

BENEFITS OF MODIFIED BREATHING AIR FOR SPACECRAFT AND PLANETARY HABITATS

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ABSTRACT

Residents of high altitude demonstrate normal physiological characteristics and show increased vitality and lesser morbidity. Subjects acclimatized to a low O₂ (hypoxic) environment (corresponds to 14.5 – 11 % O₂ at the sea level) exhibited enhanced physical endurance and increased resistance to stress – inducing and damaging factors and accelerated recovery in a variety of conditions. Hypoxic stimulation reactivates the O₂ - saving genetic program, which is active in all mammal cells during embryonic development, when O₂ partial pressure in the uterus is comparable to that in the high mountains.

CO₂ deficiency (hypocapnia) is a regular component of general stress reaction and is harmful for normal physiological functions. Positive effects of moderately increased CO₂ (physiological hypercapnia) are well documented. CO₂ has direct antioxidative action, suppressing production of superoxid - anion radicals in the mitochondria, and neutralizing the highly - aggressive radical peroxynitrit.

Application of normobaric moderately hypoxic - hypercapnic environment in manned space exploration has following biological benefits:

1. Adaptation to hypoxia result in significant enhancement of general stress - tolerance and improves general health, which increase operational reliability of crew.
2. Adaptation to hypoxia economizes oxidative metabolism, with significant reduction both of O₂ and food consumption, but without productivity decline or health hazard. It can have a special value in emergency and in long - termed interplanetary space missions, where amount of life - supporting resources is limited.
3. Inhalation of air with O₂ concentration 8.5 - 10 % is proven to induce radioprotective effect against X- rays and γ - rays. This effect finds application in cancer radiotherapy for protection of healthy tissues and can be used by astronauts for short - time radioprotection in urgent situations.
4. Hypercapnic atmosphere in the greenhouse result in significant increase of plant productivity.

BACKGROUND

It is well recognized that the technical objectives of advanced life support system for long duration space and planetary missions must include technologies that significantly reduce hazards, improve operational performance and operational reliability of the crew, as well as promote self-sufficiency, and minimize the expenditure of resources. Technology must be developed to provide effective countermeasures to deconditioning effects of zero gravity.

Many of these objectives would be achieved by providing inside a space ship or planetary habitat a modified gaseous environment with moderately reduced oxygen and increased nitrogen and carbon dioxide, that combines both fire-preventive and health-promoting properties.

The strategy of maintaining of gaseous environment in human-occupied confinements, such as those found in submarines, space ships and planetary habitats, is based mainly on the common sense presumption that the artificial breathing mixture should simulate the Earth's atmosphere as close as possible. It is commonly believed that any significant change in the proportion of constituent gases would be potentially hazardous for humans. Meanwhile, the alternative assumption is also possible. One can ask: what benefits a modified gaseous environment would provide for the crew in prolonged space missions? A comparison is possible with the use of artificial Helium-Oxygen breathing mixture that is for a long time used in saturation diving. Without this mixture no professional diving deeper than 60 - 70 m would be possible. The other example gives us the current practice of using normobaric hypoxic air for stimulating adaptation to hypoxia. The numerous advantages of adaptation to hypoxia are broadly recognized today in the field of sport and fitness training, and find growing application in the preventive and curative medicine (1, 2, 3).

OVERVIEW

Normobaric, moderately hypoxic air is similar to the altitude air of mountainous ski resorts. In the world more than million people live in the altitude between 2500 and 4000 m., where oxygen partial pressure gradually decreases from 14.7 kPa to 12.1 kPa, which corresponds from 15.4 to 12.7 % O₂ in the normobaric air. At this altitude humans and animals easily develop tolerance or adaptation to hypoxia (4). The only difference between altitude (or hypobaric) air and normobaric hypoxic air is that normobaric hypoxic air contains increased amount of nitrogen. This determines the specific fire-preventive properties of breathable normobaric hypoxic air.

It is well documented that residents of high altitude demonstrate increased vitality and lesser morbidity from common diseases (5, 6). It is proven to be the result of adaptation to hypoxia. At the beginning of hypoxia adaptation, mitochondrial respiration is decreased, thereby leading to a buildup of reducing equivalents that cannot be transferred to O₂ molecules. This condition, called reductive stress, can paradoxically lead to enhanced formation of free oxygen radicals. Free radicals mediate expression of genes, responsible for molecular adaptation to hypoxia. Induction of hypoxia-inducible transcription factor (HIF-1 α), activated at low pO₂, explain the multiple effects of hypoxia adaptation. HIF-1 α mediates the expression of possibly hundreds of genes that enable the cell to survive in a hostile environment (7).

