High-altitude Pulmonary Edema in Emergency Department

Abstract:

High altitude pulmonary Edoema (HAPE) is a severe form of high-altitude disease that, if left untreated, can result in death in up to half of those who are affected . Lowlanders who rapidly go to elevations more than 2500-3000 m are more likely to develop high altitude pulmonary Edoema (HAPE). Individual sensitivity owing to a low hypoxic ventilatory response (HVR), quick pace of climb, male sex, usage of sleep medicine, high salt consumption, chilly ambient temperature, and intense physical effort are all risk factors. HAPE may be totally and quickly reversed if caught early and correctly treated. Slow climb is the most effective technique of prevention. A fall of at least 1000 meters, is the best and most certain treatment choice in HAPE. Supplemental oxygen, portable hyperbaric chambers, and pulmonary vasodilator medications (nifedipine and phosphodiesterase-5 inhibitors) may be beneficial. In this article we'll be looking at the disease etiology, epidemiology, diagnosis and management

Introduction:

High altitude pulmonary edoema (HAPE) is a severe form of high-altitude disease that, if left untreated, can result in death in up to half of those who are affected. It is a kind of noncardiogenic pulmonary edoema that arises as a result of hypoxia. It's marked by weariness, dyspnea, and a dry cough that worsens with effort. If untreated, it can lead to restless dyspnea, rales, and cyanosis. [1] Lowlanders who rapidly go to elevations more than 2500-3000 m are more likely to develop high altitude pulmonary edoema (HAPE). Dyspnoea develops later while the patient is at rest. tachycardia, tachypnoea, and an increased body temperature of less than 38.5°C are clinical characteristics. [2]

Excessive hypoxia-mediated increases in pulmonary vascular resistance (PVR) or hypoxic pulmonary vasoconstriction (HPV), which leads to higher microvascular hydrostatic pressures despite normal left atrial pressure, is the key pathogenesis. In the absence of inflammation, the resulting hydrostatic stress can produce both dynamic changes in the permeability of the alveolar capillary barrier and

UNDER PEER REVIEW

mechanical damage, allowing big proteins and erythrocytes to escape into the alveolar space. High capillary pressure generates a high-permeability non-inflammatory-type lung edoema in humans, according to bronchoalveolar lavage (BAL) and pulmonary artery (PA) and microvascular pressure measurements. [3]

Around 33.5 percent of people live below 100 metres above sea level, while the great majority of people reside at elevations of less than 500 metres. About 1% of the population lives over 2500 metres. This population tendency is assumed to have existed throughout human history. Lowlanders' risk of HAPE increases as their height rises. Hypoxia in the body is associated with illness, trauma, and thromboembolism in the lowlands, where most human evolution took occurred. HAPE is caused by a mismatch between a lowlander's evolved environment and the unusual environment of high altitude. [4]

HAPE, the most prevalent cause of mortality associated with high altitude, may be totally and quickly reversed if caught early and correctly treated. HAPE can manifest itself in two ways. The first kind is seen in unacclimatized lowlanders who rapidly rise to heights of more than 2500-3000 m. The second kind, often known as re-entry HAPE, affects high-landers returning after a lower-altitude visit. The pathophysiology of the two kinds is most likely the same. [2]

In regions with medical facilities, supplemental oxygen is the primary therapy, but in isolated mountainous areas, quick descent is the preferred treatment. If this isn't practicable and supplementary oxygen isn't accessible, nifedipine should be used until descent is possible. Even those who are sensitive to HAPE can prevent illness if they ascend gently, with an average increase of altitude of no more than 300-350 metres per day over 2500 metres. [6]

Etiology:

HAPE, like other altitude-related disorders, occurs above 2500 metres but can even occur as low as 2000 metres. Individual sensitivity owing to a low hypoxic ventilatory response (HVR), altitude reached, quick pace of climb, male sex, usage of sleep medicine, high salt consumption, chilly ambient temperature, and intense physical effort are all risk factors. Pre-existing diseases that cause increased pulmonary blood flow, pulmonary hypertension, enhanced pulmonary vascular reactivity, or a patent foramen ovale may increase the risk of developing HAPE. [1,6-8]

