ARTICLE IN PRESS

Medical Hypotheses xxx (2010) xxx–xxx

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Hydrogen therapy may reduce the risks related to radiation-induced oxidative stress in space flight

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ARTICLE INFO

Article history:
Received 23 June 2010
Accepted 25 August 2010
Available online xxxx

SUMMARY

Cosmic radiation is known to induce DNA and lipid damage associated with increased oxidative stress and remains a major concern in space travel. Hydrogen, recently discovered as a novel therapeutic medical gas in a variety of biomedical fields, has potent antioxidant and anti-inflammatory activities. It is expected that space mission activities will increase in coming years both in numbers and duration. It is therefore important to estimate and prevent the risks encountered by astronauts due to oxidative stress prior to developing clinical symptoms of disease. We hypothesize that hydrogen administration to the astronauts by either inhalation or drinking hydrogen-rich water may potentially yield a novel and feasible preventative/therapeutic strategy to prevent radiation-induced adverse events.

Introduction

Radiation-induced oxidative stress in space

In the space flight, astronauts are exposed to a variety of potential hazardous agents including chemical contaminants and cosmic radiation from protons and high atomic number (Z) high energy (HZE) particles. Chemical contaminant exposure can be mitigated by filtration system on-board the spacecraft. However, the present technology is not capable to fully shield the astronauts from cosmic radiation. As radiation hazards in outer space present an enormous challenge for the safety of astronauts, the National Aeronautics and Space Administration (NASA) placed a high priority on crew radiation protection in space, in particular, for long-duration space flights.

One of the critical issues caused by cosmic radiation is considered to be oxidative stress due to the increased production of reactive oxygen species (ROS). Oxidative injury causes direct DNA damage or lipid peroxidation, which have been implicated in the etiology of a wide variety of chronic disease and acute pathologic states. The greatest risks from radiation are generally assumed to be cancer, cataract, [2] and possibly damage to central nerve system [8]. It has been believed that oxidative stress significantly contributes to their pathogenesis.

Although the detailed mechanisms involving radiation-induced oxidative injury have not been fully understood, experimental investigations clearly demonstrated increased oxidative stress markers and reductions in antioxidants after long-duration space flights [5,12]. Radiation-induced chromosome damage in astronauts' lymphocyte may compromise host immune system to prevent tumor development [14]. Another factor of oxidative stress is the loss of protein secondary to reductive remodeling of skeletal muscle due to undernutrition in space [12].

The efficacies of hydrogen in various biological systems

Recent basic and clinical research has revealed that hydrogen is an important physiological regulatory factor with antioxidant, anti-inflammatory and anti-apoptotic protective effects on cells and organs. Since Ohsawa et al. [10] discovered that hydrogen gas has antioxidant and antiapoptotic properties that protect the brain against ischemia–reperfusion injury and stroke by selectively neutralizing hydroxyl radicals, hydrogen gas has come to the forefront of therapeutic medical gas research. Anaerobic organisms in the large intestine obtain their energy primarily by breaking down carbohydrates, mainly from the undigested polysaccharide fraction of plant cells and starches, via hydrogenase, and generate hydrogen in human body [13].

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0306-9877/$ - see front matter © 2010 Published by Elsevier Ltd.
doi:10.1016/j.mehy.2010.08.046

Please cite this article in press as: Schoenfeld MP et al. Hydrogen therapy may reduce the risks related to radiation-induced oxidative stress in space flight. Med Hypotheses (2010), doi:10.1016/j.mehy.2010.08.046

As oxidative damage is considered to be one of the critical issues in space travel, a number of efforts using the supplements providing antioxidants have been made to reduce oxidative stress and enhance antioxidant system in astronauts. Kennedy et al. demonstrated that exposure to space radiation may compromise the capacity of the host antioxidant defence system; this adverse biological effect can be prevented at least partially by dietary supplementation with agents expected to have effects on antioxidant activities [7]. Hydrogen therapy by simply delivering the gas through inhalation or drinking water could be a promising adjunct approach with anti-oxidant properties, and easy to incorporate in the daily life of astronauts during space mission.

