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PHYSIOLOGICAL EFFECTS OF REDUCED ATMOSPHERIC PRESSURE

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Abstract. This scientific paper delves into the general analysis of the physiological effect and the mechanism of action of the reduced values of atmospheric pressure on the human body. This review provides information on the reasons, manifestations, clinical specific features, and the strategies used for the prevention of altitude sickness with reference to the available literature.

Key words: atmospheric pressure, altitude sickness, hypoxia, acute mountain disease, high-altitude cerebral edema, high-altitude pulmonary edema and prevention.

Introduction. The influence of high altitude on humans was first noted a long time ago, and the empirical experience has been accumulated over many years [1, p. 328; 2 p. 173]. The physiology of human adaptation to highlands has been studied during the investigations carried out both on high mountain slopes and in hypobaric chambers in laboratory conditions [3-7].

At high altitudes above sea level, people are affected by changes in atmospheric pressure and the associated change in oxygen pressure in the environment. With an increase in altitude above sea level, the amount of inhaled oxygen is decreased due to a decrease in the atmospheric pressure.

Altitude sickness got its name due to the fact that people encountered it, first of all, when exploring the stratosphere, although the same condition also occurs in terrestrial or more precisely underground conditions when the partial pressure of oxygen is decreased. The same can happen during underwater works, when the supply of oxygen to the diving suit is disturbed.

Health problems associated with high altitude sickness include acute mountain disease (AMD) and two life-threatening conditions: high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE) (these develop in the first 6 to 96 hours after climbing) [8]. AMD occurs relatively often, affecting ~25% of those traveling at altitudes above 2500 m [9, p. 340], and with early recognition it goes away on its own. High-altitude cerebral edema and high-altitude pulmonary edema require special treatment [10, p. 9].

Mountain disease develops in the majority of poorly trained people, and especially asthenic people who constantly live on the plains and rarely climb mountains. It should be noted that the mountain disease can be provoked by many factors:

-firstly, various climatic features of the highlands: wind, solar radiation, high difference between day and night temperatures, low absolute air humidity, presence of snow, etc.;

- secondly, there is an excessively high variability of individual sensitivity to high-altitude lack of oxygen in different people depending on gender, constitutional type, degree of training, once acquired "altitude skills", physical and mental state;

- thirdly, it is of undoubted importance that the heavy physical work done by a person also contributes to the appearance of the signs of mountain disease at lower altitudes;

- fourthly, the development of mountain disease is significantly influenced by the climbing speed: the faster the ascent, the lower the altitude threshold.

It should be noted that an altitude above 4,500 m is the level at which mountain disease develops in most people, although in some individuals the first signs of this disease can already be observed at an altitude of 1,600 to 2,000 m.

There are two forms of mountain disease:

1) acute mountain disease may occur not immediately after a fast climbing

the mountains, but after several hours (for example, after 6 to 12 hours at an altitude of 4000 m). It is characterized by various mental and neurological symptoms, headache, gastrointestinal symptoms (anorexia, nausea, vomiting), dyspnea during physical exertion, pale skin with cyanosis of the lips and pale nail beds, reduced work capacity, sleep disorder, dizziness and fatigue, with clinical severity assessed according to the Lake Louise scoring system [11, p. 273]. Symptoms of AMD can be explained by hypoventilation, impaired gas exchange, fluid retention and redistribution, and increased sympathetic activity. A characteristic diagnostic test for mountain disease is a change in handwriting, which indicates a violation of the fine motor differentiation of muscle activity and

2) chronic mountain disease that is characterized by dysfunction associated with severe hypoxia, especially during sleep, accelerated aging and neurological signs, such as reduced hypoxic respiratory stimulus and mild peripheral neuropathy [12, p. 450].

The pathophysiology of acute mountain disease (AMD) and high-altitude cerebral edema (HACE) requires additional studies, but it is apparently associated with vasodilation, permeability of the hematoencephalic barrier [13, p. 110] and the disturbance of capillaries and microvascular channels resulting in edema.

High-altitude pulmonary edema is associated with an increased pressure in the pulmonary artery caused by the pulmonary vasoconstriction that results in the pulmonary edema [14, p. 503]. Vasoconstriction and pulmonary edema can be caused by hypoxia, decreased bioavailability of nitric oxide in the lungs, inflammatory processes and impaired reabsorption of alveolar fluid [15, p. 501; 16, p. 1969].

A review of the literature showed that some studies report the acute mountain disease and altitude pulmonary edema occurring at lower altitudes of 2000 to 2500 m, and at altitudes above 2500 m the altitude sickness is more common [20, p. 733; 21, p. 50; 22, p. 465].

According to Hou Y.P., et al., women suffer a little more than men [17, p. 38], and young people, according to Gianfredi V., et al., suffer a little more than the elderly [18, p. 75]. Children suffer from acute mountain disease to the same extent as adults [19, p. 62].

