# Daily Magnesium Supplementation Effect on Magnesium Deficiency in Rats During Prolonged Restriction of Motor Activity

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**The objective of this investigation was to evaluate the effect of magnesium (Mg) supplements in rats during prolonged restriction of motor activity (hypokinesia [HK]) and in the presence of Mg deficiency, which is characterized by increased rather than decreased plasma Mg concentration, as occurs in ambulatory conditions. The studies were performed during 98 days of HK on 100 13-week-old Sprague-Dawlay male rats weighing 360 to 390 g. They were equally divided into four groups: (1) unsupplemented control animals (UCA), (2) unsupplemented hypokinetic animals (UHA), (3) supplemented control animals (SCA), and (4) supplemented hypokinetic animals (SHA). For the simulation of the hypokinetic effect, SHA and UHA were kept for 98 days in small individual wood cages that restricted their movements in all directions without hindering food and water intake. The SCA and SHA took daily with their food an additional 0.35 mg of Mg. Before and during the hypokinetic period of 98 days, Mg in plasma, urine, and feces, balance of Mg, food intake of Mg, and body weight were determined at different intervals. In SHA and UHA, plasma Mg concentration and excretion of Mg in urine and feces increased significantly compared with SCA and UCA. Magnesium balance was negative in UHA and AHA throughout the hypokinetic period. Body weight and a food intake decreased significantly in SHA and UHA when compared with SCA and UCA. Significant losses of Mg in SHA and UHA occurred in the presence of Mg deficiency and suggest that prolonged HK induces another factor that influences Mg metabolism. We conclude that prolonged HK causes significant changes in Mg values of plasma, urine, and feces and a negative Mg balance in rats, despite Mg supplements leading to Mg deficiency.**


RESTRICTION OF MOTOR ACTIVITY (hypokinesia [HK]), particularly prolonged restriction of motor activity, acts like an unusual stress stimulus, which is demonstrated by the significant release of stress hormones, catecholamines, and corticosteroids.[1,2] HK mediates the significant intensification of electrolyte losses from the body, resulting in electrolyte deficiency.[3-10] It should be remembered that electrolyte deficiency during HK causes hyperelectrolemia, and not hypoelectrolemia as happens during ambulatory and clinical conditions, indicating the involvement of some other mechanisms as being responsible for the control and regulation of electrolyte metabolism during prolonged restriction of motor activity.[3-10]

Magnesium (Mg) deficiency, which is also characterized by higher rather than lower Mg concentrations during HK and which is caused due to the significant Mg loss in the urine and feces, can be implicated in cardiovascular disorders involving thrombotic events and arrhythmias when there is underlying Mg deficiency. There is evidence that Mg deficiency contributes to sudden cardiac death. During prolonged restriction of motor activity when there is a significant Mg deficiency, as is caused by a significant excretion of Mg in urine and feces, additional Mg loss from the body might be a factor in morbidity and mortality, because additional intake of Mg supplementation cannot be used to improve Mg deficiency during prolonged HK.[3-10] The Mg deficiency persists long after termination of exposure to prolonged HK.[3-10] Animals and humans subjected to prolonged restriction of motor activity were given a diet with increased Mg content to prevent complications referable to Mg metabolism. However, despite these measures, both the animals and humans presented an increase in Mg deficiency. Addition of Mg to the diet did not normalize Mg content of extracellular fluid and did not eliminate the metabolic changes of Mg during prolonged HK.[3-10]

The present study was undertaken to determine whether daily intake of large amounts of Mg could prevent Mg deficiency in hypokinetic rats. Additionally, we hoped to learn more about the underlying mechanisms of Mg deficiency during prolonged HK, which is manifested by increased plasma concentrations of Mg.

## MATERIALS AND METHODS

One hundred 93- to 99-day-old Sprague-Dawley male rats were obtained from an International Research Laboratory (Moscow, Russia). On arrival, they were given an adaptation and rehydration period of 15 days, during which they were fed a commercial laboratory diet. Daily food consumption was determined and 90% of daily intake (15 g) was mixed with deionized distilled water (1:2 wt/vol) to form a slurry, which was fed in two meals for a 15-day adjustment period. Daily feed intake was determined during both the preexperimental period of 15 days and the experimental period of 98 days. Feed for the entire study was from the same production lot that provided 0.6 mg Mg/g diet and was maintained in a cold chamber (4°C). Rats were provided with daily deionized distilled water ad libitum. Rats were maintained in a 25°C environment with a 12-hour light-dark cycle. The animals were weighed at regular intervals between 9 and 10 AM.

