $F(4,1) = 2.195$, $P = 0.213$, respectively].

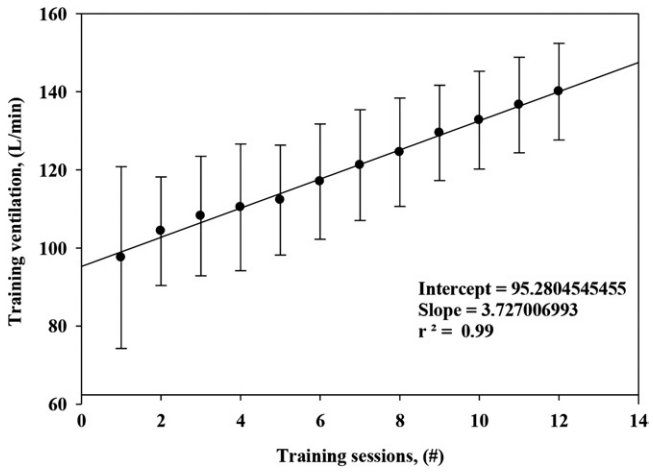

Fig. 1. The mean $\pm$ SD training ventilation that was achieved with VIHT in the present training protocol as a function of the number of training sessions.

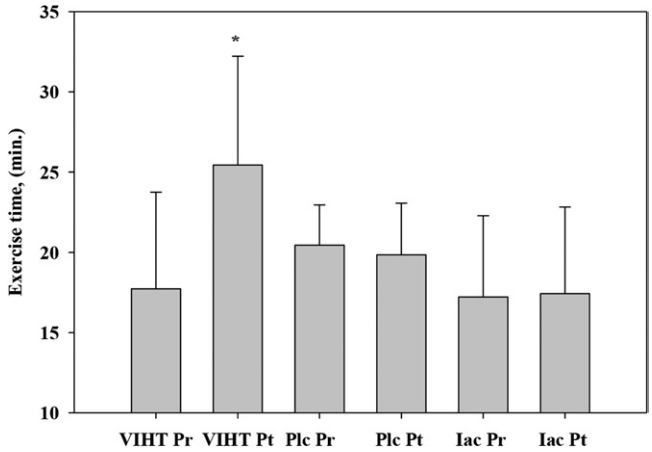

Fig. 2. Endurance exercise time (on vertical axis) is shown for pretesting (Pr) and posttesting (Pt) for the VIHT group, placebo group (Plc), and inactive control group (Iac). The * indicates a significant difference from Pre- to Post-tests.

During the exercise endurance tests, $\dot{V}O_2$ was 2.24 $\pm$ 0.20 L $\cdot$ min^{-1}. Throughout the exercise there was no change in $\dot{V}O_2$ as a function of exercise time. Furthermore, there were no differences in $\dot{V}O_2$ between pre- and post-VIHT values at any point in time [$F(9,1) = 0.685$, $P = 0.531$].

Noninvasive S_aO_2 at sea level was not different among the groups and averaged 98 $\pm$ 1%. During both rest and exercise at altitude, S_aO_2 decreased within the first 2–5 min and then was stable throughout the duration of each investigated condition. Thus, the steady state values at each condition were compared. During rest at altitude the S_aO_2 decreased from the sea level value to 88 $\pm$ 4% saturation and, as expected, these values were not significantly affected by VIHT [$F(9,1) = 1.173$, $P = 0.79$]. During exercise, S_aO_2 decreased further to 81 $\pm$ 2% pre-VIHT and, as expected, these values were not affected by VIHT [$F(9,1) = 1.23$, $P = 0.46$].

Post-VIHT data at the time where the subjects stopped on the Pre-VIHT experiment were compared to Pre-VIHT data at this point (Pre-Stop Time). The post-VIHT data at exhaustion (Post-Stop Time) were also compared to Pre-VIHT data at exhaustion.

