Treatment of Acute Mountain Sickness and High Altitude Pulmonary Oedema

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Introduction

Acute mountain sickness (AMS) and high altitude pulmonary oedema (HAPO) are common causes of morbidity and mortality seen in unacclimatized persons shortly after ascent to high altitude. High altitude is defined as altitudes more than 3000 meters while extreme high altitude is altitudes more than 5800 m [1]. Altitude related illnesses that develop shortly after ascent to high altitudes can present with either cerebral or pulmonary syndromes. AMS and high-altitude cerebral oedema (HACO) refer to the cerebral abnormalities and HAPO to pulmonary abnormalities [2]. In 2001 hospital admission rate for AMS in Indian army was reported to be 0.13/1000 personnel while admission rate for HAPO was 0.15/1000 [3]. HAPO and HACO are significant because they are potentially fatal if not treated in time.

Acute mountain sickness

Acute mountain sickness is a syndrome of nonspecific symptoms and is therefore subjective. The Lake Louise consensus group defined acute mountain sickness as the presence of headache in an unacclimatized person who has recently arrived at an altitude above 3000m plus and the presence of one or more of the following: a) gastrointestinal symptoms like anorexia, nausea or vomiting, b) insomnia, c) dizziness and d) lassitude or fatigue [2]. The pathophysiological processes that cause acute mountain sickness are unknown. However, symptoms of acute mountain sickness may be the result of cerebral swelling, either through vasodilatation induced by hypoxia or through cerebral oedema. Impaired cerebral auto regulation, the release of vasogenic mediators and alteration of the blood-brain barrier by hypoxia may also be important [2]. Similar mechanisms are thought to cause cerebral oedema at high altitude, which may represent a more severe form of acute mountain sickness. The symptoms typically develop within 6 to 10 hours after ascent, but sometimes as early as 1 hour. Importance of AMS lies in its early recognition as it may progress to HACO, clinically identified with onset of ataxia, altered consciousness or both in a person suffering from acute mountain sickness [4]. Many conditions mimic acute mountain sickness and high altitude cerebral oedema which may delay the diagnosis and early treatment. The main differential diagnoses are acute psychosis, carbon monoxide poisoning, subdural haematoma, hypoglycemia, ingestion of alcohol, seizures and stroke.

Treatment

Management of AMS follows three axioms: a) further ascent should be avoided until the symptoms have resolved, b)patients with no response to medical treatment should descend to a lower altitude and c) if and when HACO is suspected, patients should urgently descend to a lower altitude [4,5]. Descent and supplementary oxygen are the treatments of choice and for severe illness, the combination provides optimal therapy. Remarkably, a descent of only 500 to 1000 m usually leads to resolution of acute mountain sickness while high-altitude cerebral oedema may require further descent. Simulated descent with portable hyperbaric chambers, now commonly available in remote locations, are also effective. Medical therapy becomes crucial when descent is not immediately possible. Treatment is summarized in Table 1. Various drugs have been tried for high altitude illnesses with variable effect (Table 2). A small, placebo-controlled study showed that the administration of acetazolamide reduced the severity of symptoms [6]. Dexamethasone is as effective as acetazolamide and starts acting within 12 hours while acetazolamide takes around 24 hours [7]. Other drugs which have been used are ibuprofen and sumatriptan. For high altitude related insomnia acetazolamide is effective. Newer non-benzodiazepine sedatives like

