Magnesium Intake from Food and Supplements Is Associated with Bone Mineral Density in Healthy Older White Subjects

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OBJECTIVES: To determine whether magnesium intake from supplemental and dietary sources is associated with bone mineral density (BMD) in older men and women.

DESIGN: Cross-sectional.

SETTING: Memphis, Tennessee, and Pittsburgh, Pennsylvania.

PARTICIPANTS: Two thousand thirty-eight older black and white men and women aged 70 to 79 at baseline enrolled in the Health, Aging and Body Composition Study.

MEASUREMENTS: Dietary intake of magnesium was assessed using a semiquantitative food frequency questionnaire, and supplement data were collected based on a medication inventory. BMD of the whole body was obtained using a fan-beam densitometer. Additional covariates included age, body mass index (BMI), smoking status, alcohol use, physical activity, estrogen use, and supplemental calcium (Ca) and vitamin D use.

RESULTS: In white, but not black, men and women, magnesium intake was positively associated with BMD of the whole body after adjustment for age, self-report of osteoporosis or fracture in adulthood, caloric intake, Ca and vitamin D intake, BMI, smoking status, alcohol intake, physical activity, thiazide diuretic use, and estrogen use in women ($P = .05$ for men and $P = .005$ for women). BMD was 0.04 g/cm^2 higher in white women and 0.02 g/cm^2 higher in white men in the highest than in the lowest quintile of magnesium intake.

CONCLUSION: Greater magnesium intake was significantly related to higher BMD in white women and men. The lack of association observed in black women and men may be related to differences in Ca regulation or in nutrient reporting. **J Am Geriatr Soc 53:1875–1880, 2005.**

Key words: bone mineral density; nutrition; magnesium; osteoporosis; elderly

Osteoporotic fractures are a significant health problem in older adults, and the burden of osteoporosis is expected to increase as the population ages.[1] White woman have a lifetime risk of any clinical fracture approaching 75%[2] and a lifetime risk of hip fracture of 16%. White men and black women and men have a lower but still significant lifetime risk of hip fracture (3–6%).[3] The prevalence of low bone mineral density (BMD) increases with age; 50% of white women aged 80 and older have osteoporosis.[4]

Given the high prevalence of low BMD and fracture, small improvements in BMD may have a large public health effect. The study of dietary factors in osteoporosis prevention is attractive because improvements in dietary intake could be applied broadly and may represent a nonpharmaceutical approach to improving BMD. Magnesium (Mg) is a lesser-studied component of bone that may play a role in calcium (Ca) metabolism and bone strength, possibly through changes to calciotropic hormones. In Mg deficiency, there are decreased synthesis, release, and action of parathyroid hormone and 1,25 vitamin D.[5–7] This may contribute to loss of BMD via lower retention of Ca, decreased intestinal absorption of Ca, and decreased Ca resorption at the distal tubule in the kidney, but little is known about the effects of Mg intake on BMD in healthy older individuals, and no data exist to determine the optimum intake of Mg on bone health. The primary aim was to investigate the relationship between Mg intake and BMD in a biracial cohort of community-dwelling older adults enrolled in the Health, Aging and Body Composition Study (Health ABC). Differences in fracture risk and BMD between blacks and whites are attributed in part to racial

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differences in Ca metabolism,[8–10] thus a secondary aim was to examine whether there were differences in the relationship between Mg and BMD by race and sex subgroups.

METHODS

Health ABC is a prospective cohort study initiated in 1997 to examine the relationship between changes in body composition and functional decline. Participants were eligible if they were aged 70 to 79 and reported the ability to walk one-quarter of a mile or climb 10 steps without difficulty. The cohort consists of 3,075 well-functioning older adults recruited from Medicare eligibility rolls in Memphis, Tennessee, and Pittsburgh, Penneylvania. A random sample of white residents and all black residents were invited to participate. Participants were excluded from Health ABC if they reported any difficulty with activities of daily living, a life-threatening disease, or plans to relocate within 3 years of the baseline examination. Persons using oral glucocorticoids, bisphosphonates, raloxifene, calcitonin, loop diuretics, or antiepileptic medications (n = 451) were excluded from the current analysis because of their well-described effect on BMD and Mg metabolism. Also excluded were participants without a technically adequate dual x-ray absorptiometry (DXA) (n = 99), with serious errors on the food frequency questionnaire (FFQ, n = 32), with reported caloric intake less than 500 kcal/d or greater than 3,500 kcal/d in women or less than 800 or greater than 4,000 kcal/d in men (n = 446 individuals), or with reported Mg intake of more than 3 g/d (n = 1) or Ca intake of more than 3 g/d (n = 8). Caloric cutoffs are approximately the same as the criteria for exclusion used by others,[11,12] and Ca and Mg cutoffs were based upon the upper tolerable limits for Ca and Mg.[13] Thus, the study population included 2,038 persons.

