THE INFLUENCE OF TOTAL PHYSICAL INACTIVITY ON PLASMA HOMOCYSTEINE LEVELS. RISK FACTOR FOR DEVELOPMENT OF CARDIOVASCULAR DISEASE

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Abstract

Physical inactivity is the second most significant risk factor for chronic non-infectious contagious diseases in developed countries. However, conditions have slightly improved in the past few years; still, only 20 % of the population is being active in a fashion to reduce the probability of cardiovascular complications. Epidemiological research has confirmed that regular physical activity and nutrition containing sufficient quantities of folic acid, vitamins B6 and B12, reduce the level of homocysteine in blood. In our research, we studied the influence of long-lasting inactivity on the level of homocysteine and folic acid levels in blood. Ten male subjects were resting in horizontal position for 35 days in a clinical setting. After 35 days of resting we documented a statistically relevant increase in homocysteine level and decrease of folic acid concentration, despite supervised nutrition. We can conclude that prolonged physical inactivity is an autonomous, independent risk factor for the development of cardiovascular diseases.

Keywords: microgravity, physical inactivity, homocysteine, folic acid.

Introduction

Physical activity plays an important role in our lives since it is the cheapest way of strengthening our health. Of equal importance is the cognition that physical activity reduces the risk factor for the development of cardiovascular diseases which occupy the leading position.

Scientists agree that regular physical activity prevents the development of obesity, the loss of muscular mass, insulin resistance, and cardiovascular diseases in sedentary healthy people as well as in chronic disease patients (Biolo et al., 2005). Homocysteine, an amino acid in blood, which is produced during the assimilation of methionine, constitutes a risk for the development of cardiovascular diseases (Nygard et al., 1995; Shai et al., 2004). The level of homocysteine in blood is strongly influenced by habits such as nutrition, stress, alcohol, or physical inactivity (Stegnar, 2002; Van Guldener & Stehouwer, 2003; Boden-Albala & Sacco, 2000). Nutrition and alimental substances, such as folic acid, vitamins B6 and B12, which cooperate as co-enzymes during the assimilation of homocysteine, are of major importance. Several studies have confirmed that higher levels of group B vitamins are at least partly connected with lower homocysteine concentrations. Other recent proofs show that the lowest concentrations of folic acid in blood are connected with the increased risk for a severe coronary artery disease and stroke. Likewise, it is proved that physical activity reduces the concentration of total plasma homocysteine and the probability of cardiovascular diseases in healthy and sick people (El-Khairy et al., 1999; De Bree et al., 2001).

According to WHO 1.9 million people (600,000 Europeans) die annually due to inadequate physical activity. This probability increases by 50% among the physically inactive (Kraševec-Ravnik & Bevc-Stankovič, 2008).

It has been confirmed that physical activity decreases the concentrations of total plasma homocysteine and thus the probability of developing a cardiovascular disease in healthy and already sick people (Gaume et al., 2005). There were 620 persons questioned about their weekly physical activity and lifestyle and levels of their homocysteine concentration measured for the purpose of a study. The results show that physical activity is an independent lifestyle factor, linked to decreased concentrations of homocysteine in blood (Dankner et al., 2007).

In regard to the role and importance of physical activity in prevention from cardiovascular diseases we took part in the research "The influence of simulated weightlessness upon the human organism" in order to ascertain the connection between prolonged physical inactivity, homocysteine concentration, and folic acid in blood. We were interested into finding out whether physical inactivity is an independent risk factor for development of cardiovascular disease.

