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Acute high-altitude illness: a clinically orientated review

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Abstract

Acute high-altitude illness is an encompassing term for the range of pathology that the unacclimatised individual can develop at increased altitude. This includes acute mountain sickness, high-altitude cerebral oedema and high-altitude pulmonary oedema. These conditions represent an increasing clinical problem as more individuals are exposed to the hypobaric hypoxic environment of high altitude for both work and leisure. In this review of acute high-altitude illness, the epidemiology, risk factors and pathophysiology are explored, before their prevention and treatment are discussed. Appropriate ascent rate remains the most effective acute high-altitude illness prevention, with pharmacological prophylaxis indicated in selected individuals. Descent is the definitive treatment for acute high-altitude illness, with the adjuncts of oxygen and specific drug therapies.

Keywords

Acute high-altitude illness, acute mountain sickness, high-altitude cerebral oedema, high-altitude pulmonary oedema, hypoxia

Introduction

Acute high-altitude illness (AHAI) is an encompassing term for the range of pathology that the unacclimatised individual may develop when exposed to hypoxia at high altitude. This includes acute mountain sickness (AMS), high-altitude cerebral oedema (HACE) and high-altitude pulmonary oedema (HAPE). Clinically, AMS and HACO may represent parts of a spectrum of the same underlying condition, HACO being the end stage of AMS.[1] Hypoxaemia occurs at high altitude because there is a lower inspired partial pressure of oxygen (hypoxia) as a result of the decreased barometric pressure. Hypoxaemia, deficiency of oxygen in arterial blood, may in turn lead to tissue hypoxia. The onset of AHAI occurs between initial exposure to hypoxia and eventual acclimatisation, usually in a time period of hours to days.[2] AHAI can be potentially life-threatening, therefore expedition, military and pre-hospital healthcare professionals supporting groups at high altitude need to have a good understanding of its diagnosis and emergency management.

Epidemiology and risk factors

Over 35 million people are estimated to visit destinations over 3000 m each year.[3] As high-altitude travel and mountaineering become increasingly popular, the number of individuals exposed to hypobaric hypoxia at

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altitude is increasing, and the pathogenesis, prevention and treatment of AHAI have attracted more interest. AMS is common, usually benign and self-limiting if managed appropriately. HACO and HAPO are rare, with an estimated incidence of 0.1–4%,[4] but require prompt recognition if serious harm, including death, is to be avoided.

AHAI affects lowlanders who ascend to altitude rapidly. Residents from high altitude are more susceptible to chronic mountain sickness (Monge disease) and high-altitude pulmonary hypertension, which are discussed elsewhere.[5] AHAI is common; up to 50–70% of mountaineers develop symptoms of AMS,[6,7] although this incidence is dependent on both ascent rate and altitude. Ascent rate and maximum altitude are the main risk factors for AHAI, indicating a dose–response type of relationship with exposure to hypoxia in susceptible individuals.[4]

Rapid ascent profiles are recognised as a risk factor for AHAI from both retrospective[7] and prospective data. Climbers assigned to a 19-day ascent, compared with a 15-day ascent, whilst climbing Muztagh Ata (7546 m) had significantly fewer symptoms and a greater proportion climbed higher.[8] All individuals ascending at greater than 500 m a day above the level of 3000 m are at increased risk for AHAI. In addition, those who rapidly ascend over 3500 m in one day are at risk of AHAI,[9] for example when using air travel to high-altitude destinations (e.g. La Paz, Bolivia).

The incidence of AHAI is also related to maximum altitude ascended. AMS typically develops at altitudes greater than 2500 m, HAPO greater than 3000 m and HACO greater than 4000–5000 m, although susceptible individuals can be affected below these altitudes.[6]

There are a number of theories regarding individual susceptibility to AHAI, but it is likely to be derived from both genetic and environmental variables. AHAI patients normally reside permanently under 900 m.[10] Multiple genetic factors are being explored in the Tibetan and Andean populations who have adapted to hypobaria, interestingly showing very different physiological mechanisms and genetic phenotypes.[5]

