Mazur Karol, Machaj Dominik, Jastrzębska Sandra, Płaczek Alicja, Mazur Dominika. Prevention and treatment of high altitude pulmonary edema (HAPE). Journal of Education, Health and Sport. 2020;10(2):114-119. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2020.10.02.015
https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.02.015
https://zenodo.org/record/3678330

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 15.01.2020. Revised: 25.01.2020. Accepted: 21.02.2020.

Prevention and treatment of high altitude pulmonary edema (HAPE)

Karol Mazur, Dominik Machaj, Sandra Jastrzębska, Alicja Płaczek, Dominika Mazur

Karol Mazur, mazurkarol79@gmail.com, Faculty of Medicine, Medical University of Lublin, Chodźki 19 Street, 20-093 Lublin, Poland
Dominik Machaj, dominik5a4@tlen.pl, Faculty of Medicine, Medical University of Lublin, Chodźki 19 Street, 20-093 Lublin, Poland
Sandra Jastrzębska, sandra0189@gmail.com, Faculty of Medicine, Medical University of Lublin, Chodźki Street 19, 20-093 Lublin, Poland
Alicja Płaczek, alicja60@poczta.onet.pl, Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland
Dominika Mazur, dominika.hul20@gmail.com, Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland

Summary:

High-altitude pulmonary edema (HAPE) is a life-threatening form of non-cardiogenic pulmonary edema, that develops within the first 2–5 days in rapidly ascending individuals at altitudes above 2,500-3,000 m. The clinical features are cyanosis, tachypnoea, tachycardia and elevated body temperature generally not exceeding 38.5 °C. It is often severe and potentially fatal manifestation of acute mountain sickness (AMS).

The aim of this study was to assess the methods of prevention and treatment of high altitude pulmonary edema (HAPE). Our study material consisted of publications, which were found in PubMed, ResearchGate and Google Scholar databases. The first step was to find proper publications from the last 30 years .The second step was to carry out an overview of the found publications.
Gradual ascent and staged ascent are the most effective methods of prevention of HAPE Pharmacologic prophylaxis with nifedipine should only be considered for individuals with a history of HAPE. Before initiating treatment of HAPE differential diagnosis should be done. Descent should be initiated and oxygen therapy should be started when HAPE is suspected or diagnosed. If these methods are unavailable, nifedipine or Gamow bag can be used.

Key words: high altitude pulmonary edema, HAPE, prevention, treatment

INTRODUCTION AND PURPOSE

High-altitude pulmonary edema (HAPE) is a life-threatening form of non-cardiogenic pulmonary edema, that develops within the first 2–5 days in rapidly ascending individuals at altitudes above 2,500-3,000 m. It is rarely observed below these altitudes and after 1 week of acclimatization at a particular altitude. It is often severe and potentially fatal manifestation of acute mountain sickness (AMS). Altitude, rate of ascent and individual susceptibility are the most important risk factors for the occurrence of high altitude pulmonary oedema. Excessive increase in pulmonary artery pressure preceding oedema formation is the crucial pathophysiological factor. HAPE can occur in two settings: in residents of sea level or relatively low altitude who ascend to high altitude and in high-altitude natives who descend to low altitude, stay for a period of time, and then reascend to high altitude. In most cases, it is preceded by symptoms of AMS. Early symptoms of HAPE include exertional dyspnoea, subtle nonproductive cough and reduced exercise performance. As pulmonary oedema progresses, cough worsens and breathlessness at rest and sometimes orthopnoea occur. Gurgling in the chest and pink frothy sputum indicate advanced cases. The clinical features are cyanosis, tachypnoea, tachycardia and elevated body temperature generally not exceeding 38.5 °C [1].

