

Research Articles

Magnesium supplement intake and C-reactive protein levels in adults

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Abstract

Previous research has indicated that dietary magnesium may be a key component in the association between diet and inflammation; however, the role of intake from magnesium supplements has not been elucidated. The objective of this study was to determine the likelihood of elevated C-reactive protein (CRP) in people taking magnesium-containing supplements of 50 mg/d or more. We examined this issue in a study sample derived from the National Health and Nutrition Examination Survey 1999–2002, a nationally representative, survey of the civilian, noninstitutionalized population of the United States. Among US adults, 25.6% were taking a magnesium supplement of at least 50 mg daily. Only 21.9% of individuals not taking supplemental magnesium met or exceeded the recommended daily allowances (RDA) for magnesium intake compared with 60.2% of adults who were taking magnesium supplements. In adjusted logistic regression analyses, people whose total daily magnesium intake was below the RDA were significantly 40% more likely to have elevated CRP regardless of whether they were taking magnesium supplements ($P < .05$). Among people with dietary magnesium intake less than 50% RDA, individuals taking magnesium supplements were 22% less likely to have elevated CRP. Magnesium supplement intake is associated with a lower likelihood of elevated CRP in people with low dietary magnesium intake. Prospective studies are needed to examine whether magnesium supplementation can reduce levels of CRP.

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1. Introduction

Recent evidence strongly supports a significant role for inflammation in the development of cardiovascular disease. Higher levels of inflammatory markers such as C-reactive protein (CRP) indicate increased cardiovascular (CV) risk [1–4]. A large proportion of adults in the United States may be at significant risk for CV disease due to inflammation. According to data from the National Health and Nutrition Examination Survey 1999–2000 (NHANES 99–00), more than 35% of the US adult population has CRP greater than 3.0 mg/L [5]. This figure represents more than 70 million

people who have a CRP elevated in the high-risk range as designated by the American Heart Association [4]. Because of the large number of people with high CRP and the severity of conditions associated with elevated CRP, information about the role of specific diet factors in inflammation and CRP elevation is extremely important.

Previous research has indicated that dietary magnesium may be a key component in the association between diet and inflammation. Song et al [6] have documented that magnesium intake is inversely associated with systemic inflammation in middle-aged and older women. Another study [7] found a significant association between dietary magnesium and elevated CRP, but the study population did not include people taking supplements. In another investigation [8], researchers have shown that low serum magnesium levels are

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independently related to elevated CRP concentration in nondiabetic, nonhypertensive obese subjects.

Data on the influence of magnesium supplementation on CRP and inflammation are limited. Whether magnesium from magnesium supplements, essentially a purer addition of magnesium to the diet, will have the same effect on inflammatory markers is not well studied. The objective of this study was to compare the likelihood of elevated CRP among individuals with similar levels of magnesium intake from diet or from supplements to determine whether CRP elevation would be similar regardless of magnesium source.

2. Methods

We derived our study sample from the participants in the NHANES 99-02, the most recent release of this nationally representative, complex, multistage, probability based survey of the civilian, noninstitutionalized population of the United States. Detailed information about the survey design, questionnaires, laboratory analyses, and examination methodology can be found on the website for the Centers for Disease Control, National Center of Health Statistics (<http://www.cdc.gov/nchs/nhanes.htm>). For this analysis, we focused on adult participants (≥ 17 years of age) who had valid measurements for both CRP and dietary intake of magnesium ($N = 10,024$). The institutional review board at our institution has reviewed this research and it is exempt.

High sensitivity CRP was measured as part of the NHANES 99-02 physical and laboratory examination. Standard phlebotomy techniques were used to obtain specimens. The threshold for elevated CRP was defined by American Heart Association guidelines that designate CRP levels 3.0 mg/L or higher as associated with high CV risk.

Dietary intake in the NHANES 99-02 is based on recollection of foods eaten the previous day by the respondent coupled with known nutritional content of each of these foods (24 hour recall). The US Office of Dietary Supplements of the National Institutes of Health (<http://ods.od.nih.gov/index.aspx>) and the Institute of Medicine have established recommended daily allowances (RDA) of magnesium intake based on sex and age (Table 1). For each person in the study population, we calculated the percentage of the RDA that they had consumed either from dietary sources alone or from both dietary and supplement sources. For each method of determining daily magnesium consumption, 4 groups were established: less than 50% of the RDA, 50% to 74% of the RDA, 75% to 99% of the RDA, and 100% or more of the RDA.

