TURKISH JOURNAL OF EMERGENCY MEDICINE

Original Article

Access this article online
Quick Response Code:

Website:
https://turkjemergmed.com/

DOI:
10.4103/tjem.tjem_44_24

Incidence and risk factors of acute mountain sickness during ascent to Hoh Xil and the physiological responses before and after acclimatization

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Submitted: 02-03-2024
Revised: 30-05-2024
Accepted: 04-06-2024
Published: 01-10-2024

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Abstract:

OBJECTIVES: Ascending to altitudes >2500 m may lead to acute mountain sickness (AMS).

METHODS: The demographics, height, weight, body mass index (BMI), smoking, and alcohol consumption of 104 healthy controls were collected in Chengdu (500 m). Heart rate (HR), saturation of pulse oxygen (SpO2), and AMS-related symptoms were collected in Hoh Xil (4200 m). A headache with Lake Louise score ≥3 was defined as AMS.

RESULTS: The incidence of AMS was 60.58%. AMS group had a lower SpO2 and higher HR than non-AMS group. Alcohol consumption seemed a risk factor for AMS. There was no difference in the BMI, age, height, weight, and smoking between AMS and non-AMS groups. The most common AMS symptom was headache, followed by dyspnea, insomnia, dizziness, lassitude, and anorexia. Women were prone to suffer from dizziness. The value of SpO2 and HR was improved both in AMS and non-AMS groups after hypoxia acclimatization, and the value showed greater improvement in AMS group. Oxygen therapy decreased the AMS-induced tachycardia, which had no any effect on SpO2 and symptom alleviating time.

CONCLUSION: Lower SpO2 and higher HR following exposure to high altitude were associated with AMS susceptibility. The anthropometric data changes were larger in AMS group than non-AMS group before and after hypoxia acclimatization.

Keywords:
Acclimatization, acute mountain sickness, anthropometric data, Hoh Xil, risk factor

Introduction

Hoh Xil is located in the northeastern extremity of the Qinghai–Tibetan Plateau, at an average elevation of 4600 m above sea level. Since its inclusion in the UNESCO World Heritage List in 2017, the number of tourists to Hoh Xil has been continuously increasing. Rapid exposure to altitudes >2500 m will trigger the overactivation of sympathetic nervous system and the compensatory response of circulorespiratory system, the main physiological changes include heart rate, blood pressure, and saturation of pulse oxygen (SpO_2).[1,2] However, when these physiological changes fail to help the body acclimate to the hypoxic conditions, it results in acute mountain sickness (AMS).[3] AMS is a syndrome that is defined by the presence of headache in combination with dizziness, fatigue, insomnia, anorexia, nausea, and vomiting, the incidence of

How to cite this article: Ouyang Q, Yang Y, Zou D, Peng Y, Zhang W, Yang Y, *et al.* Incidence and risk factors of acute mountain sickness during ascent to Hoh Xil and the physiological responses before and after acclimatization. Turk J Emerg Med 2024;24:226-30.

Box-ED section

What is already known on the study topic?

- Ascending to altitudes>2,500 meters may lead to acute mountain sickness (AMS). Incidence of AMS varies from 9% to 84%, and symptoms including headache, dyspnea, insomnia, dizziness, lassitude and anorexia.

What is the conflict on the issue? Has it importance for readers?

- Hoh Xil is attracting increasing tourists. AMS has become a general complaint of tourists. This study is intended to provide appropriate prevention counselling and interventions for tourists before traveling to Hoh Xil.

How is this study structured?

- This was a single-center, a retrospective study that includes data from 104 subjects.

What does this study tell us?

- The incidence of AMS was 60.58%. Lower SpO2 and higher HR following exposure to high altitude were associated with AMS susceptibility. The anthropometric data changes larger in AMS group than non-AMS group before and after hypoxia acclimatization.