All procedures were in accordance with the ethical standards of the institutional review boards of the participating institutions, which approved the protocol and the consent forms. All participants signed an informed consent document.

Dietary and Supplement Assessment

Dietary Mg and Ca intake was measured using a semiquantitative FFQ (Block Dietary Data Systems, Berkeley, CA) administered by trained interviewers at the second annual examination. Food lists were based on the National Health and Nutrition Examination Survey (NHANES) III 24-hour dietary recall data for those aged 60 and older, non-Hispanic white or black, and residing in the northeast or south. The validity of a FFQ similarly modified to reflect regional and ethnic variations in type of food in older American women has been examined in the Women's Health Initiative (WHI).[14] The WHI questionnaire, like the Health ABC questionnaire, was modified to reflect regional and ethnic food choices, and the sample included 20% nonwhites. Mg intake according to the FFQ correlated well with food diary methods (Pearson correlation coefficient (r) = 0.69). The correlation coefficient for Ca was also good (0.78).

Participants were instructed to bring all prescription and over-the-counter medications used in the 2 weeks before each examination. Amounts of Ca, Mg, vitamin D, and vitamin C for each supplement were determined from an ingredient database based on the name and formulation of the supplement. If dose information was not available, doses were compiled from a search by brand name on Micromedex. If generic supplements were listed, doses were assigned using the most frequent doses from generic brands at pharmacies. Supplement use was assessed each year and cumulatively.[15]

Bone Mineral Density

A Hologic QDR Model 4500 A fan-beam densitometer (Waltham, MA) using software version 8.21 for the fan beam was used to measure BMD (g/cm^2) of the entire skeleton at the Health ABC second examination. Total hip BMD was performed at the baseline and third examinations but not the second examination. Therefore, whole-body BMD was the basis for most of this analysis. DXA Quality Assurance manual for the Health ABC was used to standardize patient positioning and scan analysis. Certified DXA technicians performed daily quality control and regular cross-calibration checks. The Health ABC strove to ensure good long-term precision (reproducibility) by using a detailed DXA operations manual, providing annual DXA operator training, and contracting the services of an experienced DXA reading center. A whole-body phantom was used throughout the study for quality control of the DXA scanners.

Covariate Information

Age at baseline was calculated from date of birth. Sex and race were self-reported on the baseline questionnaire. Body mass index (BMI, kg/m^2) was calculated from measurements taken at the second annual examination. Physician-diagnosed osteoporosis or physician-diagnosed fracture after aged 45 was self-reported at baseline and dummy-coded as yes/no. Current smoking status was assessed at baseline. Weekly alcohol intake over the previous year was ascertained at baseline and categorized into two categories: seven drinks per week or less and eight or more drinks per week. The majority of participants reported intakes below this cutpoint; therefore, further categorization was deemed unnecessary. Physical activity was calculated from a baseline questionnaire that elicited information on the participants' usual recreational activity and chores over the prior 12-month period. A summary variable was created for number of kilocalories expended per week and categorized into two categories: in the bottom decile and above the bottom decile. This categorization takes into account that substantial bone loss occurs with extremes of inactivity and that the curvilinear relationship between activity and BMD limits the effect of increasing levels of activity in active people.[16] Current use of estrogen or thiazide diuretics was transcribed from medication bottles at the second annual examination and dummy-coded as yes/no.

