Practice Guidelines

Acute Altitude Illness: Updated Prevention and Treatment Guidelines from the Wilderness Medical Society

Key Points for Practice

- Gradually increasing sleeping altitude is the best way to prevent altitude illness. Staged ascent and preacclimatization to hypoxia also reduce risk.
- Acetazolamide and dexamethasone can be used to prevent acute mountain sickness and high altitude cerebral edema, but only acetazolamide aids in acclimatization.
- The most important treatment for altitude illness is descent of 1,000 to 3,300 ft, with supplemental oxygen if available.

From the *AFP* Editors

Acute altitude illness comprises acute mountain sickness (AMS), high altitude cerebral edema (HACE), and high altitude pulmonary edema (HAPE). Symptoms of AMS, the most common form of altitude illness, include headache, nausea, vomiting, fatigue, dizziness, and insomnia. If not appropriately treated, AMS can progress to life-threatening HACE or HAPE, which can present together or separately. Although HACE presents with similar symptoms as AMS, the cerebral edema can lead to ataxia, confusion, or altered mental status. HAPE is characterized by reduced exercise tolerance, exertional dyspnea, and cough, followed by dyspnea at rest, cyanosis, and productive cough with pink frothy sputum.

Unacclimatized people are at high risk of acute altitude illness when ascending above 8,200 ft (2,500 m), but AMS can occur as low as 6,500 ft (2,000 m). HACE is typically encountered at higher elevations unless presenting with HAPE. The Wilderness Medical Society does not use specific altitude thresholds for diagnosis.

Coverage of guidelines from other organizations does not imply endorsement by *AFP* or the AAFP.

This series is coordinated by Sumi Sexton, MD, editor-in-chief.

A collection of Practice Guidelines published in *AFP* is available at https://www.aafp.org/afp/practguide.

CME **This clinical content** conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 461.

Author disclosure: No relevant financial affiliations.

Risk Assessment

Because the risk of acute altitude illness depends on acclimatization, sleeping altitude is more important than altitude reached while awake.

People without a history of AMS who do not sleep above 9,200 ft (2,800 m) are at low risk of AMS. Regardless of AMS history, people who allow at least two days to ascend to a sleeping altitude of 8,200 to 9,800 ft (2,500 to 3,000 m) are at low risk if they sleep no more than 1,600 ft (500 m) above the previous night's altitude and take a day to acclimatize after every increase of 3,300 ft (1,000 m) in sleeping altitude.

People with a history of AMS who make a one-day ascent to a sleeping altitude of 8,200 to 9,200 ft have a moderate risk of AMS. Those without a previous episode who make a one-day ascent to a sleeping altitude above 9,200 ft also have a moderate risk. Regardless of AMS history, people who ascend to a sleeping altitude above 9,800 ft are at moderate risk if they sleep more than 1,600 ft above the previous night's altitude but take a day to acclimatize after every increase of 3,300 ft in sleeping altitude.

People with a history of AMS who make a one-day ascent to a sleeping altitude above 9,200 ft have a high risk of developing AMS. All people with a history of HACE or HAPE are at high risk of AMS, regardless of sleeping elevation or rate of ascent. Regardless of AMS history, all people are at high risk of AMS if they: (1) make a one-day ascent to a sleeping altitude above 11,500 ft (3,500 m); (2) make extremely rapid ascents (e.g., climbing Mt. Kilimanjaro [19,341 ft (5,895 m)] in fewer than seven days); or (3) ascend to a sleeping altitude above 9,800 ft, then sleep more than 1,600 ft above the previous night's altitude without allowing a day off to acclimatize.