The aim of this study was to assess the methods of prevention and treatment of high altitude pulmonary edema (HAPE). Our study material consisted of publications, which were found in PubMed, ResearchGate and Google Scholar databases. In order to find the proper publications, the search has been conducted with the use of a combination of key words like: : "high altitude pulmonary edema", "HAPE", "prevention", "treatment".. The first step was to find proper publications from the last 30 years .The second step was to carry out an overview of the found publications.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Prevention

None of the studies has prospectively examined whether gradual ascent or staged ascent is effective in prevention of high altitude pulmonary edema [2]. Bartsch (1999) observed that susceptible mountaineers (with a history of HAPE) can avoid HAPE during climbing when the average daily ascent rate above 2500 m does not exceed 350–400 m per day or with a staged ascent [3]. Singh et al. and Hackett el al. (1976) in their researches revealed the clear relationship between the rate of ascent and the incidence of HAPE [4,5].

Stream et al. established the role of gradual ascent and staged ascent in the prevention of high altitude pulmonary edema [6].

Bartsch et al. (1991) assessed the use of nifedipine in the prophylaxis of high altitude pulmonary edema. 21 mountaineers with a history of HAPE were randomly assigned to receive either a slow-release nifedipine 20 mg tid (n=10) or placebo (n=11) while ascending rapidly from a low altitude to 4559 m and during the following three days at this altitude. 7 of the 11 subjects who received placebo but only 1 of the 10 subjects who received nifedipine had HAPE at 4559 m. As compared with the subjects who received placebo, those who received nifedipine had a significantly lower mean systolic pulmonary-artery pressure and alveolar-arterial pressure gradient. Therefore this research showed that nifedipine may prevent from high-altitude pulmonary edema by lowering pulmonary-artery pressure [7].

Maggiorini et al. evaluated the role of dexamethasone and tadalafil in prevention of HAPE. 29 participants of their study with a history of HAPE were randomly assigned to receive prophylactic doses of tadalafil 10 mg bid (n=8), dexamethasone 8 mg bid (n=10), or placebo (n=9) during ascent and stay at 4559 m. HAPE developed in 7 of 9 participants receiving placebo and 1 of the 8 participants receiving tadalafil but in none of the 10 participants receiving dexamethasone. At high altitude, systolic pulmonary artery pressure increased less in participants receiving dexamethasone and tadalafil than in those receiving place. Thank to that this research proved that both dexamethasone and tadalafil may reduce the incidence of HAPE by decreasing systolic pulmonary artery pressure [8].

Sartori et al. assessed the effects of prophylactic inhalation of the long-acting beta-adrenergic agonist salmeterol on the incidence of pulmonary edema during exposure to high altitudes (4559 m) in 37 subjects who were susceptible to HAPE. Their research revealed that the prophylactic inhalation of salmeterol decreased the incidence of HAPE in susceptible subjects by more than 50%, from 74% with placebo to 33%. However they used very high doses of salmeterol - 125 μg bid, that are associated with many side effects like tachycardia, dizziness, seizures, sleeplessness and faintness [9]. Because of that further research is needed before salmeterol would be recommended for HAPE prevention [2].

Gradual ascent and staged ascent remain the most effective methods of prevention of HAPE. Individuals travelling above 3000 m should not increase their sleeping elevation by more than 500 m/day and should include a rest day (ie, no ascent to higher sleeping elevation) every 3 to 4 days. Pharmacologic prophylaxis should only be considered for individuals with a history of HAPE. Nifedipine is the preferred drug in such situation because of extensive clinical experience. There is a need of further research before tadalafil or dexamethasone can

be recommended over nifedipine due to very little clinical experience in using this medications for this purpose [2].

Treatment

Rabold et al., Hackett et al. (1987), Hackett et al. (1990), Hackett et al. (2001), Schoene et al. and Tso et al. confirmed that descent is highly effective method of treatment of high altitude pulmonary edema [10,11,12,13,14,15]. Unfortunately, descending may not always be feasible owing to extreme weather conditions, concomitant trauma, or the tactical situation. Marticorena et al. and Zafren et al. proved that descent is not always necessary in cases of mild or moderate HAPE if bed rest and oxygen therapy are available [16,17]. Also descent in not essential when patients can access healthcare facilities and be closely monitored [2].