All groups had similar $\dot{V}_E$ levels during the Pre-VIHT conditions during exercise. There were no differences in pre-RMT $\dot{V}_E$ during the initial (3–6 min) exercise for any of the groups. The average values were 85.84 $\pm$ 9.16 L $\cdot$ min^{-1} for VIHT and 85.77 $\pm$ 6.93 L $\cdot$ min^{-1} for VIHTp [$F(14,2) = 1.04$, $P = 0.69$]. The averages of $\dot{V}_E$ data for Pre-VIHT and Post-VIHT for both altitude as a function of exercise time are shown in **Fig. 3**. As there were no Pre-Post differences in the control (VIHT$_{inact}$) or placebo (VIHTp) groups, the increased $\dot{V}_E$ Post-VIHT was likely due to VIHT.

Pre-VIHT, $\dot{V}_E$ at altitude (34 L $\dot{V}_E$/L $\dot{V}O_2$) was higher than at sea level (25 L $\dot{V}_E$/L $\dot{V}O_2$). This was also observed for the VIHTp

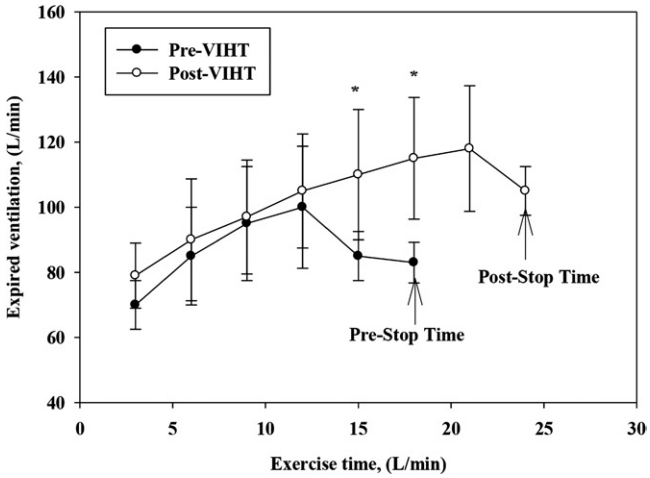

Fig. 3. Mean ± SD for exercise ventilations are plotted as a function of time for Pre-VIHT (black circles) and post-VIHT (white circles). The data points for the first gas collection at 3 min of exercise, at the time when the subject stopped exercising during the Pre-VIHT (Equal Stop) protocol and when they stooped post-VIHT (Stop post) are indicated for comparison. The * indicates that the post-VIHT values are significantly different from Pre-VIHT.

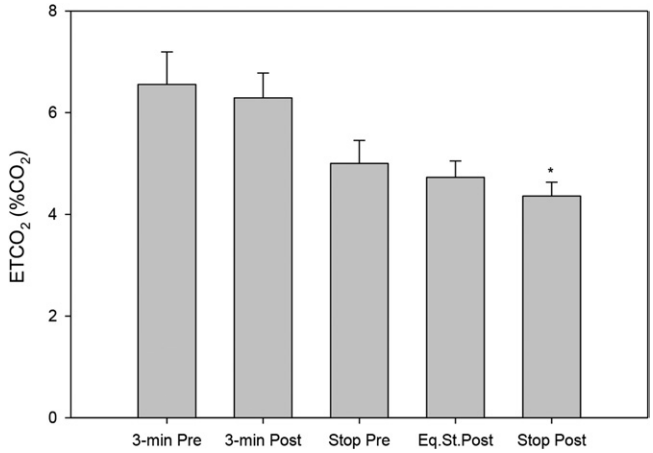

Fig. 4. Mean ± SD. End-tidal CO_2 ($P_{ET}CO_2$) is plotted for the third minute of exercise at the time when the subject stopped exercising during the Pre-VIHT (Equal Stop) protocol and when they stopped post-VIHT (Stop post) for Pre-VIHT and post-VIHT. The * indicates that the post-VIHT values are significantly different from Pre-VIHT.

