ORIGINAL ARTICLE

Sea level and acute responses to hypoxia: do they predict physiological responses and acute mountain sickness at altitude?

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Objectives: To compare a range of physiological responses to acute sea level hypoxia at simulated altitudes with the same physiological responses and acute mountain sickness (AMS) scores measured at altitude (similar to the simulated altitudes) during a 17 day trek in the Himalayas.
Methods: Twenty men and women aged 18–54 years took part in the study. End tidal CO_2 tension (P_{ETCO_2}) and saturated oxygen (Sa_{O_2}) were measured using a capnograph. Observations made at sea level and some simulated altitudes were compared with those in the Himalayas. Pairwise correlations were used to examine the correlation between variables and regression, with 95% prediction intervals providing information on how well one variable could be predicted from another for a given subject.
Results: There was only a significant correlation for a few comparisons. The 95% prediction intervals for individual Sa_{O_2} values at a range of simulated altitudes were fairly wide going from ± 4% to ± 5%. All of the correlations between laboratory and Himalayan P_{ETCO_2} values were not statistically significant. There was a significant correlation for the relation between Sa_{O_2} and P_{ETCO_2} at sea level for the laboratory data (r=–0.51; p=0.05). For the Himalayan data, there were significant correlations at Namche Bazaar (3450 m; day 3) (*r*=–0.56; p=0.01) and Dingboche (4300 m; day 6) (*r*=–0.48; p=0.03). The correlation between Sa_{O_2} and P_{ETCO_2} and AMS was generally poor.
Conclusions: The results indicate that limited information can be gained on a subject's response to altitude by assessing physiological variables at sea level and a range of simulated altitudes before the subject carries out a trek at altitude.

A decreased physical work capacity and acute mountain sickness (AMS) are common characteristics experienced by sea level dwellers who venture to altitude.[1 2] A strong hypoxic ventilatory response (HVR) is considered by some to be advantageous for climbers at high altitude, resulting in an increased arterial oxygen saturation (Sa_{O_2}) allowing them to attain greater altitudes than those with a lower HVR.[3–5] Although it is believed that climbers with a low HVR are more likely to experience AMS symptoms and are prone to body fluid retention or pulmonary oedema, the situation is confused by the fact that native altitude dwellers have a blunted ventilatory response but appear to be less susceptible to AMS than low level residents.[6 7]

Ventilatory acclimatisation to hypoxia in a mountain environment requires many days and is characterised by considerable individual variability.[8] If it were possible to predict the ventilatory acclimatisation response before a sojourn to the mountains, subjects who respond poorly to an hypoxic environment could be identified and precautions taken to avoid problems at altitude.

We considered it a great opportunity to monitor a group of 22 men and women who undertook a trek in the Himalayas at altitudes ranging from 2600 m to 5540 m. Observations made at sea level and simulated altitudes similar to those at which the group would reside in the Himalayas allowed a comparison of the acute responses to be made with those at some of the altitudes attained in the Himalayas.

The aims of the study were to compare a range of physiological responses at sea level and acute exposure to a range of simulated altitudes with physiological responses and AMS measured at altitude during a 17 day trek in the Himalayas and to compare physiological variables during the trek.

METHODS

Subjects

Twenty two men and women aged 18–54 years took part in the study. No subject had a history of pulmonary disease or respiratory symptoms and all were native sea level dwellers who had not been at altitude in the preceding three months. The subjects signed a consent form. Most were regular exercisers who took part in a range of activities including endurance running and aerobic dance. Before they left for Kathmandu, they underwent laboratory tests in Glasgow. After departure, they spent two days in Kathmandu (1300 m) before they flew to Lukla (2800 m) and carried out a trek (table 1 gives trek information). Sa_{O_2} measurements were taken in Kathmandu (1300 m), Namche Bazaar (3450 m; day 3), Dingboche (4300 m; day 6) Lobuche (4928 m; day 9), Gokyo (4750 m; day 13), and Namche Bazaar (3450 m; day 15). End tidal CO_2 tension (P_{ETCO_2}) readings were taken in the same locations apart from Gokyo and Lobuche, as these altitudes are outside the operating range for P_{ETCO_2} measurement according to the capnograph (Nellcor Puritan-Bennett NPB75, Bicester, UK) manual.

