https://doi.org/10.33266/2070-1004-2021-2-55-58
UDC 616-032:612.213:796.077.2

Rewiew article

PREVENTION AND TREATMENT OF ALTITUDE DISEASE

A.S.Samoilov[1], N.V.Rylova[1], I.V.Bolshakov[1], V.F.Kazakov[1]

[1] State Research Center – Burnasyan Federal Medical Biophysical Center of Federal Medical Biological Agency, Moscow, Russian Federation

Abstract. *The aim* of the study is to determine the tactics of effective prevention and treatment of altitude sickness in the conditions of medium and high mountains.
Materials and research methods. Domestic and foreign literature on altitude sickness are analyzed. The search was carried out using the electronic databases MEDLINE, Embase, Scopus, Web of Science, eLIBRARY for the period from 2013 to 2021. The following keywords and their combinations were used for the search: altitude sickness, treatment, prevention.
Research results and their analysis. The features of the development of altitude sickness, risk factors, modern approaches to the treatment of this pathology, as well as the possibilities of pharmacological and non-pharmacological methods of prevention are considered. It is noted that the key method of preventing altitude sickness is a gradual ascent to great heights, and a promising method for its prevention can be an early implementation of interval hypoxic training. If one needs to quickly climb to heights of over 2.5 thousand meters, it is possible to use drugs such as acetazolamide and dexamethasone. In case of ineffectiveness of prevention and of development of any form of altitude sickness, the most effective treatment is an immediate descent to lower altitudes. If the descent is impossible, the use of oxygen and pharmacotherapy is justified, it is also possible to use hyperbaric chambers.

Key words: *acute mountain sickness, altitude sickness, athletes, high-altitude cerebral edema, high-altitude pulmonary edema, prevention, treatment*

Conflict of interest. The authors declare no conflict of interest

For citation: Samoylov A.S., Rylova N.V., Bol'shakov I.V., Kazakov V.F. Prevention and Treatment of Altitude Disease. *Meditsina katastrof* = Disaster Medicine. 2021;2:55-58 (In Russ.). https://doi.org/10.33266/2070-1004-2021-2-55-58

https://doi.org/10.33266/2070-1004-2021-2-55-58
УДК 616-032:612.213:796.077.2

Обзорная статья

ПРОФИЛАКТИКА И ЛЕЧЕНИЕ ВЫСОТНОЙ БОЛЕЗНИ

А.С.Самойлов[1], Н.В.Рылова[1], И.В.Большаков[1], В.Ф.Казаков[1]

[1] ФГБУ «ГНЦ – Федеральный медицинский биофизический центр им. А.И.Бурназяна» ФМБА России, Москва, Россия

Резюме. *Цель исследования* – определение тактики эффективной профилактики и лечения высотной болезни в условиях средне- и высокогорья.
Материалы и методы исследования. Проанализированы данные отечественной и зарубежной литературы о высотной болезни. Поиск проводился с использованием электронных баз данных MEDLINE, Embase, Scopus, Web of Science, eLIBRARY за период с 2013 г. по 2021 г. Для поиска использовались следующие ключевые слова и их сочетания: высотная болезнь, лечение, профилактика.
Результаты исследования и их анализ. Рассмотрены особенности развития высотной болезни, факторы риска, современные подходы к лечению данной патологии, а также возможности фармакологических и нефармакологических методов профилактики. Отмечено, что ключевой метод профилактики высотной болезни – постепенное восхождение на большие высоты, а перспективным методом её профилактики может быть заблаговременное проведение интервальных гипоксических тренировок. При необходимости быстрого подъема на высоты свыше 2,5 тыс. м возможно применение таких препаратов, как ацетазоламид и дексаметазон. В случае неэффективности профилактики и развития любой из форм высотной болезни самое эффективное средство лечения – незамедлительный спуск на более низкие высоты. При невозможности спуска оправдано применение кислородо- и фармакотерапии, возможно также использование гипербарических камер.

