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Hypoxic irreversible brain cells damage, associated risk factors and antihypoxants

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ABSTRACT

It is reported that in the final stage of many diseases the immediate cause of biological death in humans and warm-blooded animals is hypoxic irreversible damage to brain cells. This explains the fact that to prevent biological death in all critical conditions without exception, inhalation with breathing gases containing oxygen has long been successfully used. This is also why oxygenation of the blood is considered one of the main conditions for preserving human life in all critical situations and forms the basis of emergency medical care in the intensive care unit. However, inhalation of oxygen gas and increasing blood oxygen saturation should be carried out as early as possible, and more precisely — before the onset of the stage of hypoxic irreversible damage in brain cells. The fact is that after the onset of irreversible damage brain cells die even in the presence of oxygen. In this connection, the mechanisms of adaptation of the organism to oxygen deficiency play a great role for longer preservation of brain cells viability and human life in conditions of hypoxemia. In order to increase resistance to hypoxemia, antihypoxants are traditionally used. But they can preserve the viability of brain cells not always, but only if they are introduced into the body before the onset of hypoxic irreversible damage to brain cells and in the case of unused reserves of adaptation to hypoxemia in the body. Risk factors of hypoxic irreversible damage of brain cells are indicated, among which excessively long duration of hypoxemia and hyperthermia are emphasized. It is shown that the most important circumstance for the development of hypoxic irreversible damage of brain cells is not so much the degree of hypoxemia as the degree of hypoxia of brain tissue and its duration, which exceeds the period of human resistance to hypoxia. It has been shown that human resistance to hypoxia can be assessed using the Stange test. It has been reported that fever and local cerebral hyperthermia decrease, and hibernation and local cerebral hypothermia increase, the resistance of brain cells to hypoxia. In this regard, recommendations not only to eliminate fever and local inflammatory processes in the head, but also recommendations to reduce brain temperature are highly appropriate to improve resistance to hypoxia. It is pointed out that among the methods of local therapeutic hypothermia, targeted temperature management is the most advanced. In addition, it is reported that in recent years a new group of promising antihypoxants — alkaline solutions of hydrogen peroxide — has been created. It is shown that hydrogen peroxide is able to decompose very quickly into water and oxygen gas under the action of catalase, which is found in all tissues. The peculiarities of using alkaline solutions of hydrogen peroxide as antihypoxants we all have to study in the future.

Keywords: hypoxia; aerobic metabolic rate; time; temperature; oxygen; antihypoxants; biological death; adaptation.

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Гипоксическое необратимое повреждение клеток головного мозга, ассоциированные с ним факторы риска и антигипоксанты