Research design

Measurements in the laboratory

Subjects visited a laboratory where they underwent four five minute measurements in a sitting position. They sat quietly for five minutes before performing the following sequence: breathing room air and three different oxygen mixtures of 13.6% (3450 m), 12.3% (4200 m) and 11.2% (4850 m). P_{ETCO_2} and Sa_{O_2} were measured. An attempt was made to simulate

Abbreviations: AMS, acute mountain sickness; HVR, hypoxic ventilatory response; P_{ETCO_2}, end tidal CO_2 tension; Sa_{O_2}, saturated oxygen

Table 1 Trek itinerary

Day	Date	Location	Altitude (m)	Measurement
1	29.03.00	Phakding*	2652	
2	30.03.00	Namche Bazaar	3450	
3	31.03.00	Namche Bazaar	3450	AMS 1, Sa_{O_2} & P_{ETCO_2}
4	01.04.00	Thyanboche	3867	AMS 2
5	02.04.00	Pheriche	4252	AMS 3
6	03.04.00	Dingboche	4320	AMS 4, Sa_{O_2} & P_{ETCO_2}
7	04.04.00	Dingboche	4320	AMS 5
8	05.04.00	Lobuche	4928	AMS 6
9	06.04.00	Lobuche†	4928	AMS 7‡, AMS 8, Sa_{O_2}
10	07.04.00	Pangboche	3901	AMS 9
11	08.04.00	Dole	4048	AMS 10
12	09.04.00	Machhermo	4465	AMS 11
13	10.04.00	Gokyo	4791	AMS 12, Sa_{O_2}
14	11.04.00	Dole	4048	AMS 13
15	12.04.00	Namche Bazaar	3450	AMS 14, Sa_{O_2} & P_{ETCO_2}
16	13.04.00	Phakding	2652	AMS 15
17	14.04.00	Lukla	2860	

*Walk from Lukla 2860 m.
AMS 1 refers to first AMS measurement.
†Trek to Kala Patar 5540 m.
AMS‡ On the evening of day 9, subjects were asked to give their AMS scores when they were on the summit of Kala Patar (5540 m) in the morning of day 9.
Sa_{O_2} and P_{ETCO_2} measurements were taken in the evenings between 7 and 11 pm.
AMS, acute mountain sickness score; Sa_{O_2}, Saturated oxygen; P_{ETCO_2}, end tidal CO_2 tension.

some of the altitudes at which the group would be measured in the Himalayas. It was expected that the trekking group would spend at least one night at altitudes around 3450 m, 4200 m, and 4850 m. Gas mixtures for a given altitude were calculated using target values from model atmosphere barometric pressures and calculated tracheal P_{IO_2}. On page 26, Ward *et al*[9] contend that the model atmosphere is better than the standard atmosphere, as the former reflects more accurately the high altitude sites where high altitude studies take place. Taking the recommendations of Ward *et al*,[9] gas mixtures were calculated after assessment of the P_{IO_2} for a proposed altitude using the following:

(Barometric pressure − 47 mm Hg (water vapour pressure)) × a given gas mixture

For example,

$$760 - 47 \times 0 \times 0.136 = 96.97 \text{ mm Hg.}$$

The P_{IO_2} for 4200 m was calculated as 87.69 mm Hg and for 4850 m it was 78.86 mm Hg.[9]

It is conceded that it is difficult to simulate the exact altitude at which testing would take place in the Himalayas. Barometric pressure differences caused by weather changes could not be predicted. Although the actual Himalayan villages where the group was to stay were known, possible height differences within a given village could also have a bearing on the calculations. It is acknowledged that it is the predictive capability of the laboratory measurements that is important and that actual equivalence of the simulated and true altitudes is not critical to the study.

