

ОБЗОРЫ/REVIEWS

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EFFECT OF HYPERBARIC OXYGENATION ON ERYTHROCYTE DEFORMABILITY

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INTRODUCTION. Decreased red blood cell membrane elasticity, observed in a number of pathological conditions, causes deterioration of blood rheological properties and reduced gas exchange efficiency. Hyperbaric oxygen therapy (HBO) can influence red blood cell properties, but this aspect has received little attention. Although data on the hemorheological properties of blood, and in particular red blood cell deformability, may provide important information on HBO efficacy.

OBJECTIVE. To study the effect of hyperbaric oxygenation on the deformability of red blood cells.

MATERIALS AND METHODS. The study is based on an analysis of 58 scientific publications from 1984 to 2025 in international and domestic scientific literature databases Google Scholar, PubMed, eLIBRARY, CyberLeninka, and Scopus. The literature was analyzed using keywords and various sequences of their combinations in Russian and English: hyperbaric oxygen therapy, red blood cells, erythrocytes, deformability, hemorheology, morphology, shape.

RESULTS. The effect of HBO on erythrocyte deformability was recorded: in vitro in only one of two publications (negative); in vivo in animal experiments in four of six publications (three negative, one positive); in human studies in single-chamber therapy (oxygen and air-oxygen), positive effects were reflected in all five publications; when using multi-chambers, only one of four publications noted a positive effect; in one publication on the use of a local chamber, no effect on the analyzed parameters was detected.

DISCUSSION. One of the key challenges in interpreting data on the effects of HBO on erythrocyte deformability is the use of both various procedure parameters (pressure, time, and chamber type) and the methodology for assessing hemorheology and erythrocyte deformability. Negative effects reported in a number of animal studies may be related to the use of higher pressures and longer durations of experiments compared to human studies. In the latter case, no adverse effects were observed when using routine HBO procedure parameters, and a positive effect on erythrocyte deformability was recorded in 60% of studies.

CONCLUSION. The deformability of erythrocytes can serve as an additional parameter for assessing HBO efficacy, since it affects the efficiency of gas exchange processes, which is very important in the treatment of tissue hypoxia.

KEYWORDS: marine medicine, maritime medicine, hyperbaric oxygenation, erythrocyte, deformability, rheology

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ВЛИЯНИЕ ГИПЕРБАРИЧЕСКОЙ ОКСИГЕНАЦИИ НА ДЕФОРМИРУЕМОСТЬ ЭРИТРОЦИТОВ

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ВВЕДЕНИЕ. Снижение эластичности мембраны эритроцитов, наблюдаемое при ряде патологических состояний, приводит к ухудшению реологических свойств крови и снижению эффективности газообмена. Терапия с применением гипербарической оксигенации (ГБО) может оказывать влияние на свойства эритроцитов, однако данному аспекту уделяется мало внимания, хотя данные о гемореологических свойствах крови и, в частности, деформируемости эритроцитов, могут представлять важную информацию об эффективности ГБО.

ЦЕЛЬ. Изучить влияние гипербарической оксигенации на деформируемость эритроцитов.

МАТЕРИАЛЫ И МЕТОДЫ. Исследование основано на анализе 58 научных публикаций за 1984–2025 гг. в международных и отечественных базах научной литературы Google Scholar, PubMed, eLIBRARY, КиберЛенинка, Scopus. Анализ литературных источников выполнен по ключевым словам и различным последовательностям их сочетаний на русском и английском языках: гипербарическая оксигенация / hyperbaric oxygen therapy, эритроциты / red blood cells, erythrocytes, деформируемость / deformability, гемореология / hemorheology, морфология / morphology, shape.

РЕЗУЛЬТАТЫ. Влияние ГБО на деформируемость эритроцитов было зафиксировано: в условиях *in vitro* только в одной из двух публикаций (отрицательное); в условиях *in vivo* в экспериментах с участием животных в четырех из шести публикаций (три – отрицательное, одно – положительное); в исследованиях с участием людей в условиях проведения терапии в одноместной камере (кислородной и воздушно-кислородной) положительные эффекты были отражены во всех пяти публикациях, при использовании многоместных камер только в одной из четырех публикаций отмечен положительный эффект, в одной публикации по применению локальной камеры влияние на анализируемые параметры не выявлено.

ОБСУЖДЕНИЕ. Одной из ключевых проблем в интерпретации данных о влиянии ГБО на деформируемость эритроцитов является использование как различных параметров проведения процедуры (давление, время, тип барокамеры), так и методологии оценки гемореологии и деформируемости эритроцитов. Негативные эффекты, описанные в ряде исследований с участием животных, могут быть связаны с применением более высоких значений давления и более длительными экспериментами по сравнению с исследованиями с участием человека. В последнем случае при использовании рутинных параметров проведения процедуры ГБО нежелательных эффектов не отмечено, а положительное влияние в отношении деформируемости эритроцитов было зафиксировано в 60 % исследований.