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АННОТАЦИЯ

В финальной стадии многих болезней непосредственной причиной биологической смерти людей и теплокровных животных является гипоксическое необратимое повреждение клеток головного мозга. Этим объясняется то, что для предотвращения биологической смерти при всех без исключения критических состояниях давно и успешно используют ингаляции дыхательными газами, содержащими кислород. Поэтому насыщение крови кислородом считается одним из главных условий для сохранения жизни людей во всех критических ситуациях и составляет основу оказания неотложной медицинской помощи в отделении интенсивной терапии. Однако ингаляции газа кислорода и увеличение сатурации крови кислородом должны быть осуществлены как можно раньше, а точнее — до наступления стадии гипоксических необратимых повреждений в клетках головного мозга. Дело в том, что после наступления необратимых повреждений клетки мозга погибают даже в присутствии кислорода. В связи с этим огромную роль для более длительного сохранения жизнеспособности клеток головного мозга и жизни человека в условиях гипоксемии играют механизмы адаптации организма к дефициту кислорода. С целью повышения устойчивости к гипоксемии традиционно используются антигипоксанты. Но и они могут сохранить жизнеспособность клеток головного мозга не всегда, а только в случае введения в организм до наступления гипоксического необратимого повреждения клеток головного мозга и в случае наличия в организме неиспользованных резервов адаптации к гипоксемии. Указываются факторы риска гипоксического необратимого повреждения клеток головного мозга, среди которых выделяются чрезмерно большая продолжительность гипоксемии и гипертермия. В обзоре показано, что важнейшим обстоятельством развития гипоксических необратимых повреждений клеток головного мозга является не столько степень гипоксемии, сколько степень гипоксии ткани головного мозга и ее продолжительность, превышающая по длительности период устойчивости человека к гипоксии. Устойчивость человека к гипоксии может быть оценена с помощью теста Штанге. Сообщается, что лихорадка и локальная гипертермия головного мозга снижают, а гибернация и локальная гипотермия головного мозга повышают устойчивость клеток головного мозга к гипоксии. В связи с этим высоко целесообразными для повышения устойчивости к гипоксии являются рекомендации не только по устранению лихорадки и локальных воспалительных процессов в голове, но и рекомендации по уменьшению температуры головного мозга. Среди методов локальной терапевтической гипотермии наиболее совершенным можно считать целенаправленное регулирование температуры. Кроме этого, в последние годы была создана новая группа перспективных антигипоксантов — щелочные растворы перекиси водорода. Показано, что перекись водорода способна очень быстро разлагаться на воду и газ кислород под действием каталазы, которая находится во всех тканях. Особенности использования щелочных растворов перекиси водорода в роли антигипоксантов нам всем предстоит еще изучить в будущем.

Ключевые слова: гипоксия; интенсивность аэробного метаболизма; время; температура; кислород; антигипоксанты; биологическая смерть; адаптация.

Как цитировать

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BACKGROUND

Researchers seeking solutions to the biomedical problems associated with oxygen deprivation make extensive use of the terms "hypoxia" and "hypoxemia", attempting to define by these terms the body conditions under discussion, implying but not specifying the likely hypoxic cellular damage to organs and tissues, including the brain [1–3]. Moreover, these terms are sometimes applied without emphasis on the differences underlying the concepts they define. Analysis of reports shows that the term "hypoxia" is more common and is usually used to refer to a condition of the body with decreased oxygen in the blood and a high likelihood of tissue hypoxia, including decreased oxygen in the brain and even impaired brain function, but without brain cell death [4–6]. Less commonly, the term "hypoxemia" is used, which usually refers to a condition of the body with reduced oxygen in the blood, but without tissue hypoxia or hypoxic irreversible damage to brain cells [7–10]. The depth of hypoxemia is usually taken into account in all cases (as a rule, in the form of specific values of blood oxygen saturation), which is sometimes accidentally (due to ignorance) substituted by the concept of "hypoxia depth", and, as a rule, is not associated with the dynamics of hypoxic damage of brain cells.

In other words, the current practice in the field of biomedical research shows that researchers record blood oxygen saturation and control its dynamics, using the terms "hypoxia" and "hypoxemia" to characterize the lack of oxygen in the body, but ignore the dynamics of hypoxic damage to brain cells. In our opinion, the latter is explained by the absence of a diagnostic tool that provides control of brain resistance to hypoxia. The lack of clarity about risk factors of hypoxic irreversible brain cells damage may also contribute to this.

HYPOXEMIA, BRAIN TISSUE HYPOXIA, HYPOXIC IRREVERSIBLE BRAIN CELLS DAMAGE AND OXYGEN AS AN ANTIHYPOXANT No. 1

It has been reported that in the final stages of many diseases, hypoxic irreversible brain cell damage is the immediate cause of biological death in humans and warm-blooded animals [11–14]. That is why doctors all over the world have long and successfully used oxygen gas and/or breathing gases containing oxygen to prevent biological death in all critical conditions without exception. Oxygen is the No. 1 for keeping patients alive before, during clinical reset and even for some time afterwards. Therefore, oxygenation of the blood is considered one of the main conditions for keeping people alive in all critical situations and forms the basis of emergency medical care in the ICU [15, 16].