Statistical Analysis

All dietary and supplement variables were log-transformed to normalize the data. Dietary intakes were corrected for total caloric intake using the standard multivariate model,[17] in which total energy is entered into the model. In cross-sectional analysis, BMD of the entire body was

regressed on total (diet plus supplement) Mg intake. Mg intake was modeled as a continuous variable and categorized into quintiles by race and sex subgroups. Mg intake was further categorized as above or below the recommended daily allowance ((RDA) the amount of a nutrient estimated to meet the needs of 98% of the people in an age range: 320 mg/d for women and 420 mg/d for men aged 70 and older) and the estimated average requirement ((EAR) the amount needed to meet the needs of 50% of the age group: 265 mg/d for women, 350 mg/d in men).[13]

Multivariable adjustment was used for potential confounders including study site, caloric intake, calcium intake, vitamin D intake, age, body mass index, self-reported history of osteoporosis or fracture, physical activity, current smoking, alcohol use, and in women, current estrogen use. Adjusted least-square means were calculated for BMD across categories of quintile intake separately for each race–sex subgroup. Trends were evaluated using linear regression. A linear trend fit better than a linear trend with a quadratic component. Tukey's adjustment was used for multiple comparisons between quintiles of intake of Mg. All probability values are two-tailed.

The model containing Mg intake as the nutrient of interest was compared with models that included log-transformed vitamin C (from diet and supplements), potassium, protein, and fruit and vegetable intake. The Akaike Information Criteria were used to determine the model with the best explanatory power.[18]

SAS version 9.1 for Windows was used for all analyses (SAS Systems, Inc., Cary, NC).

RESULTS

Mean values ± standard deviation (SD) for the baseline characteristics of each race–sex subgroup are presented in Table 1. Black men and women had significantly higher BMD than whites ($P<.005$ for each comparison within sex). Nearly 40% of white women had a prior history of physician-diagnosed osteoporosis (6.8%), fracture after the age of 45 (22.1%), or both (6.8%) ($P<.005$ compared with black women). This variable was included because fracture or an osteoporosis diagnosis may lead to behavioral changes (e.g., initiation of Ca supplements).

Mg Intake and Healthy Behaviors

The mean intakes of Mg by race–sex subgroup are listed in Table 2. Less than 26% of the cohort met the RDA for Mg. Although white and black women reported a similar intake of food Mg, white women had a higher total mean intake because of more-frequent use of Mg-containing supplements. White men reported higher food Mg, use of Mg-containing supplements, and total Mg intake than did black men. Twenty-five percent of the cohort took a Mg-containing supplement; the mean dose was 83 mg. Ca intake by diet and supplement use was higher in women than men ($P<.001$) and in whites than blacks ($P<.001$).

Higher Mg intake from foods or supplements may parallel higher intake of nutrients thought to be beneficial to bone.[19–29] In the entire cohort, total Mg intake was significantly correlated with fruit and vegetable fiber ($r=0.53$, $P<.001$), total (food and supplement) vitamin C intake ($r=0.36$, $P<.001$), food potassium intake ($r=0.84$, $P<.001$), protein intake ($r=0.73$, $P<.001$), and total Ca intake ($r=0.64$, $P<.001$). Correlations of similar magnitude were obtained for each of the race and sex subgroups. The nutrient intake of the individuals in the cohort reporting the highest quintile of Mg intake had lower fat intake and a more nutrient-dense diet and reported more use of Ca or Mg supplements than those in the lowest quintile after adjustment for calorie intake (Table 3). Similar findings were seen for each race and sex group (not shown).

Mg Intake and BMD

After adjustment for total energy intake, total Mg intake through food and supplements was positively associated with whole-body BMD in white ($P=.002$) but not black ($P=.37$) women. After further adjustment for study site, Ca and vitamin D intake, BMI, age, current hormone use, thiazide diuretic use, history of osteoporosis or fracture, physical activity, current smoking, and alcohol use, Mg intake remained a significant predictor ($P=.005$) in white

Table 1. Subject Characteristics by Race-Sex Subgroup (N = 2,038)

