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Contents

Journal of Aeronautic Dentistry, Medicine and Space Technology
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Editorial

Salivary Proteomics in Microgravity

Indulgenting gene expression is the key to unfolding the mechanisms behind, and ultimately, finding effective countermeasures to spaceflight-induced alterations in oral cavity. Significant progress has been made in identifying the genes responsible for these changes. Although many of these genes were observed to be either upregulated or downregulated, there is a lack of systemic study of gene and protein expression in individual cells exposed to microgravity. Models for long-term study of the effects of microgravity on cells in vitro and possible countermeasures are essential as we send astronauts on long-term missions, i.e., to Mars and back. In the future it will be important to design human bed rest and NASA studies to determine the optimal combination of countermeasures. In addition to modifications related to gravity alone, it will be important to understand the potential effects of co-exposure to cosmic radiation to provide the maximum possible protection to astronauts.

Balwant Rai
Editor-in-Chief

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Anti-oxidation actions of Indian spice in simulated microgravity

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ABSTRACT

The effect of microgravity is more pronounced after long-duration space flights and can even last for several weeks after landing. The extensive research is going on the preventation of peroxidative damage due to microgravity. It has been evident that curcumin (diferuloylmethane), a yellow pigment in curry powder exhibits antioxidant, anti-inflammatory, and proapoptotic activities. To determine the preventive effects of curcumin on peroxidative damage due to two bed rest conditions, 20 healthy male volunteers were equally divided into two groups (10 with curcumin and 10 without curcumin). They were studied in condition before, during, and just on bed rest conditions at -6° head-down-tilt (HDT) bed rest for 10 days. We measured the salivary and serum oxidative markers such as Malonaldehyde, 8-hydroxydeoxyguanosine, vitamin C and E just before HDT , during HDT experiment, and in course time of recovery with curcumin and without curcumin groups. The values of serum and salivary Vitamin C & E showed statistically significant decrease in both bed rest conditions as compared to the condition before and during the recovery stage. However, levels were not significantly lowered in curcumin groups in contrast to the groups without curcumin (Table-1, $P<0.05$) . MDA and 8-OHdG levels showed significant increase in simulating microgravity condition as compared to the condition before and in the recovery stage. Hence, curcumin prevent peroxidative damage in simulated conditions. Further study is required on antioxidation actions of curcumin in space microgravity conditions.

Key Words: Curcumin, Serum, Saliva, oxidative stress, two bed rest position, space microgravity.

INTRODUCTION

Current projects on missions to Mars results in 2 years of microgravity conditions, demands the critical need for the development of optimal nutritional programs and physical counter-measures to prevent body mass and functional alterations. On long duration space flights such as mars mission, astronauts undergo many physiological changes such as loss of bone mass, muscle strength, and cardiovascular fitness as a result of reduced metabolic activities, lower cellular and reduced tissue oxygen demand 1-12. There exists a balance in the body between oxidant production and antioxidant defence, with the balance shifted slightly in favour of oxidants 1-3. Mainly products of this "leakage" are the two ROS: superoxide radical (O2_) and H2O2 2. Other ROS includes the free radicals such as nitric oxide and compounds such as ozone and HOCl. ROS can attack and damage cellular constituents such as DNA, proteins, and membrane lipids. Oxidative damage from free radicals to DNA and lipids has been implicated in the etiology of a wide variety of chronic diseases and acute pathologic states 2-8. The chronic diseases range from oral diseases such as periodontitis and oral cancer to cardiovascular diseases and neuro-

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degenerative diseases including Alzheimer and Parkinson diseases.9-13 It has been observed that there is an increased lipid peroxidation in human erythrocytic membranes and reductions in some blood anti-oxidants after long-duration space flights 13-15 It has also been observed that there was urinary excretion of 8-iso-prostaglandin F2- and 8-oxo-7,8 dihydro-2 deoxyguanosine (8-OHdG) in six subjects during and after long-duration space flights (90 to 180 d) 16-17. Isoprostane 8-isoprostaglandin F2- and 8-OHdG are the markers for oxidative damage to lipids and DNA respectively 16-17 . Most rodent studies showed increased production of lipid peroxidation products in postflights and decreased antioxidant enzyme activity in same post-flights 18. It has been found that space flights simultaneously down regulate anti-oxidant defence capacity and elicit an oxidative stress in the liver. There was an approximately 50% increase in the liver malondialdehyde concentration with space flights19. Vitamin E is the primary chain-breaking anti-oxidant in the cell membranes 9,20,21. The protective role of vitamin C seems to lie in its ability to reduce the oxidized form of vitamin E, thereby making it reusable by the cell 9,23.