In emergency medical care, gaseous oxygen is administered to patients primarily by natural means, namely inhalation [17, 18]. Most often, inhalation of breathing gases is quite sufficient to fully supply the brain with oxygen. It has been found that inhalation of gaseous oxygen can provide rapid delivery of oxygen to brain cells in cases where the injected oxygen quickly reaches the alveoli, from where it immediately penetrates into the blood, which immediately penetrates into the erythrocytes, immediately interacts within them with the protein hemoglobin, exchanges in it for carbon dioxide, converts carbohemoglobin into oxyhemoglobin, as a result of which red blood cells with oxyhemoglobin successfully convert venous blood into arterial blood, which quickly flows from the lungs towards the head and in a few seconds reaches the brain [19].

In other words, in norm, continuous inhalation of oxygen into the respiratory system preserves the viability of brain cells if the blood continuously supplied to the human brain is not simply called arterial blood, but is actually enriched (saturated) with oxygen.

It is shown that in normal blood oxygen saturation in adults is 94–99%. In cases when the value of arterial blood saturation in people is less than 90%, a diagnosis of hypoxia, or more precisely, hypoxemia is made [20–22]. At the same time, it has been reported that the value of partial pressure of oxygen in blood does not always correlate with the oxygen content in tissues of different parts of the body [23]. The point is that different organs and tissues are differently supplied with arterial blood and use oxygen differently both in norm and pathology. In particular, in norm at normal body temperature the brain tissue of warm-blooded animals and humans is the leader in the intensity of blood supply and oxygen utilization in aerobic metabolism compared to other tissues of the body [24]. Therefore, with a sudden decrease in oxygen supply to the blood through the lungs, oxygen reserves in different organs and tissues are consumed at different rates and in different time intervals. In particular, at cessation of oxygen supply to the blood, oxygen reserves are consumed at the highest rate and for the shortest period of time in the brain tissue [25].

It has been shown that blood oxygen content in adults begins to decrease after a few seconds during apnea, an attack of laryngospasm, bronchospasm, and asphyxia by water, blood, sputum, mucus, and/or purulent masses, or by inhalation of a gas mixture devoid of oxygen gas [26, 27]. Moreover, in all cases after sudden cessation of oxygen supply to the blood of healthy people at normal body temperature, people remain alive and healthy not only for several seconds, but even for several minutes of hypoxemia. This indicates that the organism of a healthy person is ready for successful survival in conditions of short-term cessation of oxygen supply to his organism (in particular, through the lungs into the blood), first of all, precisely due to the resistance of brain cells to its hypoxia. On the other hand, timely oxygen supply to the blood eliminates hypoxemia and the danger of hypoxic irreversible damage to brain cells.

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RESISTANCE OF BRAIN CELLS TO HYPOXIA AS A RISK FACTOR FOR HYPOXIC IRREVERSIBLE BRAIN CELLS DAMAGE

Preservation of life and health of people for several minutes after complete cessation of oxygen supply to the blood of their organism would be impossible if the organism did not have a reserve of some amount of oxygen and a mechanism of adaptive redistribution of arterial blood with oxygen between parts of the body in favor of the brain. In sum, these factors of preservation of brain life in conditions of sudden cessation of respiration can be named as reserves of adaptation to hypoxia or resistance to hypoxia [27].

The duration of voluntary apnea can serve as an integral indicator of the value of human resistance to sudden acute hypoxia. This was first reported in 1914 by Vladimir A. Stange, a Russian physician from Petrograd, a graduate of the Imperial Medical and Surgical Academy [28]. He showed that only those people who have a higher tolerance to hypoxia endure longer periods of apnea. Since that time, the method of assessing a person's resistance to hypoxia, conducted by recording the duration of breath-holding against a background of deep inhalation, is known as the Stange test [29].

