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Diagnosis and Management of Mountain Sickness - A Review

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Abstract: Acute mountain sickness (AMS) is the most common form of illness at high altitude; however, it is still unclear whether age is a protective factor or a risk factor for the development of AMS in travellers. The condition generally occurs at altitudes higher than 8,000 feet (ft), or 2,500 meters (m), and is usually due to a lack of oxygen. A person who is not used to high altitudes is most at risk of developing altitude sickness. Mountain sickness is also called high altitude sickness, referring to the impact of environment on the body health at high elevation. Altitude illness is divided into 3 syndromes: acute mountain sickness, high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE). Mountain climbers are at risk of developing altitude sickness. Altitude sickness is caused by ascending too rapidly, which doesn't allow the body enough time to adjust to reduced oxygen and changes in air pressure. Symptoms include headache, vomiting, insomnia and reduced performance and coordination. Generally, it is classified into three categories based on the onset condition, namely acute mountain sickness, high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE). Hypoxic sleep disruption contributes to the symptoms of acute mountain sickness. Hypoxemia at high altitude is most severe during sleep. The sickness signifies that the human body has yet to adapt to the environment at 2500 meters or above in elevation, where low air pressure and oxygen will impair body functions. Mild cases can be treated according to symptoms (such as with painkillers for a headache), which usually go away on their own within a few days. Medicines specific for altitude sickness are also available. Acetazolamide is used to prevent and reduce the symptoms of altitude sickness. This medication can decrease headache, tiredness, nausea, dizziness, and shortness of breath that can occur when you climb quickly to high altitudes.

Keywords: Acute Mountain Sickness (AMS), High-Altitude Cerebral Edema (HACE), High-Altitude Pulmonary Edema (HAPE), High Altitude Sickness, Lake Louise Acute Mountain Sickness Score

1. Introduction

At altitude, a very common reaction is increased urinary output. The body's kidneys sense the lower level of oxygen immediately and kick into high gear. The kidneys release a hormone, erythropoetin, which commands the bone marrow to produce more red blood cells to increase the oxygen-carrying capacity of the blood. Symptoms may include headaches, vomiting, tiredness, confusion, trouble sleeping, and dizziness. Acute mountain sickness can progress to high-altitude pulmonary edema (HAPE) with associated shortness of breath or high-altitude cerebral edema (HACE) with associated confusion. Altitude sickness refers to the risk to health when the body is situated at high altitude, because the drop of atmospheric pressure means a decrease in the partial pressure of oxygen for the body to consume and the body will develop symptoms if it cannot adapt to the rising elevation [1]. The manifestation may aggravate if the individual stays up late and does not get enough rest or catch a cold, when rapidly climbing up in altitude, as these conditions will often onset at an altitude above 2500 meters or occasionally start at an altitude of 2000 meters or so. In general, the sickness can occur at any altitude above 2000 meters of sea level and almost certain to appear when crossing the threshold of 2500 meters. Mountain climbers are at risk of developing altitude

sickness. Altitude sickness is caused by ascending too rapidly, which doesn't allow the body enough time to adjust to reduced oxygen and changes in air pressure. Symptoms include headache, vomiting, insomnia and reduced performance and coordination. Common complaints may include headache, dizziness, nausea and vomiting, sleep disturbance, loss of appetite, etc. But the 2018 self-assessment questionnaire for acute altitude sickness by the Lake Louise Consensus Group, the factor of sleep disturbance was removed, since studies have shown the cause to be low blood oxygen, rather than the environment itself [2]. Slow deep breathing improves ventilation efficiency for oxygen as shown by blood oxygenation increase, and it reduces systemic and pulmonary blood pressure at high altitude but does not change pulmonary gas diffusion.

2. Clinical Features of Mountain Sickness

1) Acute Mountain Sickness (AMS) occurs when an individual rapidly climb in altitude, resulting in headache and at least one of the following symptoms, such as gastrointestinal discomfort (loss of appetite, nausea and vomiting), fatigue, lethargy, dizziness, insomnia, etc [3].
2) High altitude cerebral edema (HACE) will develop on a rapid climb in altitude that beside the symptoms of AMS, the patient will at least manifest one of the following symptoms, including unsynchronized gait to result in instability of posture, which can be tested by tandem gait, involving slowly walking in a straight line [4-6].
3) High Altitude Pulmonary Edema (HAPE) has at least two of the following cardiopulmonary symptoms, such as wheezing, coughing, chest tightness and pain, all of which are signs of decreased cardiorespiratory fitness. Also, the patient may experience a feeling of swelling in the lungs that typically the auscultation may show either rale or wheezing sound, that the individual seemingly has the shortness of breath, tachycardia and systemic cyanosis to give a purple complexion [7, 8].

