Magnesium and Calcium in Drinking Water and Death from Acute Myocardial Infarction in Women

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A relation between water hardness and cardiovascular death has been shown in previous studies. In this case-control study, we investigated the levels of magnesium and calcium in drinking water and death from acute myocardial infarction among women. The study population encompassed 16 municipalities in southern Sweden. Cases were women who had died from acute myocardial infarction between the ages of 50 and 69 years during 1982–1993 (N = 378), and controls were women who had died from cancer (N = 1,368). We obtained magnesium and calcium concentrations of the individual water sources. We divided the subjects into quartiles and found that odds ratios (ORs) were lower at higher levels of both magnesium and calcium. For the quartile with the highest magnesium levels (≥9.9 mg/liter), the OR adjusted for age and calcium was 0.70 (95% confidence interval = 0.50–0.99). For calcium, the adjusted OR for the quartile with the highest level (≥70 mg/liter) was 0.66 (95% confidence interval = 0.47–0.94). The results suggest that magnesium and calcium in drinking water are important protective factors for death from acute myocardial infarction among women. (Epidemiology 1999; 10:31–36)

Keywords: calcium, coronary disease, women, magnesium, myocardial infarction, drinking water.

An inverse relation between water hardness and death from cardiovascular disease has been shown in many studies.[1–8] Water hardness is determined by the content of calcium and magnesium. The current hypothesis is that magnesium in hard water protects against death from ischemic heart disease. Magnesium is an important enzyme activator and is essential for cell permeability and neuromuscular excitability.[9,10] Lack of magnesium has been shown to cause an increased tendency to vasoconstriction[11–14] and cardiac arrythmias.[10,15,16]

Lower levels of magnesium have been found in the uninfarcted part of the heart muscle of persons who died suddenly from ischemic heart disease, compared with persons who died from other causes.[17–22] Epidemiologic studies in the United States,[2] Canada,[23] South Africa,[24] Finland,[25,26] and Sweden[27,28] have shown an inverse relation between magnesium in drinking water and mortality from ischemic heart disease.[29] It has been suggested that it is mainly the incidence of sudden death from ischemic heart disease that is higher when water magnesium levels are lower.[30,31]

The relation between ischemic heart disease and calcium was investigated in five of the studies. In three of the studies, calcium was related to ischemic heart disease, but not as strongly as magnesium.[2,23,27] These reports, however, did not include adjustments for the correlation between the two ions. In two studies,[26,28] calcium was not materially associated with acute myocardial infarction.

The incidence of ischemic heart disease among women is only about 25% of that among men at ages below 65 years. Above this age, however, the incidence increases rapidly[32] and is the most common cause of death.[33] Previous research on ischemic heart disease has focused mainly on men,[32] as have the studies on magnesium and calcium in drinking water and ischemic heart disease. In the above-mentioned epidemiologic studies, only three included women. Anderson *et al*[23] included women together with men, commenting that subdividing data by sex made no difference. Schroeder[2] showed the same inverse relation between water hardness and cardiovascular diseases among both men and women, but when investigating the relation between specific constituents in water and coronary heart disease, he included only men. Rylander *et al*[27] studied men and women separately and found among both groups an inverse relation between both magnesium and calcium and death from ischemic heart disease. These relations were weaker for women than for men.[27]

The aim of this investigation was to study, on an individual level, the relation between the amount of the

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TABLE 1. Number of Waterworks in the Study, the Ranges of Magnesium and Calcium in Drinking Water Supplied to the Municipalities, and the Levels of Magnesium and Calcium in Water Supplied to the Most Densely Populated Areas within the 16 Municipalities