ЗАКЛЮЧЕНИЕ. Деформируемость эритроцитов может служить дополнительным параметром оценки эффективности ГБО, поскольку она оказывает влияние на эффективность процессов газообмена, что весьма важно в терапии тканевой гипоксии.

КЛЮЧЕВЫЕ СЛОВА: морская медицина, гипербарическая оксигенация, эритроцит, деформируемость, реология

Introduction. Hyperbaric oxygenation (HBO) is a method based on breathing pure oxygen under elevated pressure. The therapeutic effect of HBO is based on a significant increase in the oxygen capacity of body fluids (blood, lymph, tissue fluids, etc.), which allows for a rapid increase in oxygen tension in tissues suffering from hypoxia, restoring cellular respiration, activating oxidative phosphorylation, and stimulating energy production mechanisms [1]. HBO can serve as a primary treatment method, for example, for carbon monoxide poisoning or decompression sickness, or as a complement to surgical interventions or pharmacological therapy [2].

Since one of the key effects of HBO is an increase in oxygen capacity, the main diagnostic methods are aimed at assessing tissue perfusion and oxygenation. Among them, non-invasive and invasive methods are distinguished (body tem-

perature gradient, CT perfusion, MR perfusion, positron emission tomography, laser Doppler flowmetry, segmental blood pressure measurement, duplex ultrasound, pulse oximetry, transcutaneous oximetry, Doppler ultrasound, indocyanine green imaging, etc.) [3–7]. Based on the data obtained by these methods on blood supply and oxygen delivery to tissues, a conclusion is made about reaching target blood flow indicators and the level of blood oxygen saturation. However, the assessment of the hemorheological properties of the blood and, in particular, the deformability of erythrocytes, is often ignored [8].

One of the most important properties of the erythrocyte that ensures gas transport function is its ability to deform, which is ensured by the interaction of membrane proteins (glycophorins, band 3 protein) and cytoplasm (spectrin, ankyrin) [9]. It is known that the development of various

pathological conditions can lead to a decrease in the deformability of erythrocytes, which is accompanied by a disruption in oxygen transport both due to a deterioration in their ability to pass through microvessels and capillaries [10–14], and due to a disruption in the release of vasodilators by erythrocytes, for example, ATP and NO donors [15, 16].

Currently, several methods for measuring erythrocyte deformability are known, among which we can distinguish direct and indirect methods. Direct methods for measuring erythrocyte deformability include stretching erythrocytes with laser tweezers (optical tweezers method), video recording of erythrocytes deformed in a shear flow by viscous friction forces (rheoscopy), as well as methods of atomic force microscopy and laser diffractometry (ektacytometry). Among indirect methods we can distinguish aspiration of erythrocytes into a micropipette (microaspiration method), passing an erythrocyte suspension through an artificial capillary of small diameter, or forcing a given volume of suspension through a microporous filter. Methods of ektacytometry, rheoscopy, filtration, and perfusion involve studying cell suspensions, and methods of microaspiration, atomic force microscopy, and optical tweezers involve studying individual cells [17, 18]. In addition, of interest is the technique of electrochemically induced changes in the morphology of erythrocytes, which consists of studying the morphological changes of erythrocytes on an optically transparent electrode depending on its potential [19, 20].

However, despite the rich arsenal of methods for assessing hemorheology and a significant number of its studies in various pathological conditions, there are relatively few works devoted to the influence of HBO on hemorheology and the deformability of erythrocytes, although these methods could be very informative in this case.

Objective. To study the effect of hyperbaric oxygenation on the deformability of red blood cells.

Results. Studies on the effect of HBO on the deformability of erythrocytes and the rheological properties of blood in vitro and in vivo are presented in the table.

Discussion. Few studies on the HBO effect on the deformability of erythrocytes in vitro are quite natural due to the fact that outside the body, the structural properties of erythrocytes can be affected by factors such as temperature,

forced contact with neighboring cells due to the lack of mixing, changes in the density of the medium due to evaporation of liquid during long-term experiments, etc. [41]. Thus, in the work [21], test tubes with 2 ml of whole blood (Htc 45%) containing EDTA (1.5 mg / ml) as an anticoagulant were placed in a pressure chamber, where they were kept in an atmosphere of 100% O₂ at a temperature of 25–28 °C for 4–12 hours. Such conditions for conducting HBO (temperature different from physiological, long time outside the body, sedimentation of cells in the test tube) could well cause a change in the morphofunctional properties of erythrocytes.

In relation to the study of the HBO effect on cell morphology, the study of erythrocytes of patients with sickle cell anemia is of interest. Despite a number of early studies indicating a positive HBO effect in this pathology [42, 43], the authors [22] did not prove the HBO effect on the morphology of sickle cell erythrocytes, and they associated the previously described results with improved tissue oxygenation due to an increase in PaO₂.