Consequently, a sudden cessation of oxygen supply to the blood is quickly manifested by a decrease in the values of its oxygen saturation, i.e. hypoxemia. Indeed, after the cessation of oxygen supply to the blood, it gradually begins to lose its oxygen, but not because it consumes it itself, but because its oxygen is continuously taken by all organs and tissues of the body to ensure its aerobic metabolism. The brain uses oxygen particularly intensively. In cases where the oxygen content in the blood drops below 90%, it is assumed that hypoxemia has occurred. Moreover, a lower value of oxygen content in the blood indicates a deeper hypoxemia [9–12].

Deepening hypoxemia reduces oxygen delivery to all organs and tissues, but almost all of them have a much larger reserve of adaptation to oxygen deficiency than brain tissue. Moreover, it is not the significance of low oxygen content in blood and/or brain tissue, but the short duration of apnea that indicates a person's low resistance to sudden hypoxemia, or more precisely, to acute hypoxia of his brain tissue. Therefore, not so much hypoxemia (decreased blood oxygen saturation) and even not so much brain hypoxia as such, i. e. decrease of oxygen content in brain tissue, but rather the duration of hypoxia of brain tissue exceeding the period of human resistance to hypoxia are the most important risk factors of hypoxic irreversible damage of brain cells and biological death of a person [11, 12, 26, 29].

DURATION OF TISSUE HYPOXIA AS A RISK FACTOR FOR HYPOXIC IRREVERSIBLE BRAIN CELLS DAMAGE

Low blood oxygen levels, indicative of hypoxemia, are not the only risk factor for hypoxic irreversible brain cell damage [30]. The point is that different people with different states of their organism may have different adaptation reserves to hypoxemia and possibilities of survival in critical states [28]. It has been shown that different people can tolerate different durations of hypoxemia or periods of apnea. This has been easily detected for 110 years by the Stange test with breath-holding at maximum inspiration. It has been found that people's higher tolerance to hypoxemia provides them with longer apneas and vice versa.

Consequently, the most important risk factor for hypoxic brain cell damage is the time factor, namely, the duration of hypoxemia and/or intrathecal cerebral hypoxia and whether this time period corresponds to the maximum allowable duration of the safe period of cerebral hypoxia.

It has been reported that the significance of the temporal risk factor for the development of hypoxic brain cell damage and human biological death is shown by the following data. It has been shown that local hypothermia (local cooling of the brain) can reduce the intensity of oxygen consumption by its cells due to inhibition of the intensity of aerobic metabolism [31–33]. Therefore, local cooling of the brain during its hypoxia (or ischemia) can reduce the intensity of oxygen consumption in the brain, which, in turn, in some cases may even increase the oxygen content of brain tissue due to the delivery of oxygen with the blood flowing to it [34–36].

On this basis, it might seem that the high oxygen content of cooled brain tissue indicates that the threat of hypoxic damage to brain cells has been eliminated in the brain. However, this is not entirely true. The matter is that accurate prognosis is impossible without taking into account such a risk factor of hypoxic brain damage as duration of its tissue hypoxia before the beginning of cooling and correspondence of the period of brain hypoxia to the duration of the maximum permissible period of preservation of brain cells viability under hypoxia conditions at normothermia. The point is that without taking this factor into account, the brain can be cooled both before the onset of tissue hypoxia and at the very beginning of hypoxia, and after the development of irreversible hypoxic damage of brain cells. In other words, without taking into account the time factor, the brain can be cooled both in time, i. e. in the absence of hypoxic irreversible damage of brain cells, and with a delay, i. e. after the brain cells permanently lose their viability due to the moment of irreversible hypoxic damage development in them. Therefore, increasing the oxygen content in the cooled brain tissue in the first case will increase brain resistance to hypoxia and

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prolong the period of preservation of viability under subsequent hypoxia, while in the second case it will not, since hypoxic damage to the cells irreversibly killed them before the onset of cooling. Moreover, it is possible that in the second case the increase of oxygen content in the brain may intensify destructive processes in brain cells with the participation of additionally supplied oxygen, since oxygen can be used by metabolism of dying cells in the process of their self-damage [11, 25].

