SCIENTIFIC LETTER

Pericardial effusions in healthy lowlanders after acute ascent to high altitude

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Acute ascent to high altitude causes illness ranging from relatively trivial symptoms of acute mountain sickness (AMS) to rapidly fatal conditions including high altitude pulmonary oedema (HAPE) and high altitude cerebral oedema (HACE).¹ HAPE, HACE, and oedema in other tissues at altitude may have a common pathogenesis in increased vascular permeability. There is some evidence that this increased permeability may be caused by oxidative stress.² In conducting a trial of antioxidant supplementation in healthy adults acutely exposed to high altitude, we unexpectedly found small pericardial effusions in many subjects at high altitude. This has not been reported elsewhere.

PARTICIPANTS AND METHODS

The study was approved by the Lothian Research Ethics Committee. Eighty three lowlanders (median age 21 years, range 18–30, 44 men) participated in a randomised, placebo controlled, double blind trial of antioxidant supplementation. Subjects flew to La Paz, Bolivia (3650 m) and after 4–5 days' acclimatisation ascended over 90 minutes to the Chacaltaya laboratory (5200 m) by off road vehicle. The antioxidant group (41 subjects) received 1 g L-ascorbic acid, 400 IU α tocopherol acetate, and 600 mg α lipoic acid/day in four divided doses starting five days before ascent to 5200 m.

The primary objective of the trial was to determine whether antioxidant supplementation could reduce the symptoms of AMS. A secondary outcome was the effect of antioxidant supplementation on pulmonary artery pressure. Therefore, an experienced echocardiographer performed Doppler echocardiography (Acuson Cypress; Siemens Medical Solutions UK) with the same equipment with consistent technique at sea level and within six hours, three days, and one week at 5200 m to estimate pulmonary artery pressure. Subjects were also examined by two dimensional echocardiography at these times and pericardial effusions were detected in the first group of lowlanders to be studied. Effusions were defined as a distinct circumferential separation of pericardial layers seen on two views, not including the substernal view.³

Fisher's exact test was used to compare the proportions of effusions in the antioxidant and placebo groups. Significance was taken at $p < 0.05$. Seven subjects were excluded for the following reasons: no echocardiography data (four subjects); gastroenteritis (two); and HAPE (one). Some data are missing from five subjects because of logistical problems. Twelve subjects were evacuated from the high altitude laboratory with symptoms of severe AMS and one subject was evacuated because of high pulmonary artery pressure. Data from these subjects are included up until the time of their evacuation. Figure 1 shows the number of subjects studied at each sample day.

RESULTS

Overall, 47% (36 of 76) of the subjects had an effusion at least once at 5200 m. Five subjects developed effusions within six hours of ascent to 5200 m. The percentage of subjects in the antioxidant group who had an effusion at least once was 38%

(14 of 37) versus 56% (22 of 39) in the placebo group (absolute risk reduction 19%, 95% confidence interval –4% to 41%, $p = 0.12$) (fig 1). Although all of the effusions were small (< 5 mm), this pericardial fluid was not seen in any of the subjects at sea level before or after the expedition. The majority of effusions that developed early persisted. Those subjects with effusions had no abnormal clinical findings and effusions were not associated with pulmonary artery pressure or clinically determined jugular venous pressure. AMS was most common on day 1 at 5200 m with a prevalence of 64%, falling to 10% by day 7. The development of a pericardial effusion and AMS were not consistently related.

DISCUSSION

This is the first report of pericardial effusions in healthy subjects after ascent to high altitude. Being present after less than one week at 5200 m, effusions are likely to occur in the average visitor to high altitude. Importantly, they occurred in the absence of clinically detectable cardiac dysfunction. Also, AMS symptoms and the presence of effusions were not related in our population. The time course of the development of effusions suggests that they are unlikely to be associated with AMS, which tends to develop within the first four days at high altitude.

The antioxidant group tended to have fewer effusions than did subjects taking placebo. Further investigation of this finding in a study of > 110 subjects would have $> 80\%$ power to confirm that antioxidant supplementation reduces the prevalence of pericardial effusions and would substantially advance our understanding of the mechanisms of abnormal fluid accumulation at high altitude.

HAPE and HACE are complications of rapid ascent to high altitude. Several authors have suggested that subclinical accumulations of fluid in these organs may be common in

Figure 1 Prevalence of effusions in treatment (antioxidant group) and placebo groups. Proportion (SE) of subjects with effusions are given, with numbers of subjects studied at each time point shown in brackets.