Ключевые слова: *высокогорный отек легких, высокогорный отек мозга, высотная болезнь, острая горная болезнь, спортсмены*

Конфликт интересов. Авторы статьи подтверждают отсутствие конфликта интересов

Для цитирования: Самойлов А.С., Рылова Н.В., Большаков И.В., Казаков В.Ф. Профилактика и лечение высотной болезни // Медицина катастроф. 2021. №2. С. 55-58. https://doi.org/10.33266/2070-1004-2021-2-55-58

Contact information:
Natalia V. Rylova – Dr. Sci. (Med.), Prof., Head of the Laboratory of Sports Nutrition of the Center for Sports Medicine and Rehabilitation
Address: 46; Zhivopisnaya str., Moscow, 420012, Russia
Phone: +7-(917)-397-33-93
E-mail: rilovanv@mail.ru

Контактная информация:
Рылова Наталья Викторовна – докт. мед. наук, проф., заведующая лабораторией спортивной нутрициологии Центра спортивной медицины и реабилитации
Адрес: Россия, 420012, г. Москва, ул. Живописная, д. 46
Тел.: +7-(917)-397-33-93
E-mail: rilovanv@mail.ru

here are many activities associated with the need to climb mountains up to great heights. These include sports (mountaineering, alpine skiing, etc.), military operations, scientific expeditions, tourism, rescue operations, etc. As one climbs to a great height, one faces mane negative environmental factors: decrease in temperature and humidity, strong winds, increase in ultraviolet radiation and, most importantly, decrease in atmospheric pressure and oxygen partial pressure. It has been established that atmospheric pressure at an altitude of over 5 thousand m can decrease till 370 mm Hg and below, and partial pressure of oxygen (normal range is 90-100 mm Hg) — till 50 mm Hg and below [1, 2]. The combination of the above-mentioned unfavorable factors with hypoxia can provoke the development of the so-called "altitude sickness".

Altitude sickness has 3 forms: acute mountain sickness, high-altitude cerebral edema and high-altitude pulmonary edema. Acute mountain sickness most often develops with a rapid ascent to an altitude of 2.5 thousand meters and above. To determine the severity of acute mountain sickness, the Lake Louise test questionnaire is used, which is based on a quantitative assessment of the four most characteristic symptoms: headache, dizziness, impaired activity of the gastrointestinal tract and fatigue. On the basis of the total score, 3 degrees of severity of acute mountain sickness are distinguished: mild degree — 3-5 points; moderate degree — 6-9 points; severe degree — 10-12 points [3]. With the development of cerebral edema, neurological manifestations are added to the aforementioned symptoms: impaired consciousness and ataxia [4]. In case of pulmonary edema, the symptoms of respiratory system damage come to the fore: dry cough, tachypnea. The condition deteriorates sharply, tachycardia, wet cough, cyanosis, coma appear [5]. This syndrome is the most dangerous form of altitude sickness. It is important to note that high-altitude cerebral edema can be considered as a more severe degree of acute mountain sickness, while high-altitude pulmonary edema due to differences in pathogenesis, clinical manifestations and, as a result, in approaches to treatment, should be considered separately [6].

These conditions, especially pulmonary and cerebral edema, in certain situations endanger the health and life of not only the patient himself, but also of those persons around him. Therefore, the issue of preventing the aforementioned conditions, the effectiveness of certain methods and drugs used to treat altitude sickness is very important.

Current views on the pathophysiology of altitude sickness

When climbing to a height of 2.5 thousand meters and above, adaptive mechanisms are subjected to significant stress. Low atmospheric pressure makes it difficult for oxygen to flow through the alveolar wall by diffusion, which causes a decrease in the partial pressure of oxygen and in the level of saturation in the blood. The resulting hypoxia triggers a cascade of physiological reactions: hyperventilation develops, leading to respiratory alkalosis, hematocrit increases, erythrocyte aggregation processes accelerate, blood flow velocity in all organs and tissues (especially in the brain and lungs) increases, heart rate and hydrostatic pressure in capillary bed grow [7]. Increased pressure in the lungs microcirculation system and increased perfusion cause interstitial pulmonary edema, which further disrupts gas exchange in alveoli and aggravates hypoxia. Through the same mechanism, interstitial cerebral edema develops, which occurs mainly in the white matter and causes an increase in intracranial pressure and irritation of the sensitive fibers of the trigeminal ganglia. This process causes severe headache. The connection of sensory fibers with the autonomic centers of the brain stem explains the frequent occurrence of nausea and vomiting together with severe headache. It should be emphasized that in altitude sickness intracranial pressure at rest does not differ from normal. Its increase is observed with exercising and with an increase in intrathoracic pressure caused by coughing, vomiting, etc. [8]. Recent evidence suggests a significant role for the venous system in the pathogenesis of altitude sickness. The study showed that even a small cerebral edema if there is an individual predisposition can significantly impede venous outflow due to compression of small veins and thereby aggravate the symptoms of this condition [9]. In addition to the structural features of small veins, individual differences in the structure of the transverse sinus, the compensatory capabilities of the cerebrospinal fluid pathways and subarachnoid space, the tone of the autonomic nervous system (ANS) and the level of vascular endothelial growth factor expression can have a great influence on the development of the disease [8].