Curcumin (diferuloylmethane), a dietary pigment responsible for the yellow color of turmeric is used as a traditional medicine well documented in the Ayurveda for the treatment of numerous inflammatory conditions. Extensive research within the past half-decade has confirmed that curcumin mediates anti-inflammatory effects through the downregulation of transcription factor, nuclear factor-?B (NF-?B) , tumor necrosis factor (TNF) , interleukin-6 , interleukin-8 , adhesion molecules , inducible nitric oxide synthase (iNOS) , matrix metalloproteinase-9 (MMP-9) , cyclooxygenase-2 (COX-2) , 5-lipoxygenase (5-LOX), and glutathione reverses the inhibition 24-34 . It has been reported that Curcumin act as anti-oxidant agent 30-34. Curcumin has shown that agent can be administered safely at a oral doses of up to 8 g/d .There was no dose-limiting toxicity; dosing was limited by the number of pills that patients could or would swallow daily 35-36. Hence, this study was planned to study the effect of curcumin on serum and salivary markers of oxidative stress in simulated microgravity.

MATERIALS AND METHODS

The subjects of this investigation were 10 male volunteers aged (18-22 years, mean weight of 72.5 +_ 3.2 kg and mean height of 174.9+_ 3.4 cm) participated in an 8-hour 6° HDT bed-rest exposure (18-21 years, mean weight of 71.8 +_ 2.3 kg and mean height of 174.8+_ 3.3 cm) and bed rest position (18-24 years, mean weight of 73.6 +_ 3.4 kg and mean height of 175.1+_ 4.1 cm), who had not participated in systemic endurance training for 10 days prior to study and each subject was given a detailed explanation of the experimental protocol and were provided written and verbal consent. Each subject completed a medical and dental history questionnaire to determine the status of systemic diseases, smoking, alcoholic and drugs history as well as clinical examination for systemic diseases, chronic diseases and oral & dental diseases. Patients were excluded from study who had systemic diseases, chronic diseases, oral & dental disease, smoking, alcoholic and drugs history. Five volunteers of each HDT was selected and given a curcumin once a day and others five volunteers of each HDT was not given anything.

Curcumin- 1 g caplet form Curcumin (900 mg curcumin, 80 mg desmethoxycurcumin, and 20 mg bisdesmethoxycurcumin) from Sabinsa was obtained .

Blood and saliva samples were taken just before HDT, throughout the time course of the HDT experiment, and during recovery period. Subjects were asked to awake at 6 A.M on the day of the study and to remain seated or in standing position until arrival at the research centre. Baseline control measurements were obtained during the hour before HDT. At -9 A.M. the subjects were transferred supine to a gurney and tilted to 6' HDT, where they remained for the next 8 h. At -5 P.M. till 10 days, after 10 days the subjects returned to a

chair and stayed in seated position for the 4-h recovery period. Blood and saliva samples were prepared at the same time.

Whole unstimulated saliva was collected over a five-min period from subjects with directions to allow saliva to pool at the bottom of the mouth and drain into a collection tube, when necessary. Unstimulated whole saliva produced in a 5-min period (about 3 mL) was collected, allowed to drain into a plastic container, and centrifuged at 3,000 ×g in 4°C for 5 min to remove bacterial and cellular debris. Saliva samples were stored at -80°C until analysis. Blood samples were collected into Vacutainer tubes. The blood was centrifuged at 1,700 g for 10 minutes and the plasma was separated. Plasma was stored at -80°C until analysis. Serum and salivary levels were assessed for MDA using thiobarbituric acid (TBA) method of Buege and Aust 37 . Concentrations of both vitamins were measured using liquid chromatography 38 .Quantitative measurements of the oxidative DNA adduct 8-OHdG was performed according to the method described by Toyokuni et al.39 Briefly, the saliva samples were centrifuged at 10,000g for 10 minutes and the supernatant was used to determine 8-OHdG levels with a competitive ELISA kit (Japan Institute for the Control of Aging, Shizuoka, Japan). The determination range was 0.5-200 ng/mL. Serum 8-OHdG levels were measured in duplicate by a competitive ELISA kit (OXIS, Portland, OR, USA) according to the manufacturer's instructions. The sensitivity of the method was 1 ng/ml. All data were statistically analyzed using SPSS statistical package (SPSS, version13, Chicago,IL,USA). Data were expressed as mean ± standard deviation. Differences between pre, during and after microgravity simulation were analyzed for significant values using one-way ANOVA test. Correlation assessment was performed using the Spearman correlation analysis. Statistical significance was defined as $p< 0.05$.

RESULTS

The values of serum and salivary Vitamin C & E showed statistically significant decrease in simulating microgravity as compared to the period before and during the recovery stages, with and without Curcumin groups. It was also observed lower in recovery stage as compared to the period before when examined in microgravity conditions (Table-1&2, $P<0.05$). However decrease in curcumin groups was lower as compared to that examined in without curcumin groups. MDA and 8-OH dG levels showed statistically significant increase in both conditions as compared to period before and in recovery stages, also observed relatively higher in without curcumin groups as compared with curcumin groups (Table-1&2, $P<0.05$).