In particular, the increase in nitrogen oxides in both the acclimatisation of lowlanders and in residents at high altitude is a current research focus.[11] Tibetans have a significantly higher plasma concentration of nitric oxide by-products.[12] Impaired nitric oxide synthesis occurring with certain nitric oxide synthase polymorphisms has been suggested as a genetic cause of susceptibility to AHAI. Genetic and epigenetic variation genes that code for hypoxia-inducible factors, transcription factors that alter genetic expression in response to cellular oxygen concentrations, are also likely to be responsible for variation in individual susceptibility to AHAI.[5]

Previous history of any AHAI increases propensity for further episodes. Exercise is believed to exacerbate AMS,[13] probably by causing further oxygen desaturation. Physical fitness does not offer protection from AHAI.[14] Dehydration is associated with AMS,[15] but may not represent an independent risk factor. Individuals with low hypoxic ventilatory response (HVR) and who display a proportionally higher oxygen desaturation during exercise testing at sea level were more likely to develop AMS in one study.[16] Other studies do not show this correlation with AMS and HVR.[14] The exact role of HVR in AHAI susceptibility requires further clarification.

Anatomical variation of intracranial cerebrospinal fluid (CSF) volumes and cerebral space, allowing for less compensation during increased pressures, has also been suggested to explain individual susceptibility to AMS and HACO.[17] Known as the 'tight-fit' hypothesis, it may account for the decreased AMS incidence in individuals aged over 50 who would therefore have greater capacity to compensate for raised intracranial volume.[7] However, this finding may also reflect behaviour in an age group of those who may exert themselves less at high altitude.

Specific to HAPO, patients with raised pulmonary artery pressure and hyper-responsive pulmonary circulation to hypoxia or exercise at sea level are at a higher risk of developing HAPO when they ascend.[18] Tibetans appear to have a hyporesponsive pulmonary circulation to hypoxia compared with lowlanders.[19] It remains unclear whether or not respiratory infections increase an individual's risk for developing HAPO.[20] Variation in alveolar fluid clearance related to sodium channel phenotype may also be implicated in the pathogenesis of HAPO.[21]

Acute mountain sickness and high-altitude cerebral oedema

Clinical presentation and diagnosis

AMS usually presents between 4 and 24 hours after ascent to a new altitude, often resolving within 2 to 3 days at a consistent altitude. HACO develops in the following 24 hours.[6] The core symptom of AMS is a high-altitude headache (HAH), typically worse on exertion. Other associated symptoms include dizziness, nausea, insomnia and anorexia. Having difficulty sleeping is very common, relating to change to an unusual sleeping environment, respiratory symptoms, nausea and headaches.[2]

There are no clinical signs for AMS and the diagnosis is made in the history, collating symptom severity most commonly using the Lake Louise Score (LLS), although other questionnaires do exist. To diagnose

Table 1. The Lake Louise Score for the diagnosis of acute mountain sickness.[22]

Symptoms	Severity	Score
1. Headache	None	0
	Mild	1
	Moderate	2
	Severe/incapacitating	3
2. Gastrointestinal	None	0
	Poor appetite or nausea	1
	Moderate nausea or vomiting	2
	Severe nausea or vomiting/ incapacitating	3
3. Fatigue/weakness	None	0
	Mild	1
	Moderate	2
	Severe/incapacitating	3
4. Dizziness/lightheaded	None	0
	Mild	1
	Moderate	2
	Severe/incapacitating	3
5. Difficulty sleeping	None	0
	Not as well as usual	1
	Poor night's sleep	2
	Unable to sleep	3
A diagnosis of acute mountain sickness (AMS) requires (a) score > 3, (b) presence of headache and (c) recent ascent.		
High-altitude cerebral oedema	**With AMS**	Altered mental status *or/and* ataxia
	Without AMS	Altered mental status *and* ataxia

AMS with the LLS (Table 1), the following widely accepted criteria should be met: (1) a recent ascent to altitude, (2) the presence of a headache and one other symptom and (3) an LLS greater than 3.[22] There are alternative views as to what LLS threshold constitutes AMS, with some defining mild AMS with a LLS score as low as 2.[9]

Practically, the difficulty in identifying AMS is the non-specific nature of symptoms, which climbers may assign to fatigue or sleep deprivation. The scoring system for symptom severity is subjective and relies on self-reporting.[2] In the context of field diagnosis, it is wise to assume that such non-specific symptoms are AMS unless strong evidence is available implicating an alternative cause. It is also important not to overlook conditions with similar non-specific presentations, for example hypothermia, dehydration, hypoglycaemia and hyponatraemia.[9]

