ORIGINAL RESEARCH

Long-Term Monitoring of Oxygen Saturation at Altitude Can Be Useful in Predicting the Subsequent Development of Moderate-to-Severe Acute Mountain Sickness

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Objective.—The use of pulse oximetry (SpO_2) to identify subjects susceptible to acute mountain sickness (AMS) is the subject of debate. To obtain more reliable data, we monitored SpO_2 for 24 hours at altitude to investigate the ability to predict impending AMS.

Methods.—The study was conducted during the climb from Alagna (1154 m) to Capanna Regina Margherita (4559 m), with an overnight stay in Capanna Gnifetti (3647 m). Sixty subjects (11 women) were recruited. Each subject was fitted with a 24-hour recording finger pulse oximeter. The subjects rode a cable car to 3275 m and climbed to 3647 m, where they spent the night.

Results.—In the morning, 24 subjects (6 women) had a Lake Louise Questionnaire score (LLS) ≥ 3 (AMS^+), and 15 subjects (4 women) exhibited moderate-to-severe disease (LLS $\geq 5 = \text{AMS}^{++}$). At Alagna, SpO_2 did not differ between the AMS^- and AMS^+ subjects. At higher stations, all AMS^+ subjects exhibited a significantly lower SpO_2 than did the AMS^- subjects: at 3275 m, 85.4% vs 87.7%; resting at 3647 m, 84.5% vs 86.4%. The receiver operating characteristics curve analysis resulted in a rather poor discrimination between the AMS^- subjects and all of the AMS^+ subjects. With the cutoff LLS ≥ 5 , the sensitivity was 86.67%, the specificity was 82.25%, and the area under the curve was 0.88 ($P < .0001$) for $\text{SpO}_2 \leq 84\%$ at 3647 m.

Conclusions.—We conclude that AMS^+ subjects exhibit a more severe and prolonged oxygen desaturation than do AMS^- subjects starting from the beginning of altitude exposure, but the predictive power of SpO_2 is accurate only for AMS^{++} .

Key words: hypoxia, pulse oximetry, Lake Louise score

Introduction

Subjects who rapidly ascend to altitudes greater than 2500 m are exposed to progressive hypoxia and can develop acute mountain sickness (AMS), which is a potentially serious condition if symptoms are ignored and ascent is continued.^{1,2} It is well-known that AMS depends on the altitude, the rate of ascent, and the individual's susceptibility, independent of sex and physical fitness.^{2,3} Given its high prevalence, which is approximately 25% between 2000 and 3000 m⁴ and approximately 34% at 3650 m,⁵ in recent years many studies have focused on finding a good indicator of impending AMS.

The predictive role of oxygen desaturation as measured by pulse oximetry (SpO_2) has been studied for a long time. In some studies, both those involving simulated hypoxia and those conducted in the field, the importance of a more severe reduction of SpO_2 as a predictor of AMS development has been reported,^{6–8} and values of SpO_2 that are predictive of impending AMS at different altitudes have been proposed.^{9–11} In other studies, pulse oximetry failed to predict the development of AMS.^{12,13} According to some authors, even if the SpO_2 is on average significantly lower in subjects who are susceptible to AMS, the overlap between individuals without (AMS^-) and with AMS (AMS^+) makes it very difficult to define useful cutoff values.²

In the previous studies, SpO_2 was measured only for a few minutes either at rest or immediately after exercise; whether a single resting measurement, even if repeated,

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is reliable enough to accurately reflect an individual's SpO_2 is still debatable. In fact, it is well-known that at altitude, a short reading can provide inaccurate and variable results, especially owing to the variation in ventilation.¹⁴ It has also been shown that SpO_2 values obtained at altitude with long-term monitoring are always significantly lower than single measurements at rest.¹⁵ According to Loeppky et al,⁸ whether this early desaturation is closely correlated with the subsequent AMS remains to be tested by continuous and prolonged measurements in the same subjects. Portable devices are now available that measure SpO_2 continuously for many hours at a time. Therefore, our aim was to monitor SpO_2 for 24 hours in a large sample of climbers during one of the most popular ascents in the Alps and to relate the severity and length of oxygen desaturation to the subsequent development of AMS to determine the predictive value of this parameter.