MECHANISM OF HYPOXIA ADAPTATION

Mitochondria are able to change their morphological structure and enzyme spectrum in order to save oxygen under hypoxia influence. This results in more efficient oxygen utilization and, most important, in the reduction of basal emission of free oxygen radicals (8). Basal oxygen consumption in the body significantly decreases in adaptation to hypoxia. Remarkably, that basal oxygen consumption determines the rate of oxidative damage in DNA, which influences the individual life span, as well as onset and development of age-related diseases (9). By reducing the basal mitochondrial emission of reactive oxygen species it is possible to inhibit oxidative DNA damage and diminish age - related decline of DNA - repair mechanisms.

In the human studies it was demonstrated that reduction of basal oxygen consumption results in diminishing of excretion of oxidative DNA repair product - oxo8dG (10). This is a direct evidence of efficacy of hypoxia adaptation in reduction of basal oxidative DNA damage in humans.

In the pathologic, uncontrolled conditions, such as extreme or prolonged oxygen deprivation, hypoxia “per se”, and especially the hypoxia - reoxygenation episodes can cause destructive oxidative stress, followed by apoptosis or necrosis of involved cells. In the controlled, mild and intermittent hypoxia it would only induce enhancement of antioxidative cellular defense and adjustment of metabolic pathways (11, 12, 13).

Intermittent normobaric hypoxia can be broadly defined as repeated episodes of inhalation of ambient air, having artificially decreased oxygen content, interspersed with episodes of inhalation of air with higher oxygen content. The primary distinguishing feature of intermittent hypoxia is the presence of periods of recovery from oxygen deficit. They provide sufficient time for anabolic responses while avoiding the detrimental effects of long-term severe oxygen deprivation.

Mechanisms of adaptation to hypoxia in the mammals have deep evolutionary roots. The fertilized egg cell begins its development under very low ambient oxygen content. Partial pressure of oxygen in its microenvironment is near to that at the top of Mount Everest. Increase of oxygen concentration would kill developing organism immediately, because its antioxidative defense needs time and proper stimulation to mature.

Impulse biorhythm of cyclic pO₂ change was found in the uterus and intrauterine fetus of mammals. It is regarded as evolution-fixed, physiological mechanism aimed at increasing antioxidative defense of the fetus (14). Maintaining its capacity during the individual life seems to be crucially important mechanism that is keeping the balance between potentially destructive free radical oxydation and the reparative synthesis of damaged cellular structures. Stimulating this mechanism by adaptation to intermittent normobaric hypoxia results in more significant increase of nonspecific resistance to oxidative stress, than application of continuous, uninterrupted altitude hypoxic stimulus (3).

Moderate hypoxia, especially if combined with exercise, facilitates adaptation and improvement of aerobic metabolism. Exercising in hypoxia results in increased hormonal response and enhanced release of Growth Hormone (15). In contrast, extreme and prolonged continuous hypoxia initiates catabolic processes, which result in reduction of muscle and bone mass. Similar effects are present in the microgravity conditions of space flights and in model experiments. These effects are shown to be mediated by decreased production of GH, which accompanies detraining and disuse of muscles, ligaments and bones (16, 7).

The question is, what specific biomedical problems of manned space flights could be solved or ameliorated by implementing a normobaric hypoxic gaseous environment?

APPLICATIONS

1. Hypogravity deconditioning.

The impact of hypo-gravity deconditioning on the crew's ability to conduct subsequent surface operations is a significant concern. For example, the typical transit time for an Earth-to-Mars mission is 150 to 200 days. Because this extended time in zero gravity will contribute to bone and muscle loss in the crewmembers, these astronauts cannot be expected to walk great distances easily when they reach Mars. Current space biomedical research continues to study why bones lose more calcium during space flights, as well as changes in renal tissue, the decrease in body fluids, insulin and glucose disturbances and the development of a secondary immunodeficiency. It was shown that many of these troubles are mediated by decreased basal production and pulsatile release of Growth Hormone in hypogravity (16). GH activity goes far beyond the effect of any other hormone. It not only modulates biological aging, but also significantly improves physical and mental performance and prevents muscular atrophy and osteoporosis. Researchers have proven GH therapy can reverse the biological effects of aging by many years and dramatically improve physical fitness and bone density.