Progression to HACO is characterised by altered mental status, reduced consciousness and ataxia. In a patient with AMS, either changes in mental state or the presence of ataxia allows the diagnosis of HACO to be made. Without the presence of AMS, if both mental state changes and ataxia are present, HACO is diagnosed.[22] Papilloedema, extensor plantar reflexes or, rarely, focal neurology may be found on examination.[5] Left untreated, HACO can progress to coma within 24 hours.[2]

Pathophysiology

Although HACO is often considered the end stage of AMS clinically, it is still not established whether these conditions have the same underlying pathophysiology,[2] and the mechanisms remain poorly understood. It is also unclear whether it is solely the hypoxia that initiates AHAI or whether hypobaria exposure may also be involved. AMS occurred after exposure to both a normoxic hypobaric and a hypoxic normobaric environment, but was most rapid and severe in onset after exposure to hypoxic hypobaria.[23]

The mechanism for HACO is better understood than for AMS. Cerebral oedema develops following cerebral vasodilation secondary to hypoxia. Hypoxaemia results in overperfusion of microvasculature, an increase in hydrostatic pressure and leakage from capillaries.[1] Autopsies reveal oedema[24] and magnetic resonance imaging (MRI) studies demonstrate white matter changes in keeping with oedema in the splenium of the corpus callosum.[25]

The pathophysiology of AMS is less clear (Figure 1). Observed physiological responses in AMS include relative hypoventilation, inadequate gas exchange, increased sympathetic stimulation and relative fluid retention.[2] There are a number of theories for AMS pathogenesis. Some believe that AMS is also caused by

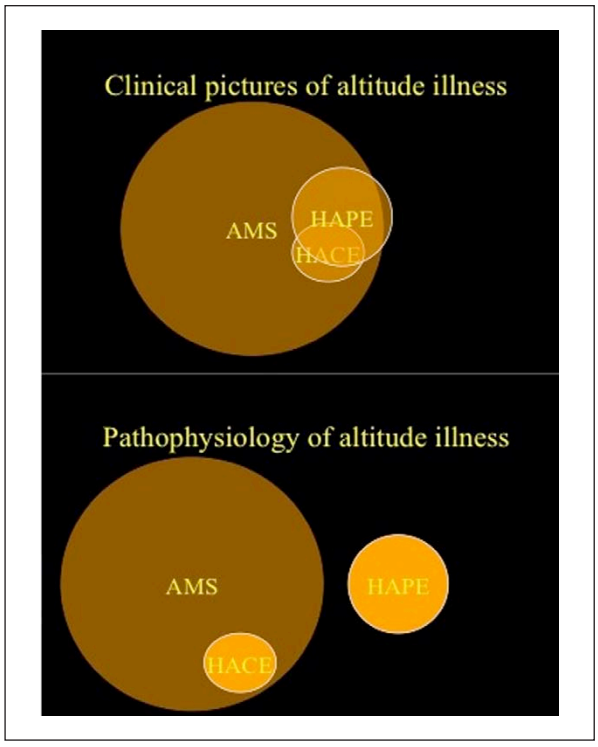

Figure 1. Acute high-altitude illness: relations in clinical presentation and pathophysiology.

raised intracranial pressure, supporting the 'tight-fit' hypothesis previously discussed.[24] Venous hypertension or sinovenous outflow obstruction may predispose individuals to intracranial hypertension that becomes clinically apparent only at high altitude.[26]

There are limited recordings of intracranial pressure at high altitude; however, increased pressure on mild exertion was recorded in an individual with AMS using a telemetric device[27] and in another study opening lumbar CSF pressures were increased after rapidly ascending to high altitude.[24] However, no study has demonstrated a significant difference in lumbar CSF pressures between those with AMS and those without.

