Acute mountain sickness susceptibility, fitness and hypoxic ventilatory response


ABSTRACT: In a party of 17 subjects who travelled together to 4,500 m, hypoxic ventilatory response (HVR) and maximum oxygen consumption (V\text{O}_2\text{max}) were measured before departure. HVR was measured under constant and varying alveolar carbon dioxide tension (P\text{ACO}_2) conditions. V\text{O}_2\text{max} was measured by both standard expired gas collection technique on a treadmill and using the "shuttle run" technique. On arrival at altitude, symptoms of acute mountain sickness (AMS) were scored daily for three days. There were no cases of severe AMS but half of the party had mild to moderate degrees of AMS. There was no correlation between AMS scores and HVR (HVRp) measured by either method of measurement or with V\text{O}_2\text{max} measured by treadmill or shuttle run.

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One of the most puzzling factors about acute mountain sickness (AMS) is the great variability in susceptibility between individuals. Rapid ascent to altitude is the major factor in its causation but amongst a group of subjects ascending together to altitude some will be unaffected, most mildly or moderately and some severely affected. On subsequent visits to altitude people tend to respond in a consistent way, i.e. some are good, some are poor acclimatizers. This leads to the idea that there must be some constitutional factor or factors which determine susceptibility to AMS.

We planned to test two hypotheses: 1) that a low hypoxic ventilatory response (HVR); or 2) that physical fitness as measured by maximum oxygen consumption (V\text{O}_2\text{max}), both measured before departure, might predict susceptibility to AMS.

A number of studies [1–3] have shown that there is a correlation between the degree of AMS and the reduction of alveolar carbon dioxide tension (P\text{ACO}_2) on arrival at altitude. That is, that subjects who are to get AMS fail to hyperventilate on arrival at altitude as much as subjects resistant to AMS. Could this in turn be due to their inherently low hypoxic ventilatory response (HVR) as measured in the laboratory at sea level? There have been a number of studies aimed at answering this question with varying results [1, 4, 5]. Our own previous study [6] failed to show any correlation between HVR and subsequent susceptibility to AMS. However, since others had claimed a relationship, we considered it worthwhile to repeat the study using different methods in the measurement of HVR, i.e. a different carbon dioxide tension (P\text{CO}_2) in the isocapnic measurement of HVR (HVRi) and to add the poikilocapnic measurement of HVR (HVRp). In this measurement the P\text{CO}_2 is allowed to fall as the inspired oxygen tension (P\text{O}_2) is lowered.

Another factor that might affect susceptibility to AMS is athletic fitness. Anecdotal evidence is that many very fit subjects do get AMS but such evidence may be biased because: 1) the unfit reporter is amused at the discom­fiture of his fit companion, so that cases are over-reported; and 2) fit subjects are likely to climb faster to altitude and so expose themselves to a greater hypoxic stress more quickly.

A Royal Navy/Royal Marines expedition to the Cordillera Real in Bolivia with a large party of disciplined subjects afforded the opportunity to test these two hypotheses.

Subjects and methods

There were 17 subjects, all male, whose ages ranged from 23–58 yrs (mean 36 yrs). Their altitude and climbing experience ranged from novice to long experience of Alpine and Himalayan climbing. Most had been on at least a few mountaineering expeditions.

Time table of ascent

All subjects travelled together from the UK to base camp. The party flew from London to La Paz airport
(4,100 m) then travelled by bus to Sorata (2,500 m) the same day. Unfortunately, due to loss of baggage the stay there was prolonged from the planned one night to seven. The party then proceeded to the roadhead by pick-up truck and spent two nights there (3,500 m), and then walked to base camp (4,500 m) the next day, taking 4–6 h. Thus, nine days were taken to reach base camp, most of this time being spent at 2,500 m.