UNDER PEER REVIEW

The susceptibility of HAPE is shown by a gene-environment mismatch. Hypoxic pulmonary vasoconstriction directs blood into healthier lungs in lowlanders with lung damage or infection, sustaining oxygenation. This technique, which is mediated by HIF-1, can be advantageous in situations when there is localised hypoxia, such as pneumonia. Widespread hypoxia in HAPE raises pulmonary blood pressure dangerously, with little benefit of shunting blood away from damaged alveoli. We argue that the adaptive response mediated by HIF-1 in trauma or illness is damaging at altitude. [4]

Epidemiology:

The severity of HAPE will be determined by a number of factors, including altitude, early detection and treatment, and medical care availability. At 4500 metres, the incidence ranges from 0.6 to 6%, whereas at 5500 metres, the incidence ranges from 2% to 15%, with a faster ascending time corresponding with a greater incidence. Those who have had HAPE before have a 60 percent chance of getting it again. It has not been established that one's degree of fitness is a protective factor. When treated, the mortality rate can be as high as 11%, and when untreated, it can be as high as 50%. Acute mountain sickness (AMS) is present in up to 50% of patients, while high altitude cerebral edoema is present in up to 14% of cases . [1]

The frequency of HAPE in tourists to ski resorts in Colorado's Rocky Mountains is believed to be between 0.01-0.1%. The frequency of HAPE in a broad alpine climbing population is 0.2 percent. Around 4% of trekkers in the Himalayas and climbers in the Alps climbing at a rate of more than 600 metres per day develop HAPE. Airlift to an altitude of 5500m was related with a HAPE prevalence of up to 15% in an unselected group of Indian troops. [2,9-13]

Subclinical or mild HAPE is more likely to develop and cause no or little symptoms that are overlooked or ascribed to other reasons. Although the true incidence of subclinical HAPE is unknown, several studies conducted at altitudes between 4,000 and 5,000 metres have suggested that up to 50% of people may have subclinical fluid accumulation in the lungs consistent with occult edoema that resolves spontaneously despite remaining at high altitude. This rate is comparable to that of acute mountain sickness (AMS), which has been linked to minor gas exchange problems. [3,14-19]

UNDER PEER REVIEW

Evaluation and diagnosis:

In lowlanders, HAPE develops within 2–5 days after arriving at high altitude. It is only infrequently seen below 2,500–3,000 metres and after 1 week of acclimatisation. The onset is comparable among high-altitude dwellers returning home after a stay at a low altitude. It is usually preceded by symptoms of AMS (headache, nausea, and lassitude), which affect up to 50% of newcomers at high altitude. As it progresses from moderate to severe, the clinical appearance of HAPE is similar to that of any other kind of pulmonary edoema. [3]

At least two of the following symptoms or complaints would be associated with HAPE: chest tightness or discomfort, cough, dyspnea at rest, and impaired activity tolerance. Two of the following exam findings would also be present: central cyanosis, rales/wheezes, tachycardia, and tachypnea. CXR may indicate patchy alveolar infiltrates with normal-sized mediastinum/heart if accessible, and ultrasonography may reveal B-lines consistent with pulmonary edoema if available. Right axis deviation and/or ischemia may be visible on an ECG. Rapid correction of clinical state and SpO2 with supplementary oxygen in a patient with infiltrates on CXR is pathognomonic of HAPE. Even if labs are available, they are of limited use, and the physician should always consider the possibility of concurrent AMS and/or HACE. [1]