Prevention of AMS and HACE

Controlling the rate of ascent—specifically, gradually increasing sleeping altitude over several days—is recommended to prevent AMS and HACE. When feasible, staged ascent and preacclimatization should be considered. Staged ascent refers to spending six to seven days at moderate altitude (7,200 to 9,800 ft [2,200 to 3,000 m]) before ascending to a higher elevation. Staged ascent allows compensatory increases in ventilation and oxygenation, and blunts the pulmonary artery pressure response. Preacclimatization refers to repeated exposure to hypoxia before ascent. Some

studies showed that preacclimatization with long-duration hypoxic exposures (at least eight hours daily for more than seven days) decreases the incidence and severity of AMS, but other studies showed no effect.

Several commercial products allow people to sleep or exercise in simulated high-altitude conditions before traveling (marketed as altitude tents or altitude training systems). The only placebo-controlled trial examining these products found that they reduced AMS incidence, but the study was limited by technical problems with the product. Benefits are more likely when they are used for at least eight hours daily for several weeks before ascent, and when sleep quality is not compromised.

No studies have examined the use of short-term supplemental oxygen—over-the-counter prefilled canisters or visits to oxygen bars—for the prevention of AMS. These measures are unlikely to be beneficial. Other over-the-counter products, such as powdered drink mixes, also lack evidence of benefit.

Forced overhydration is not effective for preventing altitude illness and increases the risk of hyponatremia. However, maintaining adequate hydration is important because symptoms of dehydration can mimic those of AMS.

PHARMACOLOGIC PROPHYLAXIS

Acetazolamide aids in acclimatization and should be strongly considered for high-altitude travelers at moderate to high risk of AMS. The recommended prophylactic dosage for adults is 125 mg every 12 hours; the dosage for children is 2.5 mg per kg (maximum: 125 mg) every 12 hours. Acetazolamide should be started the day before ascent and continued for two to four days after arrival at the target altitude. However, it still has beneficial effects if started the day of ascent. Although acetazolamide is a sulfonamide, it is extremely unlikely to cause an allergic reaction; a supervised trial can be considered before traveling. Acetazolamide is contraindicated in patients with a history of anaphylaxis or Stevens-Johnson syndrome from a sulfonamide.

Dexamethasone can prevent AMS and HACE in adults at moderate to high risk, although it does not help with acclimatization. The recommended adult prophylactic dosage is 2 mg every six hours or 4 mg every 12 hours. Dosages of 4 mg every six hours can be considered in very high-risk situations (e.g., military or search-and-rescue teams being airlifted above 11,500 ft and immediately performing physical work). Dexamethasone prophylaxis is not recommended in children. As with acetazolamide, dexamethasone should be started one day before ascent and continued for two to four days after reaching the target altitude. If dexamethasone is used for longer than 10 days, it should be tapered over one week instead of being stopped abruptly.

Ibuprofen can be used to prevent AMS in people who are allergic to, cannot tolerate, or do not wish to take acetazolamide or dexamethasone. Two studies found that 600 mg three times daily is more effective than placebo, but a smaller study found no benefit. Trials comparing ibuprofen with acetazolamide had mixed results: one showed similar benefits for preventing headache and AMS; another found ibuprofen inferior.

Chewed coca leaves, coca tea, and other coca-derived products are commonly recommended for AMS prevention in the Andes Mountains. These products have not been adequately studied and are not recommended.

Other pharmacologic options that are not recommended for AMS prevention include acetaminophen, antioxidants, dietary nitrates, ginkgo, inhaled budesonide (Rhinocort), iron, leukotriene receptor blockers, phosphodiesterase inhibitors, salicylic acid, spironolactone, and sumatriptan (Imitrex).

Treatment of AMS and HACE

Descent is indicated in patients with severe AMS, AMS that does not resolve with other treatments, or HACE. Unless terrain, weather, or injuries make descent impossible, patients should descend until symptoms resolve (typically a decent of 1,000 to 3,300 ft [300 to 1,000 m]). If descent is not practical or cannot be done expeditiously, supplemental oxygen or a portable hyperbaric chamber is a suitable alternative. Supplemental oxygen should be given at flow rates sufficient to relieve symptoms and increase oxygen saturation to more than 90%. If available, a portable hyperbaric chamber can be used for patients with severe AMS or HACE.