### *Blood, Urine, and Feces Collections*

Blood samples were obtained via cardiac puncture from ether-anesthetized animals in syringes containing heparin, which was free of Mg. Urine for each 24-hour period was collected in acidified acid-wash containers, measured, and stored at 4°C for later analysis of Mg. Feces were collected daily, dried, weighed, and frozen at −20°C for later analysis. Diet was measured at regular intervals for Mg content. Baseline results were collected on all animals for 15 days before exposure to hypokinesia and at regular intervals during the preexperimental period and before and after the intake of Mg supplementation.

### *Mg Analysis*

All samples were analyzed in duplicate and appropriate standards were used for all examined samples. Mg concentrations in plasma, urine, and feces were measured using an atomic absorption spectrophotometer (Instrumentation Laboratory, Wilmington, MA).

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All animals were randomly assigned to one of four groups. The conditions of the four groups of animals were as follows:

*Group 1.* Twenty-five unrestrained rats were housed in individual cages under ordinary vivarium conditions. Rats were not supplemented with Mg and served as unsupplemented control animals (UCA).

*Group 2.* Twenty-five restrained rats were subjected to 98 days of HK and were not supplemented with Mg. They served as unsupplemented hypokinetic animals (UHA).

*Group 3.* Twenty-five unrestrained rats were housed in individual cages under ordinary vivarium conditions and were supplemented with Mg. They served as supplemented control animals (SCA).

*Group 4.* Twenty-five restrained rats subjected to 98 days of HK and were supplemented with Mg. They served as supplemented hypokinetic animals (SHA).

Mg supplementation consisted of providing Mg lactate in drinking water. For the Mg-supplemented groups, the rats consumed 0.35 mg Mg-lactate/mL/d.

### *Simulation of HK*

For simulation of the hypokinetic effect, animals in groups 2 and 4 were kept in small individual cages made of wood. The cages dimensions of 185 × 70 × 90 mm allowed movement to be restricted in all directions without hindering food and water consumption. At the same time, the hypokinetic animals could assume a natural position and groom different parts of their bodies. When necessary, the conditions of the individual cages could be reduced using special wood inserts. The cages were constructed in such a way that their size could be changed in accordance with the size of each animal, so that the degree of restriction of motor activity could be maintained at a relatively constant level throughout the investigation.

### *Statistical Analysis*

For each variable, differences among conditions were determined using an ANOVA with repeated-measures design. This analysis was performed on data obtained from 100 rats at various sampling intervals. Comparisons between the four groups were made by using a two-way ANOVA statistical test. A significant change had occurred at $P \leq .05$.

## RESULTS

All of the animals were in good health and all had a good appetite during the experimental period. However, some of the HK animals (SHA and UHA) exhibited restlessness, nervousness, striving to escape from cages, diarrhea, and shedding of the fur. Nevertheless, none of the SHA and UHA manifested any serious disorders or deaths.

### *Body Weight*

The body weight of the SCA and UCA groups increased progressively during the experimental period (Table 1). By contrast, the body weight of the SHA and UHA groups decreased during the experimental period (Table 1). Specifically, their body weight decreased significantly by the seventh day, increased somewhat by the 42nd day, then decreased again significantly by the 70th day, and after that it remained stable until the 98th day of the hypokinetic period, but it was significantly bellow the values observed in the SCA and UCA groups (Table 1).

### *Food Intake*

The average food intake during the initial stage of the hypokinetic period was decreased significantly in SHA and UHA when compared with SCA and UCA (Table 1). After that, food intake increased somewhat, then decreased again, and by the end of the experimental period was stabilized. However, it remained significantly lower in SHA and UHA compared with SCA and UCA (Table 1).