Variable	Black Women (n = 436)	White Women (n = 534)	Black Men (n = 352)	White Men (n = 716)
Age, mean ± SD	73.6 ± 2.7	73.6 ± 2.6	73.5 ± 2.8	73.9 ± 2.8*
Bone mineral density, g/cm^2, mean ± SD	1.032 ± 0.113	0.984 ± 0.103‡	1.209 ± 0.127	1.151 ± 0.111†
Body mass index, kg/m^2, mean ± SD	29.7 ± 6.0	26.2 ± 4.5†	26.6 ± 3.8	26.8 ± 3.6
Known osteoporosis/prevalent fracture, %	28	39.9†	20.5	20.7
Smoking, %	11	7.3*	20.5	4.8†
<1/wk alcohol, %	90.1	69.0‡	73.3	55.6†
Activity, kcal/wk, mean ± SD	78.0 ± 54.6	86.1 ± 55.5*	87.2 ± 78.9	86.3 ± 70.4
Thiazide use, %	29.4	17.4‡	17.6	10.1†
Hormone replacement therapy				
Ever used, %	29.4	52.6‡	—	—
Current use, %	7.3	9.6	—	—
Duration, years, mean ± SD	2.4 ± 6.7	6.7 ± 10.4‡	—	—

Comparisons by race within each sex: $P<$ *.05, †.005, ‡.001.
SD = standard deviation.

Table 2. Magnesium (Mg) and Calcium (Ca) Intake by Race–Sex Subgroup

Mg and Ca Intake	Black Women (n = 436)	White Women (n = 534)	Black Men (n = 352)	White Men (n = 716)
Food Mg, mg/d, mean ± SD	273.0 ± 97.7	275.3 ± 90.9	290.7 ± 105.8	311.8 ± 103.8†
Total Mg, mg/d, mean ± SD	279.2 ± 115.6	307.6 ± 121.9*	304.7 ± 127.5	330.8 ± 111.9†
Meets Mg recommended daily allowance, %	32	38	13	19*
Mg supplement, %	22	34‡	13	26‡
Food Ca, mg/d, mean ± SD	732.5 ± 339.8	761.0 ± 336.6	734.5 ± 340.2	832.4 ± 374.0‡
Total Ca, mg/d, mean ± SD	855.5 ± 433.7	1055.2 ± 515.5‡	733.5 ± 363.0	888.2 ± 426.6‡
Ca supplement, %	26	51‡	10	23‡
Meets Ca adequate intake, %	20	33‡	10	21‡

Comparisons by race within each sex: $P <$ *.05, †.005, ‡.001.

women but not black women ($P = .83$). The mean parameter estimate ± standard error for the adjusted effect of log-transformed total Mg in white women was 0.052 ± 0.019; therefore, a 100-mg/d (nearly 1 SD for the group's total Mg intake) increase in intake of Mg from 220 mg/d to the RDA of 320 mg/d resulted in 0.020-g/cm^2 higher whole-body BMD, or 2% of the mean BMD.

There was a significant positive association between Mg intake and whole-body BMD for white but not black men. After adjustment only for energy intake, Mg intake was positively associated with BMD ($P = .002$) for white men. The parameter estimate for Mg in the multivariable-adjusted model was 0.039 ($P = .05$). A 100-mg/d increase in Mg intake from 320 mg/d to the RDA of 420 mg/d resulted in a 0.010-g/cm^2 increase in BMD, nearly a 1% increase in BMD from the mean. For black men, no relationship was found ($P = .55$). Mg intake above the RDA and the EAR was associated with nonsignificantly greater whole-body BMD in all race–sex subgroups than Mg intake below the RDA and the EAR.

Figure 1 presents multivariable-adjusted least-square means for whole-body BMD by quintile of Mg intake for women and men.

Total hip BMD was performed at the first and third examinations. In the multivariable-adjusted model, total Mg intake was associated with BMD at the hip at the first (parameter estimate = 0.044 ± 0.020, $P = .03$) and third (parameter estimate = 0.045 ± 0.021, $P = .03$) examinations in white women. In white men, the relationship was not as strong at the total hip at the first examination (parameter estimate = 0.032 ± 0.024, $P = .19$) or at the third examination (parameter estimate = 0.042 ± 0.026, $P = .10$).

