Endogenous Parathyroid Hormone and Renal Excretion of Magnesium in Endurance Trained Volunteers during Prolonged Restriction of Muscular Activity

Y.G. Zorbas, Y.F. Federenko, Ch.N. Saito

Zusammenfassung

Verschiedene Untersuchungen haben ergeben, daß parathyreoide Hormone (PTH) den Umgang der Nieren mit Magnesium (Mg) beeinflussen. Das Ziel dieser Studie war daher, die Auswirkung von endogener PTH im Umgang der Nieren mit Mg bei Ausdauersportlern während einer Hypokinesie (verminderter Anzahl von Laufschritten/Tag) zu bestimmen. Die Studie wurde bei 30 freiwilligen männlichen Ausdauersportlern zwischen 19 und 24 Jahren durchgeführt mit einer durchschnittlichen Sauerstoffaufnahme von 65 ml/kg−1. min−1 während einer Hypokinesie (HK) von 364 Tagen. Alle freiwilligen Teilnehmer wurden in drei gleiche Gruppen geteilt: 10 Teilnehmer mit einem ständigen Durchschnitt von 10.000 Laufschritten pro Tag, d.h. 14 km/Tag (Kontrollteilnehmer); 10 Teilnehmer mit einer ständigen HK, d.h. einem Durchschnitt von 3.000 Gehschritten/Tag (hypokinetische Teilnehmer) und 10 Freiwillige mit einer kontinuierlichen HK und einer täglichen zusätzlichen Flüssigkeits- und Salzergänzung (FSS) (30 ml Wasser/kg Körpergewicht und 0.15 g Natriumchlorid (NaCl)/kg Körpergewicht), welches zum Ziel hatte, das Serum PTH während der HK (hyperhydrierte Teilnehmer mit höherem Serum-PTH-Gehalt) zu erhöhen. Für die Simulation des hypokinetischen Effektes wurden die hypokinetischen und die hyperhydrierten Teilnehmer mit höherem Serum-PTH-Gehalt unter einem Durchschnitt von 3.000 Gehschritten/Tag, d.h. 2,5 km/Tag, gehalten. Während der prähypokinetischen Periode von 60 Tagen und während der experimentellen Periode von 364 Tagen wurden Serum-parathyroide Hormone (PTH), Serum Magnesium (sMg) und Kalzium (sCa), ultrafiltrierbares Magnesium (ufMg) und Kalzium (ufCa), Harn- Natrium (Na), Ca und Mg, glomerulose Filtrierungsraten (GFR), Hämoglobin (Hb), Hämatokrit (Hct), die Plasma-Osmolalität und der Plasma-Proteingehalt festgestellt. Das Serum PTH, ufMg und ufCa stiegen an, während Serum und Urin-Elektrolyte sowie Blutbestandteile bei den hyperhyd-

Summary

Several Studies have indicated that parathyroid hormone (PTH) influences renal handling of magnesium (Mg). Thus, the aim of this study was to determine the effect of endogenous PTH in renal handling of Mg in endurance trained volunteers during hypokinesia (decreased number of running steps/day). The studies were performed on 30 endurance trained male volunteers between 19-24 years with an average maximum oxygen uptake 65 ml. kg^{-1}. min^{-1} during 364 days of hypokinesia (HK). All volunteers were divided into three equal groups: Ten volunteers were placed continuously under an average of 10.000 running steps per day, that is 14 kilometers per day (control subjects), ten volunteers were subjected continuously to HK i.e. an average of 3.000 walking steps/day (hypokinetic subjects) and ten volunteers were submitted continuously to HK and consume daily fluid and salt supplementation (FSS) (30 ml water/kg body weight and 0.15 g sodium chloride (NaCl)/kg body weight, that aimed to increase serum PTH during HK, (hyperhydrated subjects with higher serum PTH levels). For the simulation of the hypokinetic effect the hypokinetic and hyperhydrated volunteers with higher serum PTH levels were kept under an average of 3.000 walking steps/day that is 2.5 kilometers per day. During the prehypokinetic period of 60 days and during the experimental period of 364 days serum parathyroid hormone (PTH), serum magnesium (sMg) and calcium (sCa), ultrafiltrable magnesium (ufMg) and calcium (ufCa), urinary sodium (Na), Ca and Mg, glomerular filtration rate (GFR), hemoglobin (Hb), hematocrit (Hct), plasma osmolality and plasma protein content were determined. Serum PTH, ufMg and ufCa increased, while serum and urinary electrolytes as well as blood constituents decreased in the hyperhydrated volunteers during HK. By contrast the hypokinetic volunteers displaced significantly reverse changes as compared to control and hyperhydrated volunteers during HK. It is concluded that increased serum PTH does appear to have a significant physiological effect in renal excretion of magnesium in endurance trained volun-