Pulmonary hypertension is a key link in the pathogenesis of high-altitude pulmonary edema. It is believed that in susceptible people, hypoxia causes localized pulmonary hypertension, which may be accompanied by an increased blood flow in certain areas of the lungs and by penetration of fluid from capillary bed into alveoli. Apparently, increased activity of the sympathetic nervous system and impaired absorption of sodium and fluid in the alveoli are involved in the pathogenesis of pulmonary edema [10]. Hypoxia reduces sodium transport by reducing the expression of epithelial sodium channels and sodium-potassium-dependent adenosine triphosphatase. Perhaps this effect is due to dysfunction of β2-adrenergic receptors [8]. In recent years, researchers have paid more and more attention to the role of endothelium and its production of substances such as nitrous oxide (NO) and endothelin-1. It was found that in patients with high-altitude pulmonary edema the level of NO in the exhaled air is lower than in healthy people, and the level of endothelin in their blood is higher [11].

Thus, the pathophysiology of altitude sickness is complex and multifaceted. It can be noted that the genetic characteristics of a particular person are of great importance in the development of the disease.

Risk factors for altitude sickness

The strongest risk factor for altitude sickness is a rapid ascent to a great height: the body does not have time to adapt to a progressive decrease in atmospheric pressure. With an intense physical activity symptoms of altitude sickness can appear even at relatively low altitudes. The nature of the area where the person permanently resides is of great importance. People living in lowlands are at increased risk of altitude sickness compared to those who live permanently above 900 m above sea level [12]. A previous history of altitude sickness is also a fairly important risk factor, especially if there have been cases of cerebral and pulmonary edema, regardless of how long ago they occurred. Moreover, up to 60% of people with a history of altitude sickness fall ill again when they return to the same altitude [2]. Recent studies have shown that gender and physical fitness — unlike age — do not directly affect morbidity [12]. It has been shown that people over the age of 40-60, as well as children and adolescents, are less susceptible to the development of altitude sickness, but the exact mechanisms of the development of resistance of these groups to the disease have not yet been identified. It is believed that the presence of bad habits (alcohol and smoking) does not affect the incidence of altitude sickness. However, in a recent study, it was found that people who smoke are still more likely to suffer from this pathology [13].

In the last decade, researchers have paid more and more attention to the role of genetics in the pathogenesis of altitude sickness. For example, the genetic variability of many genes may be associated with a predisposition to this condition. The strongest link was found with genes that encode angiotensin converting enzyme (ACE) and nitric oxide synthase (NO synthase) — [10]. This fact suggests that in the future it will be possible to assess the risks of altitude sickness by studying the genotype and to take the necessary measures in a timely manner before the ascent.

Prevention of altitude sickness

Preventing the development of altitude sickness should be a priority before climbing. Although the prevention strategy in most cases gives a good result, its effectiveness cannot be unequivocally guaranteed in all cases, since the response of an individual to the height can be unpredictable and depends on many individual characteristics. Gradual ascent is the best prevention tactics for all forms of altitude sickness, since applying it a person gives necessary time to his body to develop high-altitude acclimatization. If you plan to climb to an altitude of more than 2.5 thousand m, then before continuing the hike, it is recommended to spend 6-7 days at a moderate altitude — 2.2 thousand - 3 thousand m. It is also recommended at an altitude of 3 thousand not to exceed the daily climb by more than 500 m per day and to stop for rest every 3-4 days [5]. If symptoms of altitude sickness develop, the ascent should be stopped. Additionally, it should be noted that on the eve of climbing to a height, one should stop drinking alcohol, taking narcotic analgesics and avoid hard physical exertion [8]. Throughout the entire ascent, it is necessary to observe a drinking regime, since in conditions of low humidity at altitude and physical exertion, the risk of dehydration increases, which serves as an additional aggravating factor.