3. The Definitions and Risk of Mountain Sickness (Table 1)

According to the definition revised by the Lake Louise Consensus Group in 2018, there are three major categories:

A. Acute Mountain Sickness (AMS) is diagnosed by at least four symptoms that develop in six hours after achieving an altitude higher than 2500 meters and among them, headache is the primary complaint and the total score, which can be calculated by the list below, must be at least three points or more:

1) Headache: no headache (0), slight headache (1), moderate headache (2), severe headache that cannot be relieved (3). [8-11].
2) Gastrointestinal symptom: good appetite (0), nausea or loss of appetite (1), moderate nausea or vomiting (2), severe nausea or vomiting that cannot be relieved (3). [12, 13].
3) Fatigue and/or weakness: no fatigue/asthenia (0), mild fatigue/asthenia (1), moderate fatigue/asthenia (2), severe fatigue/asthenia that cannot be relieved (3).
4) Dizziness: No dizziness (0), slight dizziness (1), moderate dizziness (2), severe dizziness that cannot be relieved (3). [14, 15].

Level of Severity:

Mild acute mountain sickness will score a total of 3-5 points, as moderate acute mountain sickness will score a total of 6-9 points and severe acute mountain sickness will score a total of 10-12 points. Regardless of the severity, all cases must have symptom of headache, plus a total score of 3 or more to be diagnosed. The scoring of AMS should not begin until 6 hours after ascent to avoid interference by transient body response to the tedious climb and acute hypoxia (due to vagal reflex). And the 2018 revision removed the criterium of insomnia, because recent studies have shown that sleep disturbance is more likely to be caused by low blood oxygen and has little correlation with other symptoms. Frequently, the first symptom is headache, followed by vomiting as an indication of aggravated condition. Symptoms will start to show in 6 to 12 hours after achieving the high altitude. Mild symptoms can be relieved in a day or two, as the body starts to adapt to the environment. However, in severe case, high-altitude cerebral edema may develop [16, 17].

B. High Altitude Cerebral Edema (HACE):

This category is defined as having or not having symptoms of AMS, accompanied by unsteady gait or altered consciousness due to the onset of cerebral edema at high altitude (3000 to 4000 meters), which is rare with incidence rate of 0.5-1%. Unsteady gait can be checked by tandem gait test and is a determining criterium of high-altitude cerebral edema. If left untreated or unable to retreat to lower altitude, it may lead to coma or uncal herniation. Severe condition, if left untreated in 24 hours, will be fatal [18, 19].

C. High Altitude Pulmonary Edema (HAPE):

It involves rapid ascent and at least two of the following symptoms, including dyspnea at rest, cough, weakness or decreased activities, chest tightness or swelling, plus at least another 2 of the following conditions, such as rales or wheezing in one lung, systemic cyanosis, tachypnea or tachycardia. This category of disease occurs above 2500 meters and is the most common cause of death for patient with altitude sickness. The mortality rate is as high as 50% if left untreated and can occur in one to four days after onset. Hypobaric hypoxia is the cause, which results in an increase of pulmonary arterial pressure and permeability of pulmonary blood vessels. Due to pressure gradient, the water will rush into the lungs. Early symptoms include decreased physical activities, dry cough, fatigue, chest tightness, rapid heart rate, and rapid breathing. Late symptoms include dyspnea at rest, suffocation at night, coughing with pink foamy sputum, cyanosis (due to the drop in blood oxygen), rales, etc. The most urgent treatment for these late symptoms is oxygen therapy and to reach lower altitude to relieve the symptoms, or else, the condition may quickly develop and lead to death [20-25].

Table 1. *Risk of altitude sickness.*

risk level	risk factor
low risk	Those who do not have any history of altitude sickness and the altitude of this trip does not exceed 2500 meters above sea level; stay at an altitude of 2000-3000 meters to adapt for more than 2 days; then climb no more than 500 meters per day, and within 3 days Climbing altitude does not exceed 1000 meters.
moderate risk	Those who had a history of acute mountain sickness and climbed to an altitude above 2500 meters within 2 days; those who had no history of altitude sickness but climbed to an altitude above 2800 meters within 2 days. After arriving at an altitude of 2,800 meters, climb to an altitude of more than 500 meters every day, but stay at the original altitude for one more day for every 1,000 meters climbed.
high risk	Those with a history of high-altitude pulmonary edema or high-altitude cerebral edema, or a history of acute mountain sickness, and climbed to an altitude of more than 2,800 meters within 2 days. Those who have no history of altitude sickness but climbed to an area above 3,500 meters above sea level within 2 days; after arriving at an altitude of 3,000 meters, they climbed an average of more than 500 meters per day, and did not stay at the original altitude for every 1,000 meters. Those who suffer from altitude sickness.

4. Risk Factors

The risk factors include rapid ascent (a climb of more than 400-600 meters per day at the altitude of 2000 meters and above), previous history of the sickness, young age, genetic predisposition, strenuous exercise before acclimatization to altitude, individual oxygen consumption, etc. There is also the classification of climbing altitude, where high altitude is defined as 8,000-12,000 feet (2438-3650 meters) above sea level, very high altitude is at 12,000-18,000 feet (3650-5486 meters) and very high altitude is over 18,000 feet (>5486 meters) [26-30].