Résumé

Plusieurs études ont prouvé que les hormones parathyroïdes (PTH) excercent une influence sur la manière d'emploi des reins en ce qui concerne le magnésium (Mg). Pour cette raison le but de cette étude était de déterminer l'effet du PTH endogène sur le comportement des reins du Mg chez les sportifs entraînés avec endurance pendant une hypocinésie (HC) (nombre des pas en marche vite diminués/par jour). Les études furent faites sur 30 hommes volontaires mâles entraînés d'endurance agés de 19 á 24 avec un apport d'oxygène maximale de 65 ml kg-1. min-1 pendant 364 jours de HC. Tous les volontaires furent divides en trois groupes égales: 10 volontaires avec 10.000 pas en marche vite par jour continuellement, i.e. 14 km par jour (subjets de contrôle); 10 volontaires qui furent soumis perpetuellement à une HC, i.e. en moyenne 3.000 pas de marche par jour (personnes hypocinésiques), et 10 volontaires qui furent soumis continuellement à la HC et un additif journalier de liquide et sels (FSS) (30 ml de l'eau/kg de poids et 0.15 g de chlorure de sodium (NaCl)/kg de poids, ce qui avait le but d'augmenter le sérum PTH pendant la HC (personnes hyperhydrées avec une teneur de PTH plus élevée). Pour la simulation de l'effet hypocinétique les volontaires hypocinétiques et hyperhydrées avec une teneur élevée de sérum PTH furent soumis à 3.000 pas de marche/jour, i.e. 2,5 km per jour. Pendant la période préhypocinétique de 60 jours, et pendant la période experimentelle de 364 jours des hormones de sérum parathyroïdes (PTH), du sérum de magnésium (sMg) et de calcium (sCa), du magnésium ultrafiltrable (ufMg) et du calcium ultrafiltrable (ufCa), du sodium urinaire (Na), Ca et Mg, un taux de filtration glomérulaire (GFR), de hémoglobine (Hb), de hématicrite (Htc), de plasma osmolalité et de protéine de plasma furent déterminés. Les sérums PTH, ufMg et ufCa augmentaient, tandis que les électrolytes de sérum et urinaires et les parties constituantes diminuaient chez les volontaires hyperhydrés pendant la HC. Par contraire, les volontaires hypocinétiques montraient des changements contraires forts, comparés à les groupes des volontaires de contrôle et hyperhydrés pendant la HC. Les études permettent la conclusion que le sérum

European Institute of Environmental Cybernetics, Athens, Greece.

rierten Freiwilligen während der HK abnahmen. Im Gegensatz dazu wiesen die hypokinetischen Freiwilligen bedeutend umgekehrte Veränderungen auf, verglichen mit den Kontroll- und hyperhydrierten Freiwilligen während der HK. Es wird daraus geschlossen, daß vermehrte Serum- PTH eine bedeutende physiologische Auswirkung in der Ausscheidung von Magnesium der Niere bei Ausdauersportlern während einer verlängerten Verminderung von Muskelaktivitäten zu haben scheint.

teers during prolonged restriction of muscular activity.

PTH augmenté apparaît d'avoir un effet physiologique considérable dans l'excrétion rénale chez les volontaires entraînés d'endurance pendant une réduction prolongée d'activités musculaires.

Introduction

Magnesium is the fourth most prevalent electrolyte in the body and the second mosst abudant intracellular electrolyte [1]. Magnesium is also a cofactor for numerous enzymatic reactions [1]. Despite of prevalence and significance of Mg, little is known about the metabolism of Mg during prolonged restriction of muscular activity and what hypokinetic factors, if any, influence the metabolism of Mg during polonged restriction of muscular activity.

There it has been demonstrated that in times of Mg deprevation of hypomagnesemia, the kidney avidly conserves Mg to less than l meq/24-h period [2, 3]. In contrast, with a high Mg diet or during administration of Mg loading, the urinary excretion of Mg is increased [2, 4]. These studies indicate that the kidney is the primary organ in the fine regulation of Mg metabolism. The fine regulation of renal Mg handling may be entirely a function of the renal nephron in relation to the extra- or intracellular Mg concentrations [5] or secondary to a factor or secondary to a factor or factor(s) which may regulate renal Mg homeostasis. Since Mg is a divalent cation similar to calcium, studies have been performed to determine the possibility that those hormones involved with the maintenance of a normal serum calcium concentration might also control Mg metabolism.

Meanwhile, a number of factors have been demonstrated to influence the renal handling of magnesium, including parathyroid hormone [6, 7], vitamin D [8, 9], calcium [10], sodium [11] and chronic hyperhydration [12]. It is not known, however, if any of these factors and specifically increased serum PTH levels by means of chronic hyperhydration [13] play a physiological role in renal handling of magnesium in endurance trained volunteers during prolonged restriction of muscular activity. It was our purpose in this investigation to determine what role, if any, increased serum parathyroid hormone levels played in relation to the renal excretion of magnesium in endurance trained volunteers during prolonged restriction of muscular activity and chronic hyperhydration.

Material and Methods

Subject Selection

Thirty endurance trained male volunteers ranging in age from 19 to 24 years gave informed consent for participation in the study after a written and verbal explanation of the procedures and risks involved. All procedures were reviously reviewed and approved by the University Committee for the Protection of Human Subjects. All volunteers were long distance runners for the last three to five years and were trained in on a regular basis in order to increase their endurance capacity (5-6 times a week, (72±20 (SD) km/ week) and all of them were considered "elite athletes". All volunteers were on 14 km per day (10.000 running steps/day). Physical characteristics of volunteers are presented in the tab. 1.

Experimental Design

Each subject was placed on a metabolic diet 60 days before the starting of the study. During the initial 30 days, the diet was adjusted to maintain body weight. The adjusted diet was then maintained for the remainder of the study and was controlled for calories, fluid, and electrolyte content. The dietary composition of selected parame-

Tab. 1: Anthropometric and peak oxygen uptake changes of endurance trained male volunteers during prolonged restriction of muscular activity and chronic hyperhydration.