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Table 1

Management and prevention of high altitude illness

Clinical presentation	Management	Prevention
Mild acute mountain sickness Headahce with nausea, dizziness and fatigue during first 12 hrs after ascent to high altitude (> 3000 m)	Descend 500 m or more, rest and acclimatize; or speed acclimatization with acetazolamide (125-250 mg BD); or treat symptoms with analgesics and antiemetics	Ascend at a slow rate; spend a night at an intermediate altitude; avoid overexertion; avoid direct transport to an altitude of more than 3000 m; consider taking acetazolamide (125-250 mg BD) beginning on day before ascent and continuing for 2 days at high altitude
Moderate acute mountain sickness Moderate to severe headache with marked nausea, dizziness, lassitude, insomnia, and fluid retention at high-altitude lasting for 12 hrs or more.	Descend 500m or more; if descent is not possible, use a hyperbaric chamber or administer low-flow oxygen (1-2 lts/min); if descent is not possible and oxygen is not available, administer acetazolamide (250 mg BD), or dexamethasone (4 mg PO or IM q 6 hourly), or both until symptoms resolve.	Ascend at a slow rate; spend a night at an intermediate altitude; avoid overexertion; avoid direct transport to an altitude of more than 3000m; consider taking acetazolamide (125-250 mg BD) beginning one day before ascent and continuing for 2 days at high-altitude; treat acute moutain sickness early.
High-altitude cerebral oedema Acute Mountain Sickness for 24 hrs or more, severe lassitude, mental confusion, ataxia.	Initiate immediate descent or evacuation; if descent is not possible, use a portable hyperbaric chamber; administer oxygen (2-4 lts/min;) administer dexamethasone (8 mg PO or IM or IV initially and then 4 mg q 6 hourly); administer acetazolamide if descent is delayed.	Avoid direct transport to an altitude of more than 3000m; ascend at a slow rate; avoid overexertion; consider taking acetazolamide (125-250 mg BD) beginning one day before ascent and continuing for 2 days at high-altitude; treat acute mountain sickness early.
High-altitude pulmonary oedema dyspnea at rest, moist cough, severe weakness, drowsiness, cyanosis, tachycardia, tachypnea rales.	Administer oxygen (4-6 lts/min until condition improves, and then 2-4 lts/min to conserve supplies); descend as soon as possible, with minimal exertion, or use a portable hyperbaric chamber; if descent is not possible or oxygen is not available, administer nifedipine (10 mg PO initially and then 30 mg of extended release formulations PO q 12-24 hrs); add dexamethasone if neurological deterioration occurs.	Ascend at a slow, graded rate; avoid overexertion; people with earlier episode should avoid high altitude areas.

m - meters, PO - per orally, IM - Intra muscular, IV - Intra venous, BD -twice daily, lts - liters, q - each quantity, mg - milligrams, hrs - hours

zolpidem, which do not depress ventilation are also effective [2].

Prevention

For the prevention of high-altitude illness, the best strategy is a gradual ascent to promote acclimatization. Depending on the altitudes, acclimatization in Armed forces is carried out in three stages.

a) First stage (3000m to 3600m) acclimatization for total 06 days

b) Second stage (3600m to 4500m) acclimatization for total 04 days

c) Third stage (>4500m) acclimatization for total 04 days

In each stage a person is made to rest for the first 02 days and then gradually made to walk and subsequently climb the slopes in a graded fashion [2].

Drug treatment for prophylaxis is recommended if rapid ascent is unavoidable. Acetazolamide is the preferred drug [8]. Prophylactic aspirin can be used for prevention of headache [2].

High altitude pulmonary oedema

HAPO accounts for most deaths from high-altitude illness. In 2001, out of total number of armed forces personnel deployed in high altitude areas, 225 were admitted with HAPO while in 2003 this figure was down to 90 [9]. The pathophysiological cause of HAPO is still unknown, but several mechanisms have been proposed. One such mechanism is of patchy pulmonary hypertension, which leads to stress failure in capillaries of overperfused areas, resulting in pulmonary oedema. As is the case for acute mountain sickness, the incidence of high-altitude pulmonary oedema is related to the rate of ascent, the altitude reached, individual susceptibility

Table 2 : Medical therapy for high-altitude illness

Agent	Indication	Dose	Comments
Oxygen	All high-altitude illnesses	2-4 lts by cannula or mask initially, then 1-2 lts/min or titrate dose until SaO2 > 90%	Life saving for HAPO; improves headache within minutes in AMS
Portable hyperbaric chamber	All high-altitude illnesses	Depends on model; 2-4 psi for a minimum of 2 hrs; continued as long as necessary	Effects quivalent to administration of lowflow oxygen; can be lifesaving; does not require oxygen; can add supplemental oxygen by cannula or mask if necessary.
Acetazolamide	Prevention of AMS	Acetazolamide (125-250 mg BD) beginning one day before ascent and contining for 2 days at high-altitude.	Sulfonamide reactions possible; should be avoided by breast-feeding women; can be taken episodically for symptoms; no rebound effect.
	Treatment of AMS	250 mg PO BD until symptoms resolve.	
Dexamethasone	Prevention of AMS	2 mg q 6 hourly or 4 mg q 12 hourly PO	Can be lifesaving for AMS or HACO; effects evident in 2-8 hrs; no effect on acclimatization; no value in HAPO.
	Treatment of AMS HACO	4 mg q 6 hourly PO/IM/IV	
Nifedipine	Prevention of HAPO	20-30 mg of extended release formulation PO q 12 hourly	No value in AMS or HACO; not necessary if supplemental oxygen available.
	Treatment of HAPO	10 mg PO initially, and then 20-30 mg of extended release formulations PO q 12 hourly	
Aspirin	Prevention of headache	325 mg PO q 4 hourly for a total of 3 doses	Not proven for treatment.
Ibuprofen	Treatment of headache	400-600 mg once PO, may be repeated.	Not proven for prophylaxis