AMS reported worldwide varies from 10% to 85%.[4,5] More seriously, a small number of AMS patients may develop life-threatening high-altitude pulmonary edema or high-altitude cerebral edema.[6-8] The Lake Louise Scoring System (LLSS) is an evaluation system designed for adults to determine whether they have no, mild, or severe AMS, which has been revised in 2018 to exclude sleep-related symptoms.[9] The LLSS has demonstrated good sensitivity and specificity at different altitudes, and it is widely used for clinical diagnosis and research on AMS.[10]

Because Hoh Xil is attracting increasing tourists, AMS has become a general complaint of tourists. Therefore, this study aims to describe, in a cohort of 104 healthy lowland-dwelling subjects, the incidence, symptoms, and risk factors of AMS during ascent to Hoh Xil. We also describe physiological variables before and after hypoxia acclimatization, and the relationship between oxygen therapy and physiological variables and symptom alleviating time. This study is intended to provide appropriate prevention counseling and interventions for tourists before traveling to Hoh Xil.

Methods

Participants

A total of 104 lowland-dwelling and healthy Chinese military officers and soldiers (47 female and 57 male) aged 21–49 years were recruited in September 2020. No subjects suffered from diseases with similar clinical features to AMS, circulorespiratory system diseases, neurological diseases (including migraine and cluster headache), cerebral vascular diseases, gastrointestinal system diseases, or cancer. All subjects traveled by the same train from Chengdu to Hoh Xil in 3 days. All subjects received the same diet and would work in Hoh Xil for three months. This study was approved by the Ethical Committee of General Hospital of The Western Theater Command, and written informed consent was obtained from subjects (Number: 2023EC5-ky070, Date: 2024-02-18).

Study design

The information on demographics, smoking, and alcohol consumption of all subjects were collected, and the weight and height were measured to calculate the body mass index. The physiological parameters (heart rate [HR] and SpO_2) of all subjects were collected at 4200 m. A headache with Lake Louise score ≥3 was defined as AMS.[11] The subjects were divided into AMS group and non-AMS group, AMS group would answer a questionnaire on their AMS symptoms. If needed, oxygen therapy could be provided for AMS subjects; therefore, AMS group could be divided into oxygen therapy group and control group. Once hypoxia acclimatization, the physiological parameters of all subjects would be collected again, and AMS group would answer a questionnaire on their AMS symptom alleviating time.

Statistical analyses

Statistical analysis was performed with the SPSS 21.0 software (IBM, Armonk, NY, US) was applied for statistical analysis. The Kolmogorov–Smirnov test was used to determine the normality of continuous data. The variables were presented as the mean ± standard deviation, and comparisons between the groups were evaluated with the Student's *t*-test. Cases and percentages were used to express categorical variables, which were compared with the Chi-square test. P <0.05 indicated a statistically significant difference.

Results

Table 1: Anthropometric data of the subjects

	Total (*n*=104), mean±SD	Female (*n*=47), mean±SD	Male (*n*=57), mean±SD	*P*
BMI (kg/m^2)	22.35±2.6	20.73±2.12	23.68±2.19	<0.001**
Age (years)	35.69±6.56	36.47±6.21	35.05±6.83	0.276
Height (cm)	167.55±6.71	162.06±4.31	172.07±4.63	<0.001**
Weight (kg)	63.09±10.44	54.57±7.03	70.11±6.98	<0.001**

Two independent-sample *t*-test. BMI: Body mass index, SD: Standard deviation, **<0.001

Table 2: Demographics and anthropometric data of the subjects

Characteristics	Total (n=104), mean±SD	AMS (n=63), mean±SD	Non-AMS (n=41), mean±SD	P
Basic demographic characteristics				
BMI (kg/m^2)	22.35±2.6	22.49±2.57	22.12±2.67	0.486[a]
Age (year)	35.69±6.56	36.16±6.59	34.98±6.54	0.371[a]
Height (cm)	167.55±6.71	167.92±6.23	166.98±7.43	0.485[a]
Weight (kg)	63.09±10.44	63.73±10.1	62.1±10.98	0.438[a]
Smoker, n (%)	13 (12.50)	5 (7.94)	8 (20)	0.081[b]
Alcohol drinker, n (%)	15 (14.42)	13 (20.63)	2 (4.88)	0.025[b,*]
Physiological parameters				
SpO_2	87.03±4.4	84.67±3.53	90.66±2.85	<0.001[a,**]
HR	92.70±9.98	96.16±9.41	87.39±8.44	<0.001[a,**]

