Original Article

Sodium regulation with periodic fluid redistribution during diminished muscular activity in healthy subjects

Yury Feofil Federenko, Yury Nikita Yaroshenko, Pavel Leonid Merkov, Sergei Kirill Deno gratov

Department Biochemistry, Institute of Hypokinetic Physiology, Athens, Greece

Abstract

Background and Aim: Mineral loss is an established reaction to diminished muscular activity (Hypokinesia; HK). It has been assumed that periodic fluid redistribution (PFR) contributes to vascular volume. Fluid volume expansion could affect electrolyte metabolism. We hypothesized that chronic PFR may contribute to or improve electrolyte regulation during diminished activity. Therefore, we studied the potential benefits of sodium (Na^+) regulation with chronic PFR during HK.

Methods: The study was conducted on 40 male subjects for the duration of 390-days preexperimental period and a 364-days experimental period. They were equally divided into four-groups: Active control subjects (ACS), hypokinetic subjects (HKS), periodic fluid redistribution control subjects (PFRCS), and periodic fluid redistribution hypokinetic subjects (PFRHS).

Results: Muscle Na^+ increased ($P < 0.05$) and plasma Na^+ and Na^+ losses decreased ($P < 0.05$) in the PFRHS group compared with the HKS group. Muscle Na^+ decreased ($P < 0.05$) and plasma Na^+ and Na^+ losses increased ($P < 0.05$) in the HKS group compared with the preexperimental period levels and the values of the other groups. Muscle Na^+, plasma Na^+ and Na^+ losses were benefited much less in the PFRCS group than in the PFRHS group. Muscle Na^+, plasma Na^+ and Na^+ losses were not affected in the ACS group compared with their preexperimental values.

Conclusion: The current study shows that muscle Na^+ increases and Na^+ losses decreases with chronic PFR suggesting the potential benefits of Na^+ regulation during diminished activity.

Key words: Hypokinesia, muscle sodium, periodic head down tilt, sodium losses, sodium repletion, vascular volume

Received: 2nd July, 2014; ***Revised:*** 5th September, 2014; ***Accepted:*** 14th September, 2014

INTRODUCTION

Although periodic head down (PHD) tilt, and head-down (HD) tilt (in humans) and hindlimb suspension (in rats) share a shift in thoracic fluid volume, there are major differences in these conditions. PHD tilt and HD position are different as there are many other features specific to PHD position.[1] Specific knowledge is required to differentiate fluid redistribution (FR) with PHD position from FR in HD position and in weightlessness, water immersion, bed rest, and postoperative and/or postural manipulations. With PHD position, biochemical and physiological reactions are under different control from that with HD tilt. Plasma renin, angiotensin II, catecholamines, aldosterone and antidiuretic hormone adapt to chronic PHD position. With PHD tilt, fluid volume distribution is intravascular and intracellular, which contributes to vascular volume. Periodic fluid redistribution (PFR) induces sustainable vascular volume. Chronic PHD position produces adaptation of fluid shifting to the upper part of the body and creates a hydrostatic gradient to improve venous return and increase cardiac output and total fluid volume.[2-4] Chronic PHD position contributes to conditioning of the cardiovascular and endocrine system and increases physical capacity, energy, and strength.[1]

Periodic fluid redistribution is defined as fluid shifting to the upper part of the body beyond that of HD tilt, weightlessness, water immersion, bed rest, postoperative and/or postural manipulations. PFR counteracts the

Access this article online	
Quick Response Code:	Website: www.ijcep.org
	DOI: 10.4103/2348-8093.143475

Address for correspondence: Dr. Yury F. Federenko, Institute of Hypokinetic Physiology, Odos Eptapirgou 4, GR-162 32 Athens, Greece. E-mail: yfederenko@gmail.com

consequences of fluid shifting to the lower body parts. PFR is a factor of induction of anabolism. The aerobic glycolysis becomes more efficient. PFR contributes to or increases vascular volume and tissue perfusion. PFR condition the upper-body part tissues and regulates kidney and urinary system, endocrine and cardiovascular system and skeletomuscular system. PFR is reprogramming the different body organs and systems. PFR decreases arterial blood and interstitial fluid pressure and induces aerobic metabolism and energy production.