The tactics of preliminary hypoxic preparation for the prevention of altitude sickness is very interesting. A large number of studies have been carried out studying the effects of exposure to hypo- or normobaric hypoxia for some time before climbing. It was concluded that 15-60 min courses of hypoxia taken a few days before the ascent did not contribute to a more rapid acclimatization to the conditions of medium and high mountains. At the same time, longer courses — of more than 8 hours a day for 7 days before the ascent — are more likely to facilitate quick adaptation. Moreover, hypobaric hypoxia is more effective than normobaric hypoxia [14].

Prophylactic medication is not recommended for persons with a low risk of developing altitude sickness — climbing to an altitude below 2.5 thousand meters, with no symptoms of the disease in the anamnesis. In other cases, taking medications may be justified. The carbonic anhydrase inhibitor acetazolamide is the main drug for the prevention of acute mountain sickness and high-altitude cerebral edema. It accelerates natural mechanisms of adaptation to high mountains, reduces the severity of neurological disorders at altitude, increases physical performance under conditions of hypobaric hypoxia. At the same time, there is no data on the advantage of taking acetazolamide in a daily dose of 1000 mg compared to a daily dose of 250 mg [15]. In view of this, acetazolamide is recommended to be taken the day before the ascent at a dosage of 125 mg every 12 hours — 250 mg per day and 2.5 mg / kg - for children - until the start of the descent from the maximum reached altitude of the route [16].

If acetazolamide is intolerant, dexamethasone may be an effective prophylaxis for altitude sickness. The preferred dosage for this drug is 2 mg every 6 hours or 4 mg every 12 hours [2]. Taking dexamethasone should be discontinued after the start of descent from a height and should not last more than 7 days, since in this case there is a risk of suppression of adrenal function. Some authors recommend combination therapy with acetazolamide and dexamethasone during military and rescue operations, when there is a need for rapid ascent to an altitude of more than 3.5 thousand m [9]. Ibuprofen is also considered an alternative means of preventing altitude sickness, which has been shown to be more effective than placebo, but less effective than acetazolamide [17]. Given the fact that ibuprofen can cause gastrointestinal bleeding, this drug is recommended only if acetazolamide and dexamethasone are intolerant.

As for high-altitude pulmonary edema, the routine prophylactic use of drugs is not recommended. The only indication is a history of single or multiple cases of the disease. Among the drugs used to prevent the disease are nifedipine, tadalafil and dexamethasone. The calcium channel blocker nifedipine is the most effective drug for preventing pulmonary edema. It has been shown that this drug effectively reduces the pressure in the pulmonary vessels without development of significant systemic hypotension [18]. Prophylaxis should be started 24 hours before rising, the recommended dose is 20 mg of the slow-release drug every 8 hours. Tadalafil and dexamethasone are used only if nifedipine is intolerant.

Altitude sickness treatment

As mentioned above, when climbing to an altitude of over 2.5 thousand meters, it is necessary to prevent altitude sickness. If, despite the preventive measures taken, the disease has developed, the most effective strategy is to immediately descend to lower altitudes — an average of 300–1000 m. This is especially important if symptoms of cerebral and pulmonary edema are present. Other medical and pharmacological measures should be considered as a priority only when immediate descent is not possible.

Most patients with mild symptoms of acute mountain sickness can be cured by giving them enough time to rest. You can also use symptomatic drugs: non-opioid analgesics — for headaches; antiemetics — for nausea and vomiting. It is recommended to take ibuprofen (600 mg) and acetaminophen (650–1000 mg) as analgesics, metoclopramide (10 mg) as an antiemetic [19]. In case of ineffectiveness of symptomatic drugs when they are taken for 1-2 days or the progression of symptoms of the disease, it is recommended to use acetazolamide at a dosage of 250 mg 2 times a day or dexamethasone at a dosage of 4 mg every 6 hours with a preliminary loading dose of 8 mg [5].