Some suggest that AMS is also caused by cerebral oedema, unifying AMS and HACO as a spectrum of the same pathological process, resulting from cerebral vasodilation and overperfusion. However, T2-weighted MRIs do not always reveal cerebral oedema even in moderate to severe AMS.[28] Another theory relates to abnormalities in fluid balance, after observations that those who develop AMS gain weight at altitude.[29]

A theory proposed by Hackett and Roach for AHAI was that hypoxia increases microvascular permeability.[1] In combination with elevated capillary pressure from overperfusion, the result is cerebral and pulmonary microcirculation leakage. Sympathetic stimulation and endothelial activation would then exacerbate this process. There is currently no evidence that hypoxia directly increases microvascular permeability.

The inappropriate release of nitric oxide is probably also relevant to AMS pathogenesis.[26] It also may directly activate the trigeminovascular system in combination with overperfusion, leading to high-altitude headaches.[30] There is considerable research into the effects of hypoxia-inducible factor 1 (HIF-1), which upregulates genes causing increased synthesis of nitric oxide, vascular endothelial growth factor (VEGF) and atrial naturetic peptide. HIF-1 also stimulates erythropoiesis.[26]

In summary, AMS pathophysiology is poorly understood and may be distinct from HACO, but is likely to involve raised intracranial pressure, exacerbated by exercise in susceptible individuals. The exact role of hypoxia-induced mediators at a blood vessel level requires further clarification.

Prevention

First, AHAI prevention can be achieved by not exposing individuals at high altitude to a hypobaric, hypoxic environment. This is through either increasing barometric pressure, as employed in aircrafts using pressurised cabins, or by increasing oxygen concentrations through supplementation, a novel approach taken by high-altitude train links to Tibet. A 1% increase in oxygen concentration is the equivalent of descending by 300 m in altitude.[5]

In the absence of oxygen supplementation, an appropriate ascent profile is crucial to preventing AMS and HACO, and this has been demonstrated both retrospectively[7] and prospectively.[8] Consideration should be taken when travelling by plane or vehicle, as well as the rate of climbing once on foot. Eighty-four per cent of Himalayan tourists flying directly to 3740 m developed symptoms of AMS.[31] Individuals should not increase their sleeping altitude by greater than 300–500 m per day when over 3000 m and include a rest day every 3 or 4 days when trekking above 3000 m to minimise the risk of AMS and allow acclimatisation.[9] This guidance was developed from experience on the Everest base camp trail and is often difficult to practically apply on treks with steeper ascents. Further ascent should not be attempted until AMS symptoms resolve.[9]

The efficacy of acetazolamide for AMS prevention has been demonstrated in numerous studies, in doses as low as 250 mg daily.[32,33] The recommended prophylactic regimen from the Wilderness Medical Society (WMS) guidelines is 125 mg twice daily, with a paediatric dose of 2.5 mg/kg.[9] A randomised controlled trial comparing higher doses showed no improved AMS prophylactic efficacy and an increase in the side-effect

Table 2. The prevention and treatment of acute mountain sickness/high-altitude cerebral oedema.

Prevention	Treatment
Appropriate ascent profile	Descent
Acetazolamide 125 mg twice daily[a]	Oxygen supplementation or portable hyperbaric chamber
(Dexamethasone 8 mg daily in divided doses[a])	Acetazolamide 250 mg twice daily – *for AMS (± HACO with dexamethasone)*
	Dexamethasone 8 mg stat then 4 mg every 6 hours – *first line for HACO and used in AMS*

[a]To be considered only in high-risk individuals or for required rapid ascent profiles.

of paraesthesia, typically experienced in the extremities.[33] A recent systematic review supported this conclusion.[32] There was a lower number needed to treat (NNT) at the 750 mg dose, but this was associated with higher side-effect rates. Methazolamide, another carbonic anhydrase inhibitor, may have a better side-effect profile.[2]

Acetazolamide inhibits carbonic anhydrase, and thus reduces the conversion of carbon dioxide to bicarbonate and protons. It causes a bicarbonate diuresis and a metabolic acidosis through its inhibition in the renal system.[2] It increases poikilocapnic HVR, accelerating a mechanism that occurs usually with acclimatisation. Other potential beneficial effects include increasing carbon dioxide retention through inhibition of vascular carbonic anhydrase, and the decrease of CSF production.[34]

Dexamethasone is comparable to acetazolamide in terms of prophylactic efficacy in reducing AMS symptom scores when rapidly ascending to altitude in a randomised controlled trial,[35] but should be reserved for the emergency treatment of AMS and HACO. The mechanism of prevention is unknown but is likely to be related to vessel permeability and cytokine regulation.[2]