The effective countermeasures against detrimental effects of hypogravity used in the long orbital flights on “Mir” station, were based on the intensive treadmill exercise. Unfortunately, this exhaustive training requires more than three hours each day to achieve preventive effect. The “Mir” cosmonauts preferred to use this countermeasure only for two hours daily, which is still very expensive in resources and time-consuming.

Abundant studies confirmed that physical exercising in hypoxia result in exaggerated metabolic changes in the body (1, 3, 15, 17). An individualized protocol of hypoxic training provides a dramatic increase of GH production.

In a practical view, exercise in normobaric hypoxia would be useful for intensifying endogenous GH release in astronauts, as well as in subjects to whom heavy resistance training cannot be applied.

2. Radioprotection

It is widely known that rapid, heavy doses of radiation, released by a solar flare can cause severe cellular damage. Most of a solar flare's energy is in alpha and beta particles that can be stopped with a few centimeters of shielding.

It is well known that radiation damage in cells is augmented dramatically by increase of oxygen partial pressure (so called “oxygen effect in the radiation injury”). It is established that the molecular- biological mechanism of radiation effect on the living organisms is mediated by massive production of oxygen free radicals, released by radiolysis of water molecules.

By means of acute decrease of oxygen partial pressure in the body one can achieve the significant radioprotective effect in cells (18).

The inhalation of hypoxic air, containing 8 – 8.5 % O₂, instead of ambient air, reduces oxygen content in the tissues more than on 50 %. It results in marked, though short-termed (about 30-min.) radioprotective effect against β and γ rays. In some emergency situations this complementary technique would provide sufficient time for astronauts to reach the stationary radiation shelter. Astronauts, adapted to hypoxia, would not suffer negative effect from this low level of oxygen.

The astronauts will spend about six months traveling to Mars, eighteen months on the surface, and six months returning to Earth. The permanent habitats of the Mars base can be covered with thick layers of soil to provide full-time radiation protection, so nearly all the crew's radiation exposure would occur during the year of interplanetary travel.

The possibility of long-termed radioprotection against cosmic rays can be employed by use of the phenomenon of hypoxic hypometabolism, which develops in mammals under prolonged hypoxia. Application of uninterrupted hypoxic stimulus downregulates metabolism and decreases body temperature, especially during the night sleep. Hypoxic hypometabolism can be used both for radioprotection of crew and saving resources during interplanetary flight.

ADVANTAGES OF INCREASED CARBON DIOXIDE

The potential advantages of increased carbon dioxide (hypercapnia) in the modified gaseous environment also merit discussion.

Physiological hypercapnia is associated with a number of positive biological and therapeutic effects, such as increase in the cerebral and myocardial blood flow, acceleration of oxyhemoglobin dissociation in the capillaries and enhancement of blood perfusion in functionally active organs (19). There is abundant evidence of enhanced capillary growth, increased collateral blood vessels development under intermittent hypercapnia applications. Naturopathic medicine and balneotherapy since long time successfully explore different protocols of increased CO₂ application to produce curative effects.

It is well proven that moderate hypercapnia provides protective effect in severe hypoxia. The direct protective action of carbon dioxide against hypoxic injury during bypass operations was reported (20). Protection of blood coagulation homeostasis in severe hypoxia by carbon dioxide was shown (21). CNS tolerance to hypoxia can be increased promptly and sufficiently by purposeful elevation of inspired carbon dioxide partial pressure (22). Protective effect of increased CO₂ on calcium metabolism in immobilization osteoporosis was demonstrated (23).

It was shown recently, that carbon dioxide provide direct antioxidative action, suppressing concentration - proportionally the production of superoxide-anion radicals in the mitochondria, and neutralizing the other highly - aggressive free radical peroxynitrit (24, 25, 26,).

Actually CO₂ in proper concentration plays in the body the role of an abundant, easy available and fast acting antioxidant, which protects from depletion the other, slower functioning components of antioxidant network system of the body under condition of oxidative stress (27, 28, 29). The review of physiological effects of moderately elevated CO₂ levels presented in a joint NASA – ESA -- DARA study (30).

And last, but not least: the productivity of plants and algae in an artificial planetary ecosystem can be enhanced significantly by increased ambient CO₂.

CONCLUSIONS

We can summarize that numerous benefits of moderately hypoxic-hypercapnic gaseous environment in the space exploration human activity are highly promising. Remarkably that this approach would be synergistically favorable for space flights managing: it eliminates completely the fire hazard; it results in enhancing of general health and operational reliability of crew; it increases positive effects of exercise and reduces oxygen consumption.

The detailed questions concerning specific protocols of application of such modified atmosphere should be answered during future biomedical research in simulated space missions.

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