Methods

RECRUITMENT

Eighty-six Caucasian climbers (18 women) intending to climb to Capanna Regina Margherita (4559 m), Mount Rosa (Italy), were recruited for the study at the cable car station in Alagna Valsesia (1154 m). The purpose of the study was explained, and the subjects provided their informed consent. All subjects were asked about their medical history, usual physical activity, use of drugs, previous AMS events and anthropometric data. Mountain guides and subjects taking drugs for AMS prophylaxis were excluded from the study. The study complied with the Helsinki principles and was approved by the Ethics and Research Committee of the Medical School of the University of Ferrara, Italy.

STUDY DESIGN

All subjects were equipped with a 24-hour data memory pulse oximeter with a finger sensor (Pulsox-300i, Konica Minolta, Osaka, Japan) to monitor the arterial oxygen saturation and heart rate (HR). The instrument was previously tested at high altitude.¹⁵ A cover was provided to secure the finger probe and to avoid excessive cooling. The pulse oximeter was removed on arrival at Capanna Regina Margherita.

Subjects were also asked to complete the Lake Louise Questionnaire (LLQ; more details in next section) in Alagna before starting, at Capanna Gnifetti (on arrival, in the evening, and in the following morning), and on arrival at Capanna Regina Margherita.

After a 30- to 45-minute cable car ascent to Punta Indren (3275 m) and a 1.5- to 2-hour trek, the subjects

arrived at Capanna Gnifetti (3647 m), where they stayed overnight. On the second day, they climbed to Capanna Regina Margherita (4559 m) and descended in the same day after 1 or 2 hours of rest.

LAKE LOUISE QUESTIONNAIRE

The LLQ is designed to identify AMS, and it consists of a symptom assessment section (5 questions with a score from 0 to 3) and a clinical assessment section (3 questions).¹⁶ A total score (LLS) of less than 3 indicates the absence of AMS (AMS^-); a score between 3 and 4 with headache indicates the presence of mild AMS (AMS^+), and a score of 5 or greater indicates the presence of moderate-to-severe AMS (AMS^{++}).

DATA COLLECTION AND ANALYSIS

Data were stored at 1-second intervals and processed by the DS-5 Minolta software.

For analysis, we divided the data into 6 frames: at rest in Alagna (1), on arrival at Punta Indren (2), during the ascent to Capanna Gnifetti (3), during the rest in Capanna Gnifetti (4), during the subsequent night at the same altitude (5), and during the ascent to Capanna Regina Margherita (6). The mean values of HR, SpO_2 , and time spent under different SpO_2 values (95%, 90%, 88%, 87%, 85%, 80%, 75%, 70%) were evaluated. Exercise, rest, and sleep were individualized by the time recorded by the subjects in the LLQ and confirmed by the HR. A first analysis was performed between AMS^- and all of AMS^+ ; a second analysis was performed between AMS^- and the subgroup of moderate-to-severe AMS (AMS^{++}).

STATISTICAL ANALYSIS

Statistical analysis was performed using a statistical software package (GraphPad Prism 5; GraphPad Software, San Diego, CA). Normal distribution was checked with the Kolmogorov-Smirnov test. Comparison among groups at different altitudes was performed by using repeated-measures analysis of variance (mixed model). The Pearson correlation coefficient was used for the single correlation between LLS and SpO_2 at 3647 m (at rest and all through the night) and during the ascent to 4559 m. The receiver operating characteristics curve analysis was performed with the statistical software MedCalc (Ostend, Belgium). The level of significance was set at $P < .05$ for all analyses.

Results

The results are reported as the mean $\pm$ SD. Climbers were initially divided into 2 groups according to the LLS recorded in the morning after the first night at 3647 m:

Table 1. Characteristics of population

	AMS+	AMS-
Number of subjects	24 (6 F)	36 (5 F)
Age (y)	37 ± 9.1	35.7 ± 13.3
Height (m)	1.77 ± 0.09	1.75 ± 0.09
Weight (kg)	71.5 ± 11.3	68.2 ± 9.5
BMI (kg/m ²)	22.8 ± 2.1	22.3 ± 2.1

Data are expressed as mean ± SD.