Consequently, low values of oxygen concentration in arterial blood and in brain tissue at any given time interval do not unequivocally indicate the viability and/or nature of hypoxic damage to brain cells.

It has been shown that hypoxia is most often associated with relatively low (usually <2%) oxygen content compared to normal oxygen content in an organ, tissue, or cell type [25]. However, it has also been reported that this is not sufficient to issue a specific conclusion about the danger of hypoxia for cell viability. The fact is that the brain and its cells have variable oxygen reserves (reserves) and other mechanisms of adaptation to oxygen deficiency, the importance of which for cell viability under hypoxia varies depending on the changing role of a number of risk factors for hypoxic damage of brain cells [25, 37]. Therefore, because of the body's different resistance to hypoxia and the different role of risk factors, an equal degree of cerebral hypoxia may have different significance for brain cell viability not only in different individuals, but also in the same individual at different time intervals, under different health conditions, and in different environments.

It has been shown that hypoxia of brain tissue can induce a number of adaptive mechanisms in the body aimed at increasing the resistance of brain cells to oxygen deficiency [38]. It has been reported that the complex of adaptation changes includes mechanisms of blood circulation redistribution in favor of the brain and mechanisms of energy saving of the whole organism by minimizing the functional activity of its skeletal muscles [39]. It was found that in cases when brain resistance to hypoxia allows preserving the viability of brain cells until the end of the hypoxia episode, the mentioned adaptive changes in the organism cease to occur [40]. In this case, brain cells remain fully viable. On the other hand, in cases when the reserves of adaptation to hypoxia are exhausted before the period of brain hypoxia ends, hypoxic damage may develop in brain cells [41].

The temporal risk factor has been reported to be important not only for adults but also for fetuses within the womb. It has been shown that fetal resistance to intrauterine hypoxia is also manifested by the duration of the period of its adaptation to hypoxia. It has been found that this period can be determined by recording the duration of fetal immobility during apnea in pregnant women. This method of assessing fetal reserves to intrauterine hypoxia was developed by studying the dynamics of motor activity of fetuses inside the uterus during arbitrary apnea in pregnant women and comparing it with the dynamics of motor activity of aquarium fish in a small volume of water after hermetic closure of the container with them and cessation of air intake [42–44]. It was found that under conditions of sudden cessation of air supply to the pregnant woman's body and to the water with fish, healthy fetuses and fish behave almost identically: at the beginning of the period of beginning oxygen deficiency, they adopt a motionless state, the duration of which is the longer, the greater their reserves of adaptation to hypoxia. Then, having exhausted their adaptation reserves to hypoxia, fish and fetuses suddenly activate their motor activity and respiratory movements of the rib and/or gill arches occur. It has been reported that the duration of fetal immobility during apnea in pregnant women correlates with the magnitude of fetal reserves to intrauterine hypoxia, i. e., fetal resistance to hypoxia [29, 37, 39, 42, 43, 45].

TEMPERATURE AS A RISK FACTOR FOR HYPOXIC IRREVERSIBLE BRAIN CELLS DAMAGE

It is not a secret that body temperature is an important factor in human life activity, as the change in temperature of organs and tissues changes the intensity of all chemical, biochemical and biophysical processes occurring in them without exception [46]. The general orientation and expression of temperature dependence of metabolic bases of vital activity can be illustrated by the law of Arrhenius, which states that increasing the temperature of the interaction medium by 10°C increases the rate of chemical reactions on average by 2 times, i.e. by 100% [47]. This means that changing the temperature of a part of the human body by 1°C changes the rate of metabolic processes in it by an average of 10%.

