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Acid-Base Status Affects Renal Magnesium Losses in Healthy, Elderly Persons[1]

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Abstract

Magnesium and calcium deficiency in humans is related to a number of pathological phenomena such as arrhythmia, osteoporosis, migraine, and fatal myocardial infarction. Clinically established metabolic acidosis induces renal losses of calcium. In normal subjects, even moderate increases in net endogenous acid production (NEAP) impair renal calcium reabsorption but no information is available whether this also influences renal magnesium handling. The aim of the study was to examine the relation between NEAP and renal magnesium excretion in healthy, free-living, elderly subjects. The subjects (age 64 ± 4.7 y, $n = 85$) were randomly selected from the population register in Gothenburg (Sweden). Magnesium, calcium, and potassium were measured in 24-h urine samples and NEAP was quantified as renal net acid excretion (NAE). NAE was positively correlated with excretions of magnesium ($R^2 = 0.27$, $P < 0.0001$) and calcium ($R^2 = 0.30$, $P < 0.0001$) but not potassium. When 24-h urinary magnesium excretion was adjusted for 24-h urinary potassium excretion, a biomarker for dietary potassium intake, the association between magnesium excretion and NAE remained significant ($R^2 = 0.21$, $P < 0.0001$). The significant association between potassium-adjusted magnesiuria and NAE suggests that the acid-base status affects renal magnesium losses, irrespectively of magnesium intake. Magnesium deficiency could thus, apart from an insufficient intake, partly be caused by the acid load in the body. J. Nutr. 136: 2374–2377, 2006.

Introduction

The divalent cations magnesium and calcium are important minerals for the normal functioning of the organism and a deficiency increases the risk for health effects such as cardiovascular disease (1), osteoporosis (2), and migraine (3). The public health impact is important; in one study it was calculated that optimizing the intake of magnesium and other minerals through drinking water would lead to a yearly reduction in heart infarction death rates by 23 persons per 100,000 in females and 65 persons per 100,000 in males (4).

A deficiency of minerals can arise from a suboptimal dietary intake. An evaluation of nutritional habits during human evolution demonstrates that diets introduced when farming commenced and when industrialization took place resulted in important changes in terms of an increased intake of grains and animal proteins, a lower intake of minerals, and a higher intake of sodium and simple sugars (5,6). These changes have become even more pronounced in today's city life and fast food consumption.

The consumption of animal protein, grain, and high amounts of milk increases the acidity of the body, whereas foods rich in minerals such as green vegetables and fruit increase the alkalinity (7). Generally, the Western diet induces a chronic, low-grade metabolic acidosis (8,9). Acidosis influences the homeostasis of calcium, partly due to the influence on renal mechanisms. A number of diet intervention studies have reported a relation between an increase in the body's acid load and an increase in renal calcium losses (10,11). This mechanism may also influence the homeostasis of magnesium. There are several studies indicating a number of similarities between renal handling of magnesium and calcium (12,13) suggesting that acid-base also has an effect on magnesium, similar to that of calcium. In children with distal tubular acidosis, metabolic acidosis has been found to block the reabsorption of magnesium in the tubuli and increase urine magnesium excretion (14). There are, however, no studies on the influence of acid-base status on renal magnesium excretion in a normal population of healthy individuals.

Regarding acid-base regulation, the elderly have a decreased renal function (9) that affects the capacity of the kidneys to excrete acid, leading to a lower blood pH and a reduced plasma bicarbonate concentration (15). In view of their generally lower intake of fruit and vegetables (9,16) they thus constitute a risk group for acid conditions and hence an increased secretion of calcium and possibly magnesium.

In this study, we investigated whether the urinary excretion of magnesium was related to acid conditions in terms of net endogenous acid production (NEAP) in healthy, elderly subjects.

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Materials and Methods

Population sample. A total of 400 subjects aged 55–75 y were randomly identified using the population register from Gothenburg in the west of Sweden. The study was approved by the ethical committee at the Faculty of Medicine, University of Gothenburg, Sweden.