Each subject wore a nose clip. For the normoxia test, the subjects breathed through a tube, and end tidal samples were collected using a line manufactured by Nellcor Eden. For the hypoxia tests, a rubber mouthpiece was linked to a Hans Rudolph (model 2700) low resistance breathing valve, which was connected to the appropriate Douglas bag valve by a length of tubing. End tidal samples were collected using a line (inserted into the rubber mouthpiece) manufactured by Nellcor Puritan-Bennett, Bicester, UK. The saturation probe was attached to the index finger of the right hand.

Measurements in the Himalayas

The subjects sat for six minutes before they were attached to the capnograph. They breathed through a tube, and end tidal samples were collected using a line manufactured by Nellcor Puritan-Bennett, Bicester, UK. They each wore a nose clip. The saturation probe was attached to the index finger of the right hand. Values were recorded when the observed saturation signal was stable. AMS scores were calculated using the Lake Louise scoring system.[10] The points for each category were summed to give a total AMS score for each subject. AMS was measured in the evenings between 7 and 11 pm. On the evening of day 9, subjects were asked to give their AMS scores when they were on the summit of Kala Patar (5540 m) in the morning of day 9.

Statistical analysis

Comparison of variables at different time points was made using *t* tests. Pairwise correlations were used to examine the relation between variables and regression, and 95% prediction intervals provided information on how well one variable could be predicted from another.

RESULTS

All 22 subjects completed the trek as outlined in table 1. On day 9, all subjects reached the summit of Kala Patar at 5540 m. Two subjects took Diamox for a short period in the early part of the trek and were removed from the analysis as this medication would affect ventilatory responses. It should be noted that not all subjects were measured on all occasions.

Figure 1 gives the individual Sa_{O_2} values for the laboratory measures and those in the Himalayas, and table 2 provides the mean (SD) values. The mean (SD) laboratory sea level Sa_{O_2} was 97.5 (1.2)%. For the simulated altitudes, there was a progressive decrease with an increase in altitude. As expected, the mean Sa_{O_2} in Kathmandu (1300 m) of 97.1 (1.5)% was very similar to the mean laboratory sea level Sa_{O_2} in Glasgow ($p = 0.525$). Although the mean values for the simulated altitudes and the almost matching altitudes in the Himalayan values are generally very similar, correlations (table 3) show that there was only a significant relation for the following: simulated 3450 m Sa_{O_2} and Namche Bazaar (3450 m) Sa_{O_2} (day 3) ($r = 0.65$) ($p = 0.03$); simulated 4850 m Sa_{O_2} and Namche Bazaar (3450 m) Sa_{O_2} (day 3) ($r = 0.73$) ($p = 0.003$).

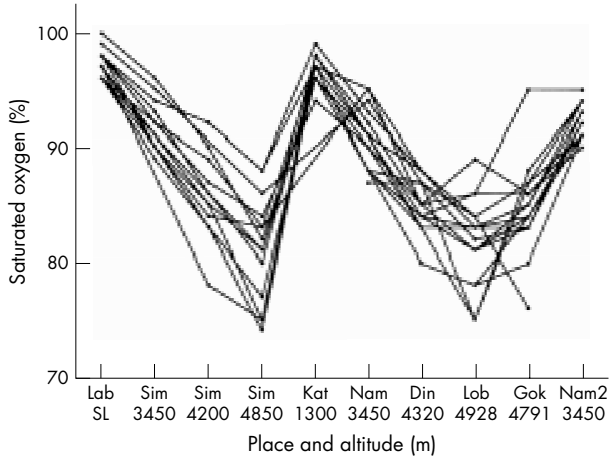

Figure 1 Subject profiles under simulated and Himalayan conditions for oxygen saturation. Lab, Laboratory; SL, sea level; Sim, simulated; Kat, Kathmandu; Nam, Namche Bazaar; Din, Dingboche; Lob, Lobuche; Gok, Gokyo.