Municipality	No. of Waterworks in the Study	Range of Magnesium in Water (mg/Liter)	Water Magnesium (mg/Liter) in the Most Densely Populated Area	Range of Calcium in Water (mg/Liter)	Water Calcium (mg/Liter) in the Most Densely Populated Area
Vellinge	2	5.9–14.0	7.8	28–59	48
Svedala	2	6.8–18.6	18.6	31–80	32
Skurup	2	7.8–10.0	8.4	39–68	58
Höör	4	7.0–13.0	11.0	40–86	71
Ystad	2	5.1–8.9	7.5	51–89	63
Trelleborg	5	6.5–19.0	16.0	32–59	38
Örkelljunga	4	3.0–8.0	6.5	11–20	18
Bromölla	4	1.3–6.3	1.3	45–95	81
Perstorp	2	4.0–9.0	9.0	18–89	64
Klippan	3	4.5–9.0	4.8	27–53	31
Åstorp	1	9.2	9.2	56	56
Kristianstad	17	1.3–14.1	6.7	24–101	85
Simrishamn	9	3.4–21.5	9.8	49–230	130
Ängelholm	3	7.0–12.0	11.0	40–76	45
Karlskrona	8	1.3–14.1	3.3	8–71	28
Karlshamn	3	1.9–5.3	2.0	28–53	30

determinants of water hardness, magnesium and calcium, in the drinking water and death from acute myocardial infarction among women.

Subjects and Methods

The study was conducted in an area in southern Sweden where the water magnesium and calcium levels varied between and within municipalities. A questionnaire was sent to all 37 municipal offices in two of the counties in that area (Skåne and Blekinge, excluding the city of Malmö) asking about drinking water hardness, acidity, and water treatment procedures. Sixteen municipalities were identified in which the water quality concerning the above parameters and treatment had been basically unchanged (change of hardness, <10%, and change of pH, <5%) since 1980.

We obtained information from the National Central Bureau of Statistics on all women in the study area who had died between the ages of 50 and 69 years during the period 1982–1993. We considered women with a diagnosis of acute myocardial infarction [*International Classification of Diseases* (ICD) code 410[34]] for the underlying cause of death as cases. Controls were women with the diagnosis of cancer (ICD codes 140–239) as the underlying cause of death.

We used parish population registers to obtain the addresses of the study subjects. Information was obtained from the municipalities on the waterworks that supplied the drinking water to each of the addresses or whether the person used a private well.

We identified 492 cases and 1,706 controls according to these criteria. Of these, we excluded 76 cases and 203 controls who were using private wells. For 38 cases and 135 controls, neither the addresses nor the water sources could be traced. The final numbers of subjects in the study were 378 cases and 1,368 controls.

Table 1 shows the number of waterworks, the range of magnesium and calcium in drinking water from the different waterworks, and the amount of magnesium in water supplied to the most densely populated area in each municipality. Within the municipalities, the number of waterworks included in the study varied between 1 and 17, and the total number was 80. The amount of magnesium in the drinking water in the municipalities varied between 1.3 and 21.5 mg/liter, and the amount of calcium ranged from 8 to 230 mg/liter. There was a weak correlation between magnesium and calcium (r_{xy} = 0.104). An estimation of the validity of the data for the water magnesium and calcium content has been made earlier.[28]

We divided the subjects into quartiles according to the levels of magnesium, calcium, and magnesium/calcium ratio in the drinking water. We calculated the crude odds ratios (ORs) with 95% confidence intervals (CIs), as well as the ORs adjusted for age and calcium and magnesium, respectively. The latter were calculated using a logistic regression model.

Results

Table 2 shows the ORs for the quartiles in relation to the magnesium content in drinking water. The ORs for death from acute myocardial infarction were lower with higher levels of magnesium in the drinking water; the OR was 0.64 (95% CI = 0.46–0.90) for the highest quartile of magnesium levels. Adjustment for age and calcium increased the ORs slightly, diminishing the effect; for the highest quartile of magnesium levels, the OR adjusted for both age and calcium was 0.70 (95% CI = 0.50–0.99). ORs were consistently farther from the null for the younger group (50–59 years) than for the older group (60–69 years).