Unfortunately, even in our modern times, it is impossible to say that we have overcome at least one of the syndromes listed above, although methods of treatment and prevention have been developed. Every year, hundreds of victims of the syndromes caused by reduced atmospheric pressure enter hospitals. Therefore, it is very important, even in our time, to know and study these pathological conditions, to understand their physiological impact on the human body, and it is also necessary to improve humanity's knowledge in this field, because although these are known since ancient times, but have quite a lot of unclear points, mechanisms of action, etc.

Purpose: investigating the mechanism of the physiological effect of reduced atmospheric pressure on the human body.

Materials and methods. The analysis of scientific data was carried out on the basis of medical databases PubMed, Scopus and Web of Science in order to collect the available research data on the effect of reduced values of atmospheric pressure on the human body.

Atmospheric pressure is the force with which the "column" of the Earth's atmosphere presses on the very surface of the planet and all the objects, including people, on it. Under normal conditions, the standard values of atmospheric pressure are considered to be 760 mmHg, or 101,325 Pa, or 101,325 n/m^2. Since this force is not small enough, in order not to be crushed by it, every living organism on the planet compensates this force with the internal pressure of the body.

Most often, people encounter conditions of reduced atmospheric pressure during climbing or a long stay high above sea level (mountains or highlands). As we climb, the atmospheric pressure drops, and accordingly, the temperature and humidity are decreased, ultraviolet radiation is increased, and more importantly, the barometric pressure and partial pressure of oxygen are decreased [23, p. 92], which plays a major role in the formation of such a pathological condition as high altitude hypoxia or "altitude sickness".

It should be noted that the main role in the formation of this pathological condition is played by a decrease in the partial pressure of gases, namely oxygen. In such conditions, in the first stages, the body turns on a number of urgent protective and adaptation mechanisms that depend on the level of altitude and duration of exposure [24, p. 310]. Adaptation mechanisms include: increased lung ventilation, tachycardia, redistribution of blood flow, physiological hypertrophy of the myocardium, etc. [25. p. 99].

These mechanisms are effective and help to normalize the body condition, but with increasing altitude, these begin to be critically lacking and starting from about 2000 meters, such problems as brain and lung edema, retinal hemorrhages, dizziness, shortness of breath, constant fatigue, exacerbation of respiratory syndromes (asthma), and exacerbation of cardiac pathologies (ischemia) can arise.

Acute and chronic reactions to altitude can be specified:

I. Acute:

1) Respiratory changes: an increase in minute volume due to hypoxic excitation (through peripheral chemoreceptors), which is mitigated by the response of central chemoreceptors to hypocapnia; decrease in $PaCO_2$ as a result of increased ventilation; hypoxia and hypocapnia lead to loss of appetite, nausea, vomiting, since alkalosis that develops during mountain disease excites the vomiting center and periodic Cheyne -Stokes breathing is observed;

2) Cardiovascular changes: tachycardia and increased cardiac output due to an increased sympathetic activity and these tend to return to almost normal levels by the end of the first week; an increase in blood pressure is insignificant and occurs as a result of an increase in cardiac output; total peripheral resistance is actually decreased.

3) Neurological changes: headache, which can be caused by the hypoxic induction of the production of nitric oxide in the brain, inflammatory reaction, increased formation of active oxygen forms, decreased cognitive functions and delirium are the consequences of acute hypobaric hypoxia and euphoria, which is characterized by the emotional and motor excitement and inappropriate behavior.

4) Kidneys and electrolytes: diuresis; decreased serum bicarbonate due to hypocapnia.

II. Chronic adaptation to low barometric pressure:

1) Respiratory changes: increased minute ventilation persists during a stay at altitude; a decrease in $PaCO_2$ as a result of increased ventilation; an increase in pulmonary arterial pressure and vascular density, which helps improve pulmonary perfusion, is insignificant; respiratory volume may gradually increase; the oxygen capacity of the blood is changed: an increase in the level of 2,3-DPG (2,3-diphosphoglycerate) in red blood cells shifts the oxygen dissociation curve to the right, facilitating the release of oxygen to tissues. There is also an increase in skeletal muscle vascularization and muscle tissue myoglobin.

2) Cardiovascular changes: heart rate and stroke volume remain elevated; high blood pressure remains to be high due to systemic vascular resistance because of the increased secretion of catecholamines at any workload, as well as due to increased blood viscosity resulting from increased hematocrit.

3) Electrolyte changes: Serum bicarbonate is decreased as a consequence of chronic hypocapnia.

4) Fluid balance and hematological changes: hematocrit is increased partly due to the loss of extracellular water, partly due to the hypoxia-stimulated erythropoiesis; the plasma volume is reduced and the fluid balance is negative compared with preacclimation values, resulting from the combined effects of brain natriuretic peptide BNP, renin, aldosterone, and a decreased level of circulating vasopressin.

It should be noted that the symptoms will sharply be increased during the first 6 to 12 hours of a stay at altitude, depending on a person's susceptibility to mountain disease, while nausea will progress faster in those who are most susceptible to this disease [26, p. 448].