Examined Parameters		Groups of Volunteers: Ambulatory Control	Unsupplemented Hypokinetic	Supplemented Hypokinetic
N		10	10	10
Age in yr		23.7 ± 7.4	22.9 ± 6.3	22.4 ± 7.5
Height, cm		175.6 ± 8.5	176.8 ± 6.4	177.7 ± 5.8
Body Mass, kg	Before	74.7 ± 5.3	75.6 ± 4.6	73.9 ± 5.4
	After	74.9 ± 4.4	70.1 ± 5.7*	76.0 ± 5.0+
Body Fat, %	Before	9.9 ± 1.2	10.3 ± 1.3	9.4 ± 1.2
	After	10.1 ± 1.3	6.6 ± 1.2*	12.5 ± 2.4+
Fat Free Body	Before	67.1 ± 6.4	67.9 ± 6.3	67.0 ± 6.5
Mass, kg	After	67.1 ± 5.5	65.5 ± 5.0	66.2 ± 5.3
VO_2 max	Before	64.3 ± 4.6	65.5 ± 6.6	65.5 ± 7.4
$ml.kg^{-1} \cdot min^{-1}$	After	65.5 ± 5.0	51.8 ± 7.4*	66.1 ± 5.0

Note: Here and in the tabs. 3, 4 and 5.

* $P < 0.05$ significant differences between hypokinetic and ambulatory control groups of volunteers.

+ $P < 0.05$ significant differences between supplemented hypokinetic and unsupplemented hypokinetic groups of volunteers.

Tab. 2: Average dietary intake per day by endurance trained male volunteers during prolonged restriction of muscular activity and chronic hyperhydration.

	Mean ± S.D.	Average
Calories, kcal	2746 ± 178	2463 – 2908
Protein, g	112.9 ± 8.5	98.7 – 127.3
Fat, g	89.5 ± 10.6	69.4 – 109.7
Carbohydrates, g	343.6 ± 13.4	275.2 – 389.5
Sodium, mg	3867.8 ± 8.7	3757 – 4265
Potassium, mg	3384.3 ± 352.6	2879 – 4093
Calcium, mg	1375.4 ± 117.5	1265 – 1520
Magnesium, mg	447 ± 34	279 – 514
Phosphorus, mg	1218.5 ± 135.7	1138 – 1445
Fluid Intake, ml	2762 ± 761	1657 – 3650

ters for the 30 volunteers are preesented in the tab. 2. To establish familiarity with the study procedures, each subject at this period of time also underwent physiological and biochemical parameters determinations at rest prior to their participation in the study.
The subjects were randomly assigned to one of the three groups:

Group 1: Ten volunteers who had exercised regularly 5-6 times per week to develop endurance and had took an average of 10.000 running steps/day for the last three to five years and had on the average a maximum oxygen uptake 65 $ml.kg^{-1}.min^{-1}$ and were continuously under an average of 14 km/day served as control subjects.

Group 2: Ten volunteers who had exercised regularly 5-6 times per week to develop endurance and had took 14 km per day (10.000 running steps/day) for the last three to five years and had on the average a maximum oxygen uptake 65 $ml.kg^{-1}.min^{-1}$ and had been restricted their muscular activity to an average of 3.000 walking steps/day (2.5 km/day) for 364 days served as hypokinetic subjects.

Group 3: Ten volunteers who had exercised regularly 5-6 times/ week to develop endurance and took 14 km per day (10.000 running steps/days) for the last three to five years and had on the average a maximum oxygen uptake 65 $ml.kg^{-1}.min^{-1}$ and had been restricted their muscular activity to an average of 2.5 kilometers per day and had consumed daily an additional amount of fluid and salt supplementation (water 30 ml/kg body weight and sodium chloride 0.15 g/kg body weight) served as hyperhydrated subjects.

Subjects were admitted to the Metabolic Study Unit, and a 30-bed clinical investigation ward, where the studies were performed. For the simulation of the hypokinetic effect the number of running steps taken per day by the volunteers was restricted to an average of 3.000 walking steps per day, while they were allowed to remain in a clinostatic position (+10°) for about 14 hours/ day that include sleeping and resting time and in an orthostatic position for about 10 hours/day that include different daily activities and moderate exercise, so that the study would approximately be like the normal life style of an non-active sedentary individual. During orthostatsis the volunteers were also allowed to walk to dining tables, lavatories, and various laboratories for a series of clinical and biochemical tests without allowing them walking upstairs and increasing the designated regime of hypokinesia and thus increasing energy expenditure. The number of steps taken/day by the hypokinetic and hyperhydrated groups of volunteers averaged to 3.000 walking steps and calculated with the use of a pedometer.

Sample Collection

On the 15th, 30th and 60th day of the prehypokinetic period and on the 60th, 120th, 180th, 240th, 300th and 364th day of the experimental period twenty four hour urine collection were obtained and frozen until analyzed for magnesium, calcium and sodium.
On the 15th, 30th and 60th day of the preexperimental period and on the 60th, 120th, 180th, 240th 300th and 364th day of the experimental period, resting blood samples (fasting) were obtained from a superficial (antecubital) arm vein each morning between 06:00 and 09:00 hours. Samples were drawn without venus stasis after the subjects had assumed a sitting position for 30 minutes. Each blood collection was about 8–10 ml. Blood for serum was allowed to clot at room temperature for 15 minutes and kept on ice for at least 60 minutes. The serum was separated by centrifugation and stored at –20°C until analyses were performed. Blood for plasma was collected in heparinized ice-chilled tubes which were centrifuged immediately in a centrifuge. The blood samples were analyzed for hemoglobin, hematocrit, plasma protein, plasma osmolality, calcium and magnesium concentrations in blood serum and serum parathyroid hormone content.