There are no obvious diagnostic test results associated with HAPE. Dehydration, stress, and prior activity might all contribute to abnormal readings. At 4,559 metres, arterial blood gas and oxygen saturation tests reveal the severity of advanced HAPE: mean arterial PO2 in the mid-20 mmHg range vs 40–45 mmHg in healthy subjects, and arterial oxygen saturations below 50% compared 70–85 percent. Early symptomatic HAPE shows a patchy and occasionally peripheral distribution of edoema on chest radiographs and CT scans. The appearance of advanced HAPE on radiographs becomes more homogeneous and diffuse. BAL tests reveal a protein-rich exudate and minor alveolar haemorrhage, which is initially noninflammatory but can evolve to a more inflammatory appearance as detailed further down. At high altitude, echocardiographic and PA catheterization tests have consistently revealed significant pulmonary hypertension. [3,20-24]

Prevention:

UNDER PEER REVIEW

Slow climb is the most effective technique of prevention, and it works even in people who are prone. Low sleeping altitudes, avoidance of alcohol and sleeping drugs, and avoidance of exertion, in addition to gradual ascent and time for acclimatisation, are the keys to avoiding HAPE. Individuals with a history of HAPE should avoid excessive activity during the initial days of altitude exposure because exercise-induced circulatory alterations might aggravate or produce pulmonary edoema. [2]

If gradual ascent is not practicable, nifedipine prophylaxis can be indicated in those with a history of unquestionable HAPE. Starting with the ascent and finishing on the third or fourth day after arrival at the ultimate height, if the stay is to be extended, or after descending to an altitude below 3000 m or one to which the individual is acclimatised, 60 mg daily of a slow-release formulation should be administered. It is important to note that while nifedipine prevents HAPE, it is ineffective in treating acute mountain sickness. Acetazolamide is a carbonic anhydrase inhibitor that works well in the treatment of acute mountain sickness (AMS). Its impact on calcium channels blunts hypoxic vasoconstriction in animals, but more study is needed to assess its usefulness in HAPE. [2,25,26]

Management:

A fall of at least 1000 metres, like with other kinds of high-altitude disease, is the best and most certain treatment choice in HAPE. Supplemental oxygen, portable hyperbaric chambers, and pulmonary vasodilator medications (nifedipine and phosphodiesterase-5 inhibitors) may be beneficial in fully aware patients with mild-moderate HAPE, or when descent is not possible. It's worth noting that the majority of HAPE therapy choices are based on case studies, a small number of observational studies, and randomised controlled trials. The major justification for employing these therapeutic alternatives is usually due to the drugs' persuasive physiologic impact mechanisms and clinical experience. Studies have shown that supplemental oxygen therapy at low flow rates combined with bed rest is a viable option for descending. As a result, in addition to bed rest, the use of supplemental oxygen to maintain an oxygen saturation level above 90% is advised. [27]

In one trial, 11 patients with HAPE were treated with bed rest, oxygen, nifedipine, and acetazolamide at a height of 4240 metres in Pheriche, Nepal. Sildenafil and

UNDER PEER REVIEW

salmeterol were utilised in the majority of patients, but not all. Seven of them had a moderate-to-severe case of HAPE. a marker of pulmonary edoema for which admission and discharge values were collected in 7 patients, was also improved at discharge (84 percent) compared to admission (59 percent). [28]

Phosphodiesterase-5 inhibitors: Phosphodiesterase-5 inhibitors provide a solid physiologic basis for use in the treatment of HAPE. Only case studies are available as evidence on this issue. When descent is not possible, oxygen/portable hyperbaric chambers, and nifedipine are not accessible, some writers recommend using 10 mg tadalafil or 50 mg sildenafil. [27]

According to one research Participants who administered dexamethasone and tadalafil had lower systolic pulmonary artery pressure at high altitude than those who got placebo. Dexamethasone and tadalafil both lower systolic pulmonary artery pressure and may lower the risk of HAPE in people with a history of HAPE, according to the findings. In these people, dexamethasone treatment may also minimise the risk of acute mountain sickness. [28,29]