Diminished muscular activity (Hypokinesia; HK) and earth gravity, affects redistribution of fluids inside the body by pulling the various body fluids downwards to the lower extremities.[3,4] Fluid shifting to the legs eventually causes fluid deficiency within the circulatory system.[3,4] Due to the fluid shifting into the lower extremities more fluid volume migrates to the pelvic region and the lower half part of the body.[3,4] This leads to retention of a large fluid volume in the lower extremities, than what is the norm for the lower part of the body contributing in lower blood volume and reduced filling with blood of the central vascular bed.[2] Fluid volume that can fit into the venous system of the lower part of the body can determine the severity in the delivery of fluid volume to the upper body part and thus extracellular and interstitial fluid volume. Reduction of total fluid volume is most detrimental to the body because it forces the body, particularly the vital organs, to work much harder than they normally should. The decreased fluid volume may contribute to higher plasma electrolyte level, which potentially may contribute to electrolyte losses and electrolyte deficiency.[5-11] To counteract the consequences of diminished muscular activity, different preventive measures[12-17] and physical exercises[12-17] have been used which, unfortunately, have shown to have limited effects. Thus, PFR that moves fluid away from the lower extremities into regional areas of the body may be one solution for normal total fluid volume and electrolyte regulation. However, limited information has been published on the effect of chronic PFR on the regulation of electrolytes during diminished muscular activity.

Periodic fluid shifting to the upper part of the body counteracts the consequences of fluid shifting to the lower part of the body. It has been assumed that chronic PFR could contribute to more fluid volume. A fluid volume expansion would then affect electrolyte metabolism. Therefore, to determine the potential benefits of Na^+ regulation with chronic PFR, we hypothesized that chronic PFR could contribute to or improve Na^+ regulation during diminished muscular activity.

MATERIALS AND METHODS

The studies have confirmed to the ethical principles of the Declaration of Helsinki. All study protocols were reviewed and approved by the Committee for the Protection of Human Subjects of the Institutional Review Board. Subjects received verbal and written explanations of all experimental and test protocols prior to providing written informed consent. The subjects had no medical problems, and none of the subjects were under any drug therapy which could have interfered with sodium metabolism. There were no drop-outs from the study. Financial incentives relative to average monthly earnings were used to encourage compliance with the protocol of the study. Forty physically healthy male subjects 24.1 ± 8.4 years of age were chosen as subjects. Subjects were instructed to run for average distances of 9.9 ± 2.0 km/day at a speed of 9.9 ± 1.7 km/h for 3-5 years. All subjects had a body weight of 75.6 ± 8.0 kg and peak oxygen uptake of 48.0 ± 7.0 mL/kg/min. In preexperimental period of 390-days all subjects were instructed to run for average distances of 9.8 ± 1.9 km/day at a speed of 9.8 ± 1.6 km/h.

Random assignment of subjects into four groups using a concealed method by an assistant blinded from the recruitment and treatment procedures was used.

Group 1: Ten subjects were instructed to run for average distances of 9.8 ± 1.7 km/day for 364-days. They were assigned to the active control subjects (ACS) group. Group 2: Ten subjects were instructed to walk an average distances of 3.5 ± 0.6 km/day for 364-days. They were assigned to the hypokinetic subjects (HKS) group. Group 3: Ten subjects were instructed to run for average distances of 9.8 ± 1.5 km/day and were subjected to PFR for 8-10 h/day for 364-days. They were assigned to periodic fluid redistribution control subjects (PFRCS) group. Group 4: Ten subjects were instructed to walk an average distances of 3.5 ± 0.5 km/day and were subjected to PFR for 8–10 h/day for 364-days. They were assigned to periodic fluid redistribution hypokinetic subjects (PFRHS) group.

Protocol

The study consisted of a 390-days preexperimental period and a 364-days experimental period. Diet were served as a 7-day menu rotation. Meals were all prepared under standard conditions in a research kitchen. Mean daily energy consumption of the metabolic diet was 3530 ± 515, 2915 ± 384, 3510 ± 555 and 3131 ± 391 SD Kcal, and the mean daily Na^+ consumption was 241.6 ± 11.6, 242.0 ± 10.4, 241.8 ± 11.8 and 242.1 ± 12.5 SD mmol for the ACS, HKS, PFRCS and PFRHS groups, respectively. Subjects housed in a facility in which humidity, temperature, activities, and dietary intakes were monitored 24 h/day and 7-day/week.

Simulation of hypokinesia through diminished muscular activity

To simulate a certain level of hypokinesia, the number of km walking per day was restricted to an average of 3.5 ± 0.7 km/day and was monitored daily by an accelerometer. The activities allowed were those that approximated normal routines of hypokinetic individuals. Subjects were allowed to walk to the dining rooms, lavatories and different laboratories where the tests were given. Climbing stairs and other activities that required greater efforts were not allowed. All subjects were mobile and were not allowed outside the experimental facility grounds so that the level of muscular activity could remain relatively constant and easily monitored.