Biochemical Methodology

All measurements were performed in duplicate: Serum and urinary magnesium and calcium concentrations were determined by atomic absorption spectrophotometry (Perkin-Elmer Model, Perkin- Elmer Corp., South Pasadena, CA, U.S.A). Urinary sodium concentrations were determined by a digital flame spectrophotometer. Blood plasma osmolality was measured by freezing point depression, hemoglobin concentration determined by the cyanomethemoglobin method, hemato-

crit index estimated by the microchematocrit method and plasma protein concentration was determined by using an automated method.
The ultrafiltrable serum magnesium (ufsMg) and ultrafiltrable serum calcium (ufsCa) fractions were obtained with the use of an Amicon Centriflo ultrafiltrations cones (Amicon Corp., Lexington, MA, USA). Three milliliters of the serum were placed in a presoaked cone under a thin layer of mineral oil and centrifuged for 10 minutes at 2000 rpm at room temperature.

Glomerular Filtration Rate
The glomerular filtration rate (GFR) was determined through the use of Glofil 125 (Sodium Iothalamate ^{125}I injection, Abbott Laboratories, North Chicago, IL, USA). A loading dose of 15 µCi was given in a 1 ml volume over 5 minutes, followed by a sustained infusion of 65 µCi in 30 ml 5% dextrose in water over an ensuing 8 h study period.

Radioimmunoassay Methodology
All measurements were performed in duplicate: The concentration of C-terminal fragment of parathyroid hormone (PTH) in blood serum was assayed by using a PTH radioimmunoassay test kit purchased from Sorin Corp., (Vicenza, Italy). Three-milliliters of aliquots of urine and plasma were placed in plastic tubes and counted in a gamma- spectrophotometer for determination of ^{125}I.

Anthropometric and Metabolic Measurements
Anthropometric variables included the measurements of body mass, and body height. The percentage of body fat was estimated from the skinfold thickmess measurements [14]. Lean body mass was obtained by substracting the estimated fat mass from the body mass. Maximum oxygen uptake was measured by using an open circuit spirometer and the volunteers were tested on a treadmill.

Statistical Analysis
The results obtained were subjected to statistical processing by using the method of analysis of variance (ANOVA) with repeated measures design. The analysis was performed on data obtained from 30 volunteers at various sampling intervals. The significance of differences among the three groups of volunteers was determined by using the statistical test of *Tukey*. A significant change had occurred if $p < 0.05$.

Results

Subjects' General Conditions
All of the tested volunteers were maximaly comfortable and were not complained of any discomfort during the experimental period. In all of the tested volunteers the appetite was good, sleep was deep and uninterrupted, lasting about 8 to 10 hours per day and during some days of the experimental period even longer.

Body and Peak VO_2 Changes
In the hyperhydrated volunteers body mass increased significantly ($P < 0.05$). Their lean body mass decreased, while body fat and maximum oxygen uptake increased as compared to the hypokinetic volunteers during the experimental period (tab. 1). By contrast, the hypokinetic volunteers displaced a significant decrease in their body weight, body fat, fat-free body mass and maximum oxygen uptake as compared to control and hyperhydrated groups of volunteers during the experimental period (tab. 1).

Body Hydration Parameters
In the hyperhydrated volunteers hematocrit index, hemoglobin concentration, plasma osmolality and plasma protein concentration decreased significantly ($P < 0.05$) as compared to the hypokinetic volunteers during the experimental period (tab. 3). In the hypokinetic volunteers hematocrit index, hemoglobin cincentration, blood plasma osmolality and plasma protein concentration increased significantly ($P < 0.05$) as compared to both control and hyperhydrated groups of volunteers during the experimental period (tab. 3). Between the control and hyperhydrated volunteers were not demonstrated any differences with regard to the blood constituents during the experimental period (tab. 3).

Glomerular Filtration Rate Changes
In the hypokinetic volunteers glomerular filtration rate decreased significantly ($P < 0.05$) as compared to the control and hyperhydrated groups of volunteers during the experimental period (tab. 4). In the hyperhydrated volunteers glomerular filtration increased as compared to the hypokinetic group of volunteers during the experimental period (tab. 4). Between the control and hyperhydrated volunteers were not demonstrated any significant differences with regard to the glomerular filtration rate during the experimental period (tab. 4).

Parathyroid Hormone
The mean serum parathyroid hormone content increased significantly ($P < 0.05$) in the hyperhydrated volunteers as compared to the hypokinetic volunteers during the experimental period (tab. 4). By contrast, the mean parathyriod concentration in blood serum of hypokinetic volunteers decreased significantly ($P < 0.05$) as compared to both control and hyperhydrated groups of volunteers during the experimental period (tab. 4). There was no significant difference between the control and hyperhydrated volunteers with regard to sereum parathyroid hormone concentration during the experimental period (tab. 4).