Measurement of HVR

HVR was measured at the Clinical Research Centre during the three months prior to the expedition. Ten of the subjects had previous experience of HVR and CO₂ response measurements. The test was carried out in the semi-recumbent posture. Subjects listened to music through earphones and were encouraged to read. Three measurements of each form of HVR, HVRi and HVRp, were made, alternating the two forms. The method used was described previously [6]. Briefly, a closed circuit system was used incorporating a dry spirometer with an electronic output giving minute ventilation. This was applied to the Y axis of an X-Y plotter. A pulse oxymeter monitored the arterial oxygen saturation (SaO₂) and the signal was applied to the X axis of the plotter. A manually operated variable bypass of a soda lime cylinder allowed the PetCO₂ to be maintained at any given level. An infrared CO₂ analyser monitored end-tidal PetCO₂ (PetCO₂) which was maintained at 5.3 kPa (40 mmHg) during the isocapnic measurement. During the poikilocapnic measurement the bypass was turned off and the PetCO₂ allowed to fall. The system was charged with air and the PetCO₂ fell as the oxygen was consumed by the subject. The slope of the inscribed response was measured as described previously and the mean result of satisfactory runs taken as the subjects' HVRi and HVRp.

Fitness

Maximum oxygen consumption (Vo₂max) was taken as a measure of fitness. This was measured in two ways in the three days prior to departure for S. America. Firstly, by a progressive exercise test on a treadmill with continuous collection, mixing and analysis of expired gas: the results of measurements of volume, PO₂ and PCO₂ were fed into a computer and the ventilation, CO₂ output, O₂ intake etc. were computed and printed each half minute. The highest VO₂ for a minute was taken as the VO₂max. Secondly, by the “shuttle run” [7] in which the subject shuttles between two marks on the ground, 20 m apart. He keeps time with a bleep from a pre-recorded audio tape. At intervals the frequency of the bleeps increases as the test goes on so that he has to increase his running speed. He continues until he is unable to keep pace with the bleeps. This point is noted and from a table his equivalent Vo₂max is read off. In both tests subjects were encouraged by their peers to continue to exhaustion. The treadmill test is generally regarded as the “gold standard” method for Vo₂max. The shuttle run test was used because we wished to have a test that we could repeat at altitude for other studies on the expedition. The type of exercise is slightly different from that required on the treadmill, a lot of acceleration and deceleration is called for which may favour some subjects. Hence, the results of both tests are reported.

AMS symptoms scoring

Subjects were asked to fill in a simple questionnaire on symptoms of AMS each morning after arrival at base camp (4,500 m) for four days by which time all symptoms had resolved. The symptoms scored were: headache, lassitude, insomnia, anorexia-vomiting. Ataxia was also included but no subject admitted to this. For each symptom there was a 0–3 scale indicating nil, mild, moderate or severe. Anorexia/vomiting was scored as follows: anorexia was given one point, nausea 2, and vomiting 3. Points were summed for the day and the three days summed to give a total AMS score. One observer was responsible for monitoring the scoring of all subjects.

Statistics

Kendall’s rank test was used to identify significant correlation between AMS cores and results of HVR and Vo₂max measurements.

Results

HVR

The mean responses were, for the isocapnic measurement (HVRi), 1.65 l·min⁻¹·%SaO₂ with a range of 3.1–0.51 and 2.61–0.29, respectively. The two measurements were closely correlated (r=0.85). The best fit regression equation was HVRp = 0.55 HVRi + 0.09, i.e. the HVRp was just over half the HVRi.

Vo₂max

Measured on the treadmill the Vo₂max of the group averaged 51.5 ml·min⁻¹·kg⁻¹ with a range 35–76 and estimated with the shuttle run was 50.4 ml·min⁻¹·kg mean range 43–62. The correlation was significant but not close (r=0.47).

AMS symptom score

Because of the delay in reaching base camp there was less AMS than had been anticipated. Nevertheless, there was enough to provide a range of sickness from one or two moderately affected subjects, the majority mildly affected and three or four essentially unaffected. The
mean score (total for three days) was 7.8, range 0–19 out of a possible maximum score of 36 (12 per day for 3 days). Symptoms of AMS were worst on the first two days after arrival at base camp for all subjects except the most affected whose symptoms were worst on the third day. If the score for the single worst day was taken, a very similar ranking of subjects is found (p=0.001, Kendall’s rank test).