Simulation of periodic fluid redistribution through periodic head down tilt

To produce PFR, the volunteers were submitted without a pillow to PHD position for 8-10 h/days during sleeping in the preexperimental period of 390-days and experimental period of 364-days. During preexperimental period, the volunteers were submitted to PFR by increasing progressively PHD position to -2, -4, -6, -8, -10 and -12 degrees every 64-71 days. For rest of the preexperimental and actual experimental period, volunteers were submitted to PFR by increasing progressively PHD tilt to -2,-4,-6,-8-12 degrees for 8-10 h/day. Procedures selection was determined from a preliminary study in establishing volunteers' adaptation ability to PHD tilt. To ensure the volunteers comfort, PHD position of -2 to-12 degrees was modified as required. The individual differences in biochemical and physiological reactions, that is, cardiovascular, renal/endocrine and metabolic reactions of volunteers and their clinical symptoms and sensitivity to different PHD positions were taken into consideration. The schedule of PHD position was alternated from time to time to conform the requirements of adaptation ability of volunteers.

Blood, urinary and fecal sample collection

To accommodate inter-individual differences in bowel habits, urine and feces were analyzed daily and were pooled to form 6-day composites while blood samples were measured every 6-day during the preexperimental and the experimental periods. The 6-day (consecutive days) pooled samples were collected. Blood samples were collected with disposable polypropylene syringes. Following overnight fasting for about 6-7 h, venous samples of blood were taken at rest and before any meals. Blood samples were drawn under the same conditions between 8.00 and 9.00 a.m., without venous stasis and after subjects had been sitting for about 30 min. The sample volume was 6-8 mL. To obtain plasma, blood samples were collected in heparinized ice-chilled tubes and were centrifuged immediately at 10.000 × g for 3 min at room temperature and separated using glass capillary pipettes that were washed in hydrochloric acid and deionized distilled water. Immediately after centrifugation plasma samples were frozen on dry ice and were stored at −20°C, until analyses were conducted for plasma Na^+. Twenty-four hour urine samples were stored at −4°C until needed for Na^+ analysis. To ensure complete 24 h urine collections creatinine loss was measured by a colorimetric method using Jaffe's reaction. Feces were collected in plastic bags, weighed and stored at −20°C for Na^+ analysis. Fecal samples were dried-ashed in a muffle furnace at 600°C overnight. Ashed samples were dissolved in 5% nitric acid. To ensure complete recovery of feces polyethylene glycol, which was used as a marker.

Muscle preparations, magnesium extraction and analysis

Muscle biopsies were performed by a percutaneous needle technique[18] under local anesthesia. Specimens were taken from the lateral portion of the quadriceps femoris muscle, 15-20 cm proximal to the knee. The muscle (mean weight 15.5 mg) was placed on a piece of quartz glass and with nonmetal tweezers carefully dissected free from all visible fat and connective tissue. Traces of blood were wiped off by rolling the specimens on the piece of quartz glass. Muscle was then placed on a platinum hook and dried in an oven at 110°C to constant weight, extracted in 1 mL of petroleum ether for 2 h and dried to constant weight and fat-free dry solids (FFDS) weight was calculated. The Na^+ extracted from muscle by treatment with 250 μL 2.5 M HNO_3 for 24 h. From each sample, 100 μL of supernatant was diluted to 10 mL with 0.25% $SrCl_2$ and analysis for Na^+ in muscle was performed by atomic absorption spectrophotometry on a Perkin-Elmer 430 Model, Perkin-Elmer Corp., Norwalk, CT, USA. The results obtained on muscle magnesium content throughout the investigation was calculated in mmol/100 g^{-1} FFDS.

Sodium measurements

Samples were analyzed in duplicate and appropriate standards were used for the measurements. The sodium levels in muscle, plasma, feces and urine were measured by a Flame Emission Spectrophotometer of a Perkin-Elmer 320 Model, Perkin-Elmer Corporation, Norwalk, CT, USA.

Statistical analysis of data

A two-way interaction (treatment [3 levels] by days [6 levels]) analysis of variance (ANOVA) was used to determine the potential benefits of muscle sodium regulation with chronic PFR. The ANOVAs with repeated measures of two-way interaction (treatment/days, preexperimental/experimental values, hypokinetic/periodic fluid redistribution hypokinetic groups, hypokinetic/control

groups) was used. The ANOVAs for each time point measurements were used. The level of significance was set at $P < 0.05$. The results obtained were reported as mean ± SD.

RESULTS

The PFRCS group and PFRHS group were reported symptoms analogous to those of HD tilt. Most common complaints were headache, dizziness, muscle aches, and pains. The subjects manifested other symptoms most of which were typical to PHD position [Table 1]; these symptoms were more pronounced in the PFRCS group than the PFRHS group. However, as the duration of PHD treatment increased and subjects adapted to PHD position, all the symptoms disappeared and by the end none of the subjects complained of any symptoms. The PFRHS group and much less the PFRCS group had gained height, energy and strength; after completion of the study the subjects have decided to continue sleeping at PHD position.