Several researches have provided evidence for oxygen therapy as a highly effective method of treatment of high altitude pulmonary edema. Marticorena et al. showed that patients with HAPE and treated with oxygen therapy combined with bed rest has significant decrease of blood pressure, heart rate, respiratory rate and more rapid alleviation of symptoms of HAPE [16]. Similar results achieved Zafren et al. in their research. All of the patients with confirmed HAPE, that were treated by bed rest and supplemental oxygen had significant decrease in blood pressure, heart rate, respiratory rate and temperature [17]. These studies established the role of oxygen therapy in HAPE treatment.

Oelz et al. demonstrated utility of nifedipine (10 mg of the short-acting version followed by 20 mg slow-release every 6 h) for HAPE treatment when oxygen or descent was not available. The use of nifedipine for individuals with HAPE resulted in clinical improvement, better oxygenation, reduction of alveolar arterial oxygen gradient and pulmonary artery pressure. Nevertheless participants of this study received a loading dose of the short-acting version of the medication that is discontinued because of the to the possibility of the provoking systemic hypotension [18].

Fagenholz et al. and Jones et al. reported using phosphodiesterase inhibitors like tadalafil or sildenafil in HAPE treatment [19,20]. However none of the studies has prospectively examined the role of this medications in HAPE treatment as mono- or adjunctive therapy. Because of that further research is needed before phosphodiesterase inhibitors would be recommended for HAPE treatment [19].

Jones et al. reported the use of dexamethasone and acetazolamide in the treatment of high altitude pulmonary edema [20]. Fagenholz et al. also noted in their study the

administration of acetazolamide in HAPE treatment [19]. Nevertheless dexamethasone and acetazolamide should not be used for HAPE treatment due to little clinical experience and lack of sufficient evidences. Also there is a need of future research to test these medications for HAPE treatment [20].

There are many studies that revealed the use of portable hyperbaric chamber (Gamow bag) in the treatment of high altitude pulmonary edema. Freeman et al. reported a case of high-altitude pulmonary edema occurring at moderate altitude in Sequoia and Kings Canyon National Parks that was successfully treated by park rangers with the portable hyperbaric chamber [21]. Markovic et al. reported the case of successful treatment of HAPE with Gamow bag, which developed on the North Col of Mount Everest, at an altitude of 7,060 m [22].

Before initiating treatment of high altitude pulmonary edema, consideration should be given to other causes of respiratory symptoms at high altitude. Differential diagnosis shall include: asthma, bronchospasm, mucous plugging, pneumonia, pneumothorax, pulmonary embolism. If HAPE is suspected or diagnosed, oxygen therapy should be started if available, and descent to lower elevation should be initiated. Individuals should try to descend at least 1000 m or until symptoms resolve. They should exert themselves as little as possible while descending because exertion can further increase pulmonary artery pressure and exacerbate edema formation. Oxygen should be delivered by nasal cannula or mask at flow rates sufficient to achieve an SpO2 >90%. If descent is infeasible or delayed, oxygen therapy should be continued or the individual should be placed in a portable hyperbaric chamber. Nifedipine can be used as an adjunct to descent, oxygen therapy or Gamow bag. It should only be used as primary therapy if none of these other measures is available [2].

CONCLUSIONS

1. Gradual ascent and staged ascent are the most effective methods of prevention of HAPE.
2. Pharmacologic prophylaxis with nifedipine should only be considered for individuals with a history of HAPE.
3. Before initiating treatment of HAPE differential diagnosis should be done.
4. Descent should be initiated and oxygen therapy should be started when HAPE is suspected or diagnosed.
5. If these methods are unavailable, nifedipine or Gamow bag can be used.

