Losartan Does Not Prove To Be Protective Against Exercise-Induced Pulmonary Oedema at 5000m

Malein WL[1], Thomas OD[2], Edsell ME[3], Myers SD[4], Bradwell AR[5], Lucase SJE[6], Imray CH[7] and the BMRES

1.Dept. Anaesthesia, NHS Tayside and BMRES 2.Dept. Anaesthesia, Taunton and Somerset NHS Trust and BMRES 3.Dept Anaesthesia, St George's Healthcare NHS Trust and BMRES. 4. Dept. Sports and Exercise Sciences, University of Chichester and BMRES. 5. The University of Birmingham and BMRES. 6. School of Sport, Exercise and Rehabilitation Sciences University of Birmingham and BMRES. 7. University Hospitals Coventry and Warwickshire NHS Trust and Warwick Medical School and BMRES

Introduction

- Relative hypoxia at high altitude leads to increased pulmonary perfusion pressures and, if capillary stress failure occurs, High Altitude Pulmonary oedema (HAPE)

- Studies exist that link ACE gene polymorphisms conveying higher ACE activity, and thus angiotensin II levels, with a higher risk of developing HAPE

- Lung ultrasound (LUS) has been used successfully to show an increase in extravascular lung water (EVLW) using the presence of ultrasound B-lines in subjects following exercise at altitude

<u>We set out with two aims:</u>

1. Further evaluate the effect of exercise at altitude on the development of EVLW in the form of B-lines using LUS
2. Investigate the effect of taking Angiotensin II blocker Losartan on EVLW following exercise at altitude

Ultrasound B-line or ‘comet tail’ artefact arising from pleura between two rib spaces

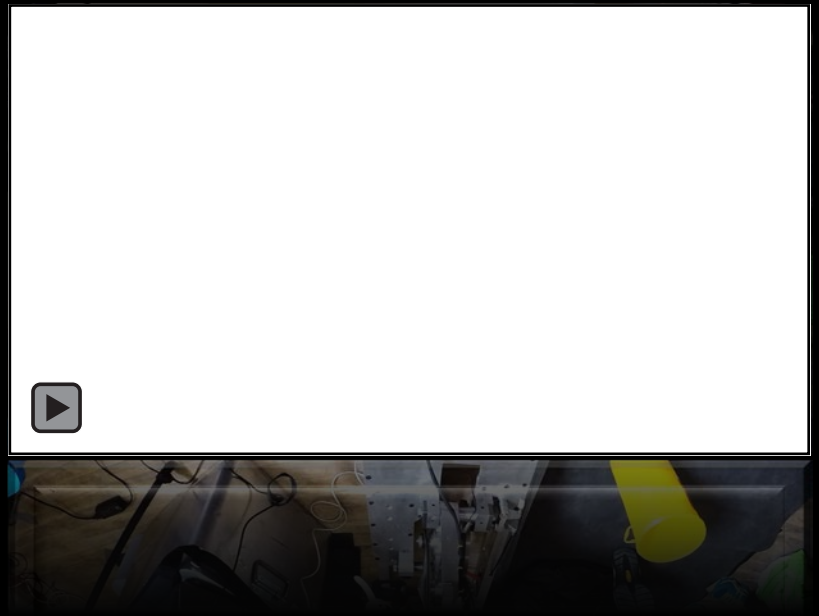
Methods

Twenty paired healthy volunteers had 8 zone LUS before and after graded exercise test to exhaustion on a recumbent cycle at the Whymper Hut, Ecuador at 5000m

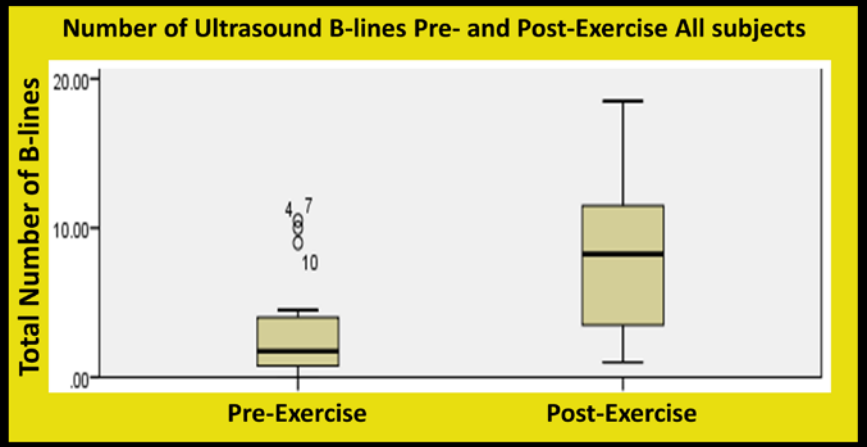
Subjects had ascended to 5000m over 7 days. They were double-blind randomised to take placebo or Losartan. Each ultrasound study was video recorded and analysed after the expedition by experienced LUS practitioners blinded to the randomisation and subject performance

The ultrasound studies were examined for the presence of B-lines, a well-recognised sign of lung interstitial oedema. Statistical analysis was performed on SPSS v22 using non-parametric Wilcoxon rank/paired *t*-test, with significance set at $p < .05$

Warm up before main testing



Results



- Significant whole cohort increase in mean number of B-lines following exercise. Mean 2.9 pre-exercise (+/- 3.3) vs mean 9.2 post-exercise (+/- 9.4) $p<.01$
- Significant fall in mean SpO_2 after exercise across both groups 76.6% (+/-7.4) pre-exercise vs 69.4% (+/-6.8%) $p<.01$

- No significant difference in mean B-lines pre- or post-exercise when Losartan compared to placebo
- No significant difference in mean SpO_2 pre- or post- exercise between Losartan and placebo groups
- No significant correlation demonstrated between number of B-lines and SpO_2

Conclusions

- Our study adds to growing evidence that exercise at high altitude can lead to an increase in pulmonary EVLW. This further supports exercise as a risk factor for HAPE.

- Despite its potential mechanism, we failed to elicit a significant protective effect of Losartan on the development of EVLW.

The recently renovated Whymper hut standing beneath Chimborazo- the furthest point on the earth's surface from its core

Discussion

- Although our failure to find a protective effect of losartan may represent an underpowered study, it may also reflect the complex multifactorial nature of the pathophysiology and susceptibilities of HAPE and development of EVLW at altitude
- We expect that the surge in pulmonary artery pressure in the hypoxic subject undertaking strenuous exercise may dilute any potential effect of Losartan. We predict that more potent pulmonary vasodilators such as Tadalafil or Nifedipine may be required to counteract the hydrostatic force created by such an exercise regime

- We agree that studies of larger and more diverse populations would be required to fully evaluate the effect of ACE inhibition or Angiotensin II blockade at altitude
- We have shown that ultrasound can be a useful tool to identify EVLW in a remote high altitude location

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