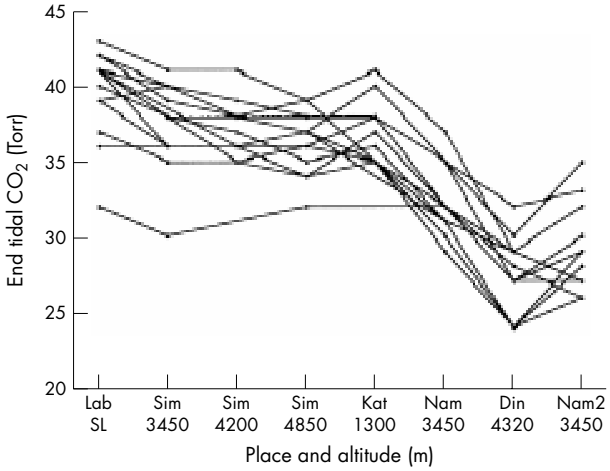

Figure 2 Subject profiles under simulated and Himalayan conditions for end tidal CO_2. Lab, Laboratory; SL, sea level; Sim, simulated; Kat, Kathmandu; Nam, Namche Bazaar; Din, Dingboche.

Table 2 Mean (SD) Sa_{O_2} and P_{ETCO_2} for laboratory values and Himalayan locations

Location	Sa_{O_2} (%)	P_{ETCO_2} (mm Hg)
Laboratory sea level	97.5 (1.2)	39.9 (3.0)
Simulated 3450 m (13.6% O_2)	92.4 (2.2)	37.4 (1.8)
Simulated 4200 m (12.3% O_2)	86.2 (3.9)	37.1 (2.9)
Simulated 4850 m (11.2% O_2)	81.2 (4.6)	36.4 (2.1)
Kathmandu 1300 m	97.1 (1.5)	37.5 (2.4)
Namche Bazaar 3450 m (day 3)	90.5 (2.6)	32.4 (2.9)
Dingboche 4320 m (day 6)	85.1 (3.0)	27.5 (2.9)
Lobuche 4928 m (day 9)	82.3 (4.8)	–
Gokyo 4791 m (day 13)	85.1 (4.0)	–
Namche Bazaar 3450 m (day 15)	92.2 (1.4)	28.6 (3.0)

Sa_{O_2}, Saturated oxygen; P_{ETCO_2}, end tidal CO_2 tension.

The 95% prediction intervals for individual Sa_{O_2} values at a range of simulated altitude saturation levels are as follows: in the case of simulated 3450 m Sa_{O_2} and Namche Bazaar (3450 m) Sa_{O_2} (day 3), the prediction error is about ± 5%; in the case of simulated 4850 m Sa_{O_2} and Namche Bazaar (3450 m) Sa_{O_2} (day 3), the prediction error is about ± 4%.

Figure 2 gives a visual impression of the individual values for P_{ETCO_2} in the laboratory and in the Himalayas. The laboratory P_{ETCO_2} mean values at sea level and simulated altitude were significantly different from each other ($p<0.05$). The Kathmandu (1300 m) mean P_{ETCO_2} of 37.5 (2.4) mm Hg is significantly lower than the mean laboratory value at sea level ($p = 0.002$). The measured mean (SD) values at Himalayan altitude are much lower than the laboratory values for the almost matching altitudes: Namche Bazaar (3450 m; day 3), 32.4 (2.9) mm Hg ($p = 0.001$); Dingboche (4320 m; day 6), 27.5 (2.4) mm Hg ($p<0.0005$); Namche Bazaar (3450 m; day 15), 28.6 (3.0) mm Hg ($p<0.0005$). As expected, the mean value for the second visit to Namche Bazaar (3450 m) is lower than for the first ($p<0.0005$).

None of the correlations between laboratory and Himalayan P_{ETCO_2} were significant (table 4). There was a significant correlation for the relation between Sa_{O_2} and P_{ETCO_2} at sea level for the laboratory data ($r=-0.51$; $p=0.05$). For the Himalayan data, table 5 shows that there were significant negative correlations for the laboratory sea level relation ($r = -0.51$; $p = 0.05$) and at the following locations: Namche Bazaar (3450 m; day 3) ($r = -0.56$; $p = 0.01$) (fig 3) and Dingboche (4320 m; day 6) ($r = -0.48$; $p = 0.03$).