Urinary Electrolytes
The mean urinary excretion of magnesium, calcium and sodium in the hyperhydrated volunteers decreased as compared to the hypokinetic volunteers during prolonged restriction of muscular activity (tab. 5). The mean urinary excretion of magnesium, calcium and sodium increased significantly ($P < 0.05$) in the hypokinetic volunteers as compared to the control and hyperhydrated groups of volunteers, reaching a maximum level by the end of the experimental period (tab. 5). In the hypokinetic volunteers urinary excretion of electrolytes increased progressively as the duration of the hypokinetic period increased (tab. 5). There was not any significant differences between the hyperhydrated and control groups of volunteers with regard to urinary excretion of electrolytes, in fact

Tab. 3: Blood biochemical changes in endurance trained male volunteers during ambulatory control, hypokinetic and hypokinetic hyperhydrated conditions (mean ± S.E.M.).

Groups of Men	Examined Parameters	Baseline	Duration of Experimental Period in days					
			60th	120th	180th	240th	300th	364th
Ambulatory Control n=10	Osmolality, mOsm/kg	278 ± 1.5	278 ± 1.4	278 ± 1.2	278 ± 1.5	278 ± 1.3	278 ± 1.3	278 ± 1.5
	Total Prot.g/dl	6.15 ± 0.07	6.15 ± 0.05	6.15 ± 0.03	6.15 ± 0.05	6.15 ± 0.04	6.15 ± 0.06	6.15 ± 0.05
	Hematocrit, %	49.5 ± 1.5	49.5 ± 1.3	49.5 ± 1.5	49.5 ± 1.4	49.5 ± 1.7	49.5 ± 1.4	49.5 ± 1.3
	Hemoglobin,g/dl	16.5 ± 0.7	16.5 ± 0.7	16.5 ± 0.5	16.5 ± 1.3	16.5 ± 1.6	16.5 ± 1.3	16.5 ± 1.5
Unsupplemented Hypokinetic n=10	Osmolality, mOsm/kg	280 ± 1.3	288 ± 1.6	296 ± 1.5*	293 ± 1.6*	290 ± 1.3*	298 ± 1.5*	307 ± 1.3*
	Total Prot. g/dl	6.16 ± 0.04	6.60 ± 0.03	7.06 ± 0.07*	6.94 ± 0.04*	6.75 ± 0.06*	7.20 ± 0.03*	7.58 ± 0.05*
	Hematocrit, %	49.8 ± 1.3	53.6 ± 1.5	56.0 ± 1.3*	55.0 ± 1.7*	53.5 ± 1.5*	56.3 ± 1.6*	58.8 ± 1.5*
	Hemoglobin, g/dl	16.6 ± 0.5	17.9 ± 0.3	18.7 ± 0.6*	18.4 ± 0.5*	17.9 ± 0.6*	19.0 ± 0.5*	20.3 ± 0.6*
Supplemented Hypokinetic n=10	Osmolality, mOsm/kg	283 ± 1.6	280 ± 1.2	277 ± 1.4+	279 ± 1.6+	281 ± 1.5+	278 ± 1.3+	274 ± 1.5+
	Total Prot. g/dl	6.18 ± 0.03	6.01 ± 0.03	5.73 ± 0.05+	5.80 ± 0.03+	5.85 ± 0.06+	5.63 ± 0.03+	5.44 ± 0.06+
	Hematocrit, %	50.4 ± 1.7	48.0 ± 1.4	45.3 ± 1.5+	46.7 ± 1.3+	47.4 ± 1.5+	45.0 ± 1.4+	42.5 ± 1.3+
	Hemoglobin, g/dl	16.8 ± 0.3	16.0 ± 0.5	15.2 ± 0.6+	15.5 ± 0.4+	15.9 ± 0.3+	15.0 ± 0.5+	14.2 ± 0.4+

Tab. 4: Glomerular filtration rate and serum parathyroid hormone concentration in endurance trained volunteers during prolonged restriction of muscular activity and chronic hyperhydration (mean ± S. E. M.) n = 30.

Groups of Men	Examined Parameters	Baseline	Duration of Experimental period in days					
			60th	120th	180th	240th	300th	364th
Control n = 10	Glomerular Filtration, ml/min	115 ± 4.4	115 ± 2.6	114 ± 5.6	115 ± 4.0	114 ± 6.5	115 ± 5.5	115 ± 5.3
	Parathyroid Hormone, ng/ml	0.18 ± 0.5	0.18 ± 0.4	0.18 ± 0.7	0.19 ± 0.3	0.18 ± 0.5	0.19 ± 0.3	0.18 ± 0.4
Hypokinetic n = 10	Glomerular Filtration ml/min	116 ± 3.5	111 ± 4.4	105 ± 5.0*	100 ± 5.5*	103 ± 3.4*	96 ± 2.4*	91 ± 3.0*
	Parathyroid Hormone ng/ml	0.19 ± 0.7	0.18 ± 0.8	0.17 ± 0.5*	0.15 ± 0.6*	0.13 ± 0.4*	0.11 ± 0.5*	0.10 ± 0.3*
Hyperhydrated n = 10	Glomerular Filtration ml/min	114 ± 2.2	117 ± 6.4	120 ± 5.5	126 ± 7.5	123 ± 4.6	128 ± 7.4	134 ± 6.0
	Parathyroid Hormone ng/ml	0.17 ± 0.4	0.19 ± 0.8	0.23 ± 0.6	0.25 ± 0.5	0.23 ± 0.4	0.25 ± 0.6	0.27 ± 0.7

urinary excretion of electrolytes was somewhat lower than in the control volunteers (tab. 5).