5. The Headache

Headache, which is the most common complication associated with altitude sickness, can manifest as high-altitude headache (HAH) or occur together with acute mountain sickness (AMS). International Classification of Headache Disorders, third Edition (ICHD-3) separate headache into high-altitude headache (HAH) or as a nervous system disorder or humoral response caused by hypoxia. The primary mechanism is the increased microvascular pressure and cerebral vasodilation due to hypoxic condition, which may lead to edema. Symptoms include headache, accompanied by sleep disturbance, fatigue, dizziness, nausea, anorexia, and unsteady gait. However, there is variation in individual response to hypoxia. Cerebral edema is the most severe outcome of AMS and occurs above 2500 meters. Brain MRI reveals edema in the subcortical white matters and corpus callosum. The high-altitude headache is treated with anti-inflammatory NSAIDs and analgesic drugs. Although the steroid treatment can reduce cytokine release and inflammation, there is still the possibility of exacerbation of the condition to result in cerebral edema [31-35].

6. Prevention and Clinical Management of Altitude Sickness

The recommended drugs for the prevention of acute mountain sickness and high-altitude cerebral edema are Diamox and Dexamethasone. Preventive medications for high altitude pulmonary edema include Nifedipine (a calcium ion blocker), Sildenafil (a.k.a. Viagra) and Cialis. Diamox, which is the Acetazolamide-type diuretics for edema, will be administered twice a day at a dosage of 125mg, in 24 hours before the climb and again in 48 hours or on the second night after reaching the highest altitude of the climb. Patient should use until 48 hours after reaching the highest altitude. When used in treating acute mountain sickness, it is administered every 8-12 hours (or 2 to 3 times a day) at a dosage of 250mg. Also, it is used to treat insomnia at high altitude by taking the medication (125mg) one hour before bedtime. The side effects include numbness and hypokalemia [36].

Dexamethasone, which is considered the second-line medication, requires the patient to observe any sign of symptoms for another 18 hours after stopping the drug. Moreover, it is not effective for high altitude pulmonary edema. However, for acute altitude sickness, it is given at 4mg every 6 hours. To treat high altitude cerebral edema, the medication starts at an initial dosage of 8mg, followed by 4 mg every 6 hours. Side effects include rebound symptoms, mood change, and hyperglycemia [32].

Nifedipine, which is a common antihypertensive drug, is ineffective in preventing AMS and HACE. But in its slow-release form, it is used to prevent HAPE by giving 20-30mg every 12 hours. On the other hand, another modality of treatment for HAPE includes an initial dose of 10mg in short-acting form and then followed by its slow-release form every 12 hours. Side effects are rapid heart rate and decreased blood pressure.

Salmeterol (beta-agonist) is bronchodilator and can be used to prevent and treat HAPE. It must be used before the climb, once every 12 hours. Sildenafil (a.k.a. Viagra) must not be used with nitrate drugs. For prevention and treatment of HAPE, it is given 20-80mg once a day. Despite that it has less hypotensive side effect than Nifedipine, there are still other issues, such as headache, flushing, dizziness, etc. Altitude sickness can be treated by medication, but lowering altitude is still the most effective way. And currently, medications for prevention altitude sickness is not 100% and thus, acclimatization is still the key before climbing. Preventive drug, such as Diamox (Acetazolamide), must be prescribed by physician. Therefore, a climber should consult beforehand. For patient with severe altitude sickness, there is also a portable pressurized bag (a.k.a. Gamow bag), which utilizes a foot pump to inflate a portable bag to simulate pressurized atmosphere for easier breathing during ascent. The effect is

equivalent of lowering the altitude by 1500 to 1800 meters. The Taiwan Field Area Emergency Rescue Association is now determined to achieve the goal of zero death from altitude sickness, in which it has provided many emergency shelters, including the well-known Song Syue Lodge on Mount Hehuan, where they also installed a portable pressurized bag on its upper floor for climbers to use in case of emergency [36]. Non-drug treatment include three major approaches and they are altitude reduction, hyperbaric bag therapy, and oxygen therapy.

7. Conclusion

It is crucial for climbers to be familiar with the early symptoms of altitude sickness and always remain alert. They are advised to take preventive drugs before the climb to avoid altitude sickness. And if the sickness occurs, they are to follow four principles, that is, to lower altitude, increase atmospheric pressure, give oxygen and rest, besides giving medication to alleviate the symptoms and increase the chance of survival.

1) Prevention of acute altitude sickness and high-altitude cerebral edema: (1) Diamox (Acetazolamide) is currently the first-line choice, which not only treat but also prevent the sickness in advance. It belongs to the sulfonamide family of drugs and thus, should be avoided for patients with favism, as they are allergic to sulfonamides. (2) Steroids, such as dexamethasone, also have both preventive and therapeutic effect. It is to note that when using it to treat acute mountain sickness or high-altitude cerebral edema, the dosage must be higher than the dosage for prevention [37].
2) Prevention of high-altitude pulmonary edema: (1) Nifedipine is not only a calcium ion blocker for preventing altitude sickness but also has been clinically proven to relieve pulmonary edema. (2) Type 5 phosphodiesterase inhibitors (including Tadalafil, Sildenafil, etc.) can prevent the increase of pulmonary arterial pressure at high altitude, but they have no therapeutic effect on patients who already have the edema.

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