The correlation between Sa_{O_2} and P_{ETCO_2} and AMS was generally poor. Tables 6 and 7 give some examples. Some significant correlations were found but these were non-systematic. As the AMS scoring system is considered to be least accurate in the low score areas as a result of non-AMS illness, the group information on AMS is presented as the number of subjects with an AMS score of 4 or above (fig 4). Figure 5 gives responses of selected subjects. The correlations between the difference in Sa_{O_2} associated with a preceding ascent or descent and AMS were significant for the fall in Sa_{O_2} from Kathmandu to Namche Bazaar (day 3) and the AMS score in Namche Bazaar (correlation 0.51; $p<0.05$). Only one other correlation just failed to reach statistical significance, the decrease in Sa_{O_2} from Dingboche to Lobuche with AMS score at Lobuche (table 8).

Table 3 Correlations between laboratory and Himalayan Sa_{O_2} (p values are given in parentheses)

	Laboratory sea level	Simulated 3450 m	Simulated 4200 m	Simulated 4850 m
Kathmandu 1300 m	0.28 (0.33)	0.14 (0.69)	–0.01 (0.98)	0.02 (0.95)
Namche Bazaar 3450 m (day 3)	0.23 (0.38)	0.65 (0.03*)	0.37 (0.21)	0.73 (0.003*)
Dingboche 4320 m (day 6)	0.01 (0.97)	0.25 (0.45)	0.04 (0.90)	0.16 (0.59)
Gokyo 4791 m (day 13)	–0.08 (0.75)	0.08 (0.82)	0.30 (0.32)	0.31 (0.27)
Lobuche 4928 m (day 9)	–0.33 (0.24)	0.19 (0.61)	–0.09 (0.77)	0.22 (0.47)
Namche Bazaar 3450 m (day15)	0.24 (0.41)	0.06 (0.88)	0.33 (0.32)	0.29 (0.36)

*Significant correlation.
Sa_{O_2}, Saturated oxygen.

Table 4 Correlations between laboratory and Himalayan end tidal CO_2 values (p values are given in parentheses)

	Laboratory sea level	Simulated 3450 m	Simulated 4200 m	Simulated 4850 m
Kathmandu 1300 m	0.19 (0.56)	0.33 (0.36)	0.30 (0.34)	0.42 (0.18)
Namche Bazaar 3450 m (day 3)	0.31 (0.26)	0.34 (0.30)	0.33 (0.27)	0.45 (0.10)
Dingboche 4320 m (day 6)	–0.09 (0.75)	–0.06 (0.85)	0.11 (0.73)	0.09 (0.77)
Namche Bazaar 3450 m (day 15)	0.23 (0.46)	0.52 (0.12)	0.45 (0.17)	0.45 (0.17)

Table 5 Correlations between oxygen saturation and end tidal CO_2 in the laboratory and in the Himalayas (p values are given in parentheses)

	Laboratory sea level	Simulated 3450 m	Simulated 4320 m	Simulated 4850 m
Correlation (p value)	–0.51 (0.05*)	–0.48 (0.14)	–0.01 (0.98)	–0.04 (0.88)
	Kathmandu 1300 m	Namche Bazaar 3450 m (day 3)	Dingboche 4320 m (day 6)	Namche Bazaar 3450 m (day 15)
Correlation (p value)	–0.44 (0.13)	–0.56 (0.01*)	–0.48 (0.03*)	–0.45 (0.08)

*Significant correlation.

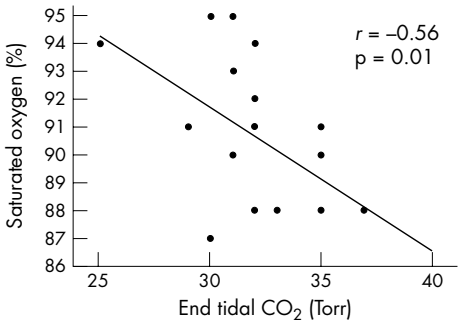

Figure 3 Oxygen saturation and end tidal CO_2 at Namche Bazaar (day 3).