Serum and Ultrafiltrable Electrolytes

Serum magnesium and serum calcium concentrations, and ultrafiltrable serum magnesium and ultrafiltrable calcium concentrations for the three groups of volunteers are presented in the (tab. 6). In the hyperhydrated volunteers serum magnesium and calcium concentrations decreased, while ultrafiltrable magnesium and calcium concentrations increased during hypokinesia as compared to the hypokinetic volunteers (tab. 6). In the hypokinetic volunteers with lower serum parathyroid hormone content serum magnesium and calcium concentrations increased significantly ($P < 0.05$) as compared to the control and hyperhydrated volunteers with high serum parathyroid hormone content (tab. 6), while ultrafiltrable serum magnesium and calcium concentrations decreased significantly ($P < 0.05$) as compared to control and hyperhydrated volunteers with higher serum parathyroid content during the experimental period (tab. 6). Between the control and hyperhydrated volunteers were not observed any significant differences with regard to serum and calcium concentrations and ultrafiltrable magnesium and calcium concentrations during the experimental period (tab. 6).

Discussion

During the experimental period none of the volunteers experienced any

Tab. 5: Urinary excretion of electrolytes (mEq/24-h) in endurance trained volunteers during prolonged restriction of muscular activity and chronic hyperhydration (mean ± S. E. M.) n = 30.

Groups of Men	Examined Parameters	Baseline	Duration of Experimental period in days					
			60th	120th	180th	240th	300th	364th
Control	Magnesium	7.3 ± 0.3	7.4 ± 0.3	7.4 ± 0.5	7.3 ± 0.7	7.3 ± 0.7	7.4 ± 0.5	7.2 ± 0.4
	Calcium	8.2 ± 0.5	8.3 ± 0.3	8.2 ± 0.6	8.3 ± 0.4	7.1 ± 0.5	7.3 ± 0.4	7.2 ± 0.5
n = 10	Sodium	140 ± 31	141 ± 50	140 ± 44	141 ± 39	140 ± 25	140 ± 55	143 ± 43
Hypo-	Magnesium	7.1 ± 0.5	7.8 ± 0.7	8.6 ± 0.4*	9.3 ± 0.4*	8.9 ± 0.5	9.6 ± 0.7*	10.3 ± 0.9*
kinetic	Calcium	8.1 ± 0.4	8.9 ± 0.6	9.7 ± 0.5*	10.5 ± 0.8*	10.1 ± 0.7*	10.9 ± 0.8*	11.7 ± 0.6*
n = 10	Sodium	139 ± 60	167 ± 57	178 ± 48*	197 ± 66*	188 ± 59*	209 ± 67*	225 ± 74*
Hyperhy-	Magnesium	7.2 ± 0.4	7.1 ± 0.6	7.0 ± 0.4	6.8 ± 0.5	6.9 ± 0.4	6.7 ± 0.6	6.5 ± 0.3
drated	Calcium	8.3 ± 0.5	8.1 ± 0.7	8.9 ± 0.5	8.6 ± 0.4	8.8 ± 0.5	8.6 ± 0.4	8.3 ± 0.5
n = 10	Sodium	141 ± 53	139 ± 35	135 ± 6	130 ± 50	135 ± 46	130 ± 48	127 ± 34

Tab. 6: Serum magnesium and calcium (mg/dl) and ultrafiltrated magnesium and calcium (mg/dl) in endurance trained volunteers during prolonged restriction of muscular activity and chronic hyperhydration (mean ± S. E. M.) n = 30.

Groups of Men	Examined Parameters	Baseline	Duration of Experimental period in days					
			60th	120th	180th	240th	300th	364th
	Serum Magnes.	1.8 ± 0.1	1.8 ± 0.1	1.8 ± 0.1	1.8 ± 0.3	1.8 ± 0.1	1.8 ± 0.2	1.8 ± 0.3
n = 10	Ultrafiltrab. Magnesium	1.4 ± 0.2	1.4 ± 0.3	1.4 ± 0.5	1.5 ± 0.2	1.4 ± 0.3	1.4 ± 0.5	1.4 ± 0.4
Control	Serum Calcium	8.7 ± 0.2	8.7 ± 0.4	8.7 ± .4	8.8 ± .3	8.7 ± 0.6	8.8 ± 0.4	8.7 ± 0.5
	Ultrafiltrab. Calcium	5.5 ± 0.2	5.5 ± 0.4	5.6 ± 0.3	5.6 ± 0.5	5.5 ± 0.2	5.6 ± 0.5	5.5 ± 0.3
	Serum Magnes.	1.7 ± 0.1	1.9 ± 0.2	2.3 ± 0.3*	2.6 ± 0.5*	2.3 ± 0.3*	2.6 ± 0.4*	2.8 ± 0.4*
n = 10	Ultrafiltrab. Magnesium	1.6 ± 0.1	1.5 ± 0.1	1.3 ± 0.2*	1.1 ± 0.3*	1.3 ± 0.2*	1.2 ± 0.3*	1.0 ± 0.1*
Hypo-	Serum Calcium	8.6 ± 0.3	9.1 ± 0.4	9.7 ± 0.5*	10.2 ± 0.7*	9.9 ± 0.4*	10.6 ± 0.6*	11.3 ± 0.5*
kinetic	Ultrafiltrab. Calcium	5.6 ± 0.2	5.3 ± 0.3	4.9 ± .2*	4.5 ± .3*	4.7 ± 0.3*	4.5 ± 0.2*	4.2 ± 0.1*
	Serum Magnes.	1.9 ± 0.2	1.8 ± 0.3	1.7 ± 0.2	1.5 ± 0.3	1.6 ± 0.2	1.5 ± 0.3	1.3 ± 0.2
n = 10	Ultrafiltrab. Magnesium	1.5 ± 0.1	2.0 ± 0.3	2.5 ± 0.6	3.3 ± 0.5	3.1 ± .4	3.7 ± 0.5	4.1 ± 0.6
Hyperhy-	Serum Calcium	8.9 ± 0.5	8.8 ± 0.6	8.7 ± 0.4	8.5 ± 0.6	8.6 ± .5	8.4 ± 0.4	8.1 ± 0.5
drated	Ultrafiltrab. Calcium	5.4 ± 0.3	5.7 ± 0.3	5.9 ± 0.5	6.1 ± 0.4	5.9 ± 0.5	6.3 ± 0.6	6.5 ± 0.3

