Current Prevention and Management of Acute Mountain Sickness

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Acute mountain sickness was known to the Chinese in ancient times, as they traversed mountain passes between the Great Headache and Little Headache mountains into present-day Afghanistan. The Jesuit priest, Father Joseph Acosta, lived in Peru during the sixteenth century; he described both this syndrome and deaths which occurred in the high Andes. The incidence of high-altitude illness will rise as previously remote sites become more accessible to trekkers and skiers. Prevention and treatment are important concerns for those physicians who wish to advise their more adventuresome patients properly. This article incorporates a selected review of pertinent investigations, in the English-language literature over the past five years, into material previously presented at travel symposia for clinicians managing the prophylaxis and treatment of acute mountain sickness.

PHYSIOLOGY

There are several excellent references on the subject of acute mountain sickness (AMS) [1–5]. This field is evolving as trekking, skiing, and rock climbing become increasingly popular. The various levels of high altitude have been divided into several zones, which are useful when considering the potential effects of high altitude on human experience [1,6]. It is quite unusual, or even rare, for significant altitude illness to occur below the 8,000-foot level. Hence, “high” altitude is arbitrarily referred to as the zone between 9,000 and 14,000 feet, where acute mountain sickness is most likely to make its first appearance [1,6]. The usual locations for base camps and the zone at which serious trekking occurs are at “very high” altitudes, between 14,000 and 18,000 feet. Acclimatization is required before any attempts are made to ascend to such levels. Above this zone, and on to Mt. Everest at more than 29,000 feet, are those peaks only approached by serious climbers who become acclimatized before even reaching such altitudes.

The physiological consequences of high altitude are both considerable and challenging. Hypoxia is the most obvious one, resulting from decreased barometric pressure in the external environment. At 18,000 feet, the available oxygen, as measured by the inspired oxygen tension, is 69 mm Hg (torr), producing an arterial oxygen tension of 44 torr, as compared with 94 torr at sea level. Probably because of the limits on pulmonary oxygen diffusion capacity at high altitude, there is an additional fall in arterial \( \text{PO}_2 \) at high altitude during exercise. This fall does not occur at sea level. In fact, exercise at sea level is usually accompanied by a slight rise in arterial \( \text{PO}_2 \) [1,6]. In addition, the decrease in ventilation during sleep, or sleep

Abbreviation: AMS: acute mountain sickness

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hyperventilation, is more marked at high altitude, resulting, at times, in markedly depressed levels of arterial oxygen saturation. In fact, the major dangers associated with sleep hyperventilation at high altitude are those due to profound decreases in arterial oxygen saturation, not respiratory acidosis. Acetazolamide may be important in reducing the periodic breathing which leads to this exacerbation of hypoxia during sleep.

The physiologic changes which predominate at high altitude include respiratory alkalosis and the slow process of renal accommodation, which can require up to two weeks to complete. Respiratory alkalosis and an initial alkalemia result from hyperventilation. This condition limits the medullary center so that it cannot respond fully to hypoxia until renal excretion of bicarbonate begins to correct the primary acid-base disturbance and to increase alveolar ventilation. During prolonged hypoxia, there is an effective decrease in plasma volume as water moves into hypoxic cells and interstitial spaces. The rapid increase in erythrocyte 2,3-diphosphoglycerate levels is of uncertain significance, but it may contribute to oxygen unloading in tissues. Of major importance is the rise in pulmonary arterial pressure associated with hypoxic pulmonary vasoconstriction. This rise in pulmonary arterial pressure varies among individuals; it is one of the physiologic responses associated with a predisposition to high-altitude pulmonary edema, a process which is not cardiac in origin, but which may be influenced by vasodilators such as nifedipine.

CLINICAL MANIFESTATIONS

Acute mountain sickness is usually manifested by tiredness, headache, anorexia, nausea, and vomiting [2,5]. By far the most severe and persistent problem is headache. Sleep patterns are also disturbed, and Cheyne-Stokes respirations may be evident; they are characterized by periods of hyperpnea and apnea with consequent changes in the arterial PO2. Sedation may worsen periods of hypoxia. Auditory and visual disturbances may appear. Memory becomes impaired, and ataxia may also occur.