Out of six animal studies, a negative effect of HBO on hemorheological parameters and erythrocyte deformability was observed in three cases [23, 24, 26], in two cases no changes were detected [25, 27], and only in one case an improvement in erythrocyte deformability was recorded [28]. Again, as in the case of in vivo studies, the experimental conditions are noteworthy. Firstly, in the studies that revealed a deterioration in hemorheological parameters, the time spent in the pressure chamber ranged from 2 to 6 hours, while in the remaining studies the time did not exceed 1.5 hours. Secondly, HBO was performed in most cases in the 2.8–3.0 ATA mode, although it is known that at pressures above 2.8 ATA, oxygen begins to exhibit a toxic effect on the body [44]. Thirdly, the measurement results may be influenced by the choice of the methodological approach to assessing erythrocyte deformability. In the work [23], when determining the deformability of erythrocytes using the filtration method and ektacytometry, the HBO effect was recorded only in the case of using the first method. This phenomenon was due to the fact that, according to the authors, the filtration method is more sensitive to changes in cell geometry and the physical properties of the membrane, and ektacytometry is more sensitive to the internal viscosity of erythrocytes. We also previously

Table

Studies on the effect of HBO on the hemorheological properties of blood

Таблица

Исследования по влиянию ГБО на гемореологические свойства крови

Study object	HBO mode (pressure, session duration, frequency)	Measurement technique	Observed effect	Literary source
<i>In vitro</i> study				
Whole blood from healthy volunteers ($n=10$)	1,0–3,0 ATA ¹ 4–16 h Single-dose	Viscometry, ektacytometry	↓ Erythrocyte deformability ↑ Blood viscosity	[21]
Whole blood from patients with sickle cell anemia ($n=10$)	3,0 ATA ¹ 15 min Single-dose	Microscopy	Doesn't affect	[22]
<i>In vivo</i> studies involving animals				
Rats (total $n=32$, HBO group $n=11$)	2,8 ATA ¹ 6 h Single-dose	Ektacytometry, filtration method, scanning electron microscopy, hematological analysis	↓ Erythrocyte deformability ↑ Echinocyte proportion	[23]
Rats (total $n=57$, HBO group $n=22$)	2,8 ATA ¹ 6 h Single-dose	Viscometry, hematological analysis	↑ Viscosity	[24]
Dogs ($n=12$)	2,4 ATA ¹ 90 min, 5 sessions per week / 10 weeks	Filtration method	Doesn't affect	[25]
Rats with diabetes (total $n = 30$; HBO group: $n = 15$)	2,8 ATA ¹ 2 h, 7 sessions	Viscometry, filtration method hematological analysis	↑ Viscosity and rigidity of erythrocytes ↓ Erythrocyte deformability	[26]
Rats, SO ₂ inhalation (total $n = 24$; HBO group: $n = 6$)	3,0 ATA ¹ 1 h, 45 sessions	Hematological analysis	Doesn't affect	[27]
Rats (total $n=43$, HBO group ГБО $n=8$)	3,0 ATA ¹ 1 h Single-dose	Ektacytometry, viscometry	Return of red blood cell deformability to normal values	[28]
<i>in vivo</i> studies involving humans				
Patients with various diseases ($n=70$)	2,0 ATA ¹ 90 min, at least 15 sessions	Filtration method viscometry	↑ Erythrocyte deformability	[29–31]
Patients with various diseases ($n=33$)	2,4 ATA ² 115 min (breathing 100 % O ₂ 3 times for 25 мин with 5-minute break) 20 sessions	Ektacytometry, viscometry, hematological analysis	Doesn't affect	[32]
Patients with toxichypoxic encephalopathy ($n=42$)	1,4–1,6 ATA ¹ 40 min 4–10 sessions	Viscometry, hematological analysis	Return of red blood cell deformability to normal values	[33]

Продолжение табл. 1 см. на стр. 11.