In the case of inadequate acclimatization, edema of the brain and lungs may develop due to the excessive perfusion of microvascular channels, increased hydrostatic capillary pressure and leakage both through the hematoencephalic barrier in the brain and through the hematoencephalic barrier in the lungs [27, p. 252].

It should be noted that hypoxia provokes the following pathological changes in the cell:

1) The lack of oxygen in the body leads to metabolic disorders and accumulation of products of incomplete oxidation (lactic acid, acetone, acetic acid) that result in the development of metabolic acidosis.

2) Intermediate products of protein metabolism are accumulated: the ammonia content is increased, the glutamine content is decreased, the exchange of phosphoproteins and phospholipids is disturbed, a negative nitrogen balance is established, and synthetic processes are retarded. The electrolyte exchange is disturbed: the amount of intracellular potassium is decreased, calcium ions are accumulated. A disturbed synthesis of the mediators of nervous system is observed.

3) As a result of biochemical disturbances, structural changes occur in the cell, in particular a decrease in pH towards the acidic side results in the damage to the lysosome membrane with the release of active proteolytic enzymes that destroy cellular structures, in particular mitochondria and nuclei.

Hypoxia also causes swelling of the brain, which leads to an increased intracranial pressure, decreased cerebral blood flow, generalized cerebral ischemia, and coma, which can lead to death [28, p. 547]. With prolonged hypoxia, inhibition is developed and the reflex activity, regulation of breathing and blood circulation are disturbed. Loss of consciousness and convulsions are complex symptoms of severe hypoxia;

Altitude pulmonary edema rarely occurs at an altitude below 3000 m [29, p. 406], and the prevalence of this disease depends on the status of acclimatization, the susceptibility of a person, the climbing rate, and the absolute altitude reached. According to Bärtsch P., Gibbs J.S. (2007) and Schoene R.B. (2008), the mountaineers suffering from high-altitude pulmonary edema are mainly young men [29, p. 410], while cerebral edema in highlanders affects both men and women [30, p. 1016]. In contrast to acute mountain disease, mortality due to the untreated high-altitude cerebral edema makes up 50% [31, p. 2297].

Let's consider the initial symptoms and signs of high-altitude pulmonary edema. The initial symptoms include: shortness of breath during exercise, accompanied by a sharp decrease in physical activity, followed by orthopnea (shortness of breath in a horizontal position with the head down), drowsiness, dry cough and pink foamy sputum [31, p. 2298.]. Signs include: productive cough and cyanosis, low peripheral oxygen saturation, wheezing, tachycardia and tachypnea [32, p. 2756]. Electrocardiography may show signs of overstrain of the right side of heart, chest X-ray shows focal infiltrates in the lungs with a normal heart size, and the absence of these infiltrates suggests an alternative diagnosis [33, p. 255].

It should be noted that these symptoms and signs are usually accompanied by a slight fever, and very often high-altitude pulmonary edema is mistaken for pneumonia. Hyperventilation syndrome and pulmonary embolism can be considered as a differential diagnosis. [31, p. 2299]. Therefore, due to the high mortality risk of high-altitude pulmonary edema, prompt diagnosis and appropriate on-site treatment are crucial.

However, the effective methods of preventing altitude sickness are available. So, for example, a system of slow climbing is used: the mountaineers are recommended to spend 6-7 days at a moderate altitude (for example, 2200-3000 m) before continuing the ascent to a higher altitude and it gives enough time to develop an adequate degree of acclimatization to the altitude [34, p. 123]. Nevertheless, some experts have another opinion, so Molano Franco D.et al. (2019) believes that the effect of preacclimatization strategies on reducing the risk of altitude sickness requires additional studies. [35, p. 35].

Also, for prevention, the mountaineers can use acetazolamide or dexamethasone. It should be noted that the use of ibuprofen for the prevention of mountain disease is currently not recommended, as its effectiveness is controversial [34, 125].

Conclusion. When climbing mountains, the human body is affected by a number of factors, the main of which are low atmospheric pressure and the resulting reduced partial pressure of oxygen in the inhaled air.

With a decrease in the partial pressure of O_2 in the inhaled air, the human body experiences the worsened transition of O_2 into the tissues and the oxygen starvation of the body, i.e. hypoxia is developed. In the mountains, human body begins to fit in and the adaptation occurs with subsequent acclimatization to unusual conditions. However, the body's adaptive reactions do not always have time to cope with oxygen deficiency. In this case, a condition called “mountain sickness” is developed, the manifestations of which are so varied and individual for each climber that it is impossible to confidently and clearly establish the symptoms of this disease.

The prophylaxis and prevention of mountain sickness require, first of all, the gradual increase in altitude and its stepwise nature.

The likelihood of the occurrence and development of mountain disease largely depends on a person’s individual resistance to highland conditions, high-altitude experience, age, sex, and his/her physical and mental state.

The problem of the effects on humans under conditions of low atmospheric pressure will exist as long as humanity exists. Unfortunately, we are adynamic to change the basic physical principles on which our body is based, especially in our time, so doctors need to know about the danger of these conditions, the mechanism of their occurrence, first symptoms, and main consequences and how to deal with them.

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