symptoms or disorders which is indicative of the fact that all of the tested volunteers tolerated very well their exposure to these experimental conditions.

Body and Peak VO_2 Changes

The possible reasons responsible for the significant reduction of body weight in the hypokinetic volunteers during prolonged restriction of muscular activity may be the following:

a) body dehydration resulting from the increased excretion of fluid and electrolytes [15, 16];

b) decreased muscle mass due to the deconditioning effect [17, 18]; and inadequate food consumption for different reasons, that is loss of appetite for some foods and loss of taste for others [19, 20]. However, since the body weight in the hyperhydrated volunteers increased significantly as compared to the hypokinetic volunteers, it can be concluded that the demonstrated increases in body weight of hyperhydrated volunteers during prolonged restriction of muscular activity may be indicative of the possibility of compensation and even exceeding metabolic losses with food and water allowance, provided a good appetite was maintained, as a result of gustatory qualities of rations, and above all a daily intake of water and salt supplementation was maintained, due to the reduction of voluntary consumption of fluid and salt which is inherent to prolonged restriction of muscular activity [15, 16].

Body Hydration Parameters

The beneficial effect of a daily intake of fluid and salt supplementation on body hydration level was apparently related to increase in circulating blood volume during hypokinesia of endurance trained volunteers. This was indicated by the significant ($P < 0.05$) decrease of hematocrit index, hemoglobin concentration, blood osmolality, plasma protein concentration and blood plasma concentration of electrolytes in hyperhydrated volunteers during prolonged restriction of muscular activity. At the same time, the hypokinetic volunteers displaced a significant ($P < 0.05$) increase in hemoglobin concentration, hematocrit index, plasma osmolality, plasma protein concentration as well as plasma concentrations of electrolytes, corresponding to the results obtained in previous experimental studies [15, 16].

Renal Handling of Magnesium

The kidney is the major organ concerned with the fine regulation of magnesium metabolism. Under ordinary muscular activity conditions a high dietary intake of magnesium results in an increase in urinary excretion magnesium [2], without a significant change in

the plasma concentration of magnesium. Under hypokinetic conditions a high dietary intake of magnesium results in a significant increease in urinary excretion of magnesium with a significant increase in the plasma concentration of magnesium [21, 22], demonstrating the inability of the organism to retain magnesium during prolonged restriction of muscular activity, since the conditions are less favorable for deposition of magnesium excess in hypokinetic volunteers due to the development of muscle atrophy and consequent changes in total magnesium content of cells during prolonged restriction of muscular activity. Conversely, during hypokinesia and chronic hyperhydration a high dietary intake of magnesium results in a decrease in urinary excretion of magnesium [21, 22]. This occurs without a significant change in the plasma concentration of magnesium or a decrease in plasma magnesium concentration.

Micropuncture studies on both rat and dog kidney tubules have indicated that magnesium is reabsorbed along the proximal tubules and the thick ascending limb of Henle [5, 23-27]. Proximal tubular magnesium accounts for 10 to 20% of magnesium reabsorbed along the nephron. The major site of magnesium reabsorption is at the ascending limb of Henle and accounts for 50 to 75% of the total magnesium reabsorbed along the nephron. This may be an active or, possibly, a passive process accompanying active chloride transport [5].

Parathyroid Hormone and Renal Handling of Magnesium

Several studies have indicated that parathyroid hormone influences renal excretion of magnesium. Acute parathyroidectomy in the rat results in an increase in renal magnesium excretion [28], and the administration of parathyroid extract reduces urinary magnesium excretion in the parathyroidectomized rat [29]. Similarly, exogenous parathyroid hormone results in a decrease in urinary magnesium excretion in the parathyroidectomized cow [30]. In the parathyroid-intact dog, parathyroid extract decreased the percentage of filtered magnesium excreted during magnesium infusions [31]. Studies in hyperparathyroid individuals revealed that the administration of parathyroid extract ressults in a decrease in urinary excretion of magnesium [6, 7]. The results obtained from these and other studies have led several investigators to conclude that parathyroid hormone does indeed results in an increase in the rate of renal tubular reabsorption of magnesium. However, data obtained form physically healthy individuals are contradictory with regard to the parathyroid hormone effect on renal excretion of magnesium. Urinary excretion of magnesium has been demonstrated to decrease [32], remain unchanged [6, 7], or increase [33] in parathyroid-intact volunteers after administration of exogenous parathyroid hormone. At the same time results obtained from endurance trained volunteers subjected to prolonged restriction of muscular activity and a daily intake of fluid and salt supplementation, which is accompanied by an increase in serum parathyroid hormone content, revealed a significant decrease in renal excretion of magnesium [21, 22].