It is believed that normal human body temperature is usually between 36.5 and 37.5°C (97.7–99.5°F) [48]. However, the actual value of body temperature varies cyclically throughout the day up to an average of 1.0°C, and this cyclical change in temperature is called a circadian rhythm [49, 50]. It has been shown that the body temperature of people around 40 years of age drops to its lowest values usually at 4 a.m. and rises to its highest values in the afternoon, namely between 4 p.m. and 6 p.m. (assuming the person is awake during the day and sleeping at night) [51]. In addition, regardless of the cyclical daily changes in total body temperature, local temperature in different parts of the body in humans can be influenced by several factors. In particular, it is influenced by external temperature influences, inflammatory processes and changes in blood supply to body parts. Thus, inflammation is accompanied by hyperthermia, and ischemia — local hypothermia. In addition, the total body temperature in the elderly decreases with increasing age [52, 53].

Taking into account the above information, it can be concluded that, all other things being equal, the intensity of vital activity and metabolism in the human body in the evening is

on average 10% higher than in the early morning. Therefore, the outcome of commensurate episodes of acute cerebral hypoxia, which occurred in a person in the early morning and in the evening, may be sadder in the evening than in the early morning.

At the same time, the physical cooling of the entire human body is hindered by the body's system for maintaining temperature homeostasis. Thanks to this system, the human body begins to produce heat more intensively to prevent cooling and maintain a normal body temperature [54]. However, the body stimulates its metabolism for increased heat production. It is shown that cold is a stress factor for humans, which activates oxidative processes in mitochondria [55]. Therefore, attempts to trivialize cooling of the whole person may increase the rate of oxygen consumption in the body to combat hypothermia, thereby reducing the person's oxygen reserves and resistance to acute hypoxia.

Therefore, localized cooling of the head is more appropriate than whole body cooling to increase brain resistance to hypoxia [56, 57]. To date, several methods have been developed for the treatment of cerebral hypoxia using localized therapeutic hypothermia, of which the most advanced is targeted temperature management [58, 59]. In particular, brain cooling through nasal cavity lavage with cold breathing gas has been shown to be possible [60–62].

It has been reported that the protective effect of local therapeutic hypothermia on the brain is analogous to hibernation, a physiological phenomenon observed in warm-blooded animals going into winter hibernation [63]. In particular, using the Arctic gopher as an example, it was shown that during winter hibernation this animal develops natural general hypothermia (hibernation), which increases its resistance to ischemic/hypoxic damage. It has also been reported that hibernation plays a universal protector role to protect the organism of warm-blooded animals not only from hypoxia but also from many other damaging factors [64–66]. Localized head hypothermia has been reported to have a good protective effect. In particular, local therapeutic hypothermia of the brain has been shown to be an effective way to increase the resistance of brain cells to hypoxic damage [67–70]. In addition, localized cooling of the brain is a universal way to preserve brain viability in damaging factors such as mechanical head trauma, cerebral hemorrhage in stroke, and sudden cardiac arrest [31, 71–73].

At the same time, it has been shown that hyperthermia may accompany inflammation of the brain, cerebral membranes, and skull bones in brain injury and therefore may reduce the brain's resistance to hypoxia. Because hyperthermia reduces the brain's resistance to hypoxia, fever prophylaxis has been proposed as a therapeutic tool to limit neuronal damage [71, 74].

Thus, local cerebral hyperthermia decreases and local cerebral hypothermia increases the resistance of brain cells to hypoxic irreversible damage.

ANTIHYPOXANTS

Our review of the literature has shown that the cause of hypoxic irreversible damage to brain cells is the high intensity of brain tissue metabolism, which is not provided with the "necessary" amount of oxygen. It is the ongoing metabolism in the cells, deprived of the normal amount of oxygen, that damages these cells [29, 37, 43, 44]. Analysis of this information allows us to conclude that under conditions of brain isolation from the body, brain cell death under oxygen deficiency can be prevented by timely increase of oxygen delivery to cells and/or inhibition of metabolism in cells to a level that will come in line with the existing reduced oxygen content. The former task can be successfully accomplished by oxygenation of brain tissue, and the latter task can be successfully accomplished by localized hypothermia of the brain.