DISCUSSION

Examination of pairwise correlations for Sao_2 values between each of the laboratory and each Himalayan data points shows that there is a fairly poor correlation between the values. Although there were some statistically significant correlations, the 95% prediction intervals for individual Sao_2 values over a range of laboratory measurements are from ± 4% to ± 5%. These predictions are of limited value.

The mean values for Sao_2 at Namche Bazaar are very similar to the mean Sao_2 score of 91% reported by Peacock and Jones.[11] As expected, the Sao_2 at Namche Bazaar increased over time and reflected ventilatory acclimatisation. The mean Sao_2 in Namche Bazaar was 90.3% on day 3 of the trek, and at Namche Bazaar on day 15 it was 92.2%. During the same time period, there was a decrease in P_{ETCO_2} from 32.6 (3.1) to 28.7 (2.9) mm Hg at Namche Bazaar, which is an indicator of ventilatory acclimatisation. The reduction in P_{ETCO_2} in the

Table 6 Correlations between oxygen saturation (Sao_2) and acute mountain sickness (AMS) score in the Himalayas (p values are given in parentheses)

	Sao_2 at:			
AMS score on:	Kathmandu 1300 m	Namche Bazaar 3450 m (day 3)	Dingboche 4320 m (day 6)	Namche Bazaar 3450 m (day 15)
31 March	0.41 (0.11)	–0.40 (0.08)	0.58 (0.007*)	–0.09 (0.73)
1 April	–0.05 (0.86)	–0.34 (0.14)	–0.12 (0.62)	–0.30 (0.28)
2 April	0.72 (0.002*)	0.09 (0.72)	0.39 (0.09)	0.18 (0.48)

*Significant correlation.

Table 7 Correlations between end tidal CO_2 tension (P_{ETCO_2}) and acute mountain sickness (AMS) score in the Himalayas (p values are given in parentheses)

	P_{ETCO_2} at:			
AMS score on:	Kathmandu 1300 m	Namche Bazaar 3450 m (day 3)	Dingboche 4320 m (day 6)	Namche Bazaar 3450 m (day 15)
31 March	–0.16 (0.59)	0.05 (0.83)	–0.28 (0.24)	–0.21 (0.42)
1 April	–0.05 (0.87)	0.11 (0.66)	0.16 (0.52)	0.11 (0.69)
2 April	–0.66 (0.01*)	–0.29 (0.21)	–0.42 (0.07)	–0.44 (0.07)

*Significant correlation.

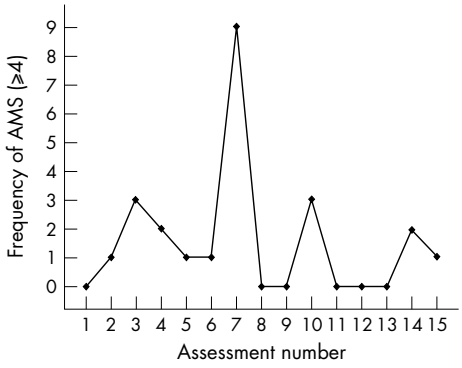

Figure 4 Frequency of the occurrence of acute mountain sickness (AMS; mountain sickness score of 4 or greater) during the trek.

Himalayas reflects increased ventilation resulting from acclimatisation. Thus, it would be expected that the simulated value at 3450 m would be lower than the 3450 m value (day 3) in Namche Bazaar. The fact that the laboratory Sa_{O_2} value is slightly higher than the Namche Bazaar score is surprising as there is evidence of ventilatory acclimatisation. According to the method of calculating simulated altitude recommended by Ward *et al*[9], the simulated altitude of 3450 m appears to be correct. However, the barometric pressure at Namche Bazaar on the testing day is not known. The capnograph was calibrated by the manufacturers before the study.

