Gender-dependent Magnesium Urinary Excretion in Healthy Adolescents and Adults

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Decreased blood and tissue magnesium may predispose to arterial hypertension, which is more frequent in males. Investigation of the physiological mechanisms of blood pressure regulation in both sexes might explain this gender-related difference. Essential hypertension is related to magnesium deficiency. It manifests in adulthood, but may have a latent onset in childhood, so investigations of magnesium turnover in children might help explain its mechanisms.

This paper presents data on urinary excretion of magnesium. We monitored urinary magnesium (both during day and night) concomitantly with blood pressure (hourly) in normal adolescents including girls during different phases of their menstrual cycle. We also monitored urinary Mg in normal young adults. Investigations showed gender-related differences in magnesium urinary excretion. The 24-h magnesium urinary excretion was significantly higher in boys than in girls. It exhibited a significant positive (direct) correlation with blood pressure in boys, especially at night. Mean blood pressure exhibited a significant positive correlation with height in boys. Girls exhibited a significant negative (inverse) correlation between magnesium nocturnal urinary excretion and blood pressure during the luteal phase of their menstrual cycle, as well as a significant negative correlation between magnesium urinary excretion and height. Young adult males (but not females) showed a significant positive correlation between body weight and urinary Mg excretion. Young adult females (but not males) exhibited a significant negative correlation between age and urinary Mg excretion.

Key words: renal excretion of magnesium, arterial blood pressure, gender

INTRODUCTION

Decreased blood and tissue magnesium may predispose to arterial hypertension (1). Decreased tissue magnesium may be related to increased vascular reactivity and predispose to a lower energy production in cardiac cells, as well as to disturbances of endothelial NO release (2). *In vitro* magnesium ions block the entry of calcium ions into smooth muscle cells, decrease the peripheral vascular resistance, relieve peripheral and coronary spasms, and decrease blood pressure (3). In experimental solutions containing no magnesium and lower than normal sodium, the tone of smooth muscle cells of female rat aortas significantly increased, but in smooth muscle cells of male rat aortas significantly decreased (4). Low levels of magnesium relieve a spasm of cerebral arterioles in rat, as well as an alcohol-induced spasm in hypomagnesemia. This effect is more prominent in male than in female rat (5).

Current epidemiological, clinical and experimental data suggest that the course of primary arterial hypertension may be gender-related. Men tend to have a higher predisposition to hypertension. The same antihypertensive treatment has different efficacy in men and women (6). To explain those phenomena, investigations of gender-related physiological differences in the regulation of blood pressure are needed.

Clinical data concerning the effects of magnesium on blood pressure are highly contradictory (7). Data on gender-related differences of magnesium turnover in children are scarce. Most of magnesium deficiency-related diseases have a latent onset in childhood and manifest clinically in adulthood, so

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investigations of gender-related differences on magnesium turnover in children might help to explain their pathogenesis.

Previous investigations suggest changes in magnesium urinary excretion to occur during sexual maturation. In obese girls magnesium excretion per kilogram body weight was significantly lower than in normal ones. This finding may be important, because obesity is a known risk factor of arterial hypertension (8).

In this article, we present data on diurnal, nocturnal, and 24-h magnesium excretion in normal adolescents and young adults, as well as on the relationship between magnesium urinary excretion and blood pressure. We also present changes in magnesium urinary excretion and blood pressure during menstrual cycle in girls.

MATERIALS AND METHODS

We monitored magnesium in the diurnal and nocturnal urine of adolescent boys (n = 29) and girls (n = 42) aged 14–17 years, as well as in young adult males (n = 37) and females (n = 27) aged 18–48 years from May to December 2000 (see Table). Diurnal urine was collected throughout the day, excluding the first urination after awakening in the morning. Nocturnal urine was collected during the first urination just upon after awakening in the morning and during awakenings at night as necessary.

In adolescent boys (n = 22) and girls (n = 22), we monitored blood pressure hourly for 24 h concomitantly with urinary Mg.

In adolescent girls (n = 15), we monitored urinary Mg concomitantly with blood pressure hourly for 24 h during different phases of their menstrual cycle. Monitored days included day 5 (follicular phase, levels of estrogens and progesterone are close to minimal), day 13 (ovulation, level of estrogens is maximal), and day 20 (luteal phase, level of progesterone is close to maximal).