DISCUSSION

In the present study, serum and salivary Vitamin C & E values were significantly lowered in condition and in both groups (Table-1, $P<0.05$) which support the previous studies 40-42. Decreased anti-oxidant defence may be one of the reasons for increased levels of ROS and subsequent tissue damage in two bed rest conditions. MDA levels in both rest conditions environment were significantly elevated in both groups in contrast to the period before and in the recovery stages. This indicates that increased lipid peroxidation due to 'free radical'-mediated injury occurs in the both rest conditions. Increased lipid peroxidation can occur if the rate of production of reactive oxygen species is higher or the antioxidant level is low which concur with the previous studies 40-44. The 8-OHdG levels were increased in both conditions as observed in the previous studies 28, 30-33. Different aspects of oxidative stress are measured by 8-OHG namely DNA damage and cell membrane damage respectively 44-48. The increased 8-OHG, MDA levels and decreased Vitamin C and E levels were low in curcumin groups as compared to the values observed in without curcumin groups in accordance with the previous studies 34 . Several reports suggest that curcumin can induce ROS 47,48 . There are also reports which suggest that curcumin quenches ROS production and thus acts as an

Table-1 Salivary and serum MDA, Vitamin C& E and 8 dihydro-2 deoxyguanosine (8-OH dG) concentrations in the plasma and saliva of 20 Normal healthy subjects in period before HDT without Curcumin (A), throughout the time course of the HDT experiment (B), during recovery (C) and before HDT with Curcumin (AA), throughout the time course of the HDT experiment (BB), during recovery (CC)

Markers	Serum and saliva	A	AA €	B	BB £,€	C	CC £
MDA	Salivary (µmol/L)	0.24±0.06*	0.22±0.13	0.34±0.12*,a	0.25±0.14	0.25±0.13*	0.24±0.23
	Serum (µmol/L)	1.14 ±0.37*	1.06 ±0.89	1.36 ±0.36*,a	1.01 ±0.68	1.18 ±0.24*	1.01 ±0.75
Vitamin C	Salivary (µg/L)	1.01±0.32*	1.56±0.66	0.82±0.21*,a	1.23±0.67	0.97±0.24*	1.29±0.68
	Serum (µg/L)	8.23±1.23*	8.96±2.46	7.56±1.89*,a	8.82±2.33	8.05±1.95*	8.88±2.86
Vitamin E	Salivary (µg/L)	0.43±0.12*	0.56±0.46	0.31±0.14*,a	0.48±0.45	0.41±0.16*	0.54±0.29
	Serum (µg/L)	8.01±1.12*	8.46±2.32	7.32±1.21*,a	8.23±3.34	7.90±1.12*	8.94±3.32
8-OH dG	Salivary (ng/ml)	0.32±0.04*	0.22±0.13	0.45±0.07*,a	0.24±0.11	0.38±0.08*	0.22±0.12
	Serum (ng/ml)	2.12 ± 1.24*	1.45 ± 1.11	2.79 ± 1.23*,a	1.89 ± 1.36	2.32 ± 1.26*	1.77 ± 1.12

*p < 0.05, as compared to after condition (C)
ap < 0.05, as compared to Before condition (A).
£p < 0.05, as compared to after condition (CC)
•p < 0.05, as compared to Before condition (AA).

antioxidant 49. Other reports suggest that curcumin quenches ROS production at low concentrations and induces ROS production at high concentrations 50. It might be like the vitamin C which acts as both a pro-oxidant and an antioxidant. Whereas the pro-oxidant mechanism mediates apoptotic effects, the antioxidant mechanism mediates NF-?B-suppressive effects.

Hence, Microgravity condition had not only systemic alterations but it also lowered the oral antioxidant levels. Antioxidant defence (vitamin E and C) was compromised and oxidative stress was higher in both rest condition. Hence, better formulations of curcumin might provide more antioxidant effects. Further study is required on the effect of curcumin as an anti-oxidant agent in microgravity & zero gravity conditions.

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Microgravity and Oral cavity: BR study review

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ABSTRACT

For many years, the prevailing concept in space human factors research has been that microgravity has an impact on human physiology and astronauts are faced with several health risks during both short and long duration spaceflights. The review of our study found that reversible effect of microgravity is oedema of face, change in taste, abnormal expression of face, teeth pain and xerostomia. The non reversible effects of microgravity such as periodontal disease, dental caries but in different pattern than normal, stone formation in salivary duct, pre cancer or cancer, fracture of maxillary and mandibular bone and xerostomia are more prevalent in astronauts as compared to normal persons. Further study will be required on large scale on long term effects of microgavity on oral cavity to prevent the adverse effects.

