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Magnesium in Drinking Water in Relation to Morbidity and Mortality from Acute Myocardial Infarction

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Abstract

We investigated the importance of magnesium and calcium in drinking water in relation to morbidity and mortality from acute myocardial infarction. Cases were men and women 50-74 years of age living in 18 Swedish municipalities who had suffered an acute myocardial infarction some time between October 1, 1994, and June 30, 1996. Controls were randomly selected from the same study base. We interviewed the surviving cases (N = 823) and controls (N = 853), focusing on risk factors for acute myocardial infarction. We collected individual data on drinking water levels of magnesium and calcium. We classified subjects by quartile of water magnesium or calcium levels. The total number of cases was similar in the four quartiles. The risk of death was 7.6% (95% confidence interval = 2.1-13.1) lower in the quartile with high magnesium levels (>=8.3 mg/liter). The odds ratio for death from acute myocardial infarction in relation to water magnesium was 0.64 (95% confidence interval = 0.42-0.97) for the highest quartile relative to the three lower ones. Multivariate analyses showed that other risk factors were not important confounders. For calcium, this study was inconclusive. The data suggest that magnesium in drinking water is associated with lower mortality from acute myocardial infarction, but not with the total incidence.

Previous studies have shown an inverse relation between magnesium in drinking water and the risk of dying from ischemic heart disease (IHD). 1-10 Other studies have not shown this relation. 11,12 Some studies have also shown an inverse relation between waterborne calcium and IHD, 1,6,8,13 but in other studies no such relation was seen. 3,7,11,12 Most of the studies were ecologic, without measurement of individual exposure. Of those studies in which individual exposures were measured, one was a cohort study 2 and three were case-control studies. 3,7,8

Magnesium is a cofactor in several important enzyme systems and is essential in normal myocardial physiology. 14,15 Magnesium deficiency increases vasoconstriction 16-19 and the risk of developing an arrhythmia. 15,20,21

The relation between calcium and death from IHD has been less pronounced, and the physiologic mechanism that could explain such a relation is not clear.

In a recent editorial, Neutra 22 highlighted several shortcomings of the previous studies in this field. He mentioned, for example, that the actual intake of magnesium and calcium from water and food had not been assessed and that other risk factors for IHD had not been determined. 22

The aim of this study was to investigate the importance of individual levels of magnesium in drinking water in relation to both mortality and morbidity from acute myocardial infarction (AMI). In addition, we investigated the importance of water calcium. To estimate the individual intake of magnesium and calcium from water and food, and to assess whether other risk factors for AMI could be confounding factors, we interviewed surviving cases and controls.

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Subjects and Methods

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Study Area

The study was conducted in 18 municipalities in the catchment area of six hospitals in the southern part of Sweden. Levels of magnesium and calcium vary substantially between and even within these municipalities. Water quality regarding hardness, acidity, and treatment procedures in these municipalities has been basically unchanged since 1980, according to a previous survey. 7

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Study Base

The study base was men and women born between 1920 and 1946, of Scandinavian origin, who had lived in any of the 18 municipalities since April 1994. We obtained a roster of the population as of April 1994 (N = 130,010), comprising birth dates, personal code numbers, and addresses, from the regional tax authorities.

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Cases

We defined the cases as men and women in the study base who during the period October 1, 1994, through June 30, 1996, suffered an AMI (*International Classification of Diseases* code 410) and at the time of the infarction were in the range of 50-74 years of age. The cases were identified from the following sources.

(1) The clinical departments treating AMIs at the six hospitals in the area reported cases of AMI, for patients who had given informed consent. The AMI diagnosis was based on strict criteria that included chest pain, electrocardiogram changes, and increases in serum enzymes.

(2) Hospital treatment records from the six hospitals were used to trace AMI patients who had not been reported by the clinical departments. These cases were contacted later, with the permission of the hospitals. In addition, we obtained information from the other hospitals in the region regarding cases from the study base.

(3) Registers at the Center for Epidemiology at the National Board of Health and Welfare were used to identify cases who died from AMI during the study period and who had not been interviewed previously.

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Controls

For each case, one control was randomly selected from the study base. These were men and women born 1 day after the birth date of the cases. Controls selected for deceased cases could either be alive or deceased. We carried out the selection of controls continuously during the study period. An extra control was selected by mistake for two of the surviving cases.

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Interviews

We conducted telephone interviews with the surviving cases and the corresponding controls. About 2 weeks after the patients had been identified, they received a letter with information about the study and were contacted 1 week later by telephone. The controls also received a letter with information about the study and were contacted about 1 week later by telephone.

The interviews were conducted by a nurse experienced with this type of work. The subjects were asked about body weight and height, marital status, number of persons in the household, education level, profession, working hours, working conditions, physical activity, stress, smoking, health status and medication, and family history of AMI. Body mass index was calculated as body weight (kg) divided by height (m 2).