AMS, acute mountain sickness; BMI, body mass index.

AMS⁺ if the LLS was 3 or greater, and AMS⁻ if the LLS was less than 3. The AMS⁺ subjects were further divided according to the severity of the disease: mild AMS when the LLS was 3 to 4 and moderate-to-severe AMS (AMS⁺⁺) when the LLS was 5 or greater.

Ten subjects were excluded from the study because they climbed directly to Capanna Regina Margherita without an overnight stay at Capanna Gnifetti. Sixteen subjects were not included for illegible data or a monitoring period that was too short. Data from 60 subjects (11 women) were therefore included. A total of 24 subjects (6 women) experienced AMS on the morning after the night at 3647 m, 15 of whom (4 women) exhibited moderate-to-severe AMS (Table 1).

Age, sex, and body mass index were not related to either AMS presence or the severity of symptoms. According to the clinical history, 55% of AMS⁺ climbers had already experienced the disease during previous ascents at altitudes between 3300 m and 5000 m.

As expected, the SpO₂ decreased significantly with increasing altitude (Table 2, upper). At baseline in

Alagna, no difference in SpO₂ was found between AMS⁺ and AMS⁻ subjects when considering the whole group; however, considering only those with moderate-to-severe disease (AMS⁺⁺), the difference was already statistically significant but within the limits of accuracy of the instrument (±2%). During high altitude exposure, the AMS⁺ subjects always exhibited SpO₂ values that were significantly lower than the AMS⁻ subjects, except during the trek to reach Capanna Gnifetti. The differences were already evident at 3275 m (Punta Indren) after 30 to 45 minutes of cable car ascent (Table 2, upper).

The time spent at rest at 3647 m with SpO₂ of 85% or greater and 80% or greater was significantly higher in the AMS⁺ subjects (Figure 1A). Similar results were found during the night at 3647 m even if at a lower SpO₂ cutoff (ie, 80%, 75%, and 70%) as reported in Figure 1B. The AMS score in the morning at 3647 m was significantly and inversely correlated with the mean SpO₂ at rest on the previous afternoon ($r = -0.32$, $P = .008$; Figure 2A) and during the previous night ($r = -0.25$, $P = .04$; Figure 2B).

Regarding the climb to 4559 m, because of bad weather conditions or illegible monitoring, data from only 34 subjects were available. Subjects were divided into AMS⁺ and AMS⁻ groups according to the LLS recorded on arrival at the summit (8 AMS⁺, 26 AMS⁻). Again, the AMS⁺ subjects maintained a lower SpO₂ during the ascent to 4559 m, spending a greater percentage of time with a lower SpO₂. In fact, the AMS⁺ subjects spent 60% of the time with SpO₂ of 75% or less, compared with 37% of AMS⁻ subjects. The LLS on

Table 2. Mean SpO₂% (upper) and HR (lower) in AMS⁺, AMS⁺⁺, and AMS⁻ at different altitudes

				<i>P value AMS⁺ vs AMS⁻</i>	
<i>Altitude</i>	<i>AMS⁺ (LLS ≥ 3)</i>	<i>AMS⁺⁺ (LLS ≥ 5)</i>	<i>AMS⁻</i>	<i>LL ≥ 3</i>	<i>LL ≥ 5</i>
SpO ₂ %					
1154 m: rest	94.6 ± 1.9	94.2 ± 1.9	95.2 ± 1.2	NS	.013
3275 m: rest	86 ± 4.1	85.4 ± 4	87.7 ± 3.5	.037	.030
3275–3647 m: exercise	82.2 ± 0.58	81.9 ± 1.2	82.4 ± 0.4	NS	NS
3647 m: rest after arrival	85 ± 2.3	83.8 ± 2	86.6 ± 2.4	.0056	.0098
3647 m: night	78 ± 4.6	76.5 ± 3.9	79.2 ± 3.7	.016	.0030
3647–4559 m: exercise	74.6 ± 4.95		76.7 ± 3.9	.008	
HR					
1154 m: rest	78.7 ± 11.4	94.3 ± 2	75.7 ± 14.6	NS	.01
3275 m: rest	72.8 ± 14.9	79.6 ± 27.2	79.8 ± 18.3	NS	NS
3275–3647 m: exercise	112.1 ± 17.7	117.5 ± 20.4	110.8 ± 20	NS	NS
3647 m: rest after arrival	93.9 ± 13	99.5 ± 12.3	87.4 ± 12.9	NS	.003
3647 m: night	76 ± 13.1	82.7 ± 12.2	70 ± 9.9	NS	.0005
3647–4559 m: exercise	120.4 ± 16.1		104 ± 19	.004	