Although there are case reports that suggest using acetazolamide to treat HAPE, there has yet to be a systematic study that evaluates the drug's effectiveness. As a result of the potential issues induced by diuretic effects such as hypotension, acetazolamide should not be administered on a regular basis. Moreover when it comes to beta-blockers, although certain case reports suggest the use of salmeterol and diuretics, no systematic studies have been conducted to assess their effectiveness in the treatment of HAPE. As a result, recommendations advise against using beta-agonists with diuretics on a regular basis. [27]

Supplemental intravenous fluids are not contraindicated in treatment of HAPE because, unlike cardiogenic pulmonary edoema, these patients' left ventricular ejection fraction is preserved, and volume overload and passive pulmonary congestion caused by elevated hydrostatic pulmonary artery pressure are not the primary pathophysiology. Acclimatization and pretreatment with acetazolamide or phosphodiesterase inhibitors should be explored with persons heading to high altitude, while acetazolamide medication is contraindicated for HAPE treatment due to increased acidosis and intravascular volume contraction concerns. [30]

Conclusion:

UNDER PEER REVIEW

High altitude pulmonary Edoema (HAPE) is a severe form of high-altitude disease that, if left untreated, can result in death in up to half of those who are affected. quick pace of climb, and physical activity increases the risk of the disease incidence and thus prevention is pretty simple which slow climb and also some medication can be used prophylaxis. HAPE may be totally and quickly reversed if caught early and correctly treated. the fall of at least 1000 meters, is the best and most certain treatment choice in HAPE. Supplemental oxygen, portable hyperbaric chambers, and pulmonary vasodilator medications (nifedipine and phosphodiesterase-5 inhibitors) may be beneficial.

UNDER PEER REVIEW

References:

1. Jensen JD, Vincent AL. High Altitude Pulmonary Edema. [Updated 2021 Jul 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430819/
2. Paralikar SJ. High altitude pulmonary edema-clinical features, pathophysiology, prevention and treatment. Indian J Occup Environ Med. 2012 May;16(2):59-62. doi: 10.4103/0019-5278.107066. PMID: 23580834; PMCID: PMC3617508.
3. Swenson ER. High-Altitude Pulmonary Edema. Textbook of Pulmonary Vascular Disease. 2010 Jun 28:871–88. doi: 10.1007/978-0-387-87429-6_61. PMCID: PMC7122766.
4. Woods P, Alcock J. High-altitude pulmonary edema. Evol Med Public Health. 2021 Jan 6;9(1):118-119. doi: 10.1093/emph/eoaa052. PMID: 33732460; PMCID: PMC7947961.
5. Bärtsch P, Mairbäurl H, Swenson ER, Maggiorini M. High altitude pulmonary oedema. Swiss Med Wkly. 2003 Jul 12;133(27-28):377-84. PMID: 12947525.
6. Derby R, deWeber K. The athlete and high altitude. Curr Sports Med Rep. 2010 Mar-Apr;9(2):79-85.
7. Gallagher SA, Hackett PH. High-altitude illness. Emerg Med Clin North Am. 2004 May;22(2):329-55, viii
8. Basnyat B, Murdoch DR. High-altitude illness. Lancet. 2003 Jun 07;361(9373):1967-74.
9. Sopocles AM., Jr High altitude pulmonary edema in Vail, Colorado, 1975-82. High Alt Med Biol. 1986;144:569–73.
10. Hochstrasser J, Nanzer A, Oelz O. Altitude edema in the Swiss Alps. Observations on the incidence and clinical course in 50 patients 1980-84. Schweiz Med Wochenschr. 1986;116:866–73.
11. Maggiorini M, Buhler B, Walter M, Oelz O. Prevalence of acute mountain sickness in the Swiss Alps. BMJ. 1990;301:853–5.
12. Hackett PH, Rales Rennie D. Peripheral edema, retinal haemorrhage and acute mountain sickness. Am J Med. 1979;67:214–8.