Key words: Mars mission, human factors, Microgravity, Aeronautic Dentistry

INTRODUCTION

For many years, the prevailing concept in space human factors research has been that microgravity has an impact on human physiology and astronauts are faced with several health risks during both short and long duration spaceflights. Some of these health problems include bone loss, muscle atrophy, cardiac dysrhythmias, and altered orientation (Herault et al., 2000; Oganov et al. 1992). Our previous studies observed some adverse effects of simulated microgravity (HDT bed rest condition) on oral cavity (Rai, 2007; Rai, 2009; Rai et al., 2010). This paper reviews the adverse effect of microgravity on oral cavity.

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RESULTS AND DISCUSSIONS

Flow rate, sodium, potassium, calcium, phosphate, protein levels were increased in simulation environments as compared to normal, while same findings were observed in urine (Rai et al, 2009; Zerwekh, 2002). Increased bone resorption contribute significantly to raise the salivary state of saturation with respect to the calcium salts, namely calcium oxalate and calcium phosphate. In addition, other environmental and dietary factors may adversely affect salivary composition and increase stone formation risk during space flight. Although observations to date have suggested that there could actually be a reduced food intake during the early phase of flight, crew members on longer-duration flights could also increase food intake and be at increased risk for salivary stone formation. The most important effect of restricting energy intake is on calcium and bone metabolism. The MIP 1 alpha level was decreased in microgravity which is potential markers of bone loss (Rai et al , 2009; Fine et al, 2009). In agreement with earlier reports (Kirsch et al., 1984; Parazynski et al., 1991; Watenpaugh et al., 1992) , they found a 9%

increase in plasma protein concentration on flight day 1, and a 17% reduction in plasma volume by 22h of flight. This agrees with the early in-flight hemoconcentration seen by others (Kirsch et al., 1984) and establishes that plasma volume contraction occurs quickly in microgravity. This hemoconcentration probably results from increased upper-body vascular pressures in microgravity (Parazynski et al., 1991) and perhaps reduced interstitial pressures ; both factors would encourage transcapillary fluid filtration into upper-body interstitial spaces, and substantial filtration can occur in minutes (Watenpaugh et al., 1992). Increased plasma protein concentration increases plasma colloid osmotic pressure and, therefore, opposes capillary filtration. An increased fluid excretion was observed in simulated microgravity leads to dehydration and finally to a reduction of plasma volume and an increase in the haematocrit. A reduction of plasma volume may result in increase in serum electrolyte levels, and therefore serum osmolality and urine osmolality increase too. The plasma volume decrease together with increases in serum and urine osmolality and electrolyte levels, influences body fluid regulation by activating hormonal regulatory factors, i.e. vasopressin, renin and aldosterone .The levels of calcium were increased in microgravity as compared to control. Insufficient calcium consumption leads to a reduction in serum calcium levels and thereby to a secretion of parathyroid hormone (PTH) and calcitriol synthesis. Both a rise in PTH and calcitriol induce an increase in calcium retention either from the intestine or from bone. Based on that, a long-lasting insufficient calcium intake together with insufficient vitamin D are the main factors leading to a decrease in bone mineral density (Bronner , 1996) . The decreased levels of vitamins E and C and increased in malonaldehyde levels denoted increased in free radical activity as in microgravity environments (Bigard et al, 1998). So, the free radical activity increased in microgravity as compared to normal gravity. The 8-hydroxy deoxyguanosine levels were increased in saliva in microgravity environments' as compared to normal, it may be due to increased in oxidative stress (Bigard et al, 1998). The threshold for MSG and capsaicin increased about 1.5 dilution step, while sodium chloride decreased about 2 dilution during microgravity as compared to normal. It might be due to fluid shift mechanism. Mild pain of teeth, facial oedema, mild pain at mandibular angle regions, pain in sublingual and submandibular opening duct regions, abnormal facial expression, loss of sensation of pain and temperature, decreased tongue and mandibular movements in simulation microgravity environment were observed. It could be due to physiological changes including an upward shift of body fluids toward the head, which may lead to an attenuation of the olfactory component in the flavour of foods, pressing the nerve regions or dysfunction of nerve as well as increased activity of b-AR agonists (Vicker et al, 2001). These results suggest that reversible effect of microgravity is oedema of face, change in taste, abnormal expression of face, teeth pain and xerostomia. The non reversible effects of microgravity such as periodontal disease, dental caries but in different pattern than normal, stone formation in salivary duct, pre cancer or cancer, fracture of maxillary and mandibular bone and xerostomia are more prevalent in astronauts as compared to normal persons.

Further study will be required on large scale and on long term effects of microgavity on oral cavity to prevent the adverse effects.

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Salivary and serum 8-hydroxydeoxyguanosine level in long term simulated microgravity

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ABSTRACT

Background: Microgravity is associated with an increased of peroxidative. The effect is more pronounced after long duration space flight and can even last for several weeks after landing. Objective: To determine the influence of a simulated microgravity on antioxidant status of the body, 10 healthy volunteers were studied in condition before, during, and just after the simulated microgravity of -6 head -down -tilt (HDT) bed rest for 120 days. We measured the salivary and serum 8-hydroxydeoxyguanosine before, during and recovery of HDT.