In the subjects with PFR, muscle Na^+ decreased, and plasma Na^+ and Na^+ losses in urine and feces increased at the initial stages of preexperimental period. However, as the duration increased the muscle Na^+ increased and plasma Na^+ and Na^+ losses in urine and feces decreased [Table 2]. With PFR Na^+ is being taken up for the deposition and used by the body, which in turn protected the net muscle Na^+, plasma Na^+ and Na^+ losses. In the HKS group and the ACS group, muscle Na^+, plasma Na^+ and Na^+ losses in urine and feces remained unchanged [Table 2].

In experimental period, muscle Na^+ increased ($P < 0.05$) and plasma Na^+ and Na^+ losses in urine and feces decreased ($P < 0.05$) in the PFRHS compared with the HKS group [Table 2]. In the HKS group, muscle Na^+ decreased ($P < 0.05$) and Na^+ losses in urine and feces increased ($P < 0.05$) compared with the preexperimental period levels and the values of the other groups [Table 2]. In the PFRCS group, muscle Na^+, plasma Na^+ and Na^+ losses in urine and feces were not benefited as much as in the PFRHS group [Table 2]. Muscle Na^+, plasma Na^+ and Na^+ losses were not affected in the ACS group compared with their preexperimental values [Table 2].

Table 1: Initial reactions of healthy subjects to chronic periodic fluid redistribution through chronic periodic head down during diminished muscular activity

Puffiness in the face
Tachycardia
Ventricular extrasystoles
Arrhythmias
Loud heart sounds
Increased excretion of urine
Tinnitus in the left and more in the right ear
Feeling of fullness (pressure) or stuffiness in the left ear and more in the right ear
Deep vein symptoms in the left and more in the right leg
Pain in the left and more the right foot
Pain in the left and more in the right gluteus muscle
Pain in the calcaneal tendon region (Achilles) in the left and more in the right leg
Pain in the left and more in the right hand
Upper body back skin itching and discoloration
Lacrimal secretion

DISCUSSION

Periodic fluid shifting to the head is not sensed by baroreceptors as excessive fluid volume but rather as simple FR and excretion mechanisms are not activated. Fluid shifting to the upper part of the body periodically provides stimulation for more fluid volume. In a normally functioning body, any means through which fluid volume is stimulated would contribute to more fluid volume and, therefore, increase the total fluid volume and extracellular fluid volume. The intuitive concept behind the potential benefits of fluid volume with PFR is grounded on the assumption that PFR is a potent stimulus for fluid volume expansion. It is further supposed that chronic PFR could contribute to or improve electrolyte regulation during diminished activity.

The current study had shown a sustainable improvement in Na^+ with chronic PFR. Muscle Na^+ may be protected or increased with chronic PFR. The chronic PFR had acted as a potent stimulus of muscle Na^+ because muscle Na^+ cannot increase with fluid shifting to the head unless it is affected by PFR. Chronic PFR is a potent stimulus for protection or increase of muscle Na^+ as was shown by the significant differences between the PFRHS group and the other groups. The lower plasma Na^+ indicates plasma volume expansion. The lower plasma Na^+ suggests Na^+ deposition because plasma Na^+ cannot reduce with Na^+ replete muscle except if it is deposited. The lower Na^+ losses indicate Na^+ regulation, because Na^+ losses cannot slow with Na^+ repleted muscle except if Na^+ is regulated. Moreover the lower Na^+ losses suggest that fluid volume shifting to the head is not sensed as excessive fluid volume because electrolyte losses cannot decrease with large fluid volume shifting upwards unless fluid shifting to the head is sensed as simple fluid volume redistribution. Once subjects have adjusted to chronic PFR they continue to show higher muscle Na^+ and lower Na^+ losses. The lower Na^+ losses with Na^+ replete muscle and higher Na^+ losses with Na^+ depleted muscle suggest that there are different mechanisms of control. Studies have shown that fluid expansion reduces electrolyte losses because fluid volume expansion is sensed by baroreceptors as simple fluid volume redistribution and excretion mechanisms are

Table 2: Muscle sodium, urinary and fecal sodium and plasma sodium measured in the control and the hypokinetic groups and the periodic fluid redistribution control and the hypokinetic groups during the preexperimental and the experimental period