Acute mountain sickness can be prevented by acclimatization in conjunction with slow ascents and a planned staging process [1,6]. It has been suggested that the rate of ascent not exceed 1,000 feet per day when climbing above the 10,000-foot level. Because exercise and hyperventilation increase insensible fluid losses, oral hydration is important, particularly if the thirst mechanism is blunted at high altitude [1,6]. “Staging” simply means spending several days at an intermediate altitude such as 7,000 feet. One additional dictum is to “sleep low and climb high,” so that the periodic breathing and hypoxia associated with sleeping at high altitude are minimized. Altitude, rate of ascent, level of physical exertion, and prior acclimatization all influence the incidence and severity of acute mountain sickness.

The consequences of AMS progression are clearly dangerous. With predisposing factors such as exposure to extreme cold and rapid ascent to high altitude, exertion and sleeping at such altitudes may result in high-altitude pulmonary edema. Children and adolescents are at greatest risk for high-altitude pulmonary edema, and symptoms worsen at night. Lack of acclimatization, even in the physically fit, may also contribute. Recurrent episodes in the same individual are common and appear to be due to an abnormally high rise in pulmonary arterial resistance [6,14], as a response to hypoxia.
PHARMACOLOGICAL INTERVENTION—PREVENTION

Is there any pharmacological intervention which can prevent either the occurrence of acute mountain sickness or minimize its consequences? Acetazolamide (Diamox®) is a well-known carbonic anhydrase inhibitor, which is used in the treatment of seizures and glaucoma, but which is a relatively poor diuretic. It does not truly prevent mountain sickness; it shortens the time of acclimatization by several days. Acetazolamide increases urinary excretion of bicarbonate, sodium, and potassium ions. The resulting hyperchloremic metabolic acidosis stimulates respiration, essentially producing, in one day, what would require about five days during the normal process of acclimatization. Its mechanism of action also appears to include ventilatory stimulation at high altitude and a decrease in resting hypoxemia, nocturnal restlessness, apnea, and oxygen desaturation at high altitude. Adams and Johnson have produced experimental data in rats regarding the respiratory effects of inhibiting carbonic anhydrase in brain tissue by infusion of acetazolamide directly into the cisterna magna [7]. The inhibition of carbonic anhydrase in medullary tissue appears to increase the ventilatory response to rebreathing CO₂. The baseline steady-state respiration during room air breathing was, however, not affected by the experimental doses of acetazolamide that were used.

The appropriate dose of acetazolamide for prevention of acute mountain sickness is not entirely clear. The recommended dose has been 250 mg by mouth every eight to 12 hours for about five days, with the subject completing therapy upon reaching the highest altitude. It has been suggested, however, that the inhibitory effects of acetazolamide on carbonic anhydrase activity in tissues may be excessive at this dosage level, and some suggest using a lower dose, such as 250 mg/day [8]. Acetazolamide should not be taken with triazolam (Halcion) or barbiturates, as it may potentiate their effects on the central nervous system, resulting in an inadequate ventilatory response [9]. Paresthesias and occasional cramping of the hands or feet should be expected, along with occasional gastrointestinal upset, somnolence, or transient myopia. Patients with sulfonamide drug sensitivity or renal disease should not utilize acetazolamide.

Miller and Miller have confirmed previous observations of altered taste (dysgeusia) less than two hours after taking 250 mg of acetazolamide for prevention of mountain sickness [10]. Altered taste for carbonated and non-carbonated beverages and food occurred in association with paresthesias of lips, tongue, and lower extremities. Patients require a warning regarding these potential side effects. The paresthesias, in particular, may be especially intolerable for patients who are visually impaired and rely on touch.

Dexamethasone is a potent glucocorticoid. It was first used to prevent acute mountain sickness largely upon the assumption that brain edema contributed to its pathogenesis. Unfortunately, corticosteroid side effects of euphoria, glucose intolerance, mania, potential gastrointestinal hemorrhage, and steroid withdrawal must also be considered. Dexamethasone has been used in doses of two to four mg every six hours, beginning on the day of ascent, continuing for three days at higher elevations, and tapering the dose over the subsequent five days. In one study, acetazolamide (250 mg, twice each day) and dexamethasone (4 mg, four times daily) were more effective than either agent alone for the prevention of acute mountain sickness [11].