Regarding calcium (Table 3), ORs for the whole group were lower in all three upper quartiles, compared with the referent quartile. Adjustments for age and magnesium altered the ORs only slightly. ORs were again farther from the null for those of lower age. For the quartile with the highest calcium values, the OR was

TABLE 2. Magnesium in Drinking Water in Relation to Number of Myocardial Infarction Cases and Controls*

Median Magnesium Concentrations (mg/Liter)	Age Groups	Number of Cases	Number of Controls	OR	95% CI	OR†	95% CI
≤3.4 quartile‡							
2.5	All	113	346	1.0		1.0	
2.0	50–59 years	17	109	1.0		1.0	
2.8	60–69 years	96	237	1.0		1.0	
3.5–6.7 quartile							
6.0	All	115	374	0.94	0.70–1.27	1.08	0.78–1.49
5.6	50–59 years	15	126	0.76	0.36–1.60	0.90	0.40–2.00
6.5	60–69 years	100	248	1.00	0.71–1.39	1.12	0.78–1.61
6.8–9.8 quartile							
7.8	All	79	310	0.78	0.56–1.08	0.93	0.64–1.34
8.4	50–59 years	9	103	0.56	0.24–1.31	0.82	0.31–2.14
7.5	60–69 years	70	207	0.83	0.58–1.20	0.96	0.64–1.42
≥9.9 quartile							
13.0	All	71	338	0.64	0.46–0.90	0.70	0.50–0.99
16.0	50–59 years	10	116	0.55	0.24–1.26	0.60	0.26–1.40
13.0	60–69 years	61	222	0.68	0.47–0.98	0.72	0.49–1.05

* ORs with 95% CIs for death from myocardial infarction among women ages 50–69 years.
† ORs adjusted for age and calcium.
‡ Referent quartile.

0.35 (95% CI = 0.14–0.87) for the younger group and 0.74 (95% CI = 0.51–1.08) for the older group.

ORs in relation to the magnesium/calcium quotient are shown in Table 4. There was no notable pattern nor any important difference in effect between the age groups.

Discussion

Most of the waterworks had information on magnesium levels only for the most recent years (1990–1993). Because we studied only those municipalities in which the water source, quality, and treatment had been stable since 1980, we made the assumption that the magnesium levels in 1990–1993 were representative of the whole period from which the mortality data were collected (1982–1993).

We determined the exposure to magnesium by tracing the individual water source of the last known address, but we had no information on how long the person had lived there. Mobility is low for this population, however, as has been reported earlier.[28] In addition, we could not estimate the daily intake of magnesium and calcium from water or food. Despite the possible misclassification of exposure, we found a strong relation; with a more precise measure of exposure, the relation would probably have been even stronger.

We had no data on other risk factors for acute myocardial infarction. It is unlikely, however, that the amount of magnesium and calcium in drinking water would covary with other risk factors. This could have been the case if densely populated areas, which are usually associated with a higher presence of risk factors such as smoking and stress, had had low levels of magnesium and calcium. Nevertheless, water magnesium in the most densely populated areas varied between 1.3 and 18.6 mg/liter, and calcium varied between 30 and 130

TABLE 3. Calcium in Drinking Water in Relation to Number of Myocardial Infarction Cases and Controls*

Median Calcium Concentrations (mg/Liter)	Age Groups	Number of Cases	Number of Controls	OR	95% CI	OR†	95% CI
≤31 quartile‡							
28	All	129	339	1.0		1.0	
28	50–59 years	20	108	1.0		1.0	
28	60–69 years	109	231	1.0		1.0	
32–45 quartile							
38	All	79	366	0.57	0.41–0.78	0.61	0.39–0.94
38	50–59 years	10	131	0.41	0.19–0.92	0.39	0.13–1.14
38	60–69 years	69	235	0.62	0.44–0.89	0.67	0.41–1.08
46–69 quartile							
57	All	88	325	0.71	0.52–0.97	0.71	0.49–1.02
56	50–59 years	13	100	0.70	0.33–1.49	0.68	0.28–1.65
58	60–69 years	75	225	0.71	0.50–1.00	0.72	0.48–1.08
≥70 quartile							
85	All	82	338	0.64	0.47–0.87	0.66	0.47–0.94
85	50–59 years	8	115	0.38	0.16–0.89	0.35	0.14–0.87
85	60–69 years	74	223	0.70	0.50–1.00	0.74	0.51–1.08

* ORs with 95% CIs for death from myocardial infarction among women ages 50–69 years.
† ORs adjusted for age and magnesium.
‡ Referent quartile.