Figure 1 shows the relationship of AMS scores to HVRI, HVRp, \(V_O_2_{\text{max}T}\) by treadmill (\(V_O_2_{\text{max}T}\)) and by shuttle run (\(V_O_2_{\text{max}S}\)). There was no correlation between AMS scores and any of these measurements. Furthermore, there was no significant correlation of either age or previous altitude (mountaineering) experience with AMS scores.

Discussion

Hyperventilation on arrival at altitude is one of the most important mechanisms of acclimatization and reduces the effect of altitude hypoxia in causing hypoxaemia. It has been claimed that those subjects who fail to hyperventilate are more likely to suffer from AMS [1–3]. It would be reasonable to suggest that these subjects may have an inherently low HVR as measured in the laboratory with a brief hypoxic test. However, we have previously failed to find any correlation between HVRI (or CO₂ ventilatory response) and subsequent AMS on going to altitude [6]. Moore et al. [4] found in a chamber experiment that the HVRp correlated with susceptibility to AMS, whereas the correlation with HVRI was not significant. Hence, we considered it worthwhile to repeat our study measuring HVRp as well as HVRI and to measure HVRI at the normal end tidal PCO₂ (5.3 kPa, 40 mmHg) used in that study.

It seems clear that under the conditions of this study, i.e. an ascent over a number of days and in relation to mild or moderate AMS, the HVR conventionally measured at sea level does not predict susceptibility to AMS. It is possible that in relation to acute pulmonary oedema of high altitude [5] or with rapid ascent as in a chamber experiment [1, 4] HVR may be predictive as claimed in previous publications. But, under the more usual conditions of mountaineering other mechanisms may be more important in achieving
the hyperventilation that characterizes the well acclimatized individual.

These mechanisms include the resetting of the medullary chemorestat for CO₂ so that the threshold of response is reduced (shift to the left of the CO₂ ventilatory response curve) and the increase in the gain or slope of this response [8]. Also, there is probably an increase of the HVR as part of the acclimatization process [9]. Both of these mechanisms have a time course of some days. Perhaps the subject resistant to AMS may be one who has a fast time course for either or both of these adaptations. Finally, the HVR is biphasic. There is an initial stimulation of ventilation which is measured by our short rebreathing test. This is followed by decline of ventilation until a new steady-state is reached in about half an hour [10]. Individual variation in the degree of this second phase of the hypoxic response might contribute to variation in susceptibility.

Amongst outdoor enthusiasts there seems to be an assumption that the athletically fit will “go well” at altitude and be free from AMS but there are many anecdotes to the contrary. RAVENHILL [11] writing in 1913 said, “There is in my experience no type of man of whom one can say he will or will not suffer from puna (AMS). Most cases... were young men to all appearances perfectly sound. Young strong and healthy men may be completely overcome. Stout, plethoric individuals... may not even have a headache.”

However, as stated in the introduction it can be argued that the fit individual will tend to climb faster and go higher more quickly than the unfit and so expose himself to a greater hypoxic stress. Also, cases of very fit individuals getting AMS may be over-reported. We know of no study that has addressed this question systematically. The protocol of this study demanded that all subjects move up to base camp together and remain there over the next five days. Thus, the hypoxic stress was controlled to a greater hypoxic stress. Individuals getting to base camp probably reduced AMS. However, as stated in the introduction it can be argued that the fitness of AMS in our subjects. There was sufficient sickness to produce a range of symptoms and these did show a significant correlation with 24 h urinary sodium excretion on the first day at base camp and with the reduction in vital capacity on the second day. Therefore, if HVR or VO₂ max were important predictors of AMS one would have expected correlations to have been found.

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References