This study has found that it is not possible to make a reasonable prediction of the ventilatory response during a trek to Nepal using P_{ETCO_2} responses. These findings are in contrast with those of Reeves *et al*,[12] who found that P_{ETCO_2} at sea level was significantly related to P_{ETCO_2} at altitude and concluded that the sea level P_{ETCO_2} results suggested interindividual differences in ventilatory control. They concluded that the sea level P_{ETCO_2} differences were predictive of the ventilatory altitude acclimatisation at 4300 m over a three week period. They conceded that the precision of the prediction is limited and that this finding is not surprising as there is great interindividual variability in the response to hypoxia. Our study has failed to confirm the findings of Reeves *et al*[12] that sea level P_{ETCO_2} is predictive of ventilatory altitude acclimatisation. Unlike the research of Reeves *et al*,[12] this study was carried out at a range of undulating altitudes, which may have produced a time/altitude interaction which may have influenced the results.

The fact that there was a significant correlation between Sa_{O_2} and P_{ETCO_2} at sea level for the laboratory data is somewhat surprising. For the Himalayan data, there were significant negative correlations at certain locations: Namche Bazaar (3450 m; day 3) ($r = -0.56$; $p = 0.01$) and Dingboche (4320 m; day 6) ($r = -0.48$; $p = 0.03$). It is to be expected that an enhanced ventilatory response would increase Sa_{O_2} and lower P_{ETCO_2}.[9]

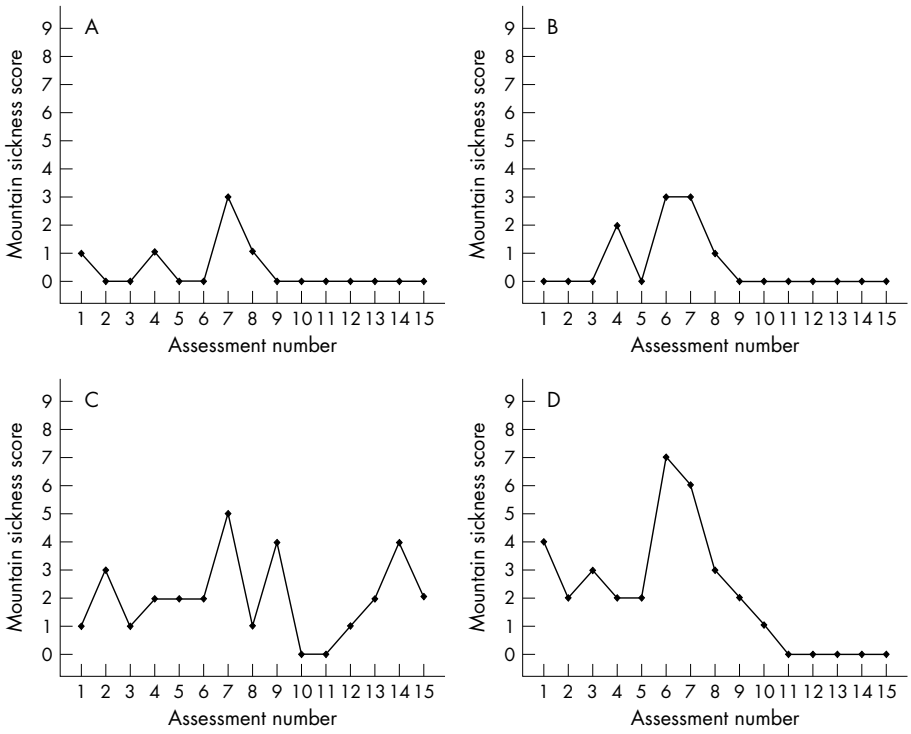

Figure 5 Acute mountain sickness responses over time in selected subjects: A, subject 3; B, subject 6; C, subject 10; D, subject 16.

Table 8 Correlations between acute mountain sickness (AMS) scores at specific time points and the changes in Sa_{O_2} associated with preceding ascent or descent (p values given in parentheses)

	AMS score at:				
	Namche Bazaar 3450 m (day 3)	Dingboche 4320 m (day 6)	Lobuche 4928 m (day 9)	Gokyo 4791 m (day 13)	Namche Bazaar 3450 m (day 15)
Preceding change in Sa_{O_2}	0.51 (<0.05*)	–0.004 (NS)	0.45 (NS)	0.11 (NS)	–0.06 (NS)

*Significant correlation.