### *Plasma Mg*

Plasma Mg concentration obtained at different intervals during the investigation was significantly higher in SHA and UHA when compared with SCA and UCA (Table 2). The plasma Mg concentration was increased more in SHA than UHA; however, this increase was statistically insignificant. The plasma Mg concentration remained statistically significant throughout the experimental period in SHA and UHA when compared with SCA and UCA (Table 2). In contrast, plasma Mg concentration in SCA was only mildly elevated when compared with UCA (Table 2), while plasma Mg concentration in UCA

**Table 1. Body Weight (g), Food Intake (g/d), and Mg Balance (mg/Mg) of Rats During Vivarium Control and Hypokinetic Conditions With Mg Supplementation (mean ± SD)**

| | | Duration of Experimental Period (d) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | Baseline | 7 | 15 | 28 | 42 | 56 | 70 | 84 | 98 |
| UCA (n = 25) | | | | | | | | | |
| Body weight | 376 ± 10.2 | 389 ± 11.5 | 420 ± 11.4 | 445 ± 15.3 | 553 ± 13.5 | 580 ± 14.0 | 591 ± 15.5 | 599 ± 13.6 | 615 ± 15.0 |
| Food intake | 32.7 ± 0.3 | 32.9 ± 0.4 | 33.7 ± 0.5 | 34.0 ± 0.4 | 33.7 ± 0.5 | 34.8 ± 0.6 | 33.6 ± 0.4 | 35.0 ± 0.5 | 34.7 ± 0.4 |
| Mg balance | +32.70 | +16.24 | +34.42 | +41.08 | +39.34 | +50.32 | +37.24 | +51.52 | +52.08 |
| UHA (n = 25) | | | | | | | | | |
| Body weight | 379 ± 11.4 | 353 ± 12.5* | 365 ± 14.4* | 350 ± 12.0* | 381 ± 15.4* | 375 ± 11.4* | 367 ± 14.6* | 367 ± 10.5* | 372 ± 10.4* |
| Food intake | 35.9 ± 0.5 | 25.0 ± 0.3* | 27.5 ± 1.4* | 25.6 ± 1.3* | 29.1 ± 1.4* | 24.1 ± 1.2* | 27.4 ± 1.4* | 22.5 ± 1.3* | 20.1 ± 1.3* |
| Mg balance | +57.15 | −78.05 | −83.44 | −166.01 | −119.42 | −226.62 | −158.62 | −200.80 | −221.6 |
| SCA (n = 25) | | | | | | | | | |
| Body weight | 375 ± 15.0 | 383 ± 13.4 | 418 ± 12.5 | 448 ± 13.4 | 551 ± 14.0 | 582 ± 13.5 | 594 ± 12.4 | 605 ± 15.0 | 619 ± 14.5 |
| Food intake | 35.1 ± 0.3 | 36.7 ± 0.5 | 37.8 ± 0.6 | 36.8 ± 0.5 | 38.6 ± 0.4 | 37.5 ± 0.6 | 39.7 ± 0.5 | 38.3 ± 0.6 | 39.1 ± 0.5 |
| Mg balance | +57.15 | +10.85 | +28.24 | +27.17 | +58.54 | +34.62 | +23.38 | +39.34 | +20.58 |
| SHA (n = 25) | | | | | | | | | |
| Body weight | 377 ± 13.5 | 353 ± 15.0* | 362 ± 13.5* | 359 ± 10.4* | 385 ± 13.4* | 374 ± 11.3* | 373 ± 10.4* | 375 ± 11.5* | 381 ± 10.3* |
| Food intake | 33.7 ± 0.6 | 23.3 ± 0.7* | 27.9 ± 0.4* | 23.7 ± 0.5* | 23.8 ± 0.6* | 27.5 ± 0.7* | 22.8 ± 0.5* | 28.0 ± 0.4* | 25.4 ± 0.5* |
| Mg balance | +37.50 | −95.69 | −70.72 | −243.35 | −369.42 | −279.30 | −251.86 | −312.34 | −287.42 |

*$P \leq .05$, significantly different between vivarium control animals (SCA and UCA) and hypokinetic animals (SHA and UHA).