Experimental period in days	Sodium			
	Muscle mmol/100/gl FFDS	Urinary mmol/days	Fecal mmol/days	Plasma mmol/L
ACS, *n*=10				
Average values preexperimental	31.1±2.2	186±10	8.1±2.2	138.2±2.0
60th	31.3±3.0	185±11	7.8±2.0	138.0±2.1
120th	31.2±2.6	184±13	8.0±2.3	138.1±2.3
180th	31.3±3.3	185±10	7.8±2.2	138.0±2.2
240th	31.5±2.7	186±12	8.0±2.0	138.1±2.3
300th	31.4±4.0	185±11	7.8±2.5	138.1±2.0
364th	31.3±2.5	186±10	8.0±2.1	138.0±2.3
HKS, *n*=10				
Average values preexperimental	31.2±2.4	185±11	8.0±2.5	138.2±2.2
60th	28.3±2.1*†	230±15*†	10.0±2.1*†	144.1±2.2*†
120th	28.7±2.4*†	228±11*†	9.8±2.3*†	144.0±2.1*†
180th	28.1±2.6*†	245±12*†	11.1±2.0*†	146.2±2.0*†
240th	28.3±3.0*†	235±13*†	10.5±2.4*†	145.8±2.2*†
300th	27.1±3.3*†	264±12*†	11.7±2.2*†	148.0±2.0*†
364th	27.5±2.5*†	258±11*†	11.3±2.0*†	147.5±2.1*†
PFRCS, *n*=10				
Average values preexperimental	30.8±3.1	198±12	8.7±2.2	138.1±2.4
60th	31.2±3.5	193±15	8.3±2.3	137.7±2.0
120th	31.0±4.0	195±13	8.5±2.3	137.8±2.1
180th	31.5±3.5	187±15	8.1±2.4	137.5±2.2
240th	31.3±4.4	190±14	8.0±2.3	137.7±2.1
300th	31.7±3.2	183±15	8.0±2.2	137.3±2.0
364th	31.5±4.0	187±12	8.3±2.0	137.5±2.2
PFRHS, *n*=10				
Average values preexperimental	30.8±3.0	198±13	8.7±2.3	138.1±2.5
60th	33.4±4.2+	173±12+	7.3±2.5+	136.0±2.1+
120th	33.0±3.4+	175±14+	7.5±2.0+	136.1±2.2+
180th	33.8±4.0+	165±15+	7.0±2.6+	136.0±2.0+
240th	33.6±5.5+	170±13+	7.3±2.5+	136.1±2.1+
300th	34.7±3.4+	155±14+	6.7±0.2.0+	136.0±2.2+
364th	34.5±4.0+	157±13+	6.9±2.3+	136.2±2.0+

All values were expressed as mean±SD. †P<0.05 significant differences between the preexperimental and experimental period values, *P<0.05 significant differences between the control and the hypokinetic groups of subjects, +P<0.05 significant differences between the hypokinetic and the periodic fluid redistribution hypokinetic groups of subjects. FFDS: Fat free dry solids, SD: Standard deviation, ACS: Active control subjects, HKS: Hypokinetic subjects, PFRCS: Periodic fluid redistribution control subjects, PFRHS: Periodic fluid redistribution hypokinetic subjects

not activated.[19-24] Studies have shown that fluid volume expansion with fluid-salt supplements may increase tissue electrolytes and decrease electrolyte losses.[25-30] It is believed that renal/endocrine system adjusts electrolyte regulating hormones to slow electrolytes losses. Later of adaptation to chronic PFR, the kidneys and the endocrine glands establish new "normal" level of electrolytes and hormones appropriate for PFR or more fluid volume. Clearly, periodic fluid shifting to the upper part of the body increases muscle Na^+ and decrease Na^+ losses.

Control subjects with and without PFR did not show significant differences in Na^+ regulation; this may be attributable to physical activity. Physical activity may counteract the PFR. Physical activity that moves fluid to the lower part of the body may determine the severity in delivery of fluid volume to the upper part of the body. It has been shown that physical activity may not contribute to fluid volume expansion.[31-35] The fluid volume is neither intravascular nor intracellular fluid and does not contribute to vascular volume. Reduced fluid volume forces the body particularly for vital organs, to work much harder than they normally would. With PFR alone, the intravascular volume increases reflecting fluid flux from the interstitium to the circulation. Physical activity may determine the efficacy of PFR because the higher physical activity, the lower PFR efficacy. Physical activity may act more as stressor rather than as a stimulus of Na^+ regulation as shown by minor changes in Na^+ regulation of the PFRCS group compared with the other groups. A much less adaptability to chronic PFR was shown in the PFRCS group than the PFRHS group. Thus, one would not see the Na^+ regulation improvements in the PFRCS group as in the PFRHS group. With physical activity, PFR did not play a significant part in Na^+ regulation. However, PFR even with physical activity is a potent stimulus of Na^+ regulation when it is used over a longer time than the time required by HKS. Physical activity may protect

Na^+ regulation as shown by the no change in the ACS group compared to the HKS group.