Data are expressed as mean ± SD.

AMS, acute mountain sickness; HR, heart rate; LLS, Lake Louise Score; NS, not significant; SpO₂, pulse oxygen saturation.

Figure 1. Percent of time spent at 3647 m with pulse oxygen saturation (SpO₂, %) ≤85% and ≤80% at rest (A) and ≤80%, 75%, and 70% during the night (B) in subjects with and without acute mountain sickness (AMS⁺ and AMS⁻, respectively).

arrival at 4559 m was significantly and inversely correlated with the mean SpO₂ during the ascent ($r = -0.5$, $P = .003$; Figure 3).

With regard to the HR, we found no difference between AMS⁻ subjects and all AMS⁺ subjects, except during the exercise to reach Capanna Regina Margherita; considering only AMS⁺⁺ subjects, the differences were always significant, except at 3275 m, and during the climb to Capanna Gnifetti (Table 2, lower).

PREDICTION OF AMS BASED ON SP_O₂ MONITORING

Because of the small sample of subjects who reached Capanna Regina Margherita and the fact that no one spent the night there, we focused the analysis on data recorded up to 3647 m to determine the predictive value of SpO₂ in AMS development after the first night at this altitude. The results of the predictive power of different values of SpO₂ at 3647 m are summarized in Table 3. A considerable overlap in the values was found, resulting in poor discrimination between AMS⁺ and AMS⁻

subjects. When the same analysis was repeated including only the subjects with moderate-to-severe AMS (ie, LLQ score ≥ 5, 15 subjects), the receiver operating characteristics curve analysis showed a sensitivity of 86.67%, a specificity of 82.25%, and an area under the curve of 0.87 ($P < .0001$) for the cutoff value of SpO₂ of 84% or less (Figure 4A). Restricting the analysis to the subjects exhibiting severe AMS (ie, LLQ score ≥ 6, 10 subjects), the sensitivity increased to 90% and the AUC was 0.91 ($P < .0001$; Figure 4B).

The same analysis repeated for the HR did not yield any useful results to accurately identify or exclude impending moderate-to-severe AMS: with the cutoff HR of 90 beats/min or greater, the sensitivity was 93.3% and the specificity was 57.9% (Figure 4C).

Discussion

To the best of our knowledge, this is the first report describing 24-hour oxygen monitoring at different altitudes in subjects with or without AMS. We hypothesized that the long-term monitoring of SpO₂ during an ascent to

Figure 2. Correlation between mean pulse oxygen saturation (SpO₂, %) measured at 3647 m at rest (A) and during the night (B) and the Lake Louise Score (LLS) recorded the subsequent morning.

Figure 3. Correlation between mean pulse oxygen saturation (SpO_2 , %) during the ascent to 4559 m and the Lake Louise Score (LLS) recorded at the arrival on the summit.

high altitude could definitively confirm the close relationship between early desaturation and subsequent AMS and could provide a more accurate prediction of impending AMS. The importance of early desaturation was already reported both in simulated altitude tests^{6–8} and in the field^{9–11}; all of these studies were based on short measurements of oxygen saturation, which were repeated,^{7,10} and they failed to find a good prediction of AMS. In fact, a cutoff with a high sensitivity usually had a low specificity and vice versa. Some authors had therefore suggested that the continuous monitoring of SpO_2 during ascent could have produced more reliable results.^{8,17}