**Table 2. Mg Changes in Plasma (mEq/L), Urine (mg/24 h), and Feces (mg/24 h) of Rats During Vivarium Control and Hypokinetic Conditions With Mg Supplementation (mean ± SD)**

| Variable | Baseline | Duration of Experimental Period (d) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 7 | 28 | 42 | 56 | 70 | 84 | 98 |
| UCA (n = 25) | | | | | | | | |
| Plasma | 2.59 ± 0.33 | 2.58 ± 0.30 | 2.59 ± 0.41 | 2.58 ± 0.33 | 2.59 ± 0.45 | 2.58 ± 0.34 | 2.59 ± 0.45 | 2.58 ± 0.31 |
| Urine | 0.44 ± 0.10 | 0.42 ± 0.16 | 0.44 ± 0.11 | 0.41 ± 0.17 | 0.43 ± 0.14 | 0.40 ± 0.15 | 0.45 ± 0.10 | 0.43 ± 0.17 |
| Feces | 17.0 ± 1.2 | 17.0 ± 1.5 | 16.8 ± 1.2 | 17.0 ± 1.6 | 16.9 ± 1.5 | 17.1 ± 1.2 | 16.9 ± 1.4 | 17.1 ± 1.6 |
| UHA (n = 25) | | | | | | | | |
| Plasma | 2.58 ± 0.28 | 2.83 ± 0.35* | 2.75 ± 0.30* | 2.92 ± 0.40* | 2.85 ± 0.35* | 3.13 ± 0.47* | 3.07 ± 0.39* | 3.23 ± 0.30* |
| Urine | 0.43 ± 0.13 | 0.55 ± 0.10* | 0.73 ± 0.15* | 0.69 ± 0.17* | 0.75 ± 0.14* | 0.67 ± 0.20* | 0.80 ± 0.16* | 0.69 ± 0.17* |
| Feces | 17.3 ± 1.4 | 25.6 ± 1.3* | 27.4 ± 1.7* | 25.3 ± 1.5* | 29.9 ± 1.6* | 27.1 ± 1.4* | 29.9 ± 1.7* | 27.2 ± 1.4* |
| SCA (n = 25) | | | | | | | | |
| Plasma | 2.60 ± 0.43 | 2.62 ± 0.33 | 2.61 ± 0.40 | 2.63 ± 0.35 | 2.62 ± 0.41 | 2.63 ± 0.39 | 2.61 ± 0.45 | 2.63 ± 0.40 |
| Urine | 0.40 ± 0.11 | 0.47 ± 0.17 | 0.49 ± 0.13 | 0.45 ± 0.17 | 0.47 ± 0.11 | 0.45 ± 0.15 | 0.47 ± 0.16 | 0.49 ± 0.14 |
| Feces | 17.2 ± 1.2 | 20.0 ± 1.4 | 19.5 ± 1.7 | 21.1 ± 1.5 | 19.2 ± 1.4 | 21.7 ± 1.7 | 19.7 ± 1.4 | 21.5 ± 1.6 |
| SHA (n = 25) | | | | | | | | |
| Plasma | 2.61 ± 0.40 | 2.99 ± 0.47* | 2.93 ± 0.34* | 3.19 ± 0.46* | 3.11 ± 0.39* | 3.35 ± 0.46* | 3.27 ± 0.35* | 3.45 ± 0.51* |
| Urine | 0.42 ± 0.17 | 0.65 ± 0.15* | 0.77 ± 0.13* | 0.71 ± 0.20* | 0.75 ± 0.17* | 0.67 ± 0.21* | 0.81 ± 0.16* | 0.77 ± 0.21* |
| Feces | 17.3 ± 2.2 | 27.0 ± 1.7* | 29.4 ± 1.9* | 27.1 ± 2.2* | 35.7 ± 2.5* | 31.0 ± 2.2* | 38.3 ± 2.4* | 35.0 ± 2.4* |

*$P \leq .05$, significantly different between vivarium control animals (SCA and UCA) and hypokinetic animals (SHA and UHA).

remained relatively stable throughout the investigation (Table 2). Nevertheless, the plasma Mg concentration in SCA and UCA did not attain statistical significance when compared with baseline values.

*Urinary Mg*

The results of urinary Mg excretion in the hypokinetic (SHA and UHA) and control (SCA and UCA) groups are presented in Table 2. During the investigation, these results showed a significant urinary excretion of Mg in the SHA and UHA groups when compared with the SCA and UCA groups (Table 2). SHA showed a much greater value for urinary Mg excretion than UHA. In contrast, SCA and UCA demonstrated no significant change in the urinary Mg excretion value at any of the tested periods during the investigation when compared with baseline values (Table 2).