With further aggravation of the symptoms of altitude sickness and the appearance of signs of high-altitude cerebral edema, urgent evacuation is necessary. If it is impossible, it is necessary to carry out oxygen treatment under the control of saturation, the target level of which is more than 90% [2]. It is also possible to use hyperbaric chambers, but in this case there is a high probability of repeated deterioration after the procedure. The use of CPAP-therapy (Constant Positive Airway Pressure), which has become widespread in the treatment of obstructive sleep apnea syndrome, is very promising [20]. When using this method, the pressure on the alveolar walls increases, which is accompanied by an increase in the alveolar volume, an improvement in the ventilation-perfusion ratio and, as a consequence, in gas exchange. However, due to the lack of full-fledged studies of the application of this method in mountain sickness, CPAP therapy is recommended to be used only when standard oxygen therapy did not give the desired effect.

If high-altitude pulmonary edema develops, it is also necessary to either take immediate descent measures, or to conduct oxygen therapy until the target saturation values are reached. In the absence of oxygen, it is recommended to take nifedipine at a dosage of 30 mg 2 times a day. It is possible to use inhibitors of phosphodiesterase-5, dexamethasone and beta-agonists. It should be noted that all types of pharmacological drugs used in high-altitude pulmonary edema should be used in the absence of the possibility of oxygen therapy, since the equal efficiency of using oxygen and its combination with drugs has been proven [9].

Currently, active research is underway on the possibility of using for the prevention and treatment of altitude sickness of such drugs as endothelin receptor antagonists type A (sitaxentan, ambrisentan), interleukin-10 activators (gabapentin), Rho-kinase inhibitors, stimulants of soluble guanylate cyclase and inducers of glutathione S- transferase [21].

Thus, altitude sickness is a dangerous condition that can cause significant harm to human health and, in some cases, even lead to death. Prevention of this disease should be carried out when climbing mountains to an altitude of more than 2.5 thousand meters, and in some cases to lower heights. This is especially true for people permanently living in flat areas or with a history of altitude sickness. Prevention of altitude sickness includes a gradual ascent to significant heights, elimination of smoking, alcohol and intense physical activity on the eve of the ascent. If you need to quickly climb to a great height, it is possible to use drugs such as acetazolamide and dexamethasone. It is also very promising to use the method of interval hypoxic training at least a week before the ascent. In case of ineffectiveness of prevention, if any form of altitude sickness develops, the most effective treatment is an immediate descent to lower altitudes. Only when it is impossible to descend, the use of oxygen therapy, pharmacotherapy, hyperbaric chambers, etc. is justified.

REFERENCES

1. Kurtzman R.A., Caruso J.L. High-Altitude Illness Death Investigation. Acad. Forensic. Pathol. 2018;8;1:83–97.

2. Davis C., Hackett P. Advances in the Prevention and Treatment of High Altitude Illness. Emerg. Med. Clin. North Am. 2017;35;2:241–260.

3. Roach R.C., Hackett P.H., Oelz O., Bärtsch P., Luks A.M., MacInnis M. J. Baillie J.K. The 2018 Lake Louise Acute Mountain Sickness Score. High Altitude Medicine & Biology. 2018;19;1:4–6.

4. Jin J. Acute Mountain Sickness. JAMA. 2017;318;18:1840.

5. Luks A.M., Auerbach P.S., Freer L., et al. Wilderness Medical Society Practice Guidelines for the Prevention and Treatment of Acute Altitude Illness: 2019 update. Wilderness Environ. Med. 2019;30;4:3-18.

6. Sagoo R.S., Hutchinson C.E., Wright A., et al. Magnetic Resonance Investigation into the Mechanisms Involved in the Development of High-Altitude Cerebral Edema. J. Cereb. Blood Flow Metab. 2017;37;1:319-331.

7. Raberin A., Nader E., Ayerbe J.L., et al. Evolution of Blood Rheology and its Relationship to Pulmonary Hemodynamic during the First Days of Exposure to Moderate Altitude. Clin. Hemorheol. Microcirc. 2020;74;2:201-208.

8. Luks A.M., Swenson, E.R., Bärtsch P. Acute High-Altitude Sickness. European Respiratory Review. 2017;26;143:160096. doi : 10.1183/16000617.0096-2016.

9. Aksel G., Çorbacıoğlu Ş.K., & Özen C. High-Altitude Illness: Management Approach. Turkish Journal of Emergency Medicine. 2019;19;4:121-126.

10. Gudbjartsson T., Sigurdsson E., Gottfredsson M., Bjornsson O.M., Gudmundsson G. High Altitude Illness and Related Diseases - a Review. Laeknabladid. 2019;105;11:499-507.