Results and conclusions: The 8-hydroxydeoxyguanosine showed significant increase in simulating microgravity. The data provides evidence that oxidative stress is among critical nutritional concerns for long duration space travellers.

Key words: Microgravity, 8-hydroxydeoxyguanosine, head -down -tilt

INTRODUCTION

On long duration space flights such as mars mission, astronauts undergo many physiological changes such as loss of bone mass, muscle strength, and cardiovascular fitness, as a result of reduced metabolic activities and lower cellular and tissue oxygen demand 1. There is a balance within the body between oxidant production and antioxidant defences, with the balance shifted slightly in favour of oxidants. Mainly products of this "leakage" are the two ROS: superoxide radical (O2_) and H2O2. Other ROS include free radicals such as nitric oxide and compounds such as ozone and HOCl. ROS can attack and damage cellular constituents such as DNA, proteins, and membrane lipids. Oxidative damage from free radicals to DNA and lipids has been implicated in the etiology of a wide variety of chronic diseases and acute pathologic states. The chronic diseases range from oral disease such as periodontitis and oral cancer to cardiovascular disease and neurodegenerative disease including Alzheimer and Parkinson diseases.2-12It has been observed that increased lipid peroxidation in human erythrocyte membranes and reductions in some blood antioxidants after long-duration space flight 13-15 It has been observed that the urinary excretion of 8-iso-prostaglandin F2_ and 8-oxo-7,8 dihydro-2 deoxyguanosine (8-OH dG) in six subjects during and after long-duration space flight (90 to 180 d). Isoprostane 8-isoprostaglandin F2_ and 8-OH dG are markers for oxidative damage to lipids and DNA, respectively 16-17. Both non-radical and radical species have been demonstrated to be capable of degrading in vivo proteoglycans, which are the main components of the basic substance of connective tissue. Hyaluronic acid depolymerization caused by ROS may be characterized by glycoside bond fragmentation

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between monomers (between glucuronic acid and acetylglucosamine) 18-19. Many other extracellular matrix components (collagen,fibronectin, laminin) have been found to be degraded to low-molecular-weight peptides. For homeostasis, extra- and intra-cellular preventive mechanisms must exist. This function is played by antioxidants, which may be regarded as those substances which, when present at low concentrations compared with those of an oxidizable substrate, will significantly delay or inhibit oxidation of that substrate 19-20.

There is no study on the correlation of blood and saliva 8-OHdG in simulating microgravity environments. Hence, this study was designed to examine oxidative marker 8 dihydro-2 deoxyguanosine (8-OH dG) concentration in the blood and saliva of Normal healthy subject in simulated microgravity condition of -6° head-down-tilt (HDT) bed rest.

MATERIALS AND METHODS

The subjects of this investigation were 10 male volunteers aged (18-22 years, mean weight of 72.5 +_ 3.2 kg and mean height of 174.9+_ 3.4 cm) participated in 6°HDT bed-rest exposure and who had not participated in systemic endurance training for 100 day prior to study and. Each Subject was given a detailed explanation of the experimental protocol and provided written and verbal consent. Each subject completed a medical and dental history questionnaire to determine the status of systemic diseases, smoking, alcoholic and drugs history as well as clinical examination for systemic disease, chronic diseases and oral & dental diseases. Persons were excluded from study who has systemic diseases, chronic diseases, oral& dental disease, smoking, alcoholic and drugs history. The average energy and calcium expended by the subjects during the simulation was 2300 kcal/ day (range 2080-3010 kcal/day) and 1200 mg/day, respectively.

Blood and saliva samples were taken just before HDT, throughout the time course of the HDT, during and recovery. Subjects were asked to awaken at 6 A.M. on the day of the study and to remain seated or standing until arrival at research centre .Baseline control measurements were obtained during the hour before HDT. At -9 A.M. the subjects were transferred supine to a gurney and tilted to 6' HDT, where they remained for the next 8 h. At -5 P.M. till 10 day, after 10 day the subjects were returned to a chair and remained in a seated position for the 4-h recovery period. Blood and saliva samples were prepared at the same time.