In general, for those without previous history of AHAI, pharmacological prophylaxis should not be required and an appropriately controlled ascent rate should be employed to prevent AMS and HACO. In high-risk situations, where (a) the individual is susceptible, (b) an altitude greater than 3500 m is attained in one day or (c) ascent must be faster than 300 m per day, acetazolamide 125 mg twice daily is considered first line.[9]

Treatment

Descent remains the most effective intervention for treatment of all forms of AHAI (Table 2); however, it is not always mandatory. Remaining at the same altitude and using simple analgesia and antiemetics may allow mild AMS to resolve before being able to continue an ascent. In severe AMS or HACO descent should be the priority.

Oxygen supplementation can be used as an alternative to descent in selected patients, or as an adjunct to descent in severe AMS or HACO. Oxygen saturations greater than 90% should be achieved.[9] Portable hyperbaric chambers can also be used, but this should not delay descent and, practically, their use in patients with severe nausea, vomiting or decreased conscious level can be challenging.

The treatment of HACO is difficult to study because the condition is rare, so much of the guidance is based on clinical experience and expert opinion rather than trial results. AMS, however, has a much greater incidence, so testing the efficacy of pharmacological intervention using trials has been more achievable.

Dexamethasone has been extensively used for treating both severe AMS and HACO.[36] It can be given intravenously or intramuscularly in patients with severe nausea or vomiting. WMS guidelines suggest an immediate 8 mg dose, continuing with 4 mg every 6 hours for HACO, with or without the addition of acetazolamide.[9] Individuals should not ascend further until they are symptom free without corticosteroid usage.

Acetazolamide was demonstrated to be effective at treating AMS at a dose of 250 mg twice daily on Mount McKinley (6194 m), improving both LLS results and arterial oxygenation.[37] No studies have compared efficacy at lower doses. It is often used in combination with dexamethasone for HACO. Dexamethasone alone can be used for the prophylaxis of AMS in individuals who have previously had a reaction to acetazolamide or other sulphur-based drugs.[9]

High-altitude pulmonary oedema

Clinical presentation and diagnosis

Exertional dyspnoea, dry cough and reduced exercise performance are typical early symptoms of HAPO. It is diagnosed when there are at least two symptoms of dyspnoea at rest, cough, decreased exercise performance or chest tightness; and two clinical signs of crackles or wheeze on auscultation, central cyanosis, tachypnoea or tachycardia, as outlined in Table 3.[22]

Table 3. The diagnosis of high-altitude pulmonary oedema.[22]

Symptom	Clinical signs
Dyspnoea at rest	Crepitations or wheeze on auscultation
Cough	Central cyanosis
Decreased exercise tolerance	Tachypnoea
Chest tightness	Tachycardia

The diagnosis of high-altitude pulmonary oedema requires at least two symptoms and two clinical signs from above.

The onset of HAPO is usually 2–4 days after ascent and is rare after 1 week at a constant altitude. A chest radiograph, if performed, demonstrates peripheral patchy pulmonary oedema in the lower zones. An electrocardiogram demonstrates sinus tachycardia, right axis deviation, right bundle branch block or right strain.[38] It is important to consider other causes of this clinical presentation, for example respiratory infection or cardiac conditions.

HAPO has the highest mortality rates within acute high-altitude illness.[1] Fifty per cent of patients with HAPO have concurrent AMS and 14% have concurrent HACO.[39] Fifty per cent of autopsies of the fatal cases of HAPO had evidence of cerebral oedema,[1] supporting the interlinked nature of AHAI pathophysiology. There may be higher rates of subclinical HAPO as patients with AMS are often found to have basal crepitations on auscultation.[5]

Pathophysiology

The mechanism for HAPO is non-cardiogenic, initiated by alveolar hypoxia resulting in pulmonary circulation vasoconstriction and the development of pulmonary hypertension.[38] Studies using pulmonary artery catheterisation have demonstrated that HAPO patients have an accentuated pulmonary vasoconstriction response to hypoxia with normal capillary wedge pressures.[40] Echocardiogram reveals that HAPO-susceptible patients have significantly increased pulmonary artery pressures during hypoxia and normoxic exercise at sea level.[18]

