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HEMODYNAMIC CHANGES IN HYPOXIC STRESS IN THE ELDERLY AND THE PHYSIOLOGICAL BASIS FOR THEIR CORRECTION WITH BIOLOGICALLY ACTIVE SUBSTANCES

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Abstract: This article analyzes hemodynamic changes in the elderly exposed to hypoxic stress. The importance of age-related vascular reactivity, endothelial function, and sympathetic regulation in the response to hypoxia is considered. The potential role of biologically active substances in hemodynamic correction is also assessed.

Keywords: aging, hypoxia, hypoxic stress, hemodynamics, endothelium, vascular reactivity, nitric oxide, antioxidants, biologically active substances.

INTRODUCTION

Oxygenation of the body is one of the vital physiological processes that ensures the stability of energy metabolism in tissues. A decrease in the amount of oxygen in arterial blood activates a number of compensatory-adaptive reactions in the body. These reactions are carried out by changing the activity of the cardiovascular system, along with the respiratory system, redistribution of peripheral vascular tone, adaptation of heart rate and blood flow to the needs of tissues.

The main task of the hemodynamic response in conditions of hypoxia is to maintain sufficient oxygen supply to vital organs in conditions of reduced oxygen partial pressure. However, with aging, the functional capabilities of a number of physiological mechanisms participating in this adaptation process change. With aging, there is an increase in arterial wall stiffness, a decrease in endothelium-dependent vasodilation, a decrease in nitric oxide bioavailability, and a reorganization of the activity of the sympathetic nervous system. Therefore, the same level of hypoxic exposure can cause different hemodynamic response in young and old organisms.

In a physiological study by Davy K.P., Jones P.P. and Seals D.R., sympathetic nerve activity was assessed in 10 young and 7 elderly healthy men during 15 minutes of breathing a gas mixture containing 10% O_2. Hypoxemia increased muscle sympathetic nerve activity in both groups, but the compensatory increase in heart rate was relatively slow in elderly participants [1]. This result indicates that some components of the cardiovascular response to hypoxia weaken during aging.

From this point of view, studying hemodynamic changes under hypoxic stress in the elderly is important not only for understanding the physiology of aging, but also for assessing the functional reserves of the body and justifying the possibilities of their targeted correction.

The purpose of the research is to analyze the physiological mechanisms of hemodynamic changes caused by hypoxic stress in elderly people based on the analysis of scientific literature, and to evaluate the prospective directions of their correction with the help of biologically active substances.

MATERIALS AND METHODS

This article is a review and analytical study. Primary experimental and randomized controlled studies indexed in the PubMed database on hypoxia, vascular reactivity, peripheral and cerebral hemodynamics, autonomic control, nitric oxide system, and antioxidant effects in elderly subjects were selected for analysis.

When analyzing the sources, special attention was paid to the nature of the hypoxic effect, the age of the participants, arterial pressure, heart rate, peripheral blood flow, vascular permeability, endothelium-dependent vasodilation, and autonomic nervous control indicators. In terms of biologically active substances, studies were analyzed that studied the effects of substances affecting the nitrate-nitrite-NO pathway and antioxidant compounds on vascular function in the elderly.

RESULTS AND DISCUSSION

In response to hypoxic stress, the body activates peripheral chemoreceptors, leading to increased respiratory and sympathetic nervous system activity. Increased heart rate and redistribution of blood flow are compensatory responses aimed at maintaining oxygen delivery. At the same time, hypoxia causes local vasodilation in peripheral tissues, which increases blood flow.

However, the effectiveness of these vasodilator mechanisms may decrease with age. Richards J.C. et al. assessed forearm blood flow and vascular permeability in 12 young and 10 elderly healthy subjects under conditions of gradual reduction of arterial oxygen saturation to 90, 85, and 80%. At 80% saturation, the increase in peripheral vascular permeability was 35±8% in young subjects, but only 4±6% in elderly subjects. The authors demonstrated that peripheral vasodilation in response to hypoxia is significantly attenuated in aging and that this cannot be explained solely by changes in sympathoadrenal control [2].