Whole unstimulated saliva was collected over a five-min period from subjects with instructions to allow saliva to pool in the bottom of the mouth and drain into a collection tube, when necessary. Unstimulated whole saliva produced in a 5-min period (about 3 mL) was collected, allowed to drain into a plastic container, and centrifuged at 3,000 ×g, in 4°C for 5 min to remove bacterial and cellular debris. Saliva samples were stored at -80°C until analysis. Blood samples were collected into Vacutainer tubes. The blood was centrifuged at 1,700 g for 10 min and the plasma was separated. Plasma was stored at -80°C until analysis. Quantitative measurement of the oxidative DNA adduct 8-OHdG was performed according to the method described by Toyokuni et al.21 Briefly, the saliva samples were centrifuged at 10,000g for 10 minutes and the supernatant was used to determine 8-OHdG levels with a competitive ELISA kit (Japan Institute for the Control of Aging, Shizuoka, Japan). The determination range was 0.5-200 ng/mL. Serum 8-OHdG levels were measured in duplicate by a competitive ELISA kit (OXIS, Portland, OR, USA) according to the manufacturer's instructions. The sensitivity of the method was 1 ng/ml.All data were statistically analyzed using SPSS statistical package (SPSS, version13, Chicago,IL,USA). Data are expressed as mean ± standard deviation. Differences between pre,during and after microgravity simulation were analyzed for significance using one-way ANOVA test. Correlation assessment was performed using the Spearman correlation analysis. Statistical significance was defined as $p < 0.05$.

RESULTS

The 8-OH dG level was statistically significant increased in simulating microgravity condition as compared to before and recovery stage , also relatively higher in recovery stage as compared to before simulation of microgravity (Table-1, P<0.05). Serum and salivary correlation ananlysis revealed strong and highly significant correlation for 8 -OHdG (r=0.89) in before , during and in recovery stimulated microgravity.

DISCUSSIONS

In present study , serum and salivary 8-OHdG levels were increased in simulated microgravity environments as compared to before & recovery simulated microgravity as in previous studies 21-23. The simplest explanation for the increased oxidative damage simulated microgravity in humans is that the increase is due to a combination of 1) the consequences of the loss of protein secondary to simulated reductive remodeling of skeletal muscle from the decreased work load on the antigravity muscles, 2) the simulated microgravity protein depletion from inadequate dietary intake, and 3) the increased anabolism associated with protein repletion. With increased generation of adenosine triphosphate, leakage of ROS from the mitochondrial electron transport chain will be increased. 2 There is another factor that can lead to decreased production of antioxidant defenses postflight, which is the suboptimal synthesis of host (defense) proteins. There is some evidence that the synthesis of host antioxidant protein defenses could be suboptimal due to competition for amino acids occurring between repleting muscle and other tissues.24 The change we identified after the exposure to microgravity are transient and reversible. Four hours the end of the exposure to microgravity 8-OHdG , we examined had returned to approximately same as that of before. If enough time is given to marsonaunts or astronauts to become its initial conditions that would result in an undetectable condition of risk. The combination of muscle decompensation and nutritional depletion would place astronauts in this category. The principal difference between the ground-based exercise studies and the space-flight situation is that the ground-based studies lack the undernutrition component. Another difference between the space-flight situation and the groundbased exercise studies is that the concerns of the latter are directed toward performance, whereas for the astronauts the concern is for long-term damage. So , in Simulated microgravity may show less oxidatative stress as compared to real microgravity condition. Providing additional dietary antioxidants during and recovery process may decrease the oxidative damage.

Table-1 Salivary and Serum 8 dihydro-2 deoxyuanosine (8-OH dG) concentration in 10 Normal healthy subject in before HDT (A), thought the time course of the HDT experiment (B), and during recovery (C)

Sr.no	8-OH dG	A	B	C
1	Salivary (ng/ml)	0.45±0.02 **(0.34-0.65)**	0.67±0.06 **(0.56-0.87)**	0.48±0.08 **(0.41-0.68)**
2	Serum	2.21±1.08 **(1.98-2.67)**	3.45±1.12 **(2.98-3.89)**	2.78±1.15 **(2.01-2.89)**

P<0.05

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Risk of Compromised EVA Performance in MDRS: A personal views

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ABSTRACT

Group program missions to the moon and Mars will include as many as 24 hours of EVA per crew member per week, which will involve the performance of exploration, science, construction, and maintenance tasks. The effectiveness and success of these missions is dependent on designing EVA systems and protocols that maximize human performance and efficiency while minimizing health and safety risks for crew members.It is very importantl to understand the effects of EVA system design variables such as suit pressure, weight/ mass, joint ranges of motion, and biomedical monitoring on the ability of astronauts to perform safe, efficient, and effective EVAs. This report describe the problems faced by MDRS health officer during two weeks MDRS mission.

INTRODUCTION

Fewer than 20 lunar EVAs were performed during the entire Apollo Program. Providing the capability for humans to work productively and safely while performing an EVA involves many

important, medically related considerations. Maintaining sufficient total pressure and oxygen, other survival enmity is vital not only to human health, but also to survival.