group (34 L $\dot{V}_E$/L $\dot{V}O_2$). At altitude $\dot{V}_E$ pre-VIHT increased 21–27% during the initial 12 min of exercise, after which it decreased 17% (Fig. 3). The increased $\dot{V}_E$ was a result of increased b_f (25–40%) because there was a 6–12% reduction in VT. In addition, the increased $\dot{V}_E$ resulted in a decrease in $P_{ET}CO_2$ (10–20%), making a decrease in arterial CO_2 highly likely. At altitude, $\dot{V}_E$ post-VIHT increased 49% during the initial 21 min of exercise, after which it decreased 11% at 24 min (Fig. 3). Post-VIHT VT was maintained during the first 21 min of exercise and the increased $\dot{V}_E$ was a result of increased b_f (9%). VT was decreased at 24 min compared to 21 min post-VIHT. The decrease in $\dot{V}_E$ and VT both pre- and post-VIHT suggest respiratory muscle fatigue, which occurred later (21 min vs. 12 min) after VIHT, but not in $VIHT_{inactive}$ or VIHTp, and was less (11% vs. 17%). These data demonstrate that VIHT, but not VIHTp, resulted in increased fatigue resistance during exercise and is likely responsible, at least in part, for the improvement in exercise time described above.

Post-VIHT $\dot{V}_E/\dot{V}O_2$ increased 11% above what it was at the EqStTm point and was 17% higher than at the Pre-VIHT-ExhstTm. At the EqStTm, b_f was 7% higher than at the Pre-VIHT-ExhstTm (which had determined said EqStTm) and 15% higher than at Pre-VIHT-StTm. VTs were not significantly different at exhaustion than at EqStTm, and were 7% higher than at Pre-VIHT-ExhstTm. $P_{ET}CO_2$ was 7% lower at Pst-VIHT-ExhstTm than at EqStTm, and the $P_{ET}CO_2$ Pst-VIHT-ExhstTm value was 10% lower than pre-VIHT (**Fig. 4**).

At altitude $\dot{V}_E$ post-VIHT when exhaustion was reached had increased 15% from the EqStTm point and was 7% higher than at the Pre-VIHT-ExhstTm. At Pst-VIHT-ExhstTm b_f was 4% higher than at EqStTm, but not different from pre-VIHT. Tidal volumes were not significantly different at exhaustion than at EqStTm, and were 9% higher than pre-VIHT. $P_{ET}CO_2$ was 11% lower at Pst-VIHT-ExhstTm than at EqStTm and this value was 7% lower than at Pre-VIHT-ExhstTm.

In the VIHTp group's pre- and post-VIHT $\dot{V}_E$, there were no differences between pre- and post-placebo training. At Pst-VIHTp-ExhstTm b_f was 13% higher than at the EqStTm, but not different from the Pre-VIHTp-ExhstTm value. The VTs were not significantly different at Pst-VIHTp-ExhstTm than at EqStTm and were also not different between Pre-VIHTp and Pst-VIHTp at any time point. End-tidal CO_2 was not significantly different at Pst-VIHTp-ExhstTm than at Pre-VIHTp-ExhstTm and at EqStTm, and these values were not different from each other.

At the same work rate as used at altitude, HR increased from 152 ± 8 bpm at sea level to 168 ± 6 bpm Pre-VIHT and 176 ± 4 bpm Pst-VIHT at the fifth min of exercise. HR increased 13 bpm during the Pre-VIHT and was 16 bpm Pst-VIHT from the fifth to the last minute of the endurance exercise. The higher HR Pst-VIHT is consistent with the longer exercise time achieved. The HR during exercise at altitude Pre-VIHT increased from the initial value (173 ± 7 bpm) to 177 ± 10 bpm at exhaustion, but these differences did not achieve significance ($P = 0.19$). In the $VIHT_{inact}$ and VIHTp groups, HR increased from the initial exercise value of 170 ± 9 bpm to 181 ± 10 bpm at exhaustion, but this difference was not significant ($P = 0.18$). There was no significant difference in HR during the exercise test between Pre- and Pst-VIHT tests at any time point in VIHT, $VIHT_{inact}$, or VIHTp groups. At exhaustion the values were 177 ± 10 bpm Pre-VIHT and 178 ± 12 bpm Pst-VIHT, and they were not different from each other ($P = 0.59$).

DISCUSSION

The present study provides evidence that VIHT performed while other muscles remain resting significantly enhanced endurance exercise duration by 44% at 75% $\dot{V}O_{2max}$ at simulated altitude up to 3600 m (11,811 ft) in contrast to the lack of improvement in the placebo and control groups. VIHT resulted

in the ability to maintain hypoxic-induced hyperventilation longer when compared to pre-VIHT and the control and placebo groups, suggesting that it delayed the onset of respiratory muscle fatigue and prolonged exercise time.