11. Murray A.J., Montgomery H.E., Feelisch M., Grocott M.P.W., Martin D.S. Metabolic Adjustment to High-Altitude Hypoxia: From Genetic Signals to Physiological Implications. Biochem Soc Trans. 2018;46;3:599-607.

12. Basnyat B., Hofmeyr R., Tölken G., De Decker R. Acute High-Altitude Illness. S. Afr. Med. J. 2017;107;12:1047-1048.

13. Ashyrbayev A.A., Tolbashiyeva G.U. Prevalence Rate of Acute Mountain Sickness and Factors Influencing on It. *Vestnik KRSU*. 2019;19;1:65-67 (In Russ.).

14. Fulco C.S., Beidleman B.A., Muza S.R. Effectiveness of Preacclimatization Strategies for High-Altitude Exposure. Exerc. Sport Sci. Rev. 2013;41;1:55-63.

15. Vetryakov O.V., Bykov V.N., Fateev I.V., Halimov Yu.Sh. The Administration of Acetazolamidum for the Symptom Prophylaxis of an Acute Mountain Sickness when Short-Term Dislocation from Middle Mountains to Highlands Takes Place. Reviews on Clinical Pharmacology and Drug Therapy. 2018;16;2:42–48 (In Russ.).

16. McIntosh S.E., Hemphill M., McDevitt M.C., et al. Reduced Acetazolamide Dosing in Countering Altitude Illness: a Comparison of 62.5 vs. 125 mg (the RADICAL Trial). Wilderness Environ. Med. 2019;30;1:12–21.

17. Burns P., Lipman G.S., Warner K., et al. Altitude Sickness Prevention with Ibuprofen Relative to Acetazolamide. Am. J. Med. 2019;132;2:247–251.

18. Simancas-Racines D., Arevalo-Rodriguez I., Osorio D., Franco J.V., Yihan Xu, Hidalgo R. Interventions for Treating Acute High Altitude Illness. Cochrane Database Syst. Rev. 2018;6;6:CD009567. doi: 10.1002/14651858.CD009567.pub2.

19. Irons H.R., Salas R.N., Bhai S.F., Gregorie W.D., Harris N.S. Prospective Double-Blinded Randomized Field-Based Clinical Trial of Metoclopramide and Ibuprofen for the Treatment of High Altitude Headache and Acute Mountain Sickness. Wilderness Environ Med. 2020;31;1:38-43.

20. Weaver T.E. Novel Aspects of CPAP Treatment and Interventions to Improve CPAP Adherence. Journal of Clinical Medicine. 2019; 8; 12: 2220.

21. Joyce K.E., Lucas S.J.E., Imray C.H.E., Balanos G., Wright, A.D. Advances in the Available Non-Biological Pharmacotherapy Prevention and Treatment of Acute Mountain Sickness and High Altitude Cerebral and Pulmonary Oedema. Expert Opinion on Pharmacotherapy. 2018;19;17:1891-1902.

СПИСОК ИСТОЧНИКОВ

1. *Kurtzman R.A., Caruso J.L.* High-altitude illness death investigation // Acad. Forensic Pathol. 2018. Vol. 8, № 1. P. 83–97.

2. *Davis C., Hackett P.* Advances in the prevention and treatment of high altitude illness // Emerg. Med. Clin. North Am. 2017. Vol. 35, № 2. P. 241–260.

3. *Roach R.C., Hackett P.H., Oelz O., Bärtsch P., Luks A.M., MacInnis M. J. Baillie J.K.* The 2018 Lake Louise Acute Mountain Sickness Score // High Altitude Medicine & Biology. 2018. Vol. 19, №1. P. 4–6.

4. *Jin J. Acute Mountain Sickness* // JAMA. 2017. Vol. 318, №18. 1840 p.

5. *Luks A.M., Auerbach P.S., Freer L. et al.* Wilderness medical society Practice guidelines for the prevention and treatment of acute altitude illness: 2019 update // Wilderness Environ. Med. 2019. Vol. 30, № 4. P. 3-18.

6. *Sagoo R.S., Hutchinson C.E., Wright A.* et al. Magnetic Resonance investigation into the mechanisms involved in the development of high-altitude cerebral edema // J. Cereb. Blood Flow Metab. 2017. Vol. 37, № 1. P. 319-331.