*Fecal Mg*

Fecal Mg excretion measurements obtained during the study showed significant differences between the hypokinetic (SHA and UHA) and the control (SCA and UCA) groups (Table 2). No significant difference was found in the rate of fecal Mg excretion between SHA and UHA during the study, although fecal Mg excretion was much greater in SHA than UHA (Table 2). The data obtained during the investigation showed a significant and progressive increase in the rate of fecal Mg excretion in SHA and UHA, which remained significantly different from the values in SCA and UCA throughout the study (Table 2). In contrast, no significant difference was found in the rate of fecal Mg excretion between the two control groups (SCA and UCA) during the investigation when compared with baseline values (Table 2).

*Mg Balance*

Throughout the study, SCA and UCA exhibited a positive daily Mg balance (Table 1). UHA and SHA manifested a significant negative Mg balance when compared with SCA and UCA during the investigation. At no time during this 98-day period of study was Mg balance positive in SHA and UHA. The mean negative Mg balance ranged from −70 to −369 mg during this period of study. Thus, during prolonged restriction of motor activity, a positive Mg balance was not produced by daily intake of Mg supplementation.

## DISCUSSION

The observed behavioral reactions of SHA and UHA, as well as their responses characterizing their general condition, are typical of prolonged restriction of motor activity,[1,2] and are considered as adaptational in nature, since all of these manifestations subsided as the duration of the hypokinetic period increased.

*Body Weight*

The significant loss of body weight in the SHA and UHA groups is inherent in hypokinetic conditions and may be due to several reasons, including prevalence of catabolic over anabolic processes,[1,2] increased fluid and electrolyte losses,[3,6,7] and a number of other factors inherent to prolonged HK.

*Food Intake*

The demonstrated changes with regard to food intake in SHA and UHA are consistent with the results obtained in previous studies.[1-3,6,7] The significant decrease in food intake in SHA and UHA may be attributable to several factors, including decreased caloric intake and prevalence of catabolism over anabolism.[1-3] The decreased intake of food consumption is inherent in prolonged restriction of motor activity.[1-3,6,7]

*Plasma Mg*

It is known that Mg deficiency during prolonged restriction of motor activity causes hypermagnesemia, and not hypomagnesemia as in ordinary and clinical conditions, indicating the involvement of some other mechanisms responsible for the

control and regulation of Mg metabolism during prolonged hypokinesia.[3,4,6-10] Rats subjected to HK alone (UHA) and combined HK with Mg supplementation (SHA) showed a significant elevation in plasma Mg concentration when compared with the control groups (SCA and UCA). This observation is consistent with the experimental findings previously reported in hypokinetic animals and humans.[3,4,6-10] Because of the presence of numerous physiological and biochemical factors known to affect Mg metabolism during prolonged restriction of motor activity, it is difficult to prove an unequivocal causal role for HK in such highly complex experimental settings. Therefore, the present investigation was designed to determine the role of HK and Mg supplementation, in isolation, by ensuring the constancy of all other experimental conditions. The results provided convincing evidence for the role of prolonged restriction of motor activity in the genesis of the observed abnormalities in Mg metabolism resulting from Mg deficiency.

With increased duration of HK, there was also a progressive and significant increase in plasma Mg concentration in the SHA and UHA groups. The following hypothesis can be postulated with regard to the causes of this phenomenon. During conditions of increased motor activity, Mg reaches the portal vein system after the intake of significant quantities of Mg and significant quantities of Mg are deposited in bone and cells of a number of tissues, which to a significant extent protect systemic circulation from rapid hypermagnesemia by performing the role of a buffer.[5] However, during prolonged restriction of motor activity, the conditions were less favorable for the deposition of Mg excess in the supplemented hypokinetic rats, which caused a significant increase in Mg concentration in peripheral blood. It may be also assumed that there was a significant increase in the concentration of Mg in the peritubular fluid, which is an important factor for the stimulation of secretion of Mg by renal tubules cells.