These results highlight the importance of local vascular control during hypoxia in the elderly. Inadequate vasodilation may limit oxygen delivery to peripheral tissues. Therefore, local vasodilator mechanisms can be considered one of the weak links of hemodynamic adaptation in aging conditions.

Age-specific differences in cerebral hemodynamics were also found. Liu X. et al. studied 12 elderly subjects aged 71±2 years and 13 young subjects aged 24±3 years under conditions of repeated 5-minute hypoxic exposure to 10% O_2. Elderly subjects had lower resting cerebral tissue oxygen saturation and lower middle cerebral artery blood flow. During hypoxia, compensatory responses of cerebral blood flow, cerebrovascular conductivity, heart rate, and respiratory rate were also less pronounced than in young subjects [3].

This does not automatically mean that the elderly organism is intolerant to hypoxemia. On the contrary, in this study, elderly subjects tolerated cyclic moderate hypoxemia satisfactorily. However, the attenuation of cerebrovascular and cardioventilatory responses in them indicates the presence of age-related reorganization of functional reserves.

One of the main components of the hemodynamic response to hypoxic stress in old age is the vascular endothelium. The endothelium is involved in the production of nitric oxide, prostacyclin, and other vasoactive substances that regulate vascular tone. Increased oxidative stress during aging may limit the bioavailability of nitric oxide, leading to a decrease in endothelium-dependent vasodilation.

In a 2024 study by Stray-Gundersen S. et al. in 12 young and 11 older participants, eight four-minute intermittent hypoxia sessions were administered, maintaining oxygen saturation at around 80%. Hypoxic exposure increased brachial artery diameter in both age groups, but did not significantly alter flow-related endothelial dilation in the acute phase. The authors noted that the vasodilatory response to a single brief intermittent hypoxia did not differ significantly by age [4].

This data seems to contradict the results of Richards et al. However, the hypoxia regimen, its duration, the degree of change in oxygen saturation, and the blood vessel pool assessed varied across studies. Therefore, it is not correct to judge the hemodynamic effects of hypoxia as “positive” or “negative” in a single direction. Its effect depends on the dose, duration, mode of repetition and the initial functional state of the organism.

Hypoxia is not always a pathological effect. Controlled, short-term, intermittent hypoxic exposure can activate adaptive mechanisms in the body. This aspect is also being studied in older individuals.

In a 2025 randomized trial, 26 participants aged 60–80 years were followed up on an eight-week intermittent hypoxic program. The experimental group received 24 passive hypoxic sessions. At the end of the study, a trend towards improved flow-dependent vasodilation was observed, and this change was statistically significant when normalized to baseline arterial diameter. However, these results do not confirm that intermittent hypoxia has a uniform effect on all hemodynamic parameters [5].

In 2026, Ladriñán-Maestro A. et al. evaluated a six-week intermittent hypoxia–hyperoxia program in 22 older participants. The study was completed by 20 participants. In the experimental group, the LF/HF heart rate variability index decreased by 1.23±0.34 conventional units, and positive changes were also noted in maximal inspiratory pressure, which reflects the strength of the respiratory muscles, and inflammation indicators. The authors noted positive trends in arterial pressure and autonomic control [6].

However, the data in this area are still mixed. For example, 24 sessions of intermittent hypoxic conditioning in individuals aged 62–79 years did not significantly improve cerebral vascular reactivity to CO_2 compared to controls [7]. This suggests that the effects of hypoxic adaptation are not uniform across vascular populations.

In selecting biologically active agents to correct hemodynamic responses to hypoxic stress in old age, their mechanism of action should be central. From a physiological point of view, two areas are of particular importance: supporting nitric oxide production and reducing oxidative stress.

Nitric oxide is an important endothelial signaling molecule involved in vascular smooth muscle relaxation and local blood flow regulation. Decreased NO bioavailability in old age is associated with endothelial dysfunction. Therefore, biologically active components that affect the nitrate–nitrite–NO metabolic pathway are one of the promising directions of hemodynamic correction.