NASA report identifies and describes the various risks and associated evidence as follows:

*Risks to Crew Performance: EVA Suit Design Parameters

*Risks to Crew Performance, Health, and Safety: EVA Biomedical Monitoring and Consumables

MANAGEMENT

*Risks to Crew Health: EVA Suit Design Parameters

*Risks to Crew Health: Decompression Sickness

*Risk to Work Efficiency: EVA Suit Design Parameters

GROUND-BASED EVIDENCE

Physiologists and physicians are using various analog environments to study the effects of suit weight, mass, CG, pressure, biomechanics, and mobility on human performance. Test activities are designed to characterize performance during ambulation and exploration-type tasks such as ambulation on both level and inclined surfaces, ambulation while carrying a load, rock collecting, shoveling, and kneeling. Other studies examine recovering from a fall and simple exploration and construction tasks using hand tools and power tools. Data collected include metabolic rates, subject anthropometrics, time series motion capture, ground reaction forces (GRFs), subjective ratings of perceived exertion (RPEs) (1), and operator compensation using a relative subjective scale. The operator compensation scale, the gravity compensation and performance scale (GCPS), is modeled after the Cooper-Harper rating scale (2) and is described.

It has been suggested that EVA performance on the lunar surface may not provide sufficient loading to protect against bone loss, thus

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indicating the continued need for exercise countermeasures (3). Recognizing that not all ambulation on the moon will be similar to that on a level treadmill, EPSP personnel have initiated studies to characterize the effects of incline and terrain on metabolic rate. Inclined walking trials have shown that the metabolic cost of the suit that is due to factors other than suit weight goes to almost zero, indicating an energy recovery component of the suit that is currently not well understood (4). The studies assessed crew performance of representative planetary exploration tasks using a single EVA suit weight with six different CG locations. A reconfigurable backpack that has repositionable weight modules was used to simulate perfect, low, forward, high, aft, and NASA baseline CG locations under the assumption of a 60-lb. suit, a 135-lb. Portable Life Support System (PLSS), and a reference 6-ft, 180-lb subject. Subjects used the GCPS rating tool to evaluate the CG locations.

Thermal homeostasis of the crew member is crucial for safe and effective EVA performance. Heat storage above 480 Btu/hr leads to performance decrements, such as a loss of tracking skills and increased errors in judgment, and tissue damage begins at 800 Btu heat storage (1-3). The observations from the Gemini experience led to the development of a liquid cooling system that could accommodate high heat production in the suit from high EVA workloads. This liquid cooling garment (LCG) consists of a system of plastic cooling tubes that run along the inside of an undergarment that is worn inside the suit. The temperature of the coolant (water) running through the tubes regulates the amount of heat that is removed from the surface of the skin. The Apollo LCG had three temperature settings: minimum (69.8°F/21°C), intermediate (59°F/15°C), and maximum (44.6°F/7°C) (4). Astronaut energy expenditure rates during Apollo lunar surface EVAs ranged from 780 to 1,200 Btu/hr, as determined by three independent methods (5). The lowest metabolic rates occurred while the astronauts drove and rode in the lunar rover vehicle, while the highest metabolic rates were observed during egress/ingress through the tight-fitting hatch of the lunar module, offloading and setup of equipment, drilling, and stowage of lunar samples. It is estimated that 60% to 80% of the heat that was generated with these workloads was dissipated through the LCG. The minimum and intermediate LCG settings were most commonly used; however, the maximum setting was frequently used during the high workload periods that were experienced during Apollo 15 and Apollo 17 EVAs .

NUTRITION, HYDRATION, AND WASTE MANAGEMENT

The longer and work-intensive EVAs that are planned for future Exploration missions will also need to account for astronaut nutrition, hydration, and waste management. Specifically, dehydration is an issue that can lead to poor crew performance.

BIOMEDICAL MONITORING

Flight surgeons and biomedical engineers (BMEs) in the Mission Control Center monitor astronaut physical parameters during EVAs to assess workload and performance. Real-time medical monitoring can provide emergency medical assistance in response to off-nominal situations. However, bioinstrumentation systems that were used in the Apollo Program and are being used in the Space Shuttle Program have been problematic.

RISK IN CONTEXT OF EXPLORATION MISSION OPERATIONAL SCENARIOS IN MDRS

Current plans call for each crew member to perform up to 24 hours of EVA per week It is evident ce section of this chapter, the risks that are associated with any inadequacies that exist in current EVA suit designs - particularly with respect to suit-induced trauma - will be greatly amplified by such frequent EVAs.

Current CxAT-Lunar mission architectures include small pressurized rovers (SPRs) as a

core element of the surface mobility system. The implications of SPRs on crew health, safety, productivity, and efficiency are potentially enormous. The availability of a pressurized safe-haven within 20 minutes at all times to provide DCS. Human Health and Performance Risks of Space Exploration Missions Chapter 14. Risk of Compromised EVA Performance and Crew Health. Due to Inadequate EVA Suit Systems 353 treatment, SPE protection, and on-site treatment of or medication for an injured crew member would significantly reduce many of the risks associated with planetary exploration. Furthermore, because crew members would be inside the SPRs during most surface translations, the overall number of in-suit EVA hours to achieve the same (or greater) science/ exploration return would be reduced. The possibility of performing single-person EVAs with a second crew member inside the SPR would further reduce total EVA hours during the lunar architecture to the same order of magnitude as during ISS construction. As a result, the number of cycles on the EVA suits would be decreased, thereby increasing the life of each EVA suit and reducing EVA risk for crew members.