The dependence of Na^+ regulation on PFR duration and PHD tilt degree suggests that the longer fluid volume is redistributed periodically into regional areas of the body and with the optimum PHD tilt degree more Na^+ is deposited and the less Na^+ is lost. This shows a common conception that PFR duration and PHD tilt degree may be vital for Na^+ regulation. It is evident that PFR and PHD position may improve Na^+ regulation. It follows that PFR and optimum PHD tilt degree may regulate muscle Na^+, plasma Na^+ and Na^+ losses. The PHD position which moves fluid from lower to the upper part of the body periodically may determine the capacity of the body to regulate vascular volume and thus extracellular and interstitial fluid volume. The large fluid volume shift from lower to the upper part of the body may be more of a stimulus rather than a stressor of Na^+ regulation. This adds an important contribution to Na^+ regulation because hypokinetic population regularly experiencing tissue electrolyte deficiency.[5-11] It is evident that subjects with chronic PFR and optimum PHD tilt may experience a less labile and more responsive Na^+ regulation.

Some studies have shown that the consequence of fluid volume expansion by a daily intake of fluid and salt supplementation in very small divided doses the brain does not interpret its blood supply as an increase in total fluid volume, but rather as simple fluid volume redistribution and the excretion mechanisms are not activated.[22-24,33-35] In response to this misperception, the brain does not signal the kidneys and other organs to reduce blood volume and other body fluids. The systems somehow turn to adapt to fluid volume expansion and the baroreceptors do not stretch and do not interpret this as an excessive fluid volume, and do not stimulate the body to urinate in an effort to eliminate the excess fluid volume. This process minimizes the loss of electrolytes that in turn contribute to more tissue electrolytes. Thus, fluid volume expansion through chronic PFR may be one solution for fluid volume expansion and more Na^+ tissue and less Na^+ losses in people living and working under diminished muscular activity conditions.

Fluid volume expansion and more tissue oxygen supply may increase oxidative phosphorylation (OP), adenosine triphosphate (ATP) synthesis, mitochondria density and aerobic metabolism contributing to intact cell mass. The synthesis of OP and ATP has a widespread effect on cellular function and morphology. Fluid volume expansion and more oxygen supply within the cell preserve or restore the cell structure and improve or regulate cell function. This eventually increases cellular transport and decreases intracellular electrolytes and maintains the integrity of cell mass leading to the stability of cellular contents that may affect cell Na^+ holding capacity. Thus, an intact cell mass may contribute to or increase muscle Na^+ and decrease Na^+ losses.[36]

The synthesis of OP and ATP is most susceptible to blood supply and oxygen delivery to the tissues. Fluid volume expansion and more tissue oxygen supply improve or normalize OP and ATP synthesis. With chronic PFR, blood supply and oxygen delivery to the tissue increases significantly. As blood flow and oxygen tension within the cell increases, OP and ATP synthesis increases during HK OP[37] and ATP synthesis[38] decreases. The increase of mitochondria density and its function is the most likely culprit to explain OP and ATP synthesis. Chronic fluid volume expansion is a potent stimulus for the mitochondria enzymes proliferation. Mitochondria density and cytochrome c which is crucially important in aerobic energy production increases during HK decrease.[39] Mitochondria density depends on the duration and intensity one can endure PFR procedures and body's ability to spare total glycogen. As OP and ATP synthesis increases, the cell shifts to aerobic glycolysis that allows ATP production from the breakdown of cellular glycogen. New glycogen synthesis is stimulated, and glycogen depots are repleted when the glycogen stores are depleted during HK.[40] Aerobic metabolic glycolysis becomes more efficient than the lower oxygen-dependent mitochondrial pathways, and cell function and morphology is eventually preserved or restored thereby stimulating Na^+ regulation contributing to more muscle Na^+ and less Na^+ losses.

Limitations of the study

The limitation of the study is the small sample size in each group. However, motivating 10 individuals to complete the study period of 364/390 days was itself a tough task.

CONCLUSION

In conclusion, chronic PFR may increase muscle Na^+ and decrease Na^+ losses, which may be attributable to more efficient Na^+ regulation. The underlying mechanisms, however, by which chronic PFR increases muscle Na^+ and decrease Na^+ losses is yet to be established. Further studies are required to determine how the body uses the mechanisms of fluid shifting to upper part of the body to counteract the consequences of fluid shifting to lower extremities to benefit electrolyte metabolism and other functions of the body.

ACKNOWLEDGMENTS

No project of this magnitude, duration and complexity could succeed without the tremendous support. We are indebted to the staff of the institute; the attending physicians and laboratory workers and most of all, our volunteers.