In the present study, we investigate the daily hypoxic profile of climbers from 1154 m to 4559 m, reporting 2 main findings. First, with an accurate description of the level of hypoxia, we can show that climbers who will subsequently experience AMS have more severe and prolonged oxygen desaturations than AMS-resistant climbers throughout the whole exposure to high altitude, beginning several hours before the onset of the first symptoms. Our data show a significant correlation between the AMS score and the previous severity and duration of oxygen desaturation detected with continuous monitoring and not only in a single moment of the climb. It is therefore confirmed that more pronounced hypoxemia characterizes the AMS^+ subjects and occurs very early at the beginning of acute exposure above 3000 m. As regard the results at 1154 m, it should be emphasized that the difference between AMS^- and AMS^+ subjects, although significant, is minimal (1%) and within the limits of accuracy of the instrument (2%). It is therefore likely that it has no clinical relevance. All the other results are above these limits, particularly as regard to the AMS^+ . Although these values, from a clinical point of view, are not relevant, they allow identification of individuals who subsequently exhibit

moderate-to-severe AMS. Obviously, when the disease is evident, the difference between healthy and sick subjects is wider. Age, sex, and body mass index do not influence AMS development and severity, as previously reported.^{5,6,9}

An intriguing result is the loss of the difference between AMS^+ and AMS^- subjects during the 1.30 to 2 hours of exercise performed from 3275 m to 3647 m. This is true whether we consider all AMS^+ subjects or whether we consider only those who later exhibit moderate-to-severe disease (AMS^{++}). Because the study design did not include any measurement of ventilation and gas exchange, we cannot identify which exercise-induced adaptations may have overwhelmed the differences in SpO_2 between AMS^+ and AMS^- subjects. However, the difference appears during the climb to the highest altitude (4559 m). Again, we have no additional data to explain this result; we can only speculate that the development of a subclinical interstitial pulmonary edema or a higher pulmonary artery pressure, both well-known causes of ventilation–perfusion mismatching and exercise desaturation, might contribute to explain the difference.^{18–23} Other potential mechanisms might be a ventilatory control instability, affecting ventilation and breathing efficiency during exercise, or the adoption by the AMS^+ subjects of a less efficient ventilatory pattern.^{24–26} The difference we found in SpO_2 is consistent with the data reported by Karinen et al¹⁰ showing a more pronounced hypoxemia during exercise up to 5300 m in subjects who will later experience AMS. However, from our results, it seems that at the beginning of exposure to lower altitudes, some compensatory responses occur during exercise, eliminating the differences.

The second important finding is the ability to predict the development of moderate-to-severe AMS after the first night at 3647 m. In fact, we report a cutoff point ($\text{SpO}_2 \leq 84\%$) with high specificity and sensitivity (81.2% and 85.7%, respectively) and an area under the curve of 0.88, which can be useful in practice. The value of SpO_2 of 85% or less at the same altitude has a high

Table 3. Prediction of AMS by continuously monitoring $\text{SpO}_2\%$ at 3647 m

$\text{SpO}_2\%$ at 3647 m	$\text{AMS}^+ \text{ LLS} \geq 3$	
	Sensitivity%	Specificity%
≤ 88	96	34
≤ 87	88	41
≤ 85	64	66
≤ 83	28	93

AMS, acute mountain sickness; LLS, Lake Louise Score; SpO_2 , pulse oxygen saturation.

Figure 4. Receiver operating characteristics curve analysis to predict impending acute mountain sickness, as indicated by a Lake Louise Score (LLS) of 5 or greater, with pulse oximetry (A and B) and heart rate (C). Sensitivity is given by the continuous lines; specificity, by the dashed lines.

sensitivity but a much lower specificity. It means that this threshold correctly identifies all subjects prone to exhibit AMS, but there is a considerable probability of including a rather high percentage of AMS⁻ subjects in the AMS⁺ group. On the contrary, the attempt to also predict mild AMS failed because of the considerable overlap.

Heart rate has not proven to have a good predictive power even for the subjects with moderate-to-severe disease.

