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Original Article

Incidence of high altitude pulmonary edema in low-landers during re-exposure to high altitude after a sojourn in the plains

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ABSTRACT

Background: There is uncertainty whether acclimatized low-landers who return to high altitude after a sojourn at low altitude have a higher incidence of pulmonary edema than during the first exposure to high altitude.

Methods: This was a prospective cohort study consisting of men ascending to 3400 m by road (N = 1003) or by air (N = 4178). The study compared the incidence of high altitude pulmonary edema during first exposure *vs* the incidence during re-exposure in each of these cohorts.

Results: Pulmonary edema occurred in 13 of the 4178 entries by air (Incidence: 0.31%, 95% CI: 0.18%–0.53%). The incidence during first exposure was 0.18% (0.05%–0.66%) and 0.36% (0.2%–0.64%) during re-exposure (Fisher Exact Test for differences in the incidence (two-tailed) $p = 0.534$). The relative risk for the re-exposure cohort was 1.95 (95% CI, 0.43%–8.80%). Pulmonary edema occurred in 3 of the 1003 road entrants (Incidence: 0.30%, 95% CI: 0.08%–0.95%). All three cases occurred in the re-exposure cohort.

Conclusion: The large overlap of confidence intervals between incidence during first exposure and re-exposure; the nature of the confidence interval of the relative risk; and the result of the Fisher exact test, all suggest that this difference in incidence could have occurred purely by chance. We did not find evidence for a significantly higher incidence of HAPE during re-entry to HA after a sojourn in the plains.

Introduction

High altitude pulmonary edema (HAPE) affects apparently healthy individuals when acutely exposed to the hypobaric hypoxia of high altitude (HA). There appear to be some geographical variations in its incidence. In the South American Andes, it is most frequent in those native residents of HA who descend to the plains for a sojourn and return to be re-exposed to hypoxia.[1] On the contrary, the incidence of HAPE is reported to be very low amongst the permanent residents of the Himalayan belt.[2–4]

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Generally, residents of low altitudes are susceptible to HAPE if acutely exposed to HA. Some suffer from HAPE during the first exposure to HA while others remain unaffected and acclimatize well. The incidence of HAPE amongst such previously unacclimatized subjects has been variously reported to range between about 0.01% and about 5%.[5,6] Most residents of low altitudes remain healthy on returning to HA after sojourns in the plains, but some suffer from HAPE during the re-exposure to hypoxia.[1,7]

In the past, prevalence data from hospital records and other cross-sectional studies have shown that, at any given time, most HAPE patients were those who had been re-exposed to HA.[6,7] These observations formed the basis of the belief that re-exposure to HA, after a sojourn in the plains, carries a higher risk for HAPE.

However, the larger absolute number of HAPE patients with a history of recent re-exposure to HA may have another explanation. Any individual enters HA for the first time only once (the first exposure) but may leave and re-enter on several occasions (re-exposures). In any group of people the total number of instances of re-exposure to HA is therefore necessarily larger than the total number of first exposures. Since the population-at-risk is larger during re-exposure it is expected that a larger number of HAPE patients at any given time will be from this group of individuals.

Most earlier estimates of the incidence of HAPE have suffered from the lack of precise estimates of the population-at-risk.[6,8–11] There have also been differences in the diagnostic criteria used for HAPE. These deficiencies in the reported incidences have been summarized recently.[12] Thus, it is not clearly known if there really is a higher incidence of HAPE during re-exposure to HA after a sojourn in the plains than during the first exposure.

Research questions

We wished to resolve this issue and designed a study that hoped to answer the following questions:

1. What is the incidence of HAPE in a cohort of healthy previously unacclimatized males during their first exposure to HA?
2. What is the incidence of HAPE in a similar cohort of healthy acclimatized males, re-exposed to HA after a sojourn in the plains?

To achieve these aims we recruited two cohorts of participants entering HA, some for the first time (first exposure, FE) and others for any subsequent exposures (re-exposure, RE). The cohorts were followed prospectively and all occurrences of HAPE amongst them were recorded. We tested the null hypothesis that there is no difference in the incidence of HAPE between the FE cohort and the RE cohort.

Material and methods

This prospective cohort study was conducted at the High Altitude Medical Research Center located at about 3400 m above sea level in the western Himalaya. The ethics committee of the research center approved the study.

All participants were male soldiers who were ascending to HA on duty. Soldiers have to be asymptomatic and free from disease before they are assigned duties at HA. Since acclimatization to HA may reduce the incidence of HA-related illnesses all soldiers follow an altitude-dependent acclimatization schedule on entering HA.[7] For an altitude of 3400 m this consisted of a two-day period of rest followed by four days of gradually increasing physical activity. On the seventh day at HA all soldiers underwent a medical examination to confirm that they were free from illness. The participants in our study consisted only of these acclimatizing soldiers. Only those soldiers who belonged to one of three military units were recruited as participants. There were two criteria for selecting these units: Firstly, they were located in close proximity to the research center, and secondly, the composition of men in these units was not restricted to any particular region of India, and therefore represented the general Indian population.

For some participants it was the first exposure to HA while for others it was a re-exposure after a sojourn in the plains. Many participants had entered HA on more than one occasion and each instance was recorded as a separate event. Some reached the HA area directly from the plains (200–300 m) after a 45–60 min journey by aircraft. These soldiers usually arrived early in the morning. Others reached after a road journey of 3–4 days. There were two possible road routes both of which involved overnight halts at camps en route. The altitude of these camps ranged between 2700 m and 4500 m. These men usually arrived at the final destination (3400 m) late in the evening of the third or fourth day after beginning their journey from low altitudes.

Data collection occurred in two phases. The first 3-month phase was from 17 April 2000 to 18 July 2000 and the next longer period extended from 10 Aug 2000 to 30 Oct 2004.

All data collection was done in the clinical laboratory where the ambient temperature ranged between 24 °C and 26 °C throughout the period of data collection.

Subjects reached the laboratory before 9:00 am. They were explained and informed about the nature of the study and their consent was obtained. A standard questionnaire was used to collect data regarding date of first exposure to HA and dates of descent, dates of re-ascent after a temporary absence from the HA area, and the mode of ascent during each exposure to HA. The questionnaire also recorded information regarding occurrence of severe AMS or admission for HAPE during any of the previous exposures to HA.

The clinical data gathered included heart rate, respiratory rate, systemic arterial blood pressure, and hemoglobin saturation. Symptoms of acute mountain sickness were elicited and recorded on standardized forms. Details of clinical examination are not given here and neither is that data presented in this paper.

Whenever any study participant fell ill he sought medical advice at the emergency department of the only hospital. All doctors in the hospital used the same criteria for diagnosis of HAPE. The diagnostic criteria included a mandatory history of recent entry to HA; the symptoms of breathlessness at rest and cough with expectoration; with tachycardia and moist breath sounds on auscultation; low saturation of hemoglobin as measured by pulse oximetry, and radiological confirmation