[a]Two independent-sample *t*-test, [b]Chi-square test. SD: Standard deviation, BMI: Body mass index, AMS: Acute mountain sickness, HR: Heart rate, SpO_2: Saturation of pulse oxygen, *<0.05,**<0.001

Subject's characteristics

All subjects undertook the requested measurements, and no emergency situation arose that required their exclusion. As shown in Table 1, the mean body mass index (BMI) of subjects was 22.35, and the average age, height, and weight were 35.69 years, 167.55 cm, and 63.09 kg, respectively. We also determined the BMI (20.73 vs. 23.68, $P < 0.001$), height (162.06 vs. 172.07 cm, $P < 0.001$), and weight (54.57 vs. 70.11 kg, $P < 0.001$) between the female and male. There was no significant statistical difference in age (36.47 vs. 35.05 years, $P = 0.276$) between females and males.

Incidence of acute mountain sickness, risk factors, and symptoms

Our study showed that 60.58% ($n = 63$) of subjects were diagnosed with AMS [Table 2]. There was no significant difference in the BMI (22.49 vs. 22.12, $P = 0.486$), age (36.16 vs. 34.98 years, $P = 0.371$), height (167.92 vs. 166.98 cm, $P = 0.485$) and weight (63.73 vs. 62.1 kg, $P = 0.438$) between AMS group and non-AMS group. The percentage of smokers was lower in AMS group than that in non-AMS group but was not statistically significant (7.94% vs. 20.00%, $P = 0.081$). In contrast, the percentage of alcohol drinkers was significantly higher in AMS group than that in non-AMS group (20.63% vs. 4.88%, $P = 0.025$). Subjects with AMS had a lower SpO2 (84.67% vs. 90.66%, $P < 0.001$) than that of subjects without AMS. In addition, the AMS group had a higher HR (96.16 vs. 87.39 bp/min, $P < 0.001$) than non-AMS group.

Besides the symptom of headache, the most common AMS symptom was dyspnea (73.00%, $n = 46$), followed by insomnia (63.50%, $n = 40$), dizziness (55.60%, $n = 35$), lassitude (55.60%, $n = 35$), and anorexia (42.90%, $n = 27$) [Table 3]. A significant difference was noted between the female group ($n = 25$) and the male group ($n = 38$) for dizziness (84.0% vs. 36.8%, $P < 0.001$), whereas other symptoms were similar between the two groups.

Table 3: Symptoms associated with acute mountain sickness

	Total (n=63), n (%)	Women (n=25), n (%)	Men (n=38), n (%)	P
Dizziness	35 (55.60)	21 (84.0)	14 (36.8)	<0.001**
Insomnia	40 (63.50)	19 (76.0)	21 (55.3)	0.094
Dyspnea	46 (73.00)	18 (72.0)	28 (73.7)	0.883
Lassitude	35 (55.60)	14 (56.0)	21 (55.3)	0.954
Anorexia	27 (42.90)	11 (44.0)	16 (42.1)	0.882

Chi-square test, **<0.001

Contrast the physiological variables before and after acclimatization

Upon acute exposure to an altitude of 4,200 m, the AMS group had a lower SpO2 (84.67% vs. 90.66%, $P < 0.001$), while a higher HR (96.16 vs. 87.39 bp/min, $P < 0.001$) than non-AMS group. The levels of SpO2 were significantly improved both in AMS group (84.67% vs. 90.22%, $P < 0.001$) and non-AMS group (90.66% vs. 92.37%, $P < 0.001$) after hypoxia acclimatization. In addition, the improvement of SpO2 in AMS group was much more obvious than that in non-AMS group (5.56% vs. 1.71%, $P < 0.001$) [Table 4]. In contrast, the HR was decreased both in AMS group (96.16 vs. 85.03 bp/min, $P < 0.001$) and non-AMS group (87.39 vs. 81.37 bp/min, $P < 0.001$) after hypoxia acclimatization. We found the HR decreased more significantly in AMS group than in the non-AMS group (−11.13 vs. −6.02 bp/min, $P < 0.001$) [Table 4].