None of the correlations between the laboratory Sa_{O_2} values and AMS scores were significant. Although there were some significant correlations between AMS scores and Sa_{O_2} in the Himalayas, most were not significant. The physiological variables showed a general trend throughout the laboratory and Himalayan measurements—that is, Sa_{O_2} and P_{ETCO_2} decreased with a lower P_{O_2}. However, there were appreciable time differences in AMS responses between subjects. The non-systematic response in the incidence of AMS compared with the fairly predictable and regular changes in the physiological variables is a possible explanation for the poor correlation between AMS scores and the physiological variables. Other factors could have contaminated the AMS results. Dehydration and gastrointestinal upset, which are fairly common features of Himalayan treks, could have had a bearing on the subjects' responses to questions on headache and gastrointestinal discomfort.

Previous studies have indicated that lowlanders with a blunted HVR are more predisposed to AMS.[13–15] However, other reports indicate that there is a poor correlation between HVR and AMS in lowlanders during their first few days at altitude.[16 17] The picture is clouded further by the fact that native high altitude residents have a blunted HVR but normally experience less AMS than lowlanders.[9] Examination of the relation between AMS score at specific time points and the change in Sa_{O_2} associated with the preceding ascent or descent showed a significant correlation of 0.51 ($p<0.05$) for the decrease in Sa_{O_2} from Kathmandu to Namche Bazaar (day 3) and the AMS score in Namche Bazaar. Changes in Sa_{O_2} may be a fairly sensitive barometer of AMS susceptibility. Hackett *et al*[15] showed that a low Sa_{O_2} was a good predictor of AMS, but found that there was a poor correlation between Sa_{O_2} and HVR. Roach *et al*[18] reported that a low Sa_{O_2} on immediate arrival is a good marker for the onset of AMS. In their review of the area on page 220, Ward *et al*[9] believe that the low Sa_{O_2} and subsequent AMS can be attributed to hypoventilation.

Although HVR responses during rapid altitude ascents such as those associated with chamber experiments are predictive of AMS, Milledge *et al*[17] consider that other factors may influence ventilatory responses during mountaineering and trekking trips where there is normally a gradual increase in altitude. They propose that changes in the ventilatory responses can be attributed to an increased HVR and or a change in the medullary responses to CO_2. Milledge *et al*[16] speculate that, in a mountain environment where the hypoxic stress is applied over a period of days unlike an acute hypoxic exposure in a chamber, there is time for ventilatory acclimatisation to take place. They believe that it is the speed of adaptation that is important rather than an HVR that has been measured at sea level. Some studies have shown an increase in HVR sensitivity ranging from four hours to 28 days after ascent.[19–21] Over a 27 day acclimatisation period, Msuda *et al*[22] found that lowlanders had a small decrease in HVR during the first three to five days but a considerable increase thereafter to 27 days. Moore *et al*[7] consider that a blunted ventilatory response may be an important factor in the development of AMS. They postulate that "altitude headaches" could result from an increased cerebral blood flow and intercranial pressure as a consequence of hypoxaemia. However, they cite the study of Reeves *et al*,[23] which showed no difference in the velocity of the internal carotid artery blood flow when AMS and control subjects were compared.

The prediction of Himalayan Sa_{O_2} from laboratory Sa_{O_2} values was limited for individual subjects. It is not possible to make a reasonable prediction of the ventilatory response using P_{ETCO_2}. There was an inverse relation between P_{ETCO_2} and Sa_{O_2} for the Himalayan data, with significant correlations at Namche Bazaar (3450m; day 3) ($r = 0.56$; $p = 0.01$) and Dingboche (4320m; day 6) ($r = -0.48$; $p = 0.03$). The prediction of AMS from physiological variables was generally poor. However, the relation between AMS score at specific time points and the change in Sa_{O_2} associated with the preceding ascent or descent is deemed to be worthy of further investigation. The results of this study indicate that limited information can be gained on a subject's response to altitude by assessing physiological variables at sea level and a range of simulated altitudes before the subject carries out a trek at altitude.

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