The role of endogenous parathyroid hormone in magnesium metabolism on endurance trained volunteers during prolonged restriction of muscular activity has not been studied very extensively. During prolonged restriction of muscular activity magnesium and calcium deficiency induced by prolonged hypokinesia resulted in a significant decrease in fractional renal reabsorption of magnesium and calcium in the hypokinetic volunteers [21, 22]. This decrease in renal reabsorption of electrolytes was dependent on the presence of parathyroid hormone levels in blood serum of hypokinetic volunteers. No increase in renal magnesium reabsorption was observed in volunteers subjected to prolonged restriction of muscular activity, despite the development of hypomagnesemia. At the same time urinary conservation of magnesium were demonstrated to be significantly greater in the hyperhydrated volunteers as compared to the hypokinetic volunteers, suggesting that the presence of increased serum parathyroid hormone does influences the handling of renal magnesium in endurance trained volunteers during prolonged restriction of muscular activity. In the hypokinetic volunteers, the serum magnesium concentration has been demonstrated to be increased significantly ($P < 0.05$) as compared to the control and hyperhydrated groups of volunteers. In previous experimental studies the serum magnesium concentration has been also found to be increased in endurance trained volunteers subjected to prolonged restriction of muscular activity [21, 22]. In the present study, it has been also demonstrated a significant ($P < 0.05$) difference in the serum magnesium and calcium concentrations among the hypokinetic and hyperhydrated groups of volunteers during exposure to hypokinesia. The effeects of increased serum parathyroid content on renal excretion of magnesium and calcium during hypokinesia and chronic hyperhydration are characterized by an increase in the capacity of the renal tubules to reabsorb these electrolytes during prolonged restriction of muscular activity [21, 22]. There is an increasee in the ability of the kidney to reabsorb magnesium and calcium in the hyperhydrated volunteers, whereas renal capacity of the kidney to reabsorb magnesium and calcium decreased significantly in the hypokinetic volunteers. The results obtained clearly demonstrate that between the hyperhydrated volunteers with high serum parathyroid hormone levels and the hypokinetic volunteers with low serum parathyroid hormone levels, there is a significant difference with regard to renal excretion of magnesium during prolonged restriction of muscular activity. These findings suggest that high serum parathyroid hormone content does indeed play an important physiological role in renal handling of magnesium on endurance trained volunteers during prolonged restriction of muscular activity and a daily intake of fluid and salt supplementation.

The demonstrated effects of serum parathyroid hormone levels on urinary excretion of magnesium in endurance trained volunteers during prolonged restriction of muscular activity could also be indirect. It is suggested that

magnesium shares a common transport system with calcium in the kidney [10]. Calcium loading tests performed on endurance trained volunteers during prolonged restriction of muscular activity, resulting in an increase in the urinary excretion of calcium, producing an increase in magnesium excretion as well [13]. This may explain why exposure to prolonged restriction of muscular activity may be associated with a negative magnesium balance [13], since during prolonged restriction of muscular activity there is an increased urinary excretion of calcium due to either a decrease in fractional reabsorption of calcium or an increase in the filtered calcium load during prolonged restriction of muscular activity. It is conceivable therefore that the decrease in urinary excretion of magnesium observeed in the hyperhydrated volunteers with high serum parathyroid hormone content may be secondary to the decrease urinary excretion of calcium in the course of prolonged restriction of muscular activity.

Conclusion

Further knowledge of the effect of endogenous parathyroid hormone on renal handling of magnesium in endurance trained volunteers during prolonged restriction of muscular activity may come from studies on individuals subjected to prolonged restriction of muscular activity by virtue of age, disease, disability, bed rest, occupation and some other factors. Prolonged restriction of muscular activity is characterized by hypermagnesemia and hypermagnesuria in the presence of hypercalcemia and hypercalciurea. The nature of these changes during prolonged restriction of muscular activity have not been studied extensively, but may be attributed to a primary change in tissular metabolism, muscle atrophy, and consequent changes in total magnesium and calcium content of cells during prolonged restriction of muscular activity. It is conceivable that the high levels of parathyroid hormone in the blood serum of the hyperhydrated volunteers during prolonged restriction of muscular activity increased the rate of renal reabsorption of magnesium and calcium. Since serum levels of parathyroid hormone remained significantly lower in the hypokinetic volunteers as compared to the control and hyperhydrated volunteers, it is likely that the increase serum parathyroid hormone content influences the handling of renal magnesium in endurance trained volunteers during prolonged restriction of muscular activity and a daily intake of fluid and salt supplementation.

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Correspondence to:
Y.F. Federenko, Hypokinetic Physiology Lab., European Institute of Environmental Cybernetics, GR-163 32 Athens, Greece.