In this study, 17 AMS subjects (26.98%, 17/63) were receiving oxygen therapy. The AMS symptoms of 55 subjects (87.30%, 55/63) were alleviated in 2 weeks, and the remaining 8 subjects (12.70%, 8/63) were alleviated in 3 weeks. In the Spearman correlation analysis [Table 5], oxygen therapy was associated with the change of HR in AMS group before and after hypoxia acclimatization ($r = 0.297$, $P = 0.018$), indicating that oxygen therapy could alleviate the AMS-induced tachycardia. However, oxygen therapy was not associated with the change of SpO2 before and after hypoxia acclimatization ($P = 0.307$) and the symptom alleviating time ($P = 0.067$).

Table 4: Anthropometric data of the subjects

Characteristics	Total (*n*=104), mean±SD	AMS (*n*=63), mean±SD	Non-AMS (*n*=41), mean±SD	*P*	
SpO_2					
1	87.03±4.4	84.67±3.53	90.66±2.85	<0.001[a,**]	<0.001[b,**]
2	91.07±2.85	90.22±2.85	92.37±2.85	<0.001[a,**]	
d(SpO_2)	4.041±2.8	5.561±2.8	1.711±2.8	<0.001[a,**]	
HR					
1	92.70±9.98	96.16±9.41	87.39±8.44	<0.001[a,**]	<0.001[b,**]
2	83.59±8.84	85.03±8.19	81.37±9.42	0.038[a,*]	
d(HR)	−9.128±9.4	−11.13±9.42	−6.023±9.4	<0.001[a,**]	

[a]Two independent-sample *t*-test, [b]Pared-samples *t*-test. 1: Acute exposure to 4200 m, 2: Hypoxia acclimatization, AMS: Acute mountain sickness, HR: Heart rate, SpO_2: Saturation of pulse oxygen, *<0.05,**<0.001

Table 5: Correlation between oxygen therapy and anthropometric parameters

Characteristics	*r*	*P*
d(SpO_2)	−0.131	0.307
d(HR)	0.297	0.018*
Symptom alleviating time (days)	−0.232	0.067

Spearman correlation. HR: Heart rate, SpO_2: Saturation of pulse oxygen, *<0.05

Discussion

In this study, we considered 104 healthy Chinese military officers and soldiers as our subjects, none of the subjects suffered from diseases with similar clinical features to AMS, circulorespiratory system diseases, neurological diseases (including migraine and cluster headache), cerebral vascular diseases, gastrointestinal system diseases or cancer. All subjects traveled from an elevation of 500–4200 m by train in 3 days, which was a continuous and gradual ascent. Some previous reports have indicated that the incidence of AMS varies from 9% to 84%.[12,13] The incidence of AMS that we reported in this study was within this range (60.58%).

In the study, we examined the risk factors associated with the development of AMS, and we found that lower SpO2 was a risk factor for AMS. Previous study has reported that SpO2 decrease under hypoxic and hypobaric conditions was positively correlated with AMS due to fluid accumulation in the pulmonary vasculature and inflammatory reactions in the peripheral airways reducing pulmonary gas exchange.[14,15] Therefore, the poor ability to self-regulation of the respiratory system may more likely to develop AMS. We also found an association between higher HR with AMS risk. The increasing of HR meant higher breathing frequency, which lead to increased strain on respiratory muscles under hypoxic and hypobaric conditions. It could be the reason for the higher incidence of AMS in these subjects. Although we found that alcohol consumption might be a risk factor for AMS, we could not make a definite conclusion due to the small number of included trials (*n* = 15).

Our data also demonstrated that the most common AMS symptoms were headache (100.00%) and dyspnea (73.00%, *n* = 46), followed by insomnia (63.50%, *n* = 40), dizziness (55.60%, *n* = 35), lassitude (55.60%, *n* = 35), and anorexia (42.90%, *n* = 27), and female were more likely to suffer from dizziness. Recent research shows that subjects with hyperresponsiveness to hypoxia may develop dizziness under hypoxic and hypobaric conditions.[16] Females were more susceptible to hypoxemia due to the relatively smaller tidal volume and higher breathing frequency, which may explain why the higher incidence of dizziness in female observed in our study.

