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Pilots' organisms: influences of radiation, hypoxia and possible prospects of their pharmacological corrections

Two damaging factors influencing on pilots' organisms were analysed – ionizing radiation and hypoxia. The brief information about these effects examined at Elbrus Medical and Biological Station of the National Academy of Sciences of Ukraine was presented. Possible prospective ways of these effects pharmacological correction by new potential pharmacological preparations (C60 fullerene, yackton, sufan, splenozide) were discussed.

The nature of ionizing radiation influences on pilots organisms during the flights. It is known that under the conditions of air flights the pilots, as well as other flights' members received significant doses of space ionizing radiation. These facts and measurements were described in numerical publications and our as well [1]. These facts were registered either during the flights near the Earth's magnetic poles, or the flights at high altitudes, since the amount of radiation doubles for approximately every two kilometers of altitude. The last phenomena can be explained by the decreasing of protective effects of the Earth atmosphere at high altitudes. Since gas molecules in the Earth's atmosphere have the ability to absorb cosmic radiation, it causes a protective effect for biological organisms (including humans) at the bottom of this "atmospheric ocean". These protective properties depend on the altitude at which the aircraft flies, on the thickness of atmospheric layer above it, and therefore its protective effect decreases with altitude increasing.

The first examples of radiation of the space origin on the Earth were registered by the Austrian Viktor Hess on 1912, and he received the Nobel Prize for this discovery on 1936 [1]. According to the last imaginations, total radiation can be subdivided into 2 components – solar radiation and galactic radiation, both have different origin and characterized by different physical components. Although atmosphere protects us from cosmic radiation enough effectively, however, at the heights of 10-12 km above sea level (a.s.l.), the density of the protective layer of residual atmosphere is 4 times lower than at sea level. Therefore, the level of radiation at the altitudes of contemporary air routes really exceeds the natural background by tens and hundreds of times. These effects are more pronounced in the polar regions of the Earth. There, the passengers can receive the maximum permissible doses of radiation, calculated for a year, in one hour of flight. And crew members who have higher standards - in 8 hours of the flight in these conditions. During powerful solar flares, the annual maximum allowable dose for passengers can generally be exceeded 10 times in one flight. As for the crews, under the

conditions of large annual raid on high-latitude routes, the doses may approach the radiation standards in the nuclear industry.

Although normal in-flight radiation levels do not exceed the maximum permissible values for adults, there are cautions for crew members spending more than 75 hours in the air per month, as well as for pregnant women. In a number of European countries, the legislation classifies aircraft crew members as people working in radiation conditions, and the dose level they receive is monitored. It is known that the maximum permissible radiation dose for a person should not exceed 0.3 roentgens per week or 15 roentgens per year. 600 roentgens are considered to be the limit dose for a person during short-term exposure [1, 2].

Some mechanisms of ionizing radiation influences on biological organisms. Success in carrying out such works is based on knowledge of the chemistry of ionizing radiation influences on biological organisms.

Since the tissues of the human body consist of 65-70% water, the initial radiation-chemical reactions develop, first of all, in the water phase [1]. At the same time, high-energy quanta knock the electrons out from the atoms of the body. These free electrons are surrounded by water molecules, and complex ions H_2O+ and H_2O- can be formed. Excited water molecules can disintegrate easily with the formation of H+ protons and H_2 hydrogen molecules, as well as number of free radicals O_2-, HO_2+, +OH and –OH.

However, later, already at the second stage of transformations of water radiolysis products in living tissues, oxygen O_2 starts to play its role. Therefore, all elementary products after interaction with O_2 acquire an oxidative properties; a number of free oxidizing radicals are formed. Basically, radiation damage is the result of the attacks on vital cellular structures by active oxidative products of radiation. Hydroperoxide radicals and hydroperoxides can be formed easily during the interaction of O_2 and oxidizing radicals of water with organic radicals (R*):

$R^* + O_2 \Rightarrow ROO^* \Rightarrow ROOH$, and

$R^* + HO_2 \Rightarrow ROO^* \Rightarrow ROOH$

Therefore, tissue oxygen acts as a radiosensitizer - a substance that increases the sensitivity of organic compounds, cells and tissues to the striking effect of radiation. This so-called “oxygen effect” characterizes the important role of oxygen in the biological action of radiation. In addition, since O_2 is an important participant of body metabolism, the radiation-induced disorganization of oxidative and energy metabolism makes an additional contribution to radiation damage of organism. From other side, O_2 plays an important role in the post-radiation recovery of the irradiated organism, acting as an active participant in the process of damaged structures repairing. Therefore, according to theoretical approaches, one can try to correct the effects of ionizing radiation within certain limits by increasing and decreasing of O_2 content in the cells of biological organism.