REFERENCES

1. Federenko YF, Merkov PL, Yaroshenko YN, Denogratov SK, Charapakhin KP, Neofitov NH. Potential benefits of potassium deposition with periodic fluid redistribution using periodic head down tilt during diminished muscular activity. Indian J Physiol Pharmacol 2014;58:30-8.
2. Smith JJ. Circulatory Response to the Upright Posture: A Review Volume. Boca Raton, Florida, US: CRC Press; 1990. p. 4-6.
3. Krotov VP. Kinetics and regulation of fluid-electrolyte metabolism in animals and man during hypokinesia, PhD thesis, Academy of Sciences USSR and Directorate of Kosmic Biology and Medicine, Ministry of Health USSR, Moscow; 1982.
4. Volozhin AV. Pathogenesis of disturbances of mineral metabolism in mineralized tissues during long-term hypokinesia PhD thesis, Interkosmos Council, Academy of Sciences USSR and Directorate of Kosmic Biology and Medicine, Ministry of Health USSR, Moscow; 1987.
5. Zorbas YG, Federenko YF, Naexu KA. Fluid electrolyte and hormonal changes in conditioned and unconditioned men under hypokinesia. Acta Astronaut 1988;17:1123-6.
6. Zorbas YG, Naexu KA, Federenko YF. Fluid electrolyte excretion during different hypokinetic body positions of trained subjects. Acta Astronaut 1994;32:393-8.
7. Zorbas YG, Federenko YF, Cherapakhin KP, Kuznetsov NK, Yarulin VL, Federov MA. Fluid electrolyte changes during prolonged restriction of motor activity in rat. J Physiol Biochem 1998;54:33-40.
8. Zorbas YG, Kakurin VJ, Kuznetsov NA, Yarullin VL, Andreyev ID, Charapakhin KP. Measurements in potassium-supplemented athletes during and after hypokinetic and ambulatory conditions. Biol Trace Elem Res 2002;85:1-22.
9. Zorbas YG, Yarullin VL, Denogradov SD, Afonin VB, Kakurin VK. Phosphate determination during hypokinesia and ambulation in establishing phosphate changes in trained and untrained subjects. Biol Trace Elem Res 2002;88:125-38.
10. Deogenov VA, Luzhkov AG, Kakuris KK, Federenko YF. Muscle calcium metabolic effects of hypokinesia in physically healthy subjects. Biol Trace Elem Res 2010;138:116-24.
11. Federenko YF, Deogenov VA, Kakuris KK, Yerullis KB. Muscle potassium and potassium losses during hypokinesia in healthy subjects. Biol Trace Elem Res 2011;143:668-76.
12. Zorbas YG, Medvedev IO. Mans desirability in performing physical exercises under hypokinesia. Int J Rehabil Res 1986;9:170-4.
13. Zorbas YG, Federenko YF, Togawa MN. Renal excretion of water in men under hypokinesia and physical exercise with fluid and salt supplementation. Acta Astronaut 1990;21:599-605.
14. Zorbas YG, Andreyev VG, Federenko YF. Effect of hyperhydration and physical exercise on fluid-electrolyte changes in healthy subjects after exposure to hypokinesia. Hung Rev Sports Med 1993;34:141-54.
15. Zorbas YG, Matveyev IO. Evaluation of efficacy of preventive measures under hypokinesia. Int J Rehabil Res 1987;10:63-8.
16. Zorbas YG, Portnoy VF, Popescu LB. Fluid electrolyte metabolism and renal function in man under hypokinesia and preventive measures. Urologia 1987;35:109-20.
17. Zorbas YG, Abratov NI, Ambrosini AN. Measures in preventing mens metabolic changes under hypokinesia and readaptation. Eur Med Phys 1987;23:141-50.
18. Bergström J. Muscle electrolytes in man determined by neutron activation analysis on needle biopsy specimens: A study on normal subjects, kidney patients and patients with chronic diarrhoea. Scand J Clin Lab Invest 1962;68:1-110.
19. Zorbas YG, Ichinose MN, Sakagamis MB. Fluid electrolyte changes in physically healthy subjects during prolonged restriction of motor activity and daily hyperhydration. Mater Med Pol 1993;25:97-107.
20. Zorbas YG, Federenko YF, Naexu KA. Calcium loading and renal function in trained subjects during restriction of muscular activity and chronic hyperhydration. Biol Trace Elem Res 1994;41:137-56.
21. Zorbas YG, Verentsov GE, Federenko YF. Fluid-electrolyte changes in physically conditioned subjects after hypokinesia and chronic hyperhydration. Acta Astronaut 1995;36:279-84.