From the population sample, 230 subjects were selected at random and contacted by letter, inviting them to join the study with the information that the purpose of the investigation was to evaluate their mineral homeostasis and acid-base conditions. From the selected sample, 112 subjects were willing to participate. They answered a questionnaire on previous and present disease. Exclusion criteria were kidney disease, diabetes, and a regular intake of medication and supplements that could influence the mineral homeostasis. Eight subjects who were taking medication that could influence the mineral balance and another 10 with serious illness were excluded.

Urine collection and analysis. Each subject collected a single 24-h urine sample and the aliquots were deep frozen immediately. They were instructed to retain their normal dietary habits during the urine collection, but dietary intake data were not collected. Dietary protein and potassium intakes were estimated from 24-h urinary nitrogen and potassium, taking average absorption coefficients (protein 75%; potassium 80%) into consideration (17,18). The urinary analysis comprised magnesium, potassium, and calcium quantified by flame atomic absorption spectrometry (12). NEAP was determined by measuring net acid excretion (NAE) according to established methods (8,19). For this, titratable acidity, ammonium, and bicarbonate were quantified and NAE was calculated as the sum of titratable acidity plus ammonium minus bicarbonate. Total nitrogen was measured by the Kjeldahl technique (Buechi 430 Digestor and Buechi Distillation Unit B-324).

Based upon the results from the urine analysis, 8 subjects were excluded because of inadequate urine sampling (subjects with creatinine <0.1 mmol $\cdot$ kg body weight^{-1} $\cdot$ d^{-1}) and one person was excluded because of an outlier NAE value (-53.2 mEq/d). The final number of subjects in the study was thus 85.

Statistical analysis. All statistical analyses were carried out with SAS procedures (Version 8.2, Statistical Analysis System) with data presentation as means ± SD. Data analyses were carried out with Student's *t* test for comparison between males and females and Pearson's correlations and linear regression analyses with age and sex as covariates. Because calcium data were not normally distributed, they were logarithmically transformed before correlation or regression analyses were run. The magnesium excretion was further adjusted for potassium excretion using the residual method (20). Urinary potassium is a biomarker for dietary potassium intake (21). As dietary magnesium and potassium intakes are highly intercorrelated (22–24), their independent effects cannot be assessed appropriately using food frequency questionnaires (24). Hence, adjusting urinary magnesium for urinary potassium gives a proxy correction for magnesium intake.

Results

The age distribution among females and males was similar (**Table 1**). The proportion of smokers was low and most of the smokers smoked only a few cigarettes per day. Protein intake, calculated from total urinary nitrogen excretion, was higher in males than in females as was potassium intake ($P < 0.0001$). Correspondingly, NAE and urinary potassium among males exceeded that of females ($P < 0.0001$).

The distribution of NAE in the urine (**Fig. 1**) was relatively normal with a mean of 60.0 ± 27.0 mEq/d and a range of 0.8 to 134. The excretion of magnesium ranged from 1.7 to 9.8 mmol/24 h with a median of 3.8 mmol/24 h.

NAE was positively associated with excretions of magnesium ($R^2 = 0.27$, $P < 0.0001$) (**Fig. 2***A*) and calcium ($R^2 = 0.30$, $P < 0.0001$) (Fig. 2*B*). The corresponding values after body surface area correction of NAE and both divalent cations were $R^2 = 0.15$ ($P = 0.0003$) and $R^2 = 0.23$ ($P < 0.0001$) for magnesium and calcium, respectively. There was no relation between potassium excretion and NAE ($R^2 = 0.06$, $P > 0.05$). The relation between NAE and magnesium excretion, adjusted for potassium excretion, was also significant ($R^2 = 0.21$, $P < 0.0001$) (Fig. 2*C*).