Continuous positive airway pressure has not been evaluated and presents logistic challenges in the field (e.g., weight, bulk, lack of access to power).

PHARMACOLOGIC TREATMENT

Although acetazolamide facilitates acclimatization and can treat mild AMS, it is not recommended for treatment of moderate to severe AMS or HACE. Dexamethasone is a more reliable treatment for moderate to severe AMS or HACE. The recommended dosage of dexamethasone for AMS treatment is 4 mg every six hours in adults, or 0.15 mg per kg (maximum: 4 mg) every six hours in children. The recommended regimen for adults with HACE is an initial 8-mg dose given orally, intravenously, or intramuscularly, then 4 mg every six hours until symptoms resolve. Acetazolamide can be used as an adjunct to dexamethasone for AMS or HACE treatment. The recommended dosage is 250 mg every 12 hours in adults or 2.5 mg per kg (maximum: 250 mg) every 12 hours in children. Further ascent should not be attempted after dexamethasone is given.

Acetaminophen and ibuprofen are effective treatments for headache at high altitudes but have not been shown to improve other symptoms of AMS or HACE.

Prevention of HAPE

Although prophylaxis of HAPE is similar to that for AMS and HACE, the different pathophysiology requires different approaches.

As with AMS and HACE, gradual ascent is the primary method to prevent HAPE. No studies have examined whether preacclimatization reduces HAPE. Although staged ascent blunts the hypoxia-induced increase in pulmonary artery pressure, the number and duration of altitude stages necessary to prevent HAPE have not been evaluated.

Pharmacologic prophylaxis should be considered only for people with a history of HAPE, especially recurrent episodes. The preferred medication is extended-release nifedipine, 30 mg every 12 hours starting the day before ascent and continuing for four to seven days after reaching target elevation or until descent. Other recommended prophylactic medications include tadalafil (Cialis), 10 mg every 12 hours, which is preferred over dexamethasone, 8 mg every 12 hours. Salmeterol (Serevent) is not recommended, and the benefit of acetazolamide is not known.

Treatment of HAPE

Before initiating treatment for HAPE, other causes of respiratory symptoms at high altitude should be considered, including asthma, bronchospasm, mucus plugging, myocardial infarction, pneumonia, pneumothorax, pulmonary embolism, and viral infection. If HAPE is suspected, supplemental oxygen should be started, and the patient should descend at least 3,300 ft while minimizing exertion. If immediate descent is not feasible, supplemental oxygen or hyperbaric treatment is recommended. If neither supplemental oxygen nor a hyperbaric chamber is available, 10 mg of immediate-release nifedipine can be given, followed by 20 mg of extended-release nifedipine every six hours. If nifedipine is not available, tadalafil and sildenafil (Viagra) are unproven alternatives.

Diuretics and acetazolamide are not recommended for the treatment of HAPE. The benefit of dexamethasone or inhaled beta agonists is unknown.

Continuous or expiratory positive airway pressure can be considered with or without supplemental oxygen, although evidence is lacking.

Although HACE often occurs with HAPE, patients with HAPE may also have neurologic dysfunction from hypoxic encephalopathy that can be confused with HACE. Dexamethasone is recommended for patients with HAPE who have neurologic dysfunction that does not resolve rapidly with supplemental oxygen.

Guideline source: Wilderness Medical Society

Evidence rating system used? Yes

Systematic literature search described? Yes

Guideline developed by participants without relevant financial ties to industry? Yes

Recommendations based on patient-oriented outcomes? Yes

Published source: *Wilderness Environ Med.* June 24, 2019; S1080-6032(19)30090-0

Available at: https://www.wemjournal.org/article/S1080-6032(19)30090-0/pdf

Carrie Armstrong
AFP Senior Associate Editor ■