The predictive power of oxygen saturation has been previously investigated at different altitudes with short recordings at rest or during exercise. The sensitivity and specificity changed depending on the cutoff values, but the findings have never been completely satisfactory. Only when other variables in addition to SpO₂ were taken into consideration was the predictive power improved. Identifying a more sensitive and specific method based on an easy measurement was therefore important. We reasoned that measurements during the periods of rest, exercise, and sleep better reflect the true oxygenation and are more reliable than a single resting measurement.¹⁵ However, to determine the predictive value, we decided to limit the analysis to the period of rest. In fact, it is difficult to standardize the exercise periods; furthermore, we have shown that in the first hours of exposure to an altitude below 3500 m, there is no difference between the groups during exercise. On the other hand, if we consider also the night values, we rule out the possibility of taking early preventive measures because the diagnosis can only be made on the following morning.

The data from other studies are always predictive of AMS development above 4200 m, and for this reason, it is difficult to compare our results to the ones reported in the literature.^{6–11} We investigated the predictive power at lower altitudes, which are altitudes that are achieved not only by climbers but also by a large number of skiers

and trekkers. We think that the possibility to predict the subsequent development of moderate-to-severe AMS at 3600 to 3700 m is an interesting and useful result. In fact, this is an altitude at which subjects often arrive quickly by cable car or plane during the approach to many trekking or mountain expeditions (for example Namche Bazar and Lhasa as well as Capanna Gnifetti).

The ability to predict the subsequent onset of moderate-to-severe AMS provides the opportunity to take some measures such as rest, avoidance of outdoor physical activity, an extra rest day, or prophylactic drugs, such as acetazolamide, if necessary. Identified at-risk subjects can also be advised to reduce the rate of ascent and to better acclimatize before climbing or spending the night at higher altitudes.²⁷

This study has some limitations. First, the results offer the possibility to predict AMS only at a given altitude (3600–3700 m) and only in subjects who arrived quickly at that altitude without previous acclimatization. Furthermore, our findings can predict the onset of moderate-to-severe AMS but not mild AMS, and the results are only valid if the SpO₂ is monitored for at least 15 minutes. A simple reading of 2 or 3 minutes can lead to inaccurate results. In the field, this may not always be easy to perform.

Another limitation is the lack of a detailed investigation of the physiological mechanisms involved in oxygen saturation to understand the disappearance of the difference between SpO₂ in AMS⁺ and AMS⁻ subjects during exercise at the beginning of altitude exposure. In fact, the large sample of subjects, which on the other hand is a strong aspect of this study, did not allow other physiological measurements, such as control of breathing, ventilation, pulmonary artery pressure, and ventilation-perfusion mismatch. In addition, having recruited the subjects at the departure station of the cable car, the sea level values were not collected.

Conclusions

The introduction of the length and severity of oxygen desaturation allow us to state with certainty that subjects who later exhibit AMS are always more hypoxemic than AMS-resistant subjects during high altitude exposure and offer a cutoff value of SpO_2 at 3600 to 3700 m with satisfactory specificity and sensitivity. These results can be useful during altitude simulation tests. In this case, we suggest monitoring oxygen saturation for at least 15 minutes during a hypoxic test simulating an altitude of approximately 3600 m (ie, 13% O_2) to better identify subjects who are at risk of moderate-to-severe AMS. If the test is used in the field, the threshold of 84% at 3600 to 3700 m can be used, provided that this altitude is reached quickly. Additionally, in this case, the SpO_2 should be measured for at least 15 minutes with subjects resting, silent, and breathing quietly. This measurement can also be performed in remote settings with simple and inexpensive equipment. The predominant value of this monitoring should be taken into account or, better yet, calculated as a time-weighted average. We suggest a minimum of 15 minutes because according to our data, this period is sufficiently long to produce stable and reliable values. However, we report that in a field study by Koele et al.²⁸ a 10-minute monitoring was sufficient to obtain significant results, providing the potential to rule out AMS.

We again emphasize that the use of these results is restricted to a single altitude, only if reached quickly, and that SpO_2 should not be self-measured but must be detected by another person, following the above-mentioned rules.

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