When the regressions were stratified by gender, there were significant associations between NAE and magnesium excretion ($R^2 = 0.30$, $P < 0.001$) and NAE and calcium excretion ($R^2 = 0.31$, $P < 0.001$) for males. For females, only calcium excretion was associated with NAE ($R^2 = 0.25$, $P < 0.001$).

TABLE 1 Subject characteristics and dietary intake of protein and potassium, and 24-h excretion of magnesium, calcium, potassium and NAE[1]

	Females, $n = 44$	Males, $n = 41$
Age, *y*	63.9 ± 4.8	64.4 ± 4.6
Smokers, *n*	8	7
Weight, *kg*	64.5 ± 8.9	84.6 ± 14.4[a]
Body mass index, *kg/m²*	23.5 ± 3.1	27.2 ± 4.0[a]
Estimated protein intake, *g/24 h*	77.2 ± 18.9	107.0 ± 25.6[a]
Estimated potassium intake, *g/24 h*	2.9 ± 0.9	3.9 ± 0.8[a]
Urinary magnesium, *mmol/24 h*	3.5 ± 0.9	4.5 ± 1.6[b]
Urinary calcium, *log mmol/24 h*	0.6 ± 0.2	0.6 ± 0.3
Urinary potassium, *mmol/24 h*	61.1 ± 16.9	82.9 ± 21.1[a]
Urinary nitrogen, *mmol/24 h*	682 ± 144	939 ± 230[a]
Net acid excretion, *mEq/24 h*	48.9 ± 20.5	72.0 ± 28.2[a]

[1] Values are means ± SD. Letters indicate different from females: [a] $P < 0.0001$; [b] $P < 0.05$.

Discussion

The aim of the study was to examine whether there was a relation between NEAP and urine magnesium excretion. The results demonstrated a close relation between NAE as indicator

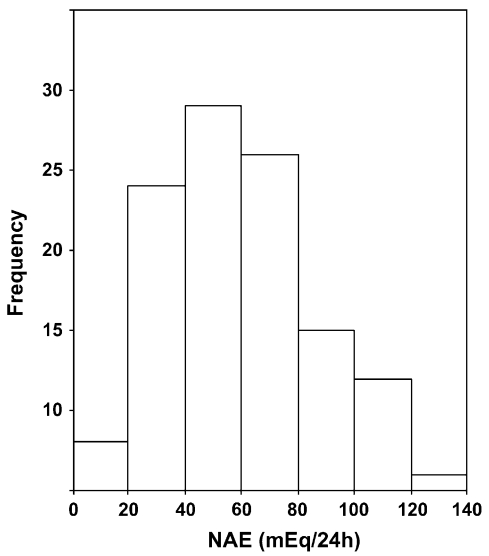

Figure 1 Distribution of the 24-h urinary NAE by 85 healthy, elderly men and women. The mean ± SD excretion was 60 ± 27 mEq/24 h. The median, percentile 10, percentile 90, minimum, and maximum excretions were: 57.1, 28.8, 99.4, 0.8, and 136.4 mEq/24 h, respectively.