7. *Raberin A., Nader E., Ayerbe J.L. et al.* Evolution of blood rheology and its relationship to pulmonary hemodynamic during the first days of exposure to moderate altitude // Clin. Hemorheol. Microcirc. 2020. Vol. 74, № 2. P. 201-208.

8. *Luks A.M., Swenson, E.R., Bärtsch P.* Acute high-altitude sickness // European Respiratory Review. 2017. Vol. 26, № 143: 160096.
doi: 10.1183/16000617.0096-2016.

9. *Aksel G., Çorbacıoğlu Ş.K., & Özen C.* High-altitude illness: Management approach // Turkish Journal of Emergency Medicine. 2019. Vol. 19, № 4. P. 121-126.

10. *Gudbjartsson T., Sigurdsson E., Gottfredsson M., Bjornsson O.M., Gudmundsson G.* High altitude illness and related diseases - a review // Laeknabladid. 2019. Vol. 105, № 11. P. 499-507.

11. *Murray A.J., Montgomery H.E., Feelisch M., Grocott M.P.W., Martin D.S.* Metabolic adjustment to high-altitude hypoxia: from genetic signals to physiological implications // Biochem. Soc. Trans. 2018. Vol. 46, № 3. P. 599-607.

12. *Basnyat B., Hofmeyr R., Tölken G., De Decker R.* Acute high-altitude illness // S. Afr. Med. J. 2017. Vol. 107, № 12. P. 1047-1048.

13. *Ашырбаев А. А., Толбашиева Г. У.* Частота распространения острой горной болезни и факторы, влияющие на нее // Вестник КРСУ. 2019. Т. 19, № 1. С. 65-67.

14. *Fulco C.S., Beidleman B.A., Muza S.R.* Effectiveness of preacclimatization strategies for high-altitude exposure // Exerc. Sport Sci. Rev. 2013. Vol. 41, № 1. P. 55-63.

15. *Ветряков О.В., Быков В.Н., Фатеев И.В., Халимов Ю.Ш.* Применение ацетазоламида для профилактики симптомов острой горной болезни при краткосрочном перемещении из среднегорья в высокогорье // Обзоры по клинической фармакологии и лекарственной терапии. 2018. Т. 16, № 2. С. 42–48.

16. *McIntosh S.E., Hemphill M., McDevitt M.C. et al.* Reduced acetazolamide dosing in countering altitude illness: a comparison of 62.5 vs. 125 mg (the RADICAL Trial) // Wilderness Environ. Med. 2019. Vol. 30, № 1. P. 12–21.

17. *Burns P., Lipman G.S., Warner K. et al.* Altitude sickness prevention with ibuprofen relative to acetazolamide // Am. J. Med. 2019. Vol. 132, № 2. P. 247–251.

18. *Simancas-Racines D., Arevalo-Rodriguez I., Osorio D., Franco J. V., Yihan Xu, Hidalgo R.* Interventions for treating acute high altitude illness // Cochrane Database Syst. Rev. 2018. Vol. 6, № 6: CD009567.
doi: 10.1002/14651858.CD009567.pub2.

19. *Irons H.R., Salas R.N., Bhai S.F., Gregorie W.D., Harris N.S.* Prospective Double-Blinded Randomized Field-Based Clinical Trial of Metoclopramide and Ibuprofen for the Treatment of High Altitude Headache and Acute Mountain Sickness // Wilderness Environ. Med. 2020. Vol. 31, № 1. P. 38-43.

20. *Weaver T.E.* Novel Aspects of CPAP Treatment and Interventions to Improve CPAP Adherence // Journal of Clinical Medicine. 2019. Vol. 8, № 12. 2220 p.

21. *Joyce K.E., Lucas S.J.E., Imray C.H.E., Balanos G., Wright, A. D.* Advances in the available non-biological pharmacotherapy prevention and treatment of acute mountain sickness and high altitude cerebral and pulmonary oedema. Expert Opinion on Pharmacotherapy. 2018. Vol. 19, № 17. P. 1891-1902.

The material was received 28.03.21; the article after peer review procedure 31.03.21; the Editorial Board accepted the article for publication 15.06.21

Материал поступил в редакцию 28.03.21; статья принята после рецензирования 31.03.21; статья принята к публикации 15.06.21