Elbrus Medical and Biological Station of Academy of Sciences of Ukraine (EMBS NASU) is a research institution at Elbrus slopes, Caucasus Mountains. The researches in this and in many other scientific directions were carried out by the great commands of Ukrainian scientists, as well as researchers from others ex-USSR institutions. Researches were initiated under the leadership of EMBS Director Prof. Sirotinin M.M. and continued by his successor-in-science Prof. Beloshitsky P.V. (with

whom Prof. Klyuchko OM worked for a long time). There, at village Terskol (2100 m a.s.l. in Caucasus Mountains, now – territory of Russia) Ukrainian Academy of Sciences (later - National Academy of Sciences of Ukraine) organized the Laboratory of Space Physiology as integral part of O.O. Bogomoletz Institute of Physiology NASU (in Kyiv, Ukraine). This Laboratory of Space Physiology in Terskol included also rehabilitation clinical department, unique thermobarochambers and obtained equipment, the best for the second half of XX c. [1, 2]. It became an international center for hypoxia problems studying and implementation of obtained results in practice of medicine (including aerospace medicine), biology (including extremal physiology), pathophysiology, ecology, sports and many other directions [1-5]. Space researches in general are impossible without the simultaneous studies in linked biological and medical areas. Consequently, many problems solutions during the space exploring require complex knowledge of professionals in different directions – engineers, programmers, professionals in medicine and biology, and others. So, the progress in contemporary aviation and astronautics cannot be imagined without united efforts of great commands of professionals. General Constructor of space technology in former USSR, the first space satellites and rockets designer, our great compatriot, S.P. Korolev who was born in Ukrainian city Zhytomyr and obtained in Ukraine his basic education, understood this perfectly well. In the result of his initiative in USSR was founded the Institute of Medical and Biological Problems (IMBP, 1963); and EMBS NANU was linked tightly with it during the time of collaboration. In the laboratory of space physiology, at EMBS of the NASU, Ukrainian scientists and doctors carried out their investigations of the effects of radiation influence on biological organisms and ways of organism rehabilitation, complex study of organisms of pilots, cosmonauts, rescuers, and persons from special contingents. It is not possible even to list all directions of investigations at EMBS NASU. The mechanisms of different organisms adaptation, influence of mountain meteorological factors on organisms aimed on the increase of organism resistance to extreme factors of space flight, as well as study of different medical preparations and substances influence in these extreme conditions were studied there [1-4]. Mathematical modeling, different novel mathematical tools were developed and applied as well in process of the research tasks solutions in framework of EMBS projects [5, 6].

Possible ways of pharmacological correction of pathological states linked with radiation damages of organisms and hypoxic states development. In connection with sometimes-increasing need for a long-term human stay in the conditions of high-altitude flights and on board of space apparatuses, scientists are looking for effective means of protection against ionizing radiation. One of the promising directions for this problem solution is the search and testing of special medical preparations that are able to prevent or at least to delay the development of radiation sickness in cases of severe radiation. Numbers of the data on this topic have already been published by the authors [4, 7, 8]. According to experimental testing of different substances with antioxidant activity by Dr. Gonchar O.O. in laboratory conditions in O.O. Bogomoletz Institute of Physiology NASU (Kyiv, Ukraine)

Substances for potential correction of hypoxic disorders - yackton, sufan, splenozide, C60 fullerene. In our previous publications we had already given the data of our experiments that potentially permitted to use the substances that demonstrate

antioxidant activity for the purposes of hypoxic disorders correction - yackton, sufan, splenozide and C60 fullerene [7, 8]. In these and other our publications we had given the information about such substances, their chemical composition, properties, details of their characteristics experimental examination and obtained results. As were mentioned above, since O_2 is an important participant of organism metabolism, the radiation-induced disorganization of oxidative and energy metabolism causes additional contribution to radiation damage of organism. From other side, hypoxia is a state of biological organism with oxygen deficiency. And the substances, which were able to influence on oxygen metabolism could to correct the effects of ionizing radiation through the regulation of oxygen metabolism in cells (within certain limits, sure). As we had previously reported, we had studied substances that may be potential medical preparations for hypoxia disorders treatment: yackton and sufan – derivatives of succinic acid, and splenozide – non-protein factor of spleen with nucleoside complex as active base. Investigations were carried on homogenates, cytosol and mitochondria fractions of liver, heart, lungs, and brain tissues of Wistar rats during acute hypoxias: hypoxic, hemic, (after the injection of sodium nitrite (6mg / 100 g/rat weight) and circulatory hypoxia (after bleeding – 2,5 ml / 100 g/rat weight). Preliminary administration of any of examined preparations – yackton, sufan and splenozide – caused the decrease of lipid peroxidation processes (malonyldialdehyde content decreased, $P<0.01$). Simultaneously increased an activity of antioxidant enzymes - superoxide dismutase, catalase, glutathione reductase, glutathione peroxidase, as well as increased a content of reduced glutathione ($P <0.05$) in comparison with hypoxia state. Increase of the rate NAD/NADH, decrease of lactate / pyruvate rate ($P < 0.05$), and lactate dehydrogenase activation evidence about the prevalence of oxidized NAD forms in comparison with reduced ones that lead to the prevention of intracellular acidosis development (typical for hypoxia). C60 fullerene demonstrated effects that could permit to use it antioxidant properties within presented paradigm too. Cell defense by studied preparations in conditions of oxygen deficiency can correct disorders in energy metabolism, hinder lipid peroxidation secondary product (PLP) activation and prevent the reduction of anti-oxidant cell potential [7, 8].

Thus, since oxygen is crucially important component in organism metabolism, the radiation-induced disorganization of energy and oxidative metabolisms causes additional pressure on radiation damage of biological system. The substances – antioxidants (including studied ones) potentially could play their positive roles in correction of disorders, caused both by hypoxia and radiation influences. So, they have good prospects to be used in future as potential medical preparations for such complex disorders treatment. Sure, after the passing of all numbers of procedures - testing, large-scale examinations of different characteristics of substances action, and etc., those are necessary for medical preparations.

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