Table 1
US RDA for magnesium (in milligrams) based on age and sex (US Office of Dietary Supplements of the National Institutes of Health)

Age group	Men	Women
14-18	410	360
19-30	400	310
31+	420	320

Demographic variables (age and sex) were included as control variables because of their known impacts on CRP [9]. In an effort to determine the independent relationship between specific eating behaviors and CRP, additional variables were included that might be linked to eating behavior or might influence CRP level. We controlled for body mass index (BMI; kg/m^2) because of its link to diet and its known association with CRP [4]. We also controlled for current smoking status and exercise. Because the quantity of magnesium consumed may be linked to the total amount of food consumed, total energy expenditure was incorporated as another control variable [5,10].

We categorized magnesium supplement intake by dividing the population into 2 groups: those taking no magnesium-containing supplements or taking a minor amount of supplemental magnesium (< 50 mg/d) and those taking 50 mg/d or higher.

Because of the complex sampling design, appropriate weighting factors (based on statistical stratification and population estimates) must be taken into account when calculating population-based frequency estimates. We used SUDAAN (Research Triangle Institute, Research Triangle, NC), a specialized statistical program that accounts for the complex weighting of the NHANES 99-02 sample [11]. Using SUDAAN allowed us to correct for unequal probabilities of selection and different response rates, ensuring that the results can be generalized to the noninstitutionalized civilian population of the United States. Thus, the percentages and odds ratios in this study represent weighted values. SUDAAN also adjusts the standard errors to account for the weighting, stratification, and clustering of the complex sampling design to ensure that expressed P values are valid [12].

Descriptive statistics for the 2 magnesium supplement groups were performed to illustrate the demographic characteristics of the 2 study populations: those taking no or only minor magnesium supplements and those who were consuming 50 mg/d or higher of supplemental magnesium.

The effects of total daily magnesium intake (from both diet and supplements) and whether an individual was taking 50 mg/d or higher of supplemental magnesium were examined using adjusted multiple regression analysis to predict elevated CRP (≥ 3.0 mg/L). The covariates age, sex, BMI, smoking, exercise, and total energy expenditure were included in the model to control for their effects. Standardized β s, P values, odds ratios, and confidence intervals were obtained from the logistic regression output. Statistical significance was defined as 0.05 or less without correction for multiple comparisons and one-sided because the specific analyses were hypothesized and planned in advance.

3. Results

Among adults (age ≥ 17) in the United States, 25.6% were taking a magnesium supplement of at least 50 mg daily (Table 2). Individuals taking magnesium supplements of at

least 50 mg/d were generally older than those taking less. They were also more likely to be female, to be nonsmokers, to exercise, to have higher dietary magnesium intake, and to have a lower total energy expenditure. Taking a magnesium supplement had a big effect on total intake of magnesium; among individuals taking less than 50 mg/d of supplemental magnesium, only 21.9% met or exceeded the RDA for magnesium intake compared with 60.2% of adults who were taking at least 50 mg/d of magnesium-containing supplements. There were no differences in the overall percent of people with elevated CRP according to magnesium supplement intake before adjustment for confounders (Table 2).

In multiple regression analysis, controlling for age, sex, smoking, BMI, exercise, and total calories in people with dietary magnesium intake less than 50% RDA, individuals

Table 2
US population demographics by amount of supplemental magnesium intake (unadjusted)

	Overall	Magnesium supplementation 0-49 mg/d	Magnesium supplementation \geq 50 mg/d	χ^2 P
Sample number	10,024	7924	2100	
US population estimate	191,326,441	142,432,768	48,893,674	
Age (mean \pm SD)	44.6 \pm 0.36	42.5 \pm 0.39	50.4 \pm 0.50	<.001 ^a
Sex				.002
Male	48.1%	49.4	44.5	
Female	51.9%	50.6	55.5	
BMI				.195
<30	71.3%	70.8	72.8	
\geq 30	28.7%	29.2	27.2	
Current smoker				<.001
Yes	28.3%	30.6	21.5	
No	71.7%	69.4	78.5	
Exercise				<.001
None	37.0%	39.1	30.9	
Some	63.0%	60.9	69.1	
Daily caloric intake				.008
<1486	24.4%	24.2	25.1	
1486-2038	25.0%	24.4	26.9	
2039-2721	25.0%	24.6	26.2	
>2721	25.5%	26.8	21.8	
Daily dietary magnesium intake				<.001
<50% RDA	23.5%	24.7	19.8	
50-74% RDA	31.1%	31.3	30.4	
75-99% RDA	22.8%	22.3	24.2	
\geq 100% RDA	22.6%	21.6	25.5	
Daily total magnesium intake				<.001
<50% RDA	18.7%	24.5	1.9	
50-74% RDA	26.6%	31.1	13.5	
75-99% RDA	23.0%	22.5	24.4	
\geq 100% RDA	31.7%	21.9	60.2	
CRP				.625
<3.0	62.4%	62.6	61.8	
\geq 3.0	37.6%	37.4	38.2	

^a t Test comparison of means.