Ellsworth et al. have added to their previous data on the efficacy of dexamethasone
for prevention of acute mountain sickness [12]. A rapid ascent of Mount Rainier was performed twice by 18 climbers in a randomized, double-blind, concurrent, placebo-controlled trial, comparing acetazolamide (250 mg), dexamethasone (4 mg), and placebo every eight hours as prophylaxis for acute mountain sickness. An environmental symptoms questionnaire and clinical interview demonstrated greater reduction in the incidence and severity of acute mountain sickness with dexamethasone than with acetazolamide or placebo. At the summit, 10 percent of subjects taking dexamethasone were “sick” by clinical interview criteria. In contrast, 75 percent of those receiving acetazolamide were ill in a similar evaluation. This study was well designed and, despite a small number of subjects, it suggests that a role for dexamethasone is emerging for those who cannot tolerate acetazolamide, or for whom it is simply ineffective. The authors also suggest using dexamethasone for those undergoing a forced rapid ascent to high altitude over a short time span when a guaranteed retreat route is available; however, potential corticosteroid side effects will continue to dictate limited use of dexamethasone prophylaxis.

TREATMENT OF ACUTE MOUNTAIN SICKNESS

Therapy of acute mountain sickness is truly immediate descent from high altitude. The role for supplementary oxygen does not include its being used as a substitute for an immediate descent from high elevations. Acetaminophen or non-steroidal anti-inflammatory agents can be used to control headaches. Retinal hemorrhages can appear at altitudes around 14,000 feet; they are common above 18,000 feet, although they resorb in days. Macular hemorrhages can affect vision and theoretically could be exacerbated by aspirin's effects on platelet function.

Grissom et al. [13] have used low-dose acetazolamide to treat acute mountain sickness in climbers on Denali (Mt. McKinley) [14]. Using two doses of 250 mg at zero and eight hours, with assessment of status at 24 hours, they demonstrated some benefit in the treatment of AMS in six subjects, compared to placebo-treated controls. Parameters measured included symptomatology, changes in alveolar to arterial oxygen pressure difference and arterial PO2. The authors conclude, from this small initial study, that acetazolamide is effective for the treatment of established cases of acute mountain sickness and its use is associated with improved pulmonary gas exchange. Dexamethasone has also been used to treat acute mountain sickness. It is clearly useful in some cases, particularly if evacuation to a lower altitude is delayed. For those clinicians who have long thought that acetazolamide offered relief of symptoms to those with acute mountain sickness, it represents a useful first alternative to corticosteroids.

Naeije and Melot recently reported a case of high-altitude pulmonary edema in a 40-year-old man, who had been a healthy subject for pulmonary hemodynamics studies six years previously [15]. He had had a normal pulmonary arterial hypoxic pressor response at that time. The authors speculate that, in this patient, use of both acetazolamide and dexamethasone so diminished his non-respiratory symptoms that he delayed his descent. Neither agent has ever been shown to improve high-altitude pulmonary edema.

Rest, supplemental O2, and rapid descent are the first modes of therapy for acute mountain sickness. Nifedipine, a calcium channel blocker, is still considered an experimental agent [16]. Bärtsch et al. have shown that the prophylactic administration of nifedipine not only prevents high-altitude pulmonary edema in susceptible subjects but also lowers the symptom score for acute mountain sickness. Side effects
of nifedipine include nausea, vomiting, headache, hypotension, and fatigue. It should not be utilized simply to prevent symptoms of acute mountain sickness.

The lightweight portable hyperbaric chamber, or Gamow bag, may be the most important recent advance in therapy. Dr. Igor Gamow developed an airtight, zippered, nylon bag which is both light and portable. The patient with acute mountain sickness is zipped into the bag and air is pumped in continuously with a foot pump to a pressure of 100 torr or two pounds per square inch (psi), simulating an altitude of 8,400 feet [6]. An air flow rate of 30 L/minute is produced with 10–15 pumps per minute, while the bag is vented through a 2 psi gauge pop-off valve in order to keep a constant bag pressure and air exchange in the bag. When rapid evacuation or descent is not possible, the positive-pressure bag provides almost immediate relief of symptoms [17].

When central nervous system manifestations of high-altitude illness progress to cerebral edema, ataxia, confusion, and somnolence, high-altitude encephalopathy has ensued. This syndrome can produce abnormal reflexes and focal neurological deficits with associated papilledema and retinal hemorrhages. Treatment, with the addition of dexamethasone, is the same as for high-altitude pulmonary edema. In each case, descent is absolutely critical. With appropriate preventive measures, much can be done to prevent acute mountain sickness. When it does occur despite such measures, it should not be ignored. To do so is to risk more life-threatening events, such as pulmonary and central nervous system complications. When in doubt, begin your descent immediately.

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