However, the brain is not normally isolated from the human body. Therefore, in the human body it is possible to prevent hypoxic irreversible damage to brain cells not only by inhalation of oxygen and cooling of the head, but also by increasing the resistance of the whole organism to hypoxia. This can be achieved by redistributing blood supply in favor of the brain, saving energy costs by relaxing skeletal muscles and making the body immobile, as well as by timely introduction of antihypoxants into the body [75, 76]. Such antihypoxants include dibunol, sodium oxybutyrate, oliphene, epofen, emoxipin, mexidol, mafusol, reamberine and some others. It is believed that the mechanism of action of these drugs lies in their ability to effectively protect the entire body from hypoxic damage. It is true that known antihypoxants are only effective if the body has a good resistance to hypoxia [75]. In addition, these antihypoxants are not used to preserve the viability of isolated organs and tissues during their preservation, despite the fact that the preservation of organs and tissues is carried out under conditions of oxygen deficiency, i. e. hypoxia. Doubt in the ability of the listed antihypoxants to preserve the life of biological objects under hypoxia conditions is strengthened also because, on the one hand, hypoxia is a lack of oxygen, and on the other hand, modern antihypoxants are neither oxygen nor its substitutes, but salts deprived of oxygen.

New hopes for effective drug-induced prevention of hypoxic irreversible brain cell damage are provided by reports that an alkaline hydrogen peroxide solution can be used as an antihypoxant [77–79]. The fact is that the main ingredient of this antihypoxant is hydrogen peroxide, which is able to decompose very quickly into water and oxygen gas under the action of the enzyme catalase located in all tissues. It has been shown that a large arsenal of alkaline hydrogen peroxide solutions has been created [80, 81]. These include drugs for inhalation and intrapulmonary injection, for administration into the stomach, for injection into the blood, and for injection directly into tissues requiring oxygen.

The prospects for the use of alkaline solutions of hydrogen peroxide are still to be explored by all of us in the future.

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CONCLUSIONS

Thus, the immediate cause of biological death of humans and warm-blooded animals in the final stage of many diseases is hypoxic irreversible damage to brain cells. Therefore, inhalation of breathing gases containing oxygen to saturate the blood with oxygen is considered one of the main conditions for preserving human life in all critical situations and forms the basis of emergency medical care in the intensive care unit. However, increasing blood oxygen saturation through the lungs is not always possible. In addition, normalization of blood oxygen saturation must be achieved before the onset of the stage of hypoxic irreversible damage in brain cells. In this connection, the mechanisms of adaptation of the organism to oxygen deficiency play a great role for longer preservation of brain cells viability and human life in conditions of hypoxemia. In order to increase resistance to hypoxemia, antihypoxants are traditionally used, which should be introduced into the body before the onset of hypoxic irreversible damage to brain cells, and their effectiveness is largely ensured by the presence in the body of unused reserves of adaptation to hypoxemia. Under these conditions, risk factors of hypoxic irreversible damage of brain cells, among which excessively long duration of hypoxemia exceeding the period of human resistance to hypoxia and hyperthermia are of great importance for exclusion of premature death of people. It has been shown that human tolerance to hypoxia can be assessed using the Stange test. It is reported that fever and localized cerebral hyperthermia decrease, and hibernation and localized cerebral hypothermia increase, the resistance of brain cells to hypoxia. It is pointed out that among the methods of local therapeutic hypothermia, targeted temperature management is the most advanced. In addition, it is reported that in recent years a new group of promising antihypoxants — alkaline solutions of hydrogen peroxide — has been created. It has been shown that hydrogen peroxide is able to decompose very quickly into water and oxygen gas under the action of catalase, which is found in all tissues. The potential of alkaline solutions of hydrogen peroxide in the role of new antihypoxants we all have yet to explore in the future.

ADDITIONAL INFO

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