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Estimations of Intake of Magnesium and Calcium

The food frequency questionnaire was based on previous knowledge of the eating habits of this age group in Sweden and was designed to elicit at least 85% of the magnesium and calcium intake. The questionnaire included 51 food items and beverages. The frequency of intake was registered according to a nine-point scale. Individuals' intake of water was covered by questions on consumption of water, coffee, and tea. We asked the subjects about drinking water sources (waterworks or wells) and the use of water filters. When the water source at work differed from that at home, we took this into account.

We calculated the individual intake of magnesium and calcium from water and food as milligrams per day, using the Swedish National Food Administration's food composition tables and estimated standard portions.

For deceased cases and the corresponding controls, age, gender, and water data were the only variables collected.

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Water Analyses

We identified magnesium and calcium content in the drinking water at the last residence for each subject. We obtained information on the levels of magnesium and calcium from each of the waterworks.

We also collected water samples from tapwater from households representing all of the waterworks (N = 79), and the samples were analyzed for magnesium and calcium. We used a mean of the values from the waterworks and the values from the analyzed water samples. We also analyzed water samples from all subjects using water filters or drinking water from private wells. For deceased cases, we could not obtain water data on those who used private wells, and they were therefore excluded. We obtained information on the controls for the deceased cases in the same way.

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Statistical Analyses

We calculated odds ratios (ORs) for AMI with surviving and deceased cases together and separately. We controlled for covariates using a logistic regression model. We categorized magnesium and calcium on the basis of quartiles of all study individuals. The three lower quartiles were combined and used as a referent. We calculated new quartiles for subgroups (men and women). We also formed quartiles for survivors on the basis of the intake of magnesium or calcium, calculated from the questionnaire.

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Results

Information on number of subjects identified and participating, respectively, is presented in Table 1. A total of 470 water samples was analyzed. Water filters were used by 15 of the cases and 23 of the controls. Private wells were used by 144 of the cases and 167 of the controls. The magnesium levels ranged from 0.0 (water filter users) to 44.0 mg/liter, and calcium from 0 to 235 mg/liter.

Table 1

Table 2 illustrates the distribution of all subjects by level of magnesium content in the drinking water. The total number of cases was similar in the four quartiles. In the quartile with the highest water magnesium content, however, the proportion of surviving cases was higher (0.81) than the corresponding proportion in the quartiles with lower magnesium values (0.74). The difference was 0.076 (95% confidence interval = 0.021-0.13). It was mainly the number of deaths occurring outside hospitals that was lower in the quartile with high magnesium levels. There were no obvious differences in distribution between the four quartiles in relation to calcium in drinking water.

Table 2

The ORs for suffering an AMI in relation to magnesium and calcium in drinking water are reported in Table 3. When all cases, survivors and deaths, were included in the analyses, we found little relations between AMI and the amount of magnesium or calcium in the drinking water. The OR for the risk of dying from AMI in relation to magnesium in drinking water was 0.64 (95% confidence interval = 0.42-0.97) for the highest quartile compared with the referent. The OR was lower for women than for men.

Table 3

We calculated the OR for the risk of suffering an AMI and surviving, both in relation to the drinking water level of magnesium and to the intake of magnesium from water, as calculated from the questionnaire. Not surprisingly, ORs were farther from the null when the calculated intake was used as the measurement of the exposure as compared with when the water magnesium level was used. Calcium in water did not affect ORs for men. For women, ORs were lower in the highest quartiles in all categories (columns in Table 3), especially for AMI fatalities. The total daily intake of magnesium and calcium from food and beverages was also calculated according to the questionnaire and analyzed similarly. The total intake of magnesium or calcium did not have an important effect on ORs. The calculated total intake of magnesium from food and beverages, excluding water, ranged from 157 to 648 mg/day. The total intake of calcium from food and beverages ranged from 120 to 2,590 mg/day. The influence of the other variables considered in the interview is reported in Table 4. Variables that were not strongly related to the OR for AMI, such as marital status, number of persons in the household, and physical activity at work, were not included in the table.

Table 4

We included variables in the logistic regression model (Table 4) if they were associated with AMI and if the ORs were affected (even if only slightly) by adjustments for water magnesium intake. The results show that ORs for the magnesium and calcium intake from water were unchanged, or even slightly farther from the null, when the other variables were controlled for. For the other risk/preventive factors, except for stress, family history of AMI, and diabetes mellitus, the OR was unchanged or slightly closer to the null.

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Discussion

Our initial aim was that all patients should be identified by the hospitals. Nevertheless, 62% of the cases had to be contacted afterward. The average lag time between the AMI and the interview was 35 (±22) days for the reported cases, as compared with 16.7 (±5.1) months for the cases contacted afterwards. It may thus have been difficult for these latter cases to recall conditions before the time of the AMI. In addition, we could not determine whether all of the criteria for the diagnosis had been fulfilled for these cases. Regarding the deceased cases, the autopsy frequency had previously been shown to be nearly the same in the four quartiles of magnesium in water (43%, 37% , 41%, and 42%, respectively). 7

We used water data for the last year in our analyses. We believe that it is present exposure that is relevant for an effect of magnesium (see below), and half a year should be enough to adapt to local water supplies. 23 Previous studies have shown that the effect of water magnesium on mortality from IHD was found at levels above about 8 mg/liter. 4-8 The cutoff limit between the highest quartile and the three lower quartiles in this study was 8.3 mg/liter of magnesium in water, corresponding to the threshold in the literature.