*Urinary Mg*

The observed increase in plasma Mg concentration in both the SHA and UHA groups during prolonged restriction of motor activity was accompanied by a significant elevation in urinary excretion of Mg. The constelletion of these findings points to reduced ability of the body to utilize or assimilate Mg during prolonged HK. With the daily administration of Mg supplementation, the Mg excretion in urine continued to increase in hypokinetic rats, despite the presence of Mg deficiency and decrease in Mg content of the body due to prolonged HK.[3-8] Accordingly, dietary factors did not appear to play an appreciable role in the prevention or inhibition of disturbances of Mg metabolism during prolonged HK. Thus, the striking abnormality found during prolonged HK was a faster excretion of Mg in the presence of Mg deficiency and probably a decrease in total Mg content of the body.[3,4,6-10] The consolidation of these findings suggests that, in all probability, the explanation for Mg loss was that significant changes develop during prolonged HK in bone and cells in a number of tissues where most Mg is deposited, with reduction of cellular mass, removal of Mg from cells, and excess Mg excreted by the kidneys. Therefore, during prolonged restriction of motor activity, one is probably dealing not only with Mg deficiency (hypermagnesemia) and diminished intracellular concentration of Mg, but also a decrease in cell mass and, consequently, limited space for Mg in the intracellular compartments that make it possible for Mg to be retained in the body. The failure to prevent or minimize Mg deficiency with daily intake of Mg supplementation may support this hypothesis.

*Fecal Mg*

Fecal Mg excretion also increased in the hypokinetic animals (SHA and UHA) and it was significantly higher when compared with control animals (SCA and UCA). Moreover, the rate of utilization and assimilation of Mg was significantly different between the hypokinetic (SHA and UHA) and control (SCA and UCA) groups according to the measured variables of the study. These observations suggest a significant reduction in deposition of Mg as a cause for the significant increase in fecal Mg excretion observed in SHA and UHA. It should be mentioned that the lack of a discernible increase in utilization and assimilation of Mg, despite a significant loss of Mg in SHA and UHA, may be considered as a typical reaction to prolonged restriction of motor activity.[3,6,7] Furthermore, this could be the result of a significant change in bone and cells of a number of tissues where most Mg is deposited, which might oppose or blunt the possible stimulating effect of Mg deficiency on the utilization and assimilation of Mg during prolonged HK.

The failure to normalize Mg metabolism in rats during prolonged restriction of motor activity and daily Mg supplementation also suggests that Mg is neither entering nor being retained by the bone and cells of numerous tissues, which would normally result in a significant increase in plasma Mg concentration and therefore a significant increase in urine and feces, which in turn would result in Mg deficiency of rats during prolonged HK.

*Mg Balance*

The Mg balance between the hypokinetic (SHA and UHA) and the control (SCA and UCA) groups was significantly different due to decreased ability of the body to retain Mg. This indicates that some homeostatic Mg mechanism had been triggered by the increased Mg metabolic disturbances and the decreased body stores of Mg. Because body weight of SHA and UHA also decreased, they could not have been in energy balance. They apparently were in a catabolic condition that could have influenced urinary, fecal, plasma, and Mg balance. Previous studies[3,6,9,10] have suggested that, during prolonged restriction of motor activity, when dietary intake of electrolytes increased, the rate of excretion of electrolytes in urine and feces also greatly increases as a result of negative electrolyte balance. Data from the current study support these observations and illustrate that supplemental Mg is excreted in urine and feces in significant amounts, primarily because significantly less amounts of Mg can be utilized by the body for synthetic processes. The result obtained from Mg supplements is a frustrating paradox: the more Mg supplements the hypokinetic subjects receive, the more deficient they become, and the more efficiently Mg is cleared from the blood stream, the less likely it is to benefit the hypokinetic animals.

Even though the supplemental Mg intake exceeded the daily

Mg requirements of animals, circulating levels of Mg, as well as the rate of urinary and fecal excretion of Mg, increased significantly in the hypokinetic animals when compared with the control groups. In addition, the overall Mg balance was negative, because the primary route of utilization and assimilation of Mg was drastically decreased, as indicated by the significant changes in the measured metabolic variables. Thus, during prolonged restriction of motor activity, negative Mg balance is induced not so much as a result of shortage of Mg in the diet, but by the impossibility of the body to utilize and assimilate Mg during prolonged HK.

*Protein-Bound Mg*

It is known that Mg exists as either a protein-bound or non–protein-bound form. It is also known that HK, particularly prolonged HK, is associated with significant protein catabolism, which is manifested by a significantly increased excretion of products of their breakdown, negative nitrogen balance, decreased absolute content of protein of tissues, and consequently protein deficiency in hypokinetic animals and humans.[11-14] Because protein, specifically albumin, combines with Mg, a deficiency of protein inhibited this binding process and contributed to extracellular build up of Mg, leading to intensification of Mg excretion in urine and feces as a result of the negative Mg balance and Mg deficiency during prolonged HK. The shortage and imbalance of Mg has an adverse effect on protein synthesis because Mg is one of the elements necessary for protein synthesis; however, most probably, the change in protein synthesis is the primary cause of insufficient utilization and assimilation of Mg: decreased uptake of Mg on the one hand and increased output on the other. Therefore, the reaction apparently develops on the order of a vicious circle, as a result of which there is an even greater shortage and imbalance of Mg and thus an even greater Mg deficiency during prolonged HK.