In a double-blind, randomized crossover study conducted by Kelly J. et al. in 12 healthy participants aged 60–70 years, plasma nitrite concentrations increased after three days of nitrate-rich beetroot juice intake. Systolic blood pressure decreased from 120±6 mm Hg to 115±9 mm Hg in placebo, and diastolic blood pressure decreased from 73±5 to 70±5 mm Hg. At the same time, the kinetics of oxygen consumption during walking accelerated [8].

However, the effects of nitrates in the elderly are not the same in all studies. There is another randomized trial in which seven days of nitrate supplementation in participants aged 60–75 years did not show a significant effect on blood pressure, central and peripheral hemodynamic parameters. Therefore, when correcting the nitrate–NO pathway, it is necessary to take into account the dose, duration of administration, the initial blood pressure of the participants and the age-specific state of NO metabolism.

A second promising direction is biologically active substances with antioxidant properties. Wray D.W. et al. examined the effect of an antioxidant complex consisting of vitamin C, vitamin E and α-lipoic acid on vascular function in 45 elderly participants. Under placebo conditions, flow-related dilation in the brachial artery of elderly participants was 5.2 ± 0.4%, but after taking the antioxidant complex it increased to 8.2 ± 0.6%. The results show that free radicals play an important role in the formation of age-related endothelial dysfunction [9].

The effects on mitochondrial oxidative stress are also of interest. Rossman M.J. et al. evaluated the effects of MitoQ 20 mg/day for six weeks in 20 subjects aged 60–79 years with impaired

endothelial function in a randomized, placebo-controlled crossover study. The results showed that mitochondrial-targeted antioxidant supplementation can improve vascular endothelial function in the elderly [10].

However, most of the studies on the above-mentioned biologically active substances were performed in the resting state or under conditions of physical exertion. They do not directly demonstrate the effectiveness of correcting the hemodynamic response during hypoxic stress in the elderly. Therefore, independent experimental studies of the effects of nitrates, α-lipoic acid, antioxidant complexes, or other biologically active substances under hypoxic conditions are needed.

It is not sufficient to assess the adaptation of the elderly organism to hypoxia based solely on arterial pressure or heart rate. The hemodynamic response to hypoxic stress is the result of the integrated activity of the heart, blood vessels, autonomic nervous system, and tissue metabolism.

Therefore, in studies, it is advisable to assess peripheral blood flow, vascular permeability, heart rate variability, and, if possible, endothelial function indicators, in addition to systolic and diastolic blood pressure, mean arterial pressure, heart rate, pulse pressure, and arterial oxygen saturation.

In particular, dynamic monitoring of hemodynamic parameters before, during, and after the administration of a corrective biologically active substance allows us to identify the physiological mechanisms of action of the substance. This approach serves to assess not only the final result of the correction, but also which stage of the adaptive response to hypoxia it affects.

CONCLUSION

In old age, the hemodynamic response to hypoxic stress is shaped by a number of physiological changes associated with aging. Available experimental data indicate that peripheral vasodilation, compensatory tachycardia, and some components of the cerebrovascular response to hypoxia may be attenuated in the elderly compared to young adults.

In hemodynamic adaptation to hypoxia, the vascular endothelium, local vasoactive mechanisms, the sympathetic nervous system, and nitric oxide bioavailability are important. At the same time, the outcome of hypoxic exposure depends on its duration and intensity, and short and controlled intermittent hypoxia can activate adaptive vascular responses under certain conditions.

Compounds that affect the nitrate-nitrite-NO system and biologically active substances with antioxidant properties are physiologically promising for correcting vascular function in old age. However, the effect of these substances on hemodynamic parameters under conditions of hypoxic stress has not been sufficiently studied.

Therefore, a comprehensive assessment of hemodynamic parameters before and after hypoxic stress in the elderly, determining their relationship with the degree of hypoxia, and studying the changes in these parameters under the influence of selected biologically active substances is one of the relevant directions of future physiological research.

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