SpO2 and HR values were better in non-AMS group than AMS group regardless of before and after hypoxia acclimatization. In addition, our data also showed that the improvement of SpO2 and HR in AMS group was more significantly than non-AMS group after hypoxia acclimatization. These results indicated that the cardiorespiratory function of non-AMS group was better tolerant to the hypoxic environment than AMS group. Previous study has indicated that the individual variation may be caused by many factors, such as the peripheral and central chemoreflex responses, respiratory center activities, cerebral blood flow, muscle CO_2 production, and gas exchange at the alveolar level.[17] Furthermore, the individual variation may also be caused by other factors, such as genetics, diet, and disease stage. In this study, all subjects are healthy Chinese people without any diseases and fed with same diet, thus, we removed these confuse factors. However, we could not rule out the possibility of genetics, which is a common and uncontrollable factor that makes individuals susceptible to AMS.[18] Previous study has shown that endothelial PAS domain-containing protein 1 (EPAS1) and vascular endothelial growth factor (VEGFA) gene variants are related to AMS susceptibility in the Chinese Han population.[19] Therefore, we suspected that the AMS group in our study was the susceptible populations of AMS, and the underlying single-nucleotide polymorphisms involved in the genesis of AMS needed further study.

Spearman correlation analysis demonstrated that oxygen therapy was positively correlated with the improvement of HR in AMS group before and after hypoxia acclimatization. Our study exhibited that oxygen therapy was effective in relieving tachycardia. Previous study has reported that hypoxemia increases catecholamine secretion and sympathetic activity, resulting in increased heart rate, blood pressure, and venous tone.[20] Therefore, oxygen therapy for high-altitude-induced hypoxia is logical. However, there is no correlation analysis conducted between oxygen therapy and the improvement of SpO2 in AMS group before and after hypoxia acclimatization. In addition, the result also showed that the oxygen therapy could not shorten the course of hypoxia acclimatization. Despite the results were unexplained, due to the limited sample size included in this study, subsequent clinical studies and systematic evaluation with large sample data are required.

Limitations

The limitations of our study are summarized as follows: (1) small sample size – total subjects included in this study are only 104; (2) subjects are mostly young despite of a wide range (21–49 years); (3) different treatment regimen. Timing of oxygen therapy is different; (4) lack of blood pressure data and erythrocyte and hemoglobin values.

Conclusion

In this study, the AMS affected 60.58% of 104 subjects that traveled to Hoh Xil, and lower SpO2 and higher HR following exposure to high altitude were associated with AMS susceptibility. The anthropometric data changes larger in AMS group than non-AMS group before and after hypoxia acclimatization. In addition, oxygen therapy has limited value for AMS, and the influence of alcohol consumption on AMS susceptibility needed a larger sample size and systematic studies. This study serves as a medical advice to help travelers with their planning for a safer travel to Hoh Xil or similar high-altitude areas.

Acknowledgments

We would like to thank Xin He, Meimin Xie, Yong Yang, Shuyong Yang, and Min Li for their assistance with data collection.

Authors' contributions

Qing Ouyang contributed to the study design, collected data, drafted the manuscript, and approved the final version of the manuscript. Yuting Yang contributed to the data cleanup and analysis, drafted the manuscript, and approved the final version of the manuscript. Dongbo Zou, Yuping Peng, and Wenxin Zhang contributed to the data cleanup and analysis. Yuan Ma and Yongjian Yang contributed to the study design and approved the final version.

Conflicts of interest

None Declared.

Ethics approval and consent to participate

This study was approved by the Ethical Committee of General Hospital of The Western Theater Command, and written informed consent was obtained from subjects (Number: 2023EC5-ky070, Date: 2024-02-18).

Funding

This project was support by the Spark Talent program of General Hospital of The Western Theater Command and Research Project of General Hospital of The Western Theater Command (2021-XZYG-C37 and 2021-XZYG-A13).

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