22. Zorbas YG, Federenko YF, Naexu KA. Effect of daily hyperhydration on fluid-electrolyte changes in endurance-trained volunteers during prolonged restriction of muscular activity. Biol Trace Elem Res 1995;50:57-78.
23. Zorbas YG, Yaroshenko YY, Kuznetsov NK, Medvedev SL. Daily hyperhydration effect on electrolyte deficiency of endurance trained subjects during prolonged restriction of muscular activity. Biol Trace Elem Res 1998;64:259-73.
24. Zorbas YG, Federenko YF, Naexu KA, Kuznetsov NK, Petrov KL. Water and electrolyte excretion in rats during prolonged restriction of motor activity and chronic hyperhydration. Physiol Chem Phys Med NMR 1998;30:99-111.
25. Zorbas YG, Federenko YF, Naexu KA. Effect of hyperhydration on bone mineralization in physically healthy subjects after prolonged restriction of motor activity. Acta Astronaut 1991;25:727-31.
26. Zorbas YG, Federenko YF, Naexu KA. Bone mineralization and plasma concentrations of electrolytes in healthy subjects after exposure to hypokinesia and hyperhydration. Wien Klin Wochenschr 1993;105:167-71.
27. Zorbas YG, Federenko YF, Togawa MN. Effect of fluid and salt supplements in preventing the development of "osteopenia" in hypokinetic rats. Acta Astronaut 1991;25:111-6.
28. Zorbas YG, Yaroshenko YY, Kuznetsov NK, Madvedev SN, Federenko YF. Electrolyte concentration in skeletal muscles and plasma of rats during and after exposure to hypokinesia and hyperhydration. Physiol Chem Phys Med NMR 1997;29:243-59.
29. Zorbas YG, Yaroshenko YY, Kuznetsov NK, Andreyev VG, Federenko YF. Bone histomorphometric changes in trained subjects during prolonged restriction of muscular activity and chronic hyperhydration. Panminerva Med 1997;39:265-74.
30. Zorbas YG, Deogenov VA, Tsiamis CB, Yerullis AL. Bone mineral density during prolonged hypokinesia and rehydration in healthy subjects. Trace Elem Electrolytes 2008;25:100-10.
31. Zorbas YG, Andreyev VG, Popescu LB. Fluid-electrolyte metabolism and renal function in men under hypokinesia and physical exercise. Int Urol Nephrol 1988;20:215-23.
32. Zorbas YG, Abratov NI, Stoikolescu CB. Renal excretion of potassium in men under hypokinesia and physical exercise with chronic hyperhydration. Urologia 1988;36:229-38.
33. Zorbas YG, Naexu KA, Federenko YF. Effect of potassium and calcium loading on healthy subjects under hypokinesia and physical exercise with fluid and salt supplements. Acta Astronaut 1995;36:183-9.
34. Tsiamis CB, Kakuris KK, Deogenov VA, Yerullis KB. Magnesium loss in magnesium deficient subjects with and without physical exercise during prolonged hypokinesia. Clin Invest Med 2008;31:E16-23.
35. Deogenov VA, Zorbas YG, Kakuris KK, Federenko YF. The impact of physical exercise on calcium balance in healthy subjects during prolonged hypokinesia. Int J Appl Basic Nutr Sci 2009;25:1029-34.
36. Kakurin LI, Arzamazov GS, Grigoryev AI. Kaliuretic renal function in man as related to different digress of exercise and bed rest. Kosm Biol I Aviakosm Med 1978;4:13-7.
37. Rassolova NP, Potapov AN, Sapelkina IM, Grebennikova II.

Effect of prolonged hypokinesia on indices of energy metabolism in skeletal muscles and internal organs. Kosm Biol Med 1973;7:26-33.
38. Mikhaleva NP, Ivanov II, Federov IV, Amdiy EM. Study of the fructional composition of skeletal muscle proteins during hypokinesia. Kosm Biol I Aviokosm Med 1970;4:42-5.
39. Grinberg LN. Changes in rat liver mitochondria respiration during prolonged hypokinesia. Vopr Med Khim 1970;16:387-90.
40. Chernyy AV. Effect of hypodynamia on animals' reactions to the administration of glucose, epinephrine and insulin referable to some parameters of carbohydrate metabolism, PhD thesis, Interkosmos Council, Academy of Sciences USSR and Directorate of Kosmic Biology and Medicine, Ministry of Health USSR, Moscow; 1981.

How to cite this article: Federenko YF, Yaroshenko YN, Merkov PL, Deno gratov SK. Sodium regulation with periodic fluid redistribution during diminished muscular activity in healthy subjects. Int J Clin Exp Physiol 2014;1:179-86.

Source of Support: Nil, **Conflict of Interest:** Nil.