The effects of the simulated altitude used in the present study on S_aO_2, $\dot{V}_E$, and $P_{ET}CO_2$ pre-VIHT are not surprising and agree with previous studies.[7,28,31] While CO is increased during submaximal exercise at altitude, maximal CO is decreased,[11] which when combined with the reduced S_aO_2 results in a significant reduction in $\dot{V}O_{2max}$. This means that the 75% of maximal sea level $\dot{V}O_2$ workload used in the endurance test was actually a higher percentage of the maximal $\dot{V}O_2$ at altitude. A further factor is the increased work of breathing[2] and energy cost of ventilation[27] that increases blood flow to the respiratory muscles. Recent studies at 1 ATA have shown respiratory muscle fatigue, even in highly trained individuals, which leads to exercise intolerance.[3,16] It has also been shown that both hypoxia and exercise result in diaphragmatic fatigue at altitude.[13] Respiratory muscles account for up to 15% of total $\dot{V}O_2$ during maximal exercise when there are hyperventilation and airflow limitations,[2,27] as is the case at altitude. The increased work of breathing and energy cost result in respiratory muscle vasodilatation and lower extremity vasoconstriction by type III–IV afferent nerves in the respiratory muscles ("stealing").[15,16] In the present study at altitude it is likely that the increased work of breathing,[2] resulting in increased energy cost[27] and respiratory muscle fatigue (in ability to sustain $\dot{V}_E$), led to stealing of blood and a decreased exercise capacity. Delaying respiratory muscle fatigue by VIHT may attenuate reflex vasoconstrictor signals sent to the limb vasculature and improve locomotor muscle blood flow and lactate clearance during exercise.[8,14,15] Further evidence for this redistribution of blood flow away from respiratory muscles and toward locomotor muscles is that some studies have reported reduced lactates post-RMT.[22,29]

There is little doubt that VIHT improves respiratory muscle exercise endurance[22,25,29] at 1 ATA, including during cycling,[5,25,29] running,[22] and swimming.[26,32] The weight of the evidence suggests that VIHT makes the ventilatory system more resistant to fatigue during exercise.[26,30] Improved respiratory and locomotor muscle endurance has been shown to be connected with reduced work of breathing,[17] increased efficiency,[17] reduced $\dot{V}O_2$ for a specific $\dot{V}_E$,[17] and enhanced oxidative metabolism in the respiratory muscles,[4,12,23] making them more fatigue resistant.

There have been other studies that have examined the potential effects of respiratory training on physiology and exercise performance at altitude or during hypoxia. A previous study[9] observed a reduced $\dot{V}_E$ during exercise in hypoxia after inspiratory muscle training, which is in agreement with a study at 1 ATA[22] and at depth[26,32] after VIHT, which was expected, but not shown in the present study. Another study that used deep breathing exercises in populations living at 2880 m (9449 ft) and 3760 m (12,336 ft) demonstrated an increase in resting S_aO_2. However, the VIHT used in the present study at altitude did not show this result at rest or during exercise, which is in agreement with other previous studies.[19,20] VIHT has been shown to blunt the altitude-induced increase in resting CO, which would increase transit time and could improve S_aO_2;[19] however, this is not likely the case during exercise where CO would be increased proportionally to the $\dot{V}O_2$, as in this study. In yet another study it was shown that yoga training resulted in less heart rate variability, lower $\dot{V}_E$, and lower b_f during altitude-induced hypoxia [5050 m (16,568 ft)],[8] which was not seen in the present study. Other studies have studied the effects of either resistive respiratory muscle training (RRMT) or VIHT, similar to what was used in the present study, on exercise capacity in hypoxia. One of these studies failed to show a benefit of VIHT on $\dot{V}O_{2max}$ during either normoxia or hypoxia.[10] This finding is not surprising as no other studies at 1 ATA[22] or greater[26,32] has shown a benefit to the cardiovascular responses to exercise, including $\dot{V}O_{2max}$. In addition, while CO at submaximal intensities is increased at altitude, maximal CO is depressed.[11] CO has also been shown not to be increased during VIHT,[32] and thus it is unlikely to be improved by VIHT.