Study object	HBO mode (pressure, session duration, frequency)	Measurement technique	Observed effect	Literary source
Patients with various diseases ($n=140$)	2,5 ATA ² 120 min (breathing 100% O ₂ 3 times for 25 min with 5-minute break) Groups - 1-20, 21-40, 41-60 and > 61 sessions	Hematological analysis	Doesn't affect	[34]
Patients with inflammatory bowel diseases ($n=16$ with Crohn's disease, $n=11$ with ulcerative colitis)	1,3-1,4 ATA ³ 40 min 5-8 sessions	Rheoscopy	↑ Erythrocyte deformability, blood rheology parameters	[35]
Patients with sensorineural hearing loss (total $n=104$, HBO group $n=52$)	2,0 ATA ³ 1 h 2 courses (10 sessions each) with a 3-day break between courses	Viscometry, hematological analysis	↓ Blood viscosity	[36]
Healthy volunteers ($n=10$), patients with chronic inflammation ($n=10$) and carbon monoxide poisoning ($n=10$)	2,5 ATA ² 120 min (breathing 100% O ₂ 90 min) 10 sessions	Ektacytometry, hematological analysis	↑ Erythrocyte deformability in patients with chronic inflammation after 1 session	[37]
Patients with diabetic foot ($n=103$)	2,4 ATA ² 120 min (breathing 100% O ₂ 3 times for 25 minutes with a 5-minute break) 20-60 sessions	Hematological analysis	Doesn't affect	[38]
Patients with diabetic foot ($n=20$)	1,5 ATA ⁴ 0,5 h Single-dose	Ektacytometry, viscometry, hematological analysis	Doesn't affect	[39]
Patients with acute cerebrovascular accident ($n=7$)	1,4-1,6 ATA ¹ 60 min 4-6 sessions	Electrochemical	↑ Erythrocyte deformability	[40]

Note: 1 – monoplace hyperbaric chamber, 2 – multiplace hyperbaric chamber, 3 – inflatable hyperbaric chamber, 4 – local hyperbaric chamber

Примечание: 1 – одноместная барокамера, 2 – многоместная барокамера, 3 – воздушно-кислородная барокамера, 4 – локальная барокамера

noted a difference in the sensitivity of the methods for determining deformability, when studying the morphology of erythrocytes under hypothermic storage conditions, a reliable difference in the deformability index measured by the filtration method was noted only by the 42nd day, while when using electrochemically induced changes in morphology, reliable differences were recorded much earlier [45].

In contrast, out of ten studies involving humans, six cases [29, 33, 35–37, 40] showed an im-

provement in erythrocyte deformability, while no significant changes were found in four cases [32, 24, 38, 39]. When analyzing the presented data, it was noted that, in contrast to studies involving animals, in the human studies the maximum pressure during HBO was 2.5 ATA, and in this case multiplace hyperbaric chambers were used. Interestingly, in the case of multi-place chambers, even despite the use of modes with a pressure of at least 2.4 ATA [32, 34, 37, 38], only one case showed a positive effect of HBO on eryth-

rocyte deformability [37]. No significant HBO effect on erythrocyte deformability was shown either when using a local hyperbaric chamber in the treatment of patients with diabetic foot [39]. At the same time, in all studies where monoplace pressure chambers were used, both oxygen [29, 33, 40] and air-oxygen [35, 36], a significant positive HBO effect on the hemorheological parameters of blood and the deformability of erythrocytes was noted.

There are still many questions regarding the understanding of the pathophysiology of the HBO influence on the morphofunctional properties of erythrocytes. On the one hand, according to a number of studies, HBO leads to an increase in the content of reactive oxygen species, which, in turn, causes increased peroxidation of lipids and proteins of the erythrocyte membrane and can lead to changes in their morphology [46–49]. In support of the thesis about the effect of increased oxidation processes on the morphology of erythrocytes during HBO, reference is made to studies involving animals under normobaric conditions with an increased oxygen content (up to 82.2%), where the phenomenon of a decrease in the proportion of discocytes and an increase in the proportion of echinocytes was recorded, although the duration of the experiment (24 hours) should be considered [50]. On the other hand, there is a growing body of research confirming that HBO has a positive effect on the balance of oxidants and antioxidants in the body [51–54] and activates components of the body's antioxidant

defense system [55–58], and these effects may be more pronounced in the presence of pathology [59]. In addition, it has recently been shown that when using “soft” HBO regimens (1.5 ATA) compared to regimens with higher pressure (2.5 ATA), a clear antioxidant effect is observed, prevailing over oxidative stress [60].

The positive HBO effect may be manifested in relation to the elastic properties of erythrocyte membranes. Increased deformability and redistribution of morphological forms towards discocytes should positively affect the efficiency of oxygen transport. Thus, more elastic cells better pass through capillaries, which plays an important role both at the stage of oxygen binding in the alveolar capillaries and at the stage of its release in the capillaries of organs and tissues. Considering the fact that HBO is accompanied by vasoconstriction [61], an increase in cell elasticity should have an important therapeutic effect. With regard to the influence of morphology on gas exchange, it is known that discocytes, compared with other morphological forms of erythrocytes, have the largest surface area (150 μm^2) [62, 63], which ensures the maximum oxygen exchange area.

Conclusion. The analysis of literature sources suggests a predominantly positive effect of HBO on erythrocyte deformability, which should influence the efficiency of gas exchange processes and, consequently, a reduction in tissue hypoxia. Thus, erythrocyte deformability can be used as an additional parameter when assessing the effectiveness of hyperbaric oxygen therapy.

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