Possible mechanisms of hydrogen as a therapeutic strategy

Although disparate mechanisms for the tissue and cellular protection afforded by hydrogen exposure have been proposed, the role of hydrogen as an antioxidant has been advocated. The antioxidant capabilities of hydrogen include activities as a scavenger of free radicals. Hydrogen selectively reduces hydroxyl (·OH) and peroxynitrite (ONOO−) radicals, which are the very strong oxidants that react indiscriminately with nucleic acids, lipids and proteins resulting in DNA fragmentation, lipid peroxidation, and protein inactivation. Biochemical experiments, using fluorescent probes and electron resonance spectroscopy spin traps, suggest that the effects of hydrogen against peroxynitrite are less potent than those against hydroxyl radicals [1]. Another possible mechanism underlying the cellular protection afforded by hydrogen may be an increase in antioxidant enzymes such as catalase, superoxide dismutase or heme oxygenase-1 [12,13].

The hypothesis

Based on preliminary experimental data, showing that hydrogen has potent protective effects for oxidative cellular/organ injury, we hypothesize that hydrogen gas may prevent oxidative injury related to cosmic radiation during space missions. The hydrogen gas at safe concentrations (<4.6% in air by volume) may be administered to astronauts via inhalation as room air in spacecraft. Another option can be the administration of solubilized hydrogen which may be delivered as drinking water. This may be more practical in daily life and more suitable for daily consumption for therapeutic use. Hydrogen-rich drinking water can be generated by several methods including dissolving electrolyzed hydrogen into pure water, dissolving hydrogen into water under high pressure, and utilizing electrochemical reaction of magnesium with water ($Mg + 2H_2O \rightarrow Mg(OH)_2 + H_2$). This study will open a new preventative/therapeutic avenue combining the field of therapeutic medical gases and space radiation.

Cosmic radiation results in the selective detrimental effects of HZE particles on the dopaminergic system, which is similar to the pathophysiology of Parkinson's disease [8]. In addition, diabetogenic problem associated with increased C-peptide excretion and insulin resistance [15], as well as constipation due to malfunction of intestine. We assume that countermeasures with hydrogen therapy for these events coincided in space travel may ameliorate symptoms, as the effects of hydrogen for diabetes [6], Parkinson's disease [4] and bowel dysfunction [3] have been shown in relevant ground-based (animal) models.

Evaluation of the hypothesis

The rationale behind this hypothesis is as follows: Qian et al. [11] reported that treating cells with hydrogen-rich cultured media before irradiation could significantly inhibit ionizing irradiation-induced Human lymphocyte AHH-1 cells apoptosis and increase cells viability *in vitro*. This group also show that hydrogen-rich saline intraperitoneal injection in a mice model before radiation exposure can protect gastrointestinal endothelia from radiation-induced injury, decrease plasma malondyaldehyde and intestinal 8-hydroxydeoxyguanosine (8-OHdG) levels and increase plasma endogenous antioxidant, including superoxide dismutase (SOD) and glutathione reductase.

The safety of hydrogen for humans is demonstrated by its application in Hydreliox, an exotic breathing gas mixture of 49% hydrogen, 50% helium and 1% oxygen, which is used for the prevention of decompression sickness and nitrogen narcosis during very deep technical diving [1]. Also no adverse effects have been found using drinking hydrogen water in a human study [6,9]. While hydrogen gas mixtures have the potential to create fire, deflagration and detonation hazards, the potential for such hazards can be addressed through proper precautions. If the spacecraft cabin pressure is comprised of hydrogen and air and contained less than 3.9 vol.% of hydrogen, the atmosphere would not be flammable. Furthermore, these limits vary depending upon the temperature, amount of hydrogen, and the amount and type of gas mixture.

More studies are warranted to apply hydrogen therapy for space travel. The issues associated with the dissolution of hydrogen in water are the ability to dissolve and maintain the desired concentrations of dissolved gas within the water prior to consumption. However, we believe that hydrogen represents a potentially novel therapeutic and preventative strategy for radiation-induced oxidative injuries during space missions.

Conflicts of interest statement

None declared.

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