CONCLUSION

The CxP will be more dependent on EVA excursions away from a pressurized habitat or vehicle than any program in the history of NASA. EVAs will be required to conduct planned scientific expeditions, assemble structures, perform nominal maintenance, and intervene and solve problems outside of the vehicle that cannot be solved either robotically or remotely. The ultimate success of future Exploration missions is dependent on the ability to perform EVA tasks efficiently and safely in these challenging environments.

With lunar missions planned for up to 30 times more EVA hours than during the Apollo era, exploration missions to the moon and Mars will present many new challenges with regard to crew health, safety, and performance. To date, our understanding of human health and performance parameters in partial-gravity environments is limited to observations of, and lessons learned from, Apollo-era astronauts who performed EV.

As on the lunar surface. Since the Apollo Program, and using lessons learned from microgravity EVAs aboard the space shuttle and ISS, new prototype suits have been in development for future space exploration activities. However, to date there has been limited quantification of the physiological and biomechanical variables associated with suited activities in unit and partial gravity. The integrated human testing program that is under way at NASA will help to better characterize the impacts to crew health and performance of the various parameters that are involved in EVA suit design.

Collaborative work is also under way to enable the development of suit technologies that enhance crew comfort and efficiency; provide for optimal nutrition, hydration, and waste management; and reduce suit-induced trauma and fatigue. These efforts will provide objective data to enable informed requirements and the design of Constellati on suit systems that will provide sufficient protection and life support for nominal zero-G and surface activities, as well as survival for contingency operations.

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6. Human Health and Performance Risks of Space Exploration Missions Chapter 14.
7. Risk of Compromised EVA Performance and Crew Health Due to Inadequate EVA Suit Systems 357.

APPENDIX A: GRAVITY COMPENSATION AND PERFORMANCE SCALE 24

The Cooper-Harper scale, which has been in wide use since the late 1960s, permits quantification of pilot perceptions of aircraft handling characteristics. Most of the participants in EPSP studies are astronauts, many of whom are pilots and familiar with the use of this scale; however, the scale itself assumes a certain level of consistency in both pilot skills and specifications of the desired aircraft performance. In the development of next-generation EVA suits for Exploration missions, NASA requires controlled evaluations of varied suit concepts across an ambitious range of activities. These evaluations must be performed by astronauts or test subjects whose skills are limited to microgravity and/or simulated partial-gravity environments - far from equivalent to the skilled pilot population for whom the Cooper-Harper scale was originally designed.

EVA suit development for lunar and martian surface operations will require a wide range of evaluationsencompassing tasks as varied as habitat building, traversing rocky terrain, core sampling, shoveling, and, potentially, rescuing an incapacitated crew member. In addition, suit concepts vary widely in mass, weight, CG, and pressure, and each must be evaluated across this range of tasks. NASA does not currently have rigorous performance measures for such tasks, and the EPSP Project personnel have begun the process of characterizing human-suit system performance under a variety of conditions and suit concepts using available analog facilities.

Due to the many limitations of using the Cooper-Harper scale under these circumstances, scientists in the EPSP Project adapted the Cooper-Harper scale to reflect handling/controllability characteristics of task performance in reduced-gravity environments when compared relative to one's own shirt-sleeved performance of the same task in 1g. This modified scale, the GCPS, is shown on the following page. Using this scale, a rating of 2 during a suited experimental trial is perceived by the subject to be equivalent to his/her unsuited performance of the same task in 1g, thereby providing a quantitative rating of desired task performance in the suit.

As an example, a subject who is performing a shoveling task while wearing a suit that has a high-and-aft CG may rate the task performance as a 5 because the selected CG setting requires considerable effort/ compensation compared to performing the same task unsuited with nominal CG. This new tool is useful for comparing multiple subjects' ratings of operator compensation that is required to perform a variety of simulated surface exploration tasks across a wide range of suit concepts, configurations, and gravity levels. 24 Modified from the Cooper-Harper scale.

Chapter 14 Human Health and Performance Risks of Space Exploration Missions 358 Risk of Compromised EVA Performance and Crew Health due to Inadequate EVA Suit Systems.

GRAVITY COMPENSATION AND PERFORMANCE SCALE (GCPS)

CONTROL

Risk of Operational Impact of Prolonged Daily Required Exercise 359.

CHAPTER 15

135. Risk of Operational Impact of Prolonged

DAILY REQUIRED EXERCISE

Jancy C. McPhee
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Muscle

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