We analyzed urinary Mg by spectrophotometry using special kits (*Seneca*, Poland). We monitored arterial blood pressure with an Auto-cuff automatic outpatient blood pressure monitor (model ABP-1001, *Biotrac*, USA).

The impact of various factors on Mg excretion and the relation of Mg excretion to blood pressure have been investigated by means of correlation analysis. To show statistical significance of difference between 2 means, we used a Student's t test.

RESULTS

Urinary level and excretion of magnesium. We found a 24-h urinary excretion of magnesium in boys to be significantly higher than in girls (see Table). The level of magnesium in the nocturnal urine of boys and girls was significantly higher than in diurnal.

Young adult males showed a significant correlation between the 24-h Mg excretion and body weight ($r = 0.40$, $p < 0.05$). Young adult females exhibited an opposite tendency ($r = -0.13$, NS). A gender-related difference in the correlation between 24-h Mg excretion and body weight in young adults was significant ($p < 0.05$, Fig. 1).

Young adult females showed a significant correlation between the 24-h Mg excretion and age ($r = -0.46$, $p < 0.05$). Such relationship was absent in young adult males ($r = 0.05$, NS). The gender-related difference in the correlation between 24-h Mg excretion and age in young adults was significant ($p < 0.05$, Fig. 2).

Blood pressure. Nocturnal systolic blood pressure was significantly higher in boys (100 ± 6 mm Hg) than in girls (105 ± 9 mm Hg).

Correlation between magnesium urinary excretion and blood pressure. Nocturnal magnesium excretion had a significant positive correlation with nocturnal blood pressure (systolic $r = 0.67$, diastolic $r = 0.56$, and mean $r = 0.63$; $p < 0.05$; Figs. 3 and 4) in adolescent boys. Such a correlation between diurnal urinary magnesium excretion and blood pressure was not significant. Adolescent girls exhibited a significant negative correlation between nocturnal urinary