*Conclusion*

In conclusion, prolonged restriction of motor activity of SHA and UHA results in a sustained Mg deficiency induced primarily by the impaired ability of the body to utilize and assimilate Mg. Measurement of Mg concentration in plasma showed evidence of Mg deficiency, since Mg depletion during prolonged HK causes hypermagnesemia and not hypomagnesemia, as is the case during ordinary and clinical conditions. In fact, contrary to expectation, Mg concentrations in plasma increased significantly. Fecal and urinary elimination of Mg also increased significantly in SHA and UHA, while their Mg balance was negative. The failure to normalize Mg metabolism with the use of a daily intake of Mg supplementation suggests that Mg deficiency during prolonged HK is not a matter of shortage of Mg in the diet, but of the decreased ability of the body to utilize and assimilate Mg for maintaining Mg balance. These results also suggest that Mg perhaps is not entering or being retained by the bone and numerous tissue cells, where most Mg is deposited, which normally results in the intensification of Mg loss from the body and thus in Mg deficiency in hypokinetic animals.

## REFERENCES

1. Krupina TN, Mikhaylovskiy GP, Tizul Y: Adaptation to Muscular Activity and Hypokinesia. Novosibirsk, Meditsina, 1970

2. Kovalenko YA, Gurovskiy NN: Hypokinesia. Moscow, Meditsina, Russia, 1980

3. Krotov VP: Kinetics and regulation of fluid-electrolyte metabolism in animals and man during hypokinesia, PhD thesis. Interkosmos Council, Academy of Sciences USSR and Directorate of Cosmic Biology and Medicine, Ministry of Health USSR, Moscow, Russia, 1978

4. Grigoryev AI: Regulation of fluid-electrolyte metabolism and renal function in man during cosmic flights, PhD thesis. Interkosmos Council, Academy of Sciences USSR and Directorate of Cosmic Biology and Medicine, Ministry of Health USSR, Moscow, Russia, 1980

5. Kakurin LI, Arzamazov GS, Grigor'yev AI: Kaliuretic renal function in man as related to different degree of exercise during bed rest. Kosmicheskaya Biol 12:13-17, 1978

6. Zorbas YG, Federenko YF, Naexu KA: Renal excretion of magnesium in rats subjected to prolonged restriction of motor activity and magnesium supplementation. Magnesium Bull 16:64-70, 1994

7. Zorbas YG, Alexeyev NB, Nikolescu ZA: Water mineral metabolism in muscles and tissues of rabbits under hypokinesia. Materia Medica Polona 22:267-275, 1990

8. Zorbas YG, Federenko YF, Naexu KA: Phosphate-loading tests influences on endurance trained volunteers during restriction of muscular activity and chronic hyperhydration. Biol Trace Element Res 48:51-65, 1995

9. Zorbas YG, Federenko YF, Saito CN: Endogenous parathyroid hormones and renal excretion of magnesium in endurance trained volunteers during prolonged restriction of muscular activity. Magnesium Bull 16:104-112, 1994

10. Zorbas YG, Kakuzim AK, Kuznetsov NK, et al: Magnesium loading effect on magnesium deficiency in endurance trained subjects during prolonged restriction of muscular activity. Biol Trace Element Res (in press)

11. Fedorov IV, Vinogradov VN, Milov YI, et al: Synthesis of tissue proteins in animals during hypodynamia. Kosmicheskaya Biol 1:53-57, 1967

12. Fedorov IV, Grishanina LA: Nitrogen metabolism in animals exposed to hypokinesia. Kosmicheskaya Biol 1:43-48, 1967

13. Fedorov VI: Intensity of autolysis of animal tissues during hypodynamia. Kosmicheskaya Biol 5:82-84, 1971

14. Fedorov IV, Chernyy AV, Fedorov AI: Synthesis and catabolism of tissue proteins in animals during hypodynamia and resumption of muscular activity. Fiziol Zh SSR 63:1128-1133, 1977