Hypoxic pulmonary vasoconstriction has been proposed as being non-uniform throughout the pulmonary circulation, causing regional overperfusion.[41] Endothelial dysfunction may also be instigated. Endothelial nitric oxide synthase gene polymorphisms confer genetic suspectibility, and therefore impaired nitric oxide synthesis may be an underlying mechanism in HAPO.[42]

Alveolar capillaries develop stress failure secondary to pulmonary artery hypertension, which is exacerbated by exercise.[43] There is leakage of large molecules into the alveolar space, resulting in high-permeability pulmonary oedema, supported by high-molecular-weight proteins being found in oedema of HAPO patients.[40] Exercise at altitude significantly increases this leakage when examined using broncho-alveolar lavage following exercise.[43]

More recently, it has been found that there is also impaired clearance of alveolar fluid, against this background of increased production. HAPO-susceptible individuals have a defective transepithelial sodium transport in their alveoli, and the impairment may be exacerbated at high altitude.[21] Both salmeterol and dexamethasone decrease the incidence of HAPO in highly susceptible individuals,[44,45] probably through increasing transepithelial respiratory sodium transport.

In summary, stress failure of pulmonary microcirculation combined with overperfusion is exacerbated by exercise in a hyper-responsive pulmonary circulation, resulting in insufficient gaseous exchange and hypoxaemia. Decreased nitric oxide synthesis and impaired sodium transport are mechanisms predisposing individuals to HAPO. Prevention aims to counter pulmonary artery hypertension or improve alveolar fluid absorption, whilst treatment focuses on correcting hypoxaemia.

Prevention

Slow ascent remains the best preventative measure of HAPO, as with other forms of AHAI. Those susceptible to HAPO should not ascend greater than 300 m per day.[38] High-intensity exercise shortly after ascent should also be minimised as this exacerbates pulmonary artery hypertension.[43]

Drug prevention aims to prevent pulmonary artery hypertension. Traditionally, nifedipine 20 mg slow-release three times a day has been used, after reducing the incidence of HAPO from 63% to 10% when ascending over 4500 m.[46] Tadalafil 10 mg twice daily has similar efficacy in HAPO prevention.[44] Sildenafil, at a dose of 50 mg three times a day, is another phosphodiesterase-5 inhibitor option.[9] However, in a recent randomised controlled trial testing sildenafil for HAPO prophylaxis, AMS severity was increased.[47]

The role of acetazolamide in HAPO is unclear. Pulmonary artery pressures were not reduced in a recent study,[48] but have inhibited vasoconstriction in animal hypoxia models.[49] Dexamethasone is also an effective prophylactic in HAPO-susceptible individuals, probably through improving alveolar fluid absorption, but must be taken prior to ascent to be effective.[38,44]

Salmeterol has been trialled for prophylaxis of HAPO as it also increases transepithelial sodium channel

Table 4. The prevention and treatment of high-altitude pulmonary oedema.

Prevention	Treatment
Appropriate ascent profile Nifedipine 60 mg modified-release in divided doses[a]	Descent Supplementary oxygen (oxygen saturations >90% ± positive airway pressure) Portable hyperbaric chamber Nifedipine 60 mg modified release in divided doses

[a]HAPO-susceptible patient only.

function. The efficacy is less than for calcium channel blockers and phosphodiesterase-5 inhibitors, but it is still effective, reducing incidence from 74% to 33% when ascending over 4500 m.[45] Very high doses (125 µg twice daily) were required.

The difficulty in interpreting many of the HAPO prevention and treatment trials mentioned here is that subjects selected are often those who are known to be highly susceptible to HAPO. It is not clear whether or not these results can be extrapolated to a general population of lowlanders.

WMS guidelines recommend using only 60 mg nifedipine modified-release daily (divided in two or three doses) in HAPO-susceptible individuals. This should be started 1 day prior to ascent and continued for 5 days. Salmeterol, tadalafil, acetazolamide and dexamethasone are not currently recommended because of the lack of clinical experience and their limited trial data in the wider population.[9]

Treatment

HAPO treatment aims to increase oxygenation using rapid descent, oxygen supplementation or hyperbaric treatment with a portable chamber (Table 4).[38] Descent is the most effective intervention, as with other forms of AHAI, and is the recommended first-line treatment in the remote setting. Initial descent should be by at least 1000 m, or further until symptoms resolve.[9] This should be done with minimal exertion to prevent exacerbation of pulmonary artery hypertension. Oxygen or portable hyperbaric chambers may be used whilst awaiting evacuation.