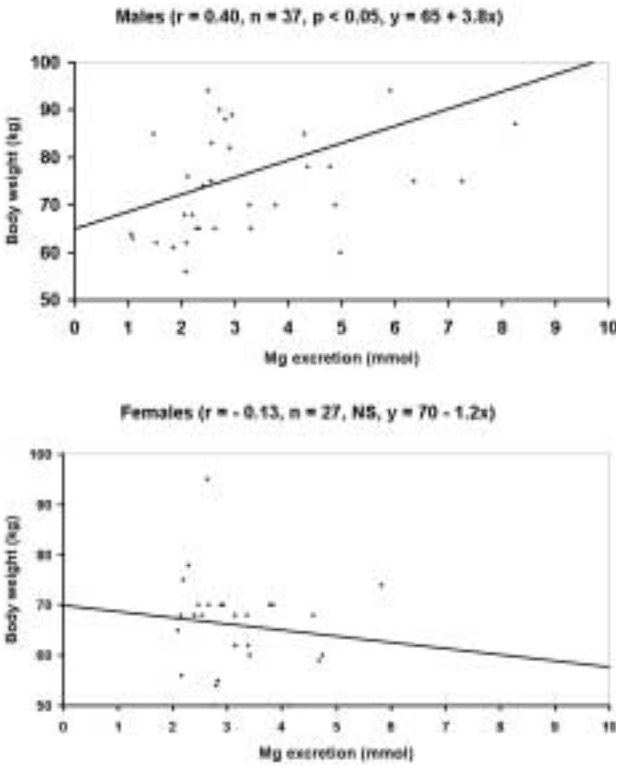

Fig. 1. Correlation between 24h Mg excretion and body weight in young adults

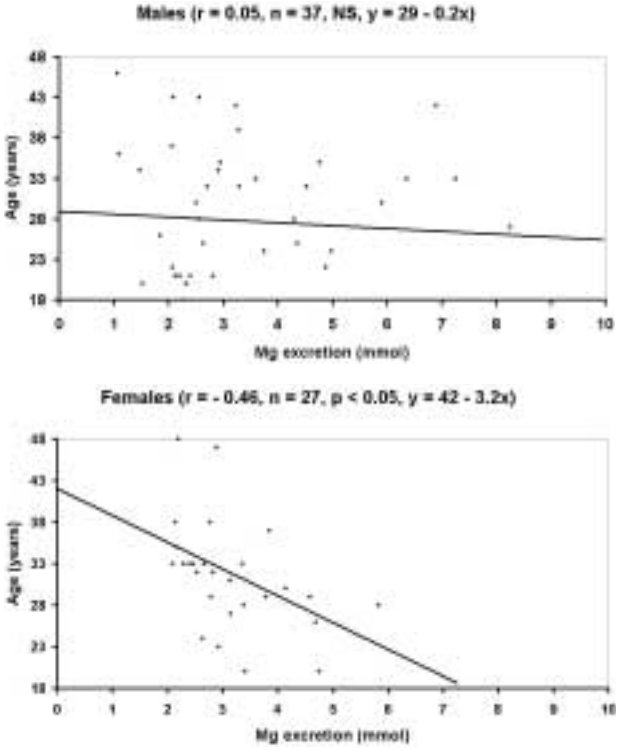

Fig. 2. Correlation between 24 h Mg excretion and age in young adults

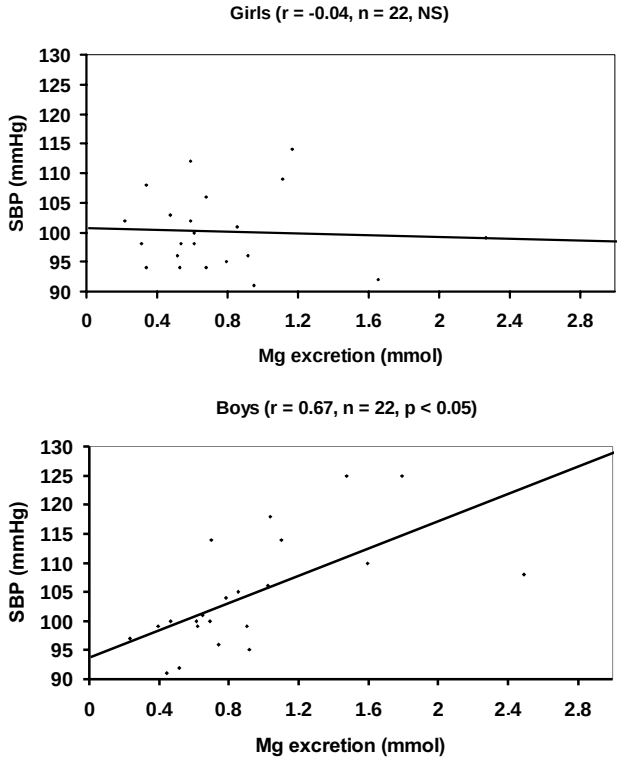

Fig. 3. Correlation between Mg excretion and systolic blood pressure at night in healthy adolescents

magnesium and diastolic blood pressure (r = –0.6, p < 0.05) as well as between nocturnal urinary magnesium and mean arterial pressure (r = –0.65, p < < 0.05) during luteal phase (Figs. 3 and 4).

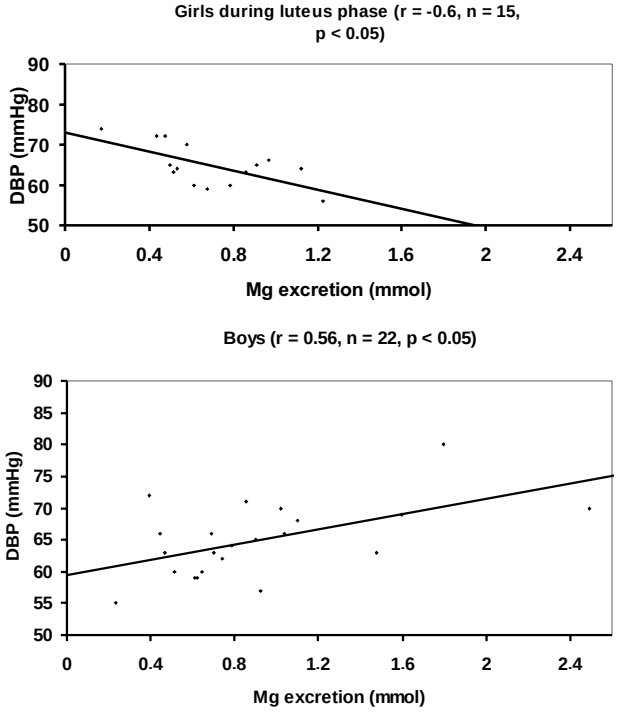

Fig. 4. Correlation between Mg excretion and diastolic blood pressure at night in healthy adolescents

Adolescent boys showed a significant positive correlation between mean diurnal blood pressure and height (r = 0.55, p < 0.05). No such relationship was observed in adolescent girls (r = 0.02, NS). The gender-related difference in the correlation between blood pressure and height in adolescents was significant (p < 0.05).