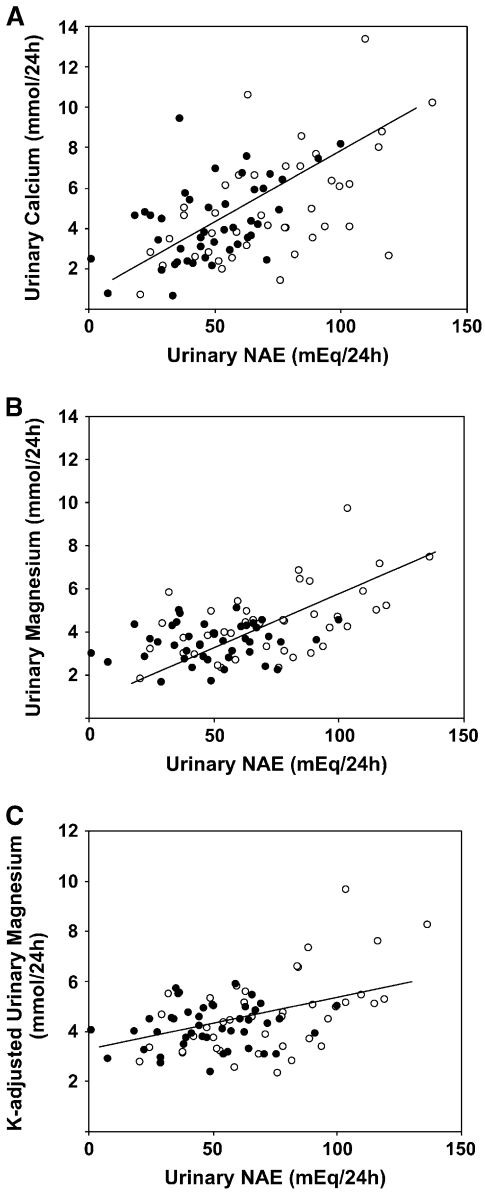

Figure 2 Relations between urinary NAE and excretions of calcium (R^2 = 0.30, $P < 0.0001$) (*A*), magnesium ($R^2 = 0.27$, $P < 0.0001$) (*B*), and magnesium adjusted for 24-h potassium ($R^2 = 0.21$, $P < 0.0001$) (C) in 85 healthy, elderly men (open circles) and women (closed circles).

of NEAP and the excretion of both magnesium and calcium. The average net acid load of 60 mEq/d in the group studied corresponded to the NAE usually observed among persons consuming Western diets (17,25).

There are some methodological issues to consider. No measurements were made of dietary intake of magnesium and calcium. It is known, however, that the amount of urinary calcium is not related to dietary calcium (26). Furthermore magnesiuria is only weakly associated with dietary magnesium intake (12,27,28). Because food records do not allow a reasonable prediction of the absorption of divalent cations (12,26), dietary assessments of magnesium and calcium intake were not considered useful.

No analyses were made of calcium and magnesium in serum. Serum concentrations do not relate to urinary excretion because they are highly regulated by hormonally controlled tubular uptake mechanisms (22,29). Measurements of serum pH and bicarbonate were not made because determinations at one time point are inappropriate to assess overall daily acid load. The daily acid load is appropriately reflected by NAE (8).

The potential dietary influence of high or low magnesium intake on renal magnesium excretion was controlled for by adjusting for 24-h urinary potassium excretion, a biomarker for dietary potassium intake (23). Dietary potassium and magnesium intake are highly interrelated (24) because potassium-rich foods are usually magnesium-rich (30). In a study on young adults (Dortmund Nutritional and Anthropometric Longitudinally Designed study), the highest correlation coefficients among various mineral intakes were for dietary magnesium and dietary potassium, averaging around 0.85 (our unpublished data).

The urinary magnesium excretion was significantly associated with NAE, both before and after body surface area correction and also after adjusting for varying magnesium intakes with the biomarker potassium. When the regressions were run stratified by gender, this relation was significant for males but not for females. This is probably a reflection of lower NAE and magnesium excretion for females, partly due to their smaller body size (or BMI). At the same time, the relation to calcium for females was significant, suggesting that calcium excretion is less dependent on body size and more sensitive to alterations in acid-base-conditions than magnesium. The conclusion that the acid load could be a determinant of renal magnesium excretion is supported by results from animal experiments where alkalinization/acidification was found to regulate renal magnesium and calcium reabsorption proteins (13). However, our findings need to be tested in controlled intervention experiments in humans living in metabolic wards.

Whether the urinary excretion of magnesium is related to NEAP in other age groups as well, including children, needs to be examined in future studies. These are important in view of the potential influence of inappropriate dietary habits on the magnesium and calcium homeostasis and hence health status. The results also suggest that investigations on magnesium homeostasis should control for a possible acid-base dependent excretion of magnesium.

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