UNDER PEER REVIEW

13. Singh I, Roy SB. High altitude pulmonary edema: Clinical, hemodynamic, and pathologic studies. In: Command UA, Ra D, editors. Biomedicine of high terrestrial elevation problems. Washington D.C: 1969. pp. 108–20
14. Cremona G, Asnaghi R, Baderna P, et al. Pulmonary extravascular fluid accumulation in recreational climbers: a prospective study. Lancet. 2002;359:303–309.
15. Mason NP, Petersen M, Mélot C, et al. Serial changes in nasal potential difference and lung electrical impedance tomography at high altitude. J Appl Physiol. 2003;94:2043–2050.
16. Jaeger JJ, Sylvester JT, Cymerman A, Berberich JJ, Denniston JC, Majer JT. Evidence for increased intrathoracic fluid volume in man at high altitude. J Appl Physiol. 1979;47:670–676.
17. Senn O, Clarenbach CF, Fischler M, et al. Do changes in lung function predict high-altitude pulmonary edema at an early stage? Med Sci Sports Exerc. 2006;38:1565–1570.
18. Grissom CK, Roach RC, Sarnquist FH, Hackett PH. Acetazolamide in the treatment of acute mountain sickness: clinical efficacy and effect on gas exchange. Ann Intern Med. 1992;116:461–465.
19. Bärtsch P, Bailey DM, Berger MM, Knauth M, Baumgartner RW. Acute mountain sickness: controversies and advances. High Alt Med Biol. 2004;5:110–124.
20. Vock P, Fretz C, Franciolli M, Bärtsch P. High-altitude pulmonary edema: Findings at high-altitude chest radiography and physical examination. Radiology. 1989;170:661–666.
21. Vock P, Brutsche MH, Nanzer A, Bärtsch P. Variable radiomorphologic data of high altitude pulmonary edema – features from 60 patients. Chest. 1991;100:1306–1311.
22. Schoene RB, Swenson ER, Pizzo CJ, et al. The lung at high altitude: bronchoalveolar lavage in acute mountain sickness and pulmonary edema. J Appl Physiol. 1988;64:2605–2613.
23. Swenson ER, Maggiorini M, Mongovin S, et al. Pathogenesis of high-altitude pulmonary edema: inflammation is not an etiologic factor. J Am Med Assoc. 2002;287:2228–2235.

UNDER PEER REVIEW

24. Kubo K, Hanaoka M, Hayano T, et al. Inflammatory cytokines in BAL fluid and pulmonary hemodynamics in high-altitude pulmonary edema. Respir Physiol. 1998;111:301–310.
25. Swenson ER. Carbonic anhydrase inhibitors and ventilation: A complex interplay of stimulation and suppression. Eur Resp J. 1998;12:1242–7.
26. Deem S, Hedges R, Ker M, Swenson ER. Acetazolamide reduces the rate and magnitude of hypoxic pulmonary vasoconstriction in isolated perfused rabbit lung. Respir Physiol. 2000;123:109–19.
27. Aksel G, Çorbacıoğlu ŞK, Özen C. High-altitude illness: Management approach. Turk J Emerg Med. 2019 Sep 19;19(4):121-126. doi: 10.1016/j.tjem.2019.09.002. PMID: 31687609; PMCID: PMC6819752.
28. Rohit Goyal, Zab Mosenifar, et al. High-Altitude Pulmonary Edema (HAPE) Treatment & Management. medscape Updated: Apr 07, 2020. https://emedicine.medscape.com/article/300716-overview
29. Mounier R, Amonchot A, Caillot N, et al. Pulmonary arterial systolic pressure and susceptibility to high altitude pulmonary edema. Respir Physiol Neurobiol. 2011 Dec 15. 179 (2-3):294-9.
30. Walker C, Miner B, Bolotin T. High-Altitude Pulmonary Edema in Ohio at an Elevation of 339 Meters. Open Access Emerg Med. 2021 Mar 31;13:151-153. doi: 10.2147/OAEM.S297752. PMID: 33833596; PMCID: PMC8020123.

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