Finally, statistical models with protein intake, fiber from fruits and vegetables, and vitamin C intake did not perform as well as the model containing Mg as the nutrient of interest. Potassium, also abundant in fruits and vegetables, was significantly associated with BMD in white women (parameter estimate = 0.049 ± 0.022, $P = .03$) and white men (parameter estimate = 0.060 ± 0.021, $P = .004$).

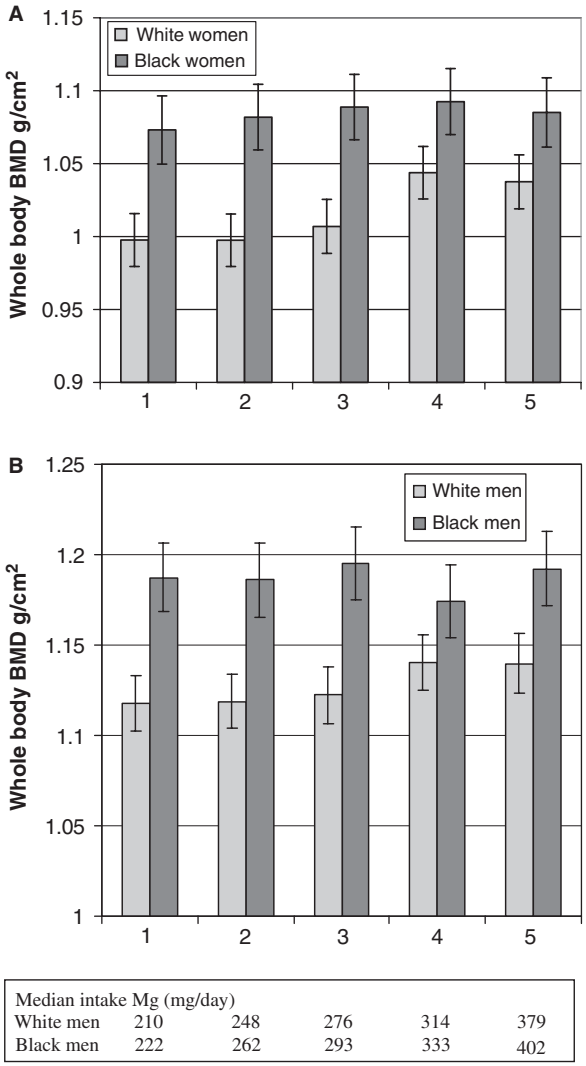
DISCUSSION

Higher Mg intake through diet and supplements was positively associated with total-body BMD in older white men and women. For every 100-mg/d increase in Mg (somewhat less than 1 SD), there was an approximate 2% increase in whole-body BMD. This effect size parallels the effect of Ca intake on BMD. In the Study of Osteoporotic Fractures, a 400-mg/d (approximately 1 SD within the group) increase

Table 3. Difference in Nutrient Intake Beneficial to Bone Between Quintile 1 and Quintile 5 of Total Magnesium (Mg) Intake (N = 2,038)

Variable	Quintile 1*	Quintile 5†
Fat, g/1,000 kcal per day, mean ± SD	41.15 ± 7.34	32.33 ± 8.82‡
Protein, g/1,000 kcal per day, mean ± SD	32.30 ± 6.78	40.30 ± 7.70‡
Carbohydrate, g/1,000 kcal per day, mean ± SD	125.38 ± 20.45	141.59 ± 22.18‡
Food Mg, mg/1,000 kcal per day, mean ± SD	115.72 ± 12.31	207.91 ± 31.61‡
Food calcium, mg/1,000 kcal per day, mean ± SD	322.09 ± 95.65	540.63 ± 201.29‡
Food vitamin D, IU/1,000 kcal per day, mean ± SD	85.10 ± 43.85	145.90 ± 85.95‡
Food potassium, mg/1,000 kcal per day, mean ± SD	1,210.50 ± 188.40	1,991.90 ± 382.65‡
Food vitamin C, mg/1,000 kcal per day, mean ± SD	62.69 ± 30.87	98.82 ± 43.57‡
Fruit and vegetable fiber, g/1,000 kcal per day, mean ± SD	2.60 ± 1.07	5.57 ± 2.56‡
Mg supplement ≥50 mg/d, %	1.5	57.7‡
Calcium supplement ≥100 mg/d, %	11.3	53.3‡

Mg intake: *247.84 ± 82.3 mg/d, †394.22 ± 153.9 mg/d.
Comparisons between quintiles 1 and 5: ‡$P < .001$.
SD = standard deviation.