LIST OF REFERENCES:

1. Bartsch P, Mairbauri H, Swenson ER, Maggiorini M. High altitude pulmonary edema. Swiss Med Wkly. 2003;133:377–84.
2. Luks A.M., Auerbach P.S., Freer L., Grissom C.K., Keyes L.E., Intosh M.C. et al. Wilderness Medical Society Practice Guidelines for the prevention and treatment of acute altitude illness: 2019 update. Wilderness Environ Med. 2019; 30: S3–S18.
3. Bärtsch P. High altitude pulmonary edema. Med Sci Sports Exerc 1999;31(1):S23–S27.
4. Singh I., Kapila C.C., Khanna P.K., Nanda R.B., Rao B.D.P. Highaltitude pulmonary oedema. Lancet 1965;I;229–34.
5. Hackett P.H., Rennie D., Levine H.D. The incidence, importance, and prophylaxis of acute mountain sickness. Lancet. 1976 ;2;1149–1155.
6. Stream, J.O., Grissom C.K. Update on high-altitude pulmonary edema: pathogenesis, prevention, and treatment. Wilderness Environ Med. 2008; 19: 293–303.
7. Bartsch P., Maggiorini M., Ritter M., Noti C., Vock P., Oelz, O. Prevention of high-altitude pulmonary edema by nifedipine. N Engl J Med. 1991; 325: 1284–1289.
8. Maggiorini M., Brunner-La Rocca, H.P., Peth S., Fischler M., Bohm T., Bernheim A. et al. Both tadalafil and dexamethasone may reduce the incidence of high-altitude pulmonary edema: a randomized trial. Ann Intern Med. 2006; 145: 497–506.
9. Sartori, C., Allemann Y., Duplain H., Lepori M., Egli M., Lipp, E. et al. Salmeterol for the prevention of high-altitude pulmonary edema. N Engl J Med. 2002; 346: 1631–1636.
10. Rabold M. High-altitude pulmonary edema: A collective review. Am J Emerg Med. 1991;7:426–433.
11. Hackett PH, Roach RC. Medical therapy of altitude illness. Ann Emerg Med. 1987;16:980–986.
12. Hackett PH, Roach RC. High altitude pulmonary edema. J Wild Med. 1990;1:3–26.
13. Hackett PH, Roach RC. High-altitude medicine. In: Auerbach PS, ed. Wilderness Medicine. 4th ed. St Louis, Mo:Mosby; 2001: Chap 1: 2–43.
14. Schoene RB. Pulmonary edema at high altitude: Review, pathophysiology, and update. Clin Chest Med.1985;6(3):491–507.
15. Tso EL, Wagner TJ Jr. What's up in the management of high-altitude pulmonary edema? Md Med J. 1993;42:641–645.
16. Marticorena, E. and Hultgren, H.N. Evaluation of therapeutic methods in high altitude pulmonary edema. Am J Cardiol. 1979; 43: 307–312
17. Zafren, K., Reeves, J.T., and Schoene, R. Treatment of high-altitude pulmonary edema by bed rest and supplemental oxygen. Wilderness Environ Med. 1996; 7: 127–132
18. Oelz, O., Maggiorini, M., Ritter, M., Waber, U., Jenni, R., Vock, P. et al. Nifedipine for high altitude pulmonary oedema. Lancet. 1989; 2: 1241–1244
19. Fagenholz, P.J., Gutman, J.A., Murray, A.F., and Harris, N.S. Treatment of high altitude pulmonary edema at 4240 m in Nepal. High Alt Med Biol. 2007; 8: 139–146
20. Jones, B.E., Stokes, S., McKenzie, S., Nilles, E., and Stoddard, G.J. Management of high altitude pulmonary edema in the Himalaya: a review of 56 cases presenting at Pheriche medical aid post (4240 m). Wilderness Environ Med. 2013; 24: 32–36.
21. Freeman K., Shalit M., and Stroh, G. Use of the Gamow bag by EMT-basic park rangers for treatment of high-altitude pulmonary edema and high-altitude cerebral edema. Wilderness Environ Med. 2004; 15: 198–201
22. Markovic D, Kovacevic H. Recompression therapy of mountain sickness. Arhiv Za Higijenu Rada i Toksikologiju. 2002;1:3–6.