Methods

Participants and bed rest

Participants

The influence of simulated weightlessness on the human organism was studied as *Bed rest* (BR) in research participants who rested in horizontal position for 35 days. Among all registered volunteers there were ten examinees with no history of neuromuscular or cardiovascular disorders (age 24.3 § 2.6 years) selected on the bases of the following criteria: non-smokers, non-alcoholics, male, defined age between 20 and 30, personal interview, and medical check. Participants were included in the research after passing preliminary medical tests and signing their consent. They were informed in detail about the procedures and risks. The project was carried out in July and August 2007 at the Valdoltra Orthopaedic Hospital Slovenia, which offered its nursing and technical support. Participants carried out all their daily activities in horizontal position. Physical activity was strongly forbidden during all the research period of 35 days. There was passive limb motion and massage lead by a physiotherapist organized three times a week. With the aim to maintain the body weight the diet was individually dimensioned taking into consideration healthy eating principles. When the research started the participants' basal metabolism was considered in calculating the diet's compositional and quantitative balance. During the study the calculations were repeated at weekly intervals to maintain body weight and fat mass unchanged. The ingredients and the quantity of meals were balanced; participants had to consume entire meals with no additional intake.

All the participants' activities were video-monitored 24 hours a day. The study was approved by the Slovenian National Medical Ethics Committee and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Body weight and height

In order to prevent the loss of body mass we provided for regular and individual meals three times a day and followed the participants' daily consumption. Body weight (BW in kg) and height (BH in cm) were measured with the use of common measuring instruments. In addition the body mass index (BMI in kg/m^{-2}) was also monitored. Body height was measured before and after the research, while the body weight was registered every week.

Taking blood samples

We took blood samples from the participants before and after the bed rest study. Venous blood was taken on an empty stomach in the morning (between 7.00 and 7.30 a.m.) into 4 ml vacuum test tubes (Beckton-Dickinson, Rutherford, USA). We measured the concentration of total plasma homocysteine and the concentration of folic acid.

Statistics

All data are expressed as the mean ± SD with *n* being the number of participants. Statistical significance was assessed using the SPSS 15.0 with Student's paired t-test.

Results

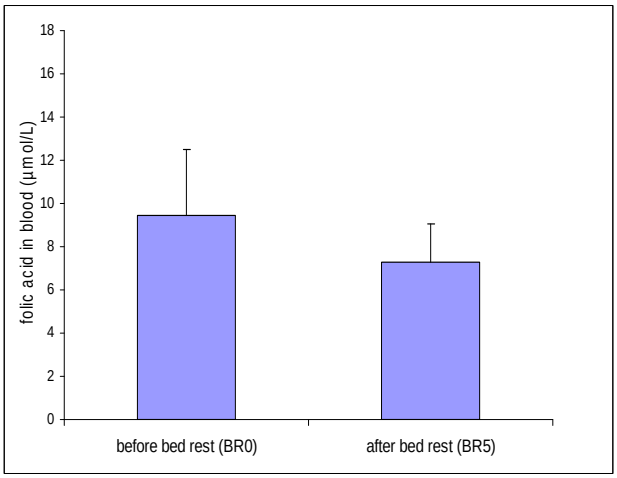
Body height and body weight

The body height did not change statistically during the bed rest research, while the body weight started to decrease after the third week (BR3) till the fifth week of rest (BR5). The loss of body weight in the third week (BR3) amounted to 1.6 %, (P<0.001) and in the fifth week (BR5) to 3 %, (P<0.001).

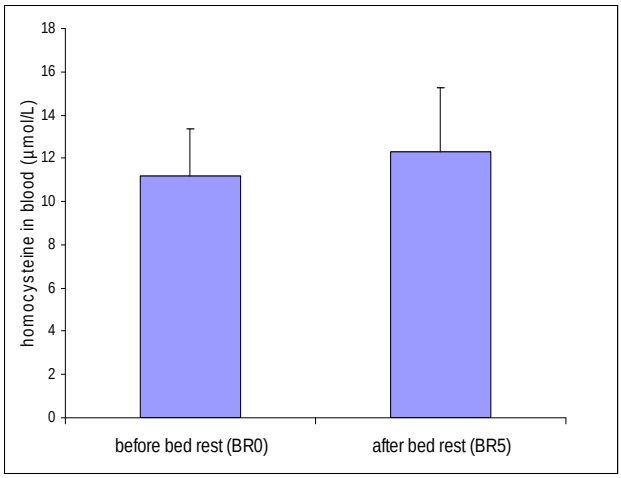
Homocysteine and folate levels

The values of total homocysteine and folates were compared before the bed rest study (BR0) and during the last, fifth week, right before the getting up (BR5). The research has showed statistically characteristic changes in the concentration of homocysteine which amounted to 11.19 ± 2.19 μmol/L before the study, and 12.28 ± 2.96 μmol/L after it, (p=0.014), *n*= 10; graph 1. Likewise, the concentration of folates in blood characteristically decreased during the research, from 9.46 ± 3.06 μmol/L to 7.28 ± 1.80 μmol/L, (p=0.007), *n*= 10; graph 2.