One study did demonstrate an improvement in $\dot{V}O_{2max}$ in hypoxia ($F_IO_2 = 0.12$) and normoxia[19] after VIHT; however, it was conducted in conjunction with aerobic exercise training (50% $\dot{V}O_{2max}$ for 1 h). Yet studies in normoxia do not show an improvement in $\dot{V}O_{2max}$ after VIHT.[5,22] In hypoxic conditions, respiratory limitations to $\dot{V}O_{2max}$ have been reported,[6] but in another study VIHT did not improve $\dot{V}O_{2max}$ in hypoxia.[10] One study reported that VIHT did not improve exercise endurance at 80% of $\dot{V}O_{2max}$ in hypoxia,[19,20] which is not in agreement with the present study, which shows significant improvement in exercise endurance at 75% of sea level $\dot{V}O_{2max}$ at simulated altitude. However, that previous study did show improvement in exercise endurance at 80% of $\dot{V}O_{2max}$ in normoxia,[19] which is in agreement with many previous studies.[5,22,25] The weight of the evidence suggests that VIHT makes the ventilatory system more resistant to fatigue during endurance exercise.[30]

The present study showed that VIHT allowed the subjects to sustain $\dot{V}_E$ significantly longer and the reduction in $\dot{V}_E$ at exhaustion was less. Another study reported increased $\dot{V}_E$ during submaximal and maximal exercise as well as during an endurance run at 80% of $\dot{V}O_{2max}$[19] after VIHT, which is in agreement with the present study.

Perhaps an explanation of why inspiratory resistance respiratory muscle training did not improve exercise endurance at altitude is that, in addition to inspired flow resistance in individuals at altitude during higher-intensity exercise,[18] there is also increased expiratory flow resistance.[2] This further increases the work of breathing and is not subject to changes during inspiratory muscle training, but is during VIHT. This point is supported by observations that unloading the respiratory muscles reduces the work of breathing during cycling at altitude,[21] resulting in a reduction of $\dot{V}O_2$ and CO at 1 ATA.[15] This could also be effective in hypoxia as previously shown.[14] The potential differences in the results of exercise endurance in the present study at altitude and the previous study in hypoxia[19] could be differences in S_aO_2, the absence of barometric pressure effects in hypoxia that are there at altitude, the differences in work rate (75% vs. 80% $\dot{V}O_{2max}$, respectively), and that in the previous

study the work rate was the same in both conditions. The reduced $\dot{V}O_{2max}$ in hypoxia would mean the exercise intensities used in the present study would have been at a higher percentage of $\dot{V}O_{2max}$ than in normoxia.

A major difference in 1 ATA and altitude and the hyperbaric environment, in addition to changes in S_aO_2, is gas density. One might expect that the lower gas density at altitude, but not in hypoxia at 1 ATA, would reduce the work of breathing and energy cost of ventilation and, thus, VIHT would not improve exercise performance. However, the work of breathing at altitude is increased as mentioned above. One study showed that assisted ventilation at moderate altitude reduced the work of breathing.[21] Examining the effects of VIHT at 1 ATA results in about a 30% improvement in exercise performance. At depth (increased gas density) the improvement was reported to be 86%. Therefore, a 43% improvement at altitude would appear to be reasonable.

The effect of reduced barometric pressure and consequently reduced P_{O_2} in inhaled air resulted in the expected reduction in arterial oxygen saturation at altitude, particularly during exercise. The effect of reduced oxygen saturation was a compensatory increase in ventilation compared to when exercising at the surface. The reduced oxygen delivery and respiratory muscle fatigue likely resulted in reductions in exercise performance before VIHT had been performed as the subjects could not sustain ventilation during the endurance exercise. VIHT resulted in an increase in voluntary exercise time to exhaustion (43%) in young male subjects. Importantly, there were no significant changes in exercise endurance for the placebo or inactive control groups. The findings of the present study suggest that VIHT can substantially benefit trekkers and military personnel who are working at altitude. The results of the present study have to be confirmed for female subjects and at different altitudes.

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