Median intake Mg (mg/day)					
White men	210	248	276	314	379
Black men	222	262	293	333	402

Figure 1. Least-squares means ± standard error for bone mineral density (BMD) by quintile of energy-adjusted magnesium (Mg) intake in women (A) and men (B). Median value (mg/d) for Mg intake by quintile is shown beneath quintile number. Least-square means are adjusted for study site; caloric, calcium, and vitamin D intake; age; body mass index; self-reported history of osteoporosis or fracture; physical activity; current smoking; alcohol use; and in women, current estrogen use. For white women only, the 0.04 g/cm^2 BMD increase between the lowest and highest quintile of intake was significant ($P = .004$, test for trend = .002).

in food Ca resulted in a 1% to 3% increase in density at the femoral neck, no increase at the spine, and less than a 1% increase at the radius in multivariable-adjusted analysis.[30]

Previous cross-sectional studies have shown positive associations between Mg and BMD or bone mineral content in premenopausal white women,[27,28] older white men and women,[20] and Japanese-American men and women.[29]

Mg may exert its effect on BMD in part via calciotropic hormones. Mg may also act as a buffer for the acid produced by the typical Western diet. Dietary sources of Mg include green, leafy vegetables, unpolished grains and nuts, meats, starches, and milk—foods that are also high in potassium and Ca.[31] The theory of bone benefit from more-alkaline diets has gained support in the last few years, with studies indicating that diets higher in potassium, higher potassium-to-protein ratios,[32] and lower net endogenous acid production are beneficial to BMD.[33]

A third potential mechanism for the effect of Mg on bone is that divalent cations may substitute for Ca in crystal formation of bone hydroxyapatite and exert structural changes in the apatite crystal.[34] Strontium, another divalent cation, has beneficial effects on BMD and fracture prevention in humans.[35]

It is not clear why there was a racial difference in the association between Mg and BMD, but previous works support racial differences in bone response to dietary variables. Data from NHANES III show that early milk intake had positive effects on hip BMD in white but not black postmenopausal women.[36] It is not apparent why milk is protective in whites but not blacks, but the authors postulate that racial differences in calciotropic hormones or vitamin D receptor polymorphisms or response to other nutrients in milk could play a role. Milk is an important source of dietary Mg as well as Ca. Other studies have shown racial differences in Ca absorption and retention in adolescent women,[37] in levels of calciotropic hormones in women and men,[8,38–40] and in the strength of the association between vitamin D levels and hip BMD in men and women.[41]

Using the FFQ to estimate Mg intake is associated with measurement error. There are differences in how obese and nonobese subjects[42] report food intake. Because the black female participants in the Health ABC cohort were more likely to be obese than were the white female participants, the effect of body weight on caloric underreporting may be an additional explanation for the lack of association between Mg intake and BMD in the black participants. Memory change with the aging process may interfere with valid collection of data,[43] and the extent to which dietary and supplement use remains stable over time or reflects the important exposure period for effect on BMD is unclear.[44,45]

Strengths of this analysis include the use of a large dataset, the inclusion of black and white men and women, the ascertainment of supplemental and food Mg, and the consideration of multiple confounders of the relationship between Mg intake and BMD. After adjustment for numerous confounders, the significant positive relationship between Mg intake and BMD persisted, although the relationship was attenuated.

In conclusion, this investigation shows that Mg intake is associated with total-body BMD in older white women and men. The effect size of the finding is small but no smaller than the effect of Ca in one important study.[30] Whether higher levels of Mg intake translate into fracture protection is not investigated in this study. Dietary surveys show that a large percentage of older adults do not meet the RDA or even the EAR for Mg, resulting in a population at risk for Mg deficiency.[13] Higher Mg intake through dietary change or supplementation may provide an additional strategy for the prevention of osteoporosis.

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