HAPO - high altitude pulmonary oedema, AMS - acute mountain sickness, psi - pounds per square inch HACO - high altitude cerebral oedema, PO - per orally, q - each quantity, hrs - hours, SaO2 - saturation of oxygen in blood, BD - twice daily, mg - milligrams, lts - liters

and exertion; cold, which increases pulmonary-artery pressure by means of sympathetic stimulation, is also a risk factor [10]. Abnormalities of cardiopulmonary circulation increase the risk of high-altitude pulmonary oedema.

Early diagnosis is critical. Symptoms of HAPO occur most commonly two to three days after arrival at altitude and consist of dyspnoea with exercise, progressing to dyspnoea at rest, a dry cough, weakness and poor exercise tolerance. As the disease worsens, severe dyspnoea and frank pulmonary oedema are obvious, followed by coma and death. Early clinical signs include tachycardia and tachypnoea, mild pyrexia, basal crepitations and dependent oedema. Patients with HAPO tend to have lower oxygen saturations than unaffected people at same altitude, but the degree of desaturation by itself is not a reliable sign of HAPO. HAPO should be differentiated from asthma, bronchitis, pneumonia and left ventricular failure. Electrocardiography demonstrates sinus tachycardia and often, right ventricular strain. Chest radiography typically reveals a normal-sized heart, full pulmonary arteries, patchy and fluffy infiltrates, which are generally confined to the right middle and lower lobes in mild cases and are found in both lungs in more severe cases.

Management

Increasing alveolar and arterial oxygenation is the highest priority. It is mainly achieved by supplemental oxygen and descent. Patients with severe pulmonary oedema must be immediately moved to a lower altitude [10]. Hyperbaric chamber may be used till the time patient is being transported to a lower altitude. Medication like nifedipine has been tried only when supplemental oxygen is unavailable or descent is impossible [11]. In clinical studies, although nifedipine reduced pulmonary-artery pressure by approximately 30 percent, it barely increased the partial pressure of arterial oxygen. Inhaled beta-agonists have also been used in the prevention as well as treatment of high-altitude pulmonary oedema, as they appreciably increase the clearance of fluid from the alveolar space and might also lower pulmonary artery pressure [2]. Antibiotics are used if there is any evidence of infection such as purulent sputum or high grade fever. Oxygen

Fig. 1 : Portable hyperbaric chamber

administration is monitored by measuring oxygen saturation by a pulse oximeter with the aim of maintaining oxygen saturation above 90%. After an episode of high altitude pulmonary oedema, a person should avoid high altitude areas. In armed forces after an episode of HAPO, a person is not posted to high altitude areas again.

Newer developments

Portable hyperbaric chamber

Portable hyperbaric chambers are increasingly being used in treatment of high-altitude illnesses when rapid descent is not possible. With the use of these chambers at a pressure of 2 psi (13.8 kPa), the equivalent altitude is roughly 2000 m lower than the ambient altitude. These chambers are available in armed forces hospitals in high altitude areas (Fig 1).

Inhaled nitric oxide

Inhaled NO produces rapid decrease in pulmonary artery pressure thereby improving arterial oxygenation [12]. Mixture of 15 parts per million (ppm) of nitric oxide gas and 50 percent oxygen is generally used. The two gases in mixture work through two independent ion channels that regulate the expansion and constriction of blood vessels. Inhaled nitric oxide has shown lot of promise during initial trials at armed forces hospitals in high altitude areas.

Sildenafil

Sildenafil is a phosphodiesterase inhibitor, which causes vasodilatation. Though initially used for erectile dysfunction it has also been shown to benefit patients of primary pulmonary hypertension. It was found effective in hypoxia induced pulmonary arterial hypertension. Trials are being planned at several centers for using sildenafil in high altitude pulmonary oedema [13,14].

Conclusions

AMS and HAPO are seen in unacclimatized personnel exposed to high altitude. They can easily be prevented by gradual ascent to promote acclimatization. Early detection is the key in preventing deaths. Treatment of choice for both acute mountain sickness and high altitude pulmonary oedema is descent to lower altitude and supplemental oxygen. When immediate descent is not possible various drugs can be used. New developments like portable hyperbaric chamber and inhaled nitric oxide have shown promise in various trials.

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