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ORIGINAL RESEARCH

High-Intensity Intermittent Exercise Increases Pulmonary Interstitial Edema at Altitude But Not at Simulated Altitude

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Objective.—Ascent to high altitude leads to a reduction in ambient pressure and a subsequent fall in available oxygen. The resulting hypoxia can lead to elevated pulmonary artery (PA) pressure, capillary stress, and an increase in interstitial fluid. This fluid can be assessed on lung ultrasound (LUS) by the presence of B-lines. We undertook a chamber and field study to assess the impact of high-intensity exercise in hypoxia on the development of pulmonary interstitial edema in healthy lowlanders.

Methods.—Thirteen volunteers completed a high-intensity intermittent exercise (HIIE) test at sea level, in acute normobaric hypoxia (12% O_2, approximately 4090 m equivalent altitude), and in hypobaric hypoxia during a field study at 4090 m after 6 days of acclimatization. Pulmonary interstitial edema was assessed by the evaluation of LUS B-lines.

Results.—After HIIE, no increase in B-lines was seen in normoxia, and a small increase was seen in acute normobaric hypoxia (2 ± 2; $P < .05$). During the field study at 4090 m, 12 participants (92%) demonstrated 7 ± 4 B-lines at rest, which increased to 17 ± 5 immediately after the exercise test ($P < .001$). An increase was evident in all participants. There was a reciprocal fall in peripheral arterial oxygen saturations (Spo_2) after exercise from $88\% \pm 4\%$ to $80\% \pm 8\%$ ($P < .01$). B-lines and Spo_2 in all participants returned to baseline levels within 4 hours.

Conclusions.—HIIE led to an increase in B-lines at altitude after subacute exposure but not during acute exposure at equivalent simulated altitude. This may indicate pulmonary interstitial edema.

Key words: altitude, exercise, ultrasound, high altitude pulmonary edema

Introduction

Ascent to high altitude leads to a reduction in ambient pressure and a subsequent fall in available oxygen. The vascular response to hypoxemia is vasodilatation, whereas in the human lung, it leads to vasoconstriction and a rise in pulmonary artery pressure.[1,2] This in turn increases microvascular hydrostatic pressure and may lead to the accumulation of a high-permeability type interstitial fluid (a capillary stress failure) in the presence of normal cardiac function.[3] In certain individuals, this can lead to a clinical deterioration, further hypoxemia, and the development of high altitude pulmonary edema (HAPE), a potentially life-threatening condition for climbers and trekkers in remote locations.[1,4]

Compared with sea level, completing the same aerobic work (eg, walking) at high altitude will be more strenuous because of the reduction in the maximal rate of oxygen uptake ($\dot{V}o_2max$) experienced at high altitude, meaning they will be working at a higher percentage of it.[5,6] Strenuous exercise has long been proposed as a potential risk factor for the development of HAPE.[7] Even in the absence of HAPE, most climbers and trekkers experience a degree of dyspnea and decreased

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performance at altitude, and it has been hypothesized that this may be related to an increase in interstitial lung fluid.[8]

Lung ultrasound (LUS) is a noninvasive technique for the assessment of a range of pulmonary and pleural disease.[9,10] Interstitial edema is characterized on LUS by the presence of B-lines, also known as ultrasound lung comets.[10,11] In hospital practice, B-lines have been correlated with chest x-ray and computed tomography scan assessments of interstitial edema as well as invasive measurements of extravascular lung water (EVLW) using thermodilution.[4,12,13]

The LUS technique has been used as both a clinical and research investigation at high altitudes, and its strength and weakness when used in this environment have been discussed in reviews by Fagenholz et al[14] and Wimalasena et al.[15]

Fagenholz et al[14] first reported the use of LUS as a diagnostic tool for HAPE in a prospective case-control study of patients admitted to the Himalayan Rescue Station in the Khumbu valley (5400 m). In their observational study, patients with a HAPE had a higher number of lung comets than controls, and their presence was negatively correlated with peripheral oxygen saturation.[16]

The use of LUS to describe subclinical pulmonary edema (also described as clinically silent HAPE) was first reported in a study by Pratali et al in 2010.[17] The authors performed LUS on 18 participants during a 2-week trek to Everest Base Camp. Fifteen participants exhibited B-lines at 3440 m, and all participants showed evidence of increased B-lines at 4790 m. In 2012, they followed up this study using LUS to show that patients who had chronic mountain sickness experienced a rapid increase in pulmonary interstitial fluid after exercise at altitude compared with healthy high altitude dwellers.[18]

Exercise-induced pulmonary edema and ventricular function during exercise at sea level have also been evaluated using LUS, with Agricola et al[19] reporting that exercise alone can lead to elevation of pulmonary arterial pressure sufficient to induce pulmonary edema.

Strenuous exercise at altitude has long been proposed as a potential risk factor for the development of HAPE, with many experienced climbers following the old adage that "slow and steady wins the race."[7] We hypothesized that high-intensity intermittent exercise (HIIE) at altitude would not only increase hypoxemia but also cause surges in pulmonary artery (PA) pressure that may lead to a capillary stress failure. Therefore, the primary objective of this study was to evaluate the hypothesis that strenuous exercise in a hypoxic environment will lead to an increase in B-lines in otherwise healthy individuals. The secondary objective was to compare whether any response would differ between acute normobaric and subacute hypobaric exposures.

Methods

PARTICIPANTS

Thirteen participants (3 women, 10 men; age, 37 ± 10 years [mean ± SD]; height, 179 ± 9 cm; body mass, 79 ± 12 kg) volunteered for the study. None of the participants had been to altitude in the 3 months before undergoing hypoxic testing. All participants were nonsmokers with no medical history of chronic lung disease. Participants gave their written informed consent, and ethical approval was granted by the University of Chichester Research Ethics Committee (protocol number 1011_39).

The study involved a HIIE test completed at sea level (Chichester, UK, 29 m) and acute hypoxia in a normobaric chamber (TISS model 201003=1, TIS Services UK, Medstead, UK) simulating an altitude of 4090 m (O_2 12.6%; CO_2 0.04%; N_2 balance) following a crossover design. Participants were subsequently tested in hypobaric hypoxia during the 2012 Birmingham Medical Research Expeditionary Society (BMRES) expedition to Bhutan (Jomulhari Base Camp, Jangothan, Bhutan). The acclimatization period comprised a 6-day ascent to the test altitude of 4090 m following a gentle ascent profile (approximately 400 m/d). The testing took place in a windproof hut, with the participants kept warm using sleeping bags and duvet jackets when required. All participants completed the tests in acute hypoxia and at high altitude, but 2 participants were unavailable for their scheduled sea level session.

HIGH-INTENSITY INTERMITTENT EXERCISE TEST

The HIIE test was developed as a practical means of applying a maximal exercise insult to all participants that required a contribution from both the aerobic and anaerobic energy systems, without the need to set a prescribed resistance related to either a threshold (eg, ventilatory or lactate threshold) or maximal rate of oxygen uptake ($\dot{V}O_2$max). The use of a prescribed resistance would have required participants to complete additional tests in each condition to develop individual power–$\dot{V}O_2$ regressions to estimate a set intensity above $\dot{V}O_2$max. The test was completed on a custom-made supine cycle ergometer (Alticycle, BMRES, Birmingham, UK) the details of which have been described in a previous publication.[20] Briefly, in use the Alticycle requires the individual to lie supine, constrained by a shoulder harness, with feet strapped into the pedals. Multistage