In adolescent girls there was a significant correlation between 24-h magnesium urinary excretion and height (r = –0.34, p < 0.05). Such a relationship was absent in adolescent boys (r = 0.10, NS).

DISCUSSION

Current knowledge suggests magnesium to play a role of antihypertensive cofactor, though not a factor. Clinical evidence suggests magnesium supplementation to be sometimes a useful treatment adjunct in hypertension (7). Glomerular filtration is the main mechanism involved in urinary excretion of magnesium. Urinary excretion of magnesium is mainly related to serum magnesium, meanwhile examination of serum magnesium in children didn't show gender-related differences (9, 10). Gender-related differences in serum magnesium were not found in normal adults, either (11). Increased urinary magnesium was not found to be associated with hypermagnesemia (12). Extensive trials didn't show any significant correlation between urinary excretion and dietary intake of magnesium in children (13).

No clear correlation between the dose of oral magnesium supplements and urinary excretion of magnesium in adults was found (14). Therefore some other gender-related factors and mechanisms are supposed to be involved in the renal excretion of magnesium and its depletion. Experimental data show age- and gender-related differences in reabsorption of divalent ions in renal tubules, but the molecular mechanisms of such differences remain to be investigated (15). Hypomagnesemia may be associated with relative insulin resistance, impaired glucose tolerance and hyperinsulinemia in normal subjects (16). Physiological doses of insulin markedly increase renal magnesium excretion (17). Gender-related differences in insulin resistance of cells and tissues are known to exist. Insulin resistance is higher in male rats and men than in female rats and women (18).

Patients suffering from hypertension tend to be magnesium-deficient (1, 7), which may be related to chronic insufficient dietary intake, constitution, and an increased urinary excretion of magnesium. Magnesium depletion may be implicated in the pathogenesis of essential hypertension. Investigation of gender-related differences in magnesium turnover might explain the higher prevalence of hypertension in men as well as some mechanisms involved in the progression of this disease. Some changes capable of contributing to hypertension in future may be found in childhood. We found a significant positive correlation between nocturnal urinary magnesium excretion and blood pressure (systolic, diastolic, and mean) in boys. Nocturnal systolic blood pressure was significantly higher in boys than in girls. Consequently, nocturnal magnesium depletion may contribute to the higher nocturnal blood pressure in boys.

There are gender-related differences in tissue magnesium. Magnesium content is significantly higher in the hair of girls than of boys (24). Muscle magnesium levels are significantly higher in women than in men (25). The reasons for such differences haven't been disclosed yet, but they may be associated with the above-mentioned gender-related differences in magnesium urinary excretion. Our investigations showed different patterns of magnesium excretion in boys and girls. Gender-related differences in diurnal and nocturnal excretion of magnesium may be associated with different mechanisms of magnesium homeostasis. We found 24-h urinary magnesium excretion in adolescent boys to be significantly higher than in adolescent girls. Differences in both 24-h urinary excretion and urinary level of magnesium may result from gender-related physiological differences in its turnover. We found a relation between higher body weight and urinary loss of Mg in young adult males, but not females. Overweight is a known risk factor of hypertension.

Girls exhibited a significant negative correlation between their nocturnal magnesium excretion and blood pressure (diastolic and mean) during the luteal phase of their menstrual cycle, therefore progesterone might supposedly protect the female body from magnesium depletion. Clinical evidence shows serum-ionised and total magnesium to be significantly lower during the luteal than the follicular and ovulation phase (21). Placebo-controlled clinical trials showed hormone replacement therapy with estrogens and progesterone to produce a significant decrease in urinary excretion of magnesium (22). We failed to find any literature data on the physiological mechanisms of the effect of female sex hormones on renal magnesium excretion. Ovarectomy and estrogen supplementation had no effect on intestinal magnesium absorption in female rats (23).