Within a hospital setting, supplementary oxygen may be used as the first-line intervention and descent may not be required. Continuous positive airway pressure is to be considered here,[9] following case reports of expiratory positive airway pressure being effective in supporting oxygenation in HAPO.[50] Inhaled nitric oxide improves oxygenation in HAPO, but is impractical to administer.[51] However, it does provide an interesting insight into the mechanisms of HAPO.

Nifedipine 60 mg modified-release in divided doses can be used when descent or oxygen supplementation is not possible.[52] It is recommended as the first-line adjunct in WMS guidelines,[9] although a recent study in HAPO recovery found no extra benefit if descent and oxygen supplementation are adequate.[20] The short-acting preparation should be avoided because of the risk of cerebral hypoperfusion.

The use of sildenafil for HAPO is appealing because of its primary vasodilator action on pulmonary rather than systemic vessels, perceivably decreasing the risk of systemic hypotension and cerebral hypoperfusion when compared with nifedipine. No robust studies of phosphodiesterase inhibitors in HAPO treatment have yet been conducted and there is some clinical experience that it increases AMS severity,[47] so its use is not currently recommended.[9]

Current guidelines focus on descent in the remote setting with supplementary oxygen or nifedipine adjuncts. Hyperbaric therapy should not delay descent but can be used whilst awaiting evacuation. There is no role for diuretics in HAPO treatment.[6,9]

Conclusion

AHAI covers a spectrum of diseases, ranging from the very common high-altitude headaches to the rare but life-threatening high-altitude cerebral or pulmonary oedema. Diagnosis can be challenging in practice owing to reliance on self-reporting of symptom severity, but the LLS offers a useful tool for diagnosing and grading AMS.

Prevention remains the best approach to all forms of AHAI, primarily through appropriate ascent rate rather than pharmacological prophylaxis. Acetazolamide is effective for AMS prevention in those susceptible, but should not be required routinely. Nifedipine for HAPO prevention is indicated only in patients with a past medical history of HAPO or pulmonary artery hypertension.

The priorities for the emergency treatment of AHAI are descent and oxygen supplementation. Descent is not always required within a hospital setting but should be the main focus in the remote setting. Nifedipine is first line for HAPO, whilst dexamethasone with or without acetazolamide is used extensively for AMS and

HACO treatment. Late diagnosis and delayed descent are common practical problems encountered when managing AHAI in the field.

Many of the underlying mechanisms of AHAI remain unclear, but research in this area may have wider benefits to understanding hypoxia in other clinical settings, as well as improving the prevention and management of this growing clinical problem.

Multiple-choice questions

Which is the single correct answer for each of the following questions on acute high-altitude illness?

Question 1: The Lake Louise Score for acute mountain sickness
All the following are required for a diagnosis of acute mountain sickness, except:

A. The presence of a headache and at least one other symptom
B. A Lake Louise score of 3 of more
C. Altered mental status on examination
D. Recent ascent to a higher altitude

Question 2: Acute mountain sickness pathophysiology
The following physiological observations are made in patients with acute mountain sickness compared with controls at high altitude, except:

A. Relative fluid diuresis
B. Inadequate gaseous exchange
C. Increased sympathetic stimulation
D. Relative hypoventilation

Question 3: Acute mountain sickness prevention
The following have demonstrated efficacy for acute mountain sickness prevention, except:

A. Acetazolamide 125 mg, twice daily
B. Sildenafil 50 mg, three times daily
C. Appropriate ascent rate
D. Dexamethasone 4 mg, twice daily

Question 4: Nifedipine in high-altitude illness
The use of nifedipine modified-release is the first-line pharmacological intervention for which acute high-altitude illness?

A. High-altitude cerebral oedema
B. High-altitude headache
C. High-altitude pulmonary oedema
D. Acute mountain sickness

Multiple-choice answers

1. C
2. A
3. B
4. C

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