Graph 1



Graph 2



Graph 1: Plasma folate concentration in participants' blood before the bed rest study (BR0) and in the fifth week (BR5) of bed rest. The concentration statistically characteristically decreases in the fifth week (p= 0.007).

Graph 2: Plasma homocysteine concentration in the participants' blood before the bed rest study (BR0) and in the fifth week (BR5) of bed rest. In the last blood sample taking during the fifth week of bed rest (BR 5), the concentration of homocysteine statistically typically increased (p=0.014).

Discussion

All ten volunteers participating in the research successfully passed a 35-day horizontal bed rest as well as a couple of weeks of rehabilitation. Since the participants' diet was managed individually in order to assure a neutral energetic balance, the participants had to consume entire meals with no additional intake. As the calorie intake was calculated on the bases of weekly measurements of participants' weight a major loss of weight was prevented, and gaining of excessive fat mass suppressed. Despite the fact that the nutrition was monitored with controlled intake of singular ingredients and micronutrients, folic acids being among them, the folic acid decreased significantly after the five-week bed rest, yet within the reference value range. A moderate homocysteinemia was also recorded after five weeks, the level of dangerous homocysteine increased significantly, exceeding the reference values. The latter demonstrates the inverse ratio between folic acid and homocysteine concentration, already confirmed by previous studies (Siri et al., 1998). Increased homocysteine is presumably responsible for at least a 10 % risk for the development of atherotrombotic vascular disease (Clarke et al., 2001), and a moderate homocysteinemia is nearly as important risk factor for development of atherotrombosis as smoking and hyperlipidemia (Chen et al., 1999).

The "Bed rest" or "The influence of simulated weightlessness upon the human organism" is an international research of interdisciplinary nature involving numerous foreign and domestic scientists. Its objective is to study the influence of inactivity upon the human body, and above all, the effect of simulated weightlessness on skeleton-muscular, thermo-regulatory, as well as cardiovascular system. Such studies are important not just for the space flights' preparation but also for the investigation of consequences of prolonged bed rest after a surgery. It is thus at this point that interests of "spatial" and "terrestrial" medicine intersect.

Along with the building of the international space station Freedom human presence in space has been steadily increasing. Until now, astronauts have spent a year at the most in space. On the basis of such space experience as well as terrestrial experiments, we have become aware of the fact that a non-gravity condition causes certain changes which can be harmful after a long stay in space. The ongoing terrestrial researches are aimed at the comprehension of the causes of these changes and at the development of precautions which could prevent harmful physiological changes. In our research, we have followed and tried to determine in what way long-lasting rest or inactivity affects the level of homocysteine in blood and to establish the linkage between the level of homocysteine and folates in nutrition. The results of the research will be useful not only for space workers of future but also for the comprehension of physiological changes among immobilized patients.

Horizontal bed rest (BR) or microgravity is one of the most frequently used methods of monitoring the consequences of total physical inactivity (Adams et al., 2003; Eiken and Mekjavić, 2002). Since several studies indicate physical activity as an independent lifestyle factor connected with lower homocysteine concentration (Danker et al., 2007), our research could confirm that physical inactivity is an independent risk factor for the development of cardiovascular diseases, although we cannot state with accuracy that after five weeks the level of dangerous homocysteine increased above the critical level due to physical inactivity or folic acid decrease.

Conclusion

Our research findings confirmed the importance of exercise and physical activity in the prevention of cardiovascular diseases. It has been evidenced that prolonged rest increases the levels of homocysteine in blood, negatively influencing the cardiovascular system. The latter makes it clear that the same consequences can result from prolonged physical inactivity in everyday life.

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