Our investigations revealed a significant positive correlation of height with nocturnal and diurnal blood pressure in boys, but not in girls. Girls exhibited a significant negative correlation between 24-h urinary excretion of magnesium and height. Height may be a risk factor of hypertension in boys (19, 20).

We found the urinary loss of Mg to decrease with age in young adult females, but not males. This may partially protect young adult females against blood pressure increase with age. There is a clear-cut evidence of a relationship between calcium and magnesium homeostasis, and there are known gender-related differences in calcium transport across the cell membrane, metabolism, and excretion (26–28). Diurnal and nocturnal calcium urinary excretion differs in men and women. This phenomenon may be associated with gender-related circadian changes in serum growth hormone and parathyroid hormone (29). The growth hormone increases the urinary excretion of magnesium (30). A possible association between gender-related differences in calcium homeostasis and magnesium excretion cannot be ruled out.

Investigation of the mechanisms of the above-mentioned gender-related differences in children might explain a predisposition to magnesium deficiency-related conditions in adult males. These mechanisms could also suggest prophylactic means of magnesium deficiency-related diseases.

CONCLUSIONS

1. Magnesium urinary excretion is related to gender, age, height, body weight, circadian rhythm, and blood pressure.

2. In boys, the risk of magnesium deficiency-related conditions is related to blood pressure, especially nocturnal. It may also be related to their height.

3. Progesterone may protect female body against magnesium depletion.

4. Higher body weight may be a gender-related risk factor of Mg depletion in young adult males.

5. Urinary Mg loss may decrease with age in females (contrary to males) during their young adulthood.

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SVEIKŲ PAAUGLIŲ IR SUAUGUSIŲJŲ SU LYTIMI SUSIJUSI MAGNIO EKSKRECIJA SU ŠLAPIMU

S a n t r a u k a

Sumažėjusi magnio koncentracija kraujyje ir audiniuose gali būti susijusi su arterine hipertenzija, kuri dažniau pasireiškia vyrams. Šio su lytimi susijusio polinkio sirgti pirmine hipertenzija priežastys nėra žinomos. Dažniausiai ši liga kliniškai pasireiškia suaugus, tačiau jos užuomazga gali nepastebimai prasidėti vaikystėje. Todėl magnio apykaitos vaikų organizme tyrimai gali padėti suprasti pirminės hipertenzijos raidą. Straipsnyje pateikiami magnio ekskrecijos su šlapimu duomenys. Mes tyrėme magnio koncentraciją abiejų lyčių paauglių dienos ir nakties šlapime, kartu 24 valandas kas valandą matuodami arterinį kraujospūdį. Taip pat tyrėme mergaičių šlapimą įvairių mėnesinių ciklo fazių metu, kartu matuodami Mg ekskreciją bei 24 valandas kas valandą – arterinį kraujospūdį. Taip pat tyrėme jaunų suaugusių vyrų ir moterų Mg ekskreciją šlapime. Tyrimai parodė su lytimi susijusius magnio ekskrecijos su šlapimu skirtumus. Magnio kiekis berniukų paros šlapime buvo patikimai ($p < 0,05$) didesnis negu mergaičių. Berniukams nustatyta patikima ($p < 0,05$) teigiama koreliacija tarp nakties magnio ekskrecijos ir nakties sistolinio kraujospūdžio bei patikima ($p < 0,05$) teigiama koreliacija tarp dienos vidutinio arterinio kraujospūdžio ir ūgio. Mergaitėms nustatyta patikima ($p < 0,05$) neigiama koreliacija tarp magnio kiekio nakties šlapime ir nakties kraujospūdžio menstruacinio ciklo geltonkūnio fazėje, taip pat patikima ($p < 0,05$) neigiama koreliacija tarp magnio ekskrecijos paros šlapime ir ūgio. Jauniems vyrams nustatyta patikima ($p < 0,05$) teigiama koreliacija tarp kūno svorio ir paros magnio ekskrecijos, o jaunoms moterims tokia koreliacija nebūdinga. Jaunoms moterims nustatyta patikima ($p < 0,05$) neigiama koreliacija tarp amžiaus ir paros magnio ekskrecijos šlapime, o tai nebūdinga jauniems vyrams.

Raktažodžiai: magnio ekskrecija su šlapimu, arterinė hipertenzija, lytis