Table 3

Relative likelihood (odds ratio) of having elevated CRP (>3.0 mg/L) among individuals whose dietary magnesium intake is less than 50% of the RDA

	Odds ratio
Age	1.019*
Sex	
Male	1
Female	1.857*
BMI	
<30	1
\geq 30	3.038*
Current smoker	
Yes	1.537*
No	1
Exercise	
None	1.495*
Some	1
Daily caloric intake	
<1486	1
1486-2038	0.898
2039-2721	0.910
>2721	0.823
Daily magnesium supplement (mg)	
<50	1
\geq 50	0.777 [†]

* Significantly greater than 1.0 ($P < .05$).

[†] Significantly less than 1.0 ($P < .05$).

taking at least 50 mg of magnesium supplements daily were 22% less likely to have elevated CRP in adjusted analyses ($P < .05$). People whose total daily magnesium intake was below the RDA were significantly 40% more likely to have elevated CRP ($P < .05$) (Table 3).

4. Discussion

The key finding in this study is that magnesium intake from supplements has an impact on the likelihood of having elevated CRP, separate from and in addition to dietary magnesium intake. People with very low intake of magnesium from dietary sources (<50% of the RDA) who take magnesium supplements of at least 50 mg daily have a 22% lower risk of elevated CRP than people not taking supplements. The association was maintained after controlling for confounding factors: age, sex, BMI, smoking, exercise, and energy expenditure.

Although total magnesium intake appears to be the critical factor associated with elevation of CRP, intake from supplements plays a key role; only 22% of persons reach the RDA for magnesium without taking a supplement. Furthermore, our demonstration that the same results can be achieved by magnesium supplementation as from a diet rich in magnesium-containing foods supports a key role for magnesium itself outside of other nutritional "riders" in magnesium-rich foods.

The implications of these findings are that magnesium supplementation intake may be a viable alternative for reducing inflammation in people who do not achieve the RDA for magnesium through dietary sources alone. The

findings also have some implications on whether magnesium plays a direct and important role in regulating inflammation. Magnesium functions in many important metabolic pathways and is a coenzyme for cardiac muscle contraction. Magnesium has also been found to play a key role in endothelial metabolism [13]. Because people with elevated CRP frequently also have other accompanying CV risk factors [5,14,15], maintaining sufficient magnesium for important physiologic processes is especially important. Magnesium supplementation may present a simple and straightforward way to assure adequate magnesium intake for these vital metabolic pathways.

Previous studies have demonstrated an association between diet and elevation of CRP. Most notably, high dietary fiber intake has been associated with lower CRP [7,15,16]. In those studies, other nutrients were notably not found to be associated with CRP levels, including carbohydrates and saturated fats [7,15]. However, dietary fiber intake was found to be highly correlated with magnesium intake. The question arises as to whether the lower levels of CRP are due to the intake of fiber, magnesium, or some other nutrient in foods that are a common source of both (eg, bran). By evaluating magnesium intake from supplements separately from dietary sources, the current study seems to support a more direct association between magnesium intake and inflammation separate from other dietary components of foods containing magnesium. Further prospective studies are needed to confirm this relationship.

The study has some important limitations that should be taken into account. First, dietary information was obtained from a 24-hour dietary recall, which may not accurately represent an individual's intake over the last several weeks or months. However, the method may be the most reasonable for use in population-based studies, particularly when looking at CRP levels, which have a half-life less than 24 hours [17,18]. Second, participants may have exaggerated or overestimated their intake of healthy foods such as vegetables and legumes, which are relatively high in magnesium. If so, then population estimates of magnesium are likely lower in reality, and the bias may have blunted the significance of the association we examined, making the association even stronger than we have illustrated. Third, the strength of the association between magnesium supplement intake and CRP is modest and may be because of other unmeasured factors. Furthermore, we can make no definitive statement regarding cause and effect in a cross-sectional analysis.

In conclusion, magnesium supplement intake higher than 50 mg daily is associated with a lower likelihood of elevated CRP in people with low dietary magnesium intake.

Prospective studies are needed to examine whether magnesium supplementation can reduce levels of CRP and ultimately CV risk.

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