For practical reasons, we could not measure blood lipids, which is an important risk factor for AMI. It is, however, unlikely that this variable would covary independently with magnesium in drinking water. Still, there could be an inverse causal relation between magnesium intake and levels of blood lipids, as has been shown in previous studies. 24-28

We found that the magnesium levels in the water did not affect the total incidence of AMI, but the proportion of cases surviving AMI was larger among the group with higher magnesium levels in the drinking water, and in particular the number of deaths from AMI occurring outside of hospitals was smaller in the high-level magnesium group. This finding supports the hypothesis that magnesium prevents sudden death from AMI, rather than all IHD deaths. 29-33

Magnesium is needed to maintain the normal gradient of potassium and calcium over the cell membranes 19,35 and is necessary to keep up intracellular levels of potassium. This effect is accomplished by blocking the outward passage in potassium channels and by being an activator of Na/K-ATPase. Magnesium has a similar function in Ca-ATPase. Magnesium also has a direct effect on potassium and calcium channels. 15,26,36,37 Furthermore, magnesium is an activator of adenylate cyclase, which is involved in the synthesis of cyclic adenosine monophosphate, a vasodilator. It also acts as a natural calcium antagonist, competing for calcium-binding sites in the vascular smooth muscle. 15,38,39 In addition, the vasoconstrictive actions of hormones such as angiotensin, serotonin, and acetylcholine are enhanced in the case of magnesium deficiency. 19

For calcium, we found that calcium lowered the total incidence of AMI in women, but not in men. This finding supports the hypothesis of the underlying mechanism discussed previously, 8 that a low calcium intake may increase the blood pressure level. 40,41 Menopausal women have been shown not only to have a deficient intake, but also to have a lower absorption rate. 42

An important question is whether the relatively small amount of magnesium provided from water, compared with the intake from food, could be responsible for the effect seen. 22 It has been suggested that for those who have a low dietary intake and use water with high magnesium levels, the quantitative contribution of water magnesium may be crucial for body magnesium status. 31,43

In this study, a large number of the subjects had a lower intake of magnesium than the recommended dietary amount (6 mg/kg/day). The subject with the lowest intake, 157 mg magnesium per day, used drinking water with 3.5 mg/liter, which means a 4.5% addition to the magnesium intake from food. If she instead had used water with 40 mg/liter, the addition would have been 50%, and the total daily intake would have been 240 mg/day. In addition, cooking food in magnesium-poor water leaches out magnesium, whereas cooking in magnesium-rich water diminishes this loss. 44,45

It has also been suggested that magnesium in water, appearing as hydrated ions, has a higher bioavailability than magnesium in food, which is bound in different compounds that are less easily absorbed. 44,46 Plants cultivated in areas with magnesium-rich water may have a higher magnesium content, especially if the soil is magnesium-rich and the cultivation is irrigated with magnesium-rich water. If persons living in such areas eat vegetables and fruits that are locally grown, this might also add to the total magnesium intake. There may thus be some uncertainty with regard to the correctness of mineral content in food composition tables. Genetic factors, however, appear to have a greater effect on plant magnesium composition than do soil and environmental factors. 47

Some previous studies have shown relations between water magnesium and body magnesium content. One experimental pilot study showed that waterborne magnesium was better absorbed than dietary magnesium. 48 In a study on baboons, tapwater was more effective than dietary supplementation in increasing serum levels of magnesium and zinc. 49 Other studies have shown relations between water magnesium levels and the magnesium content in the heart muscle, 50 coronary arteries, 51 and skeletal muscle. 52 The importance of waterborne magnesium for the body status has also recently been shown in a study using an oral loading test. 53

In summary, we showed that magnesium in drinking water did not affect the risk of suffering an AMI, but the probability of surviving the infarction was greater for those who had high magnesium levels in their drinking water. The findings for calcium in drinking water were inconclusive.

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Keywords: calcium; coronary disease; drinking water; gender; magnesium; myocardial infarction

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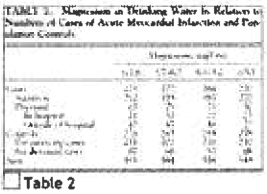
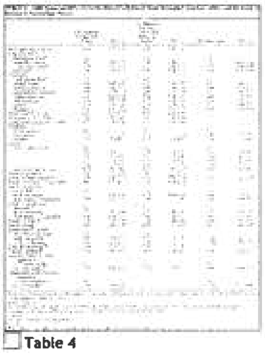


TABLE 2. Magnesium in Drinking Water in Relation to Numbers of Cases of Acute Myocardial Infarction and Population Controls

Table 2

Table 3



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