TABLE 4. Magnesium/Calcium Ratios in Drinking Water in Relation to Number of Myocardial Infarction Cases and Controls*

Median Magnesium/Calcium Ratios (mg/Liter)	Age Groups	Number of Cases	Number of Controls	OR	95% CI
≤0.075 quartile†					
0.067	All	76	308	1.0	
0.067	50–59 years	12	111	1.0	
0.067	60–69 years	64	197	1.0	
0.076–0.118 quartile					
0.103	All	122	367	1.35	0.97–1.86
0.103	50–59 years	15	108	1.28	0.58–2.87
0.103	60–69 years	107	259	1.27	0.89–1.82
0.119–0.205 quartile					
0.140	All	86	338	1.03	0.73–1.46
0.144	50–59 years	10	113	0.82	0.34–1.97
0.140	60–69 years	76	225	1.04	0.71–1.53
≥0.206 quartile					
0.275	All	94	355	1.07	0.77–1.51
0.361	50–59 years	14	122	1.06	0.47–2.39
0.262	60–69 years	80	233	1.06	0.72–1.55

* ORs with 95% CIs for death from myocardial infarction among women ages 50–69 years.
† Referent quartile.

mg/liter (Table 1). Furthermore, the municipalities were all medium sized and located within a relatively small geographical area, and the levels of magnesium and calcium were different not only between but also within the municipalities.

The controls were women who had died from cancer. For several common diseases, such as cerebrovascular and respiratory disease, there are data showing a possible relation with magnesium.[2,35] We therefore excluded these diseases as control diagnoses, as well as diseases of the digestive organs, because of possible interference with the absorption of magnesium and calcium. We also excluded "accidental death" as a control diagnosis, because in many accidental deaths alcohol is involved, and alcohol affects magnesium status.[36] Of the diagnoses that remained, 85% of individuals had some form of cancer. No clear evidence exists that magnesium affects the risk of death from cancer.

The diagnoses were based on death certificates. Autopsies were carried out in 41% of cases and 16% of controls, respectively; hospital examination before death occurred in 47% and 83%, respectively; and medical examination outside of the hospital before death or examination after death occurred in 8% and 3%, respectively. For the clinical diagnosis of acute myocardial infarction, certain strict criteria have to be fulfilled, so the risk of misclassification should be small for those examined in the hospital before death.

The OR for the quartile with the highest magnesium level in this study was about the same for women as that reported for men in an earlier study with similar design in the same area.[28] Thus, although the risk factors for ischemic heart disease differ between men and women,[37,38] the protective effect of high levels of magnesium in drinking water is similar, when measured on a ratio scale.

The results indicate that magnesium in water has a substantial effect, although the contribution of magnesium in water to the total intake is much lower than that from food. The recommended dietary amount of magnesium is about 350 mg/day.[39] In modern western society, the intake is often lower, mainly owing to increased industrial treatment of food, which decreases normal magnesium levels by 80–95%.[40] If the total daily intake is 250 mg/day, the proportional magnesium contribution from water for the quartile with the highest magnesium levels (median, 13.0 mg/liter) is about 10%, and for those with the highest levels in this study (21.5 mg/liter), nearly 20%. For the use of water in the lower range, the contribution of water magnesium is less than 1%. The relative contribution of water magnesium could be more important among persons with a low dietary intake of magnesium. In addition, magnesium in water is thought to have a higher bioavailability than magnesium in food, which is bound in different compounds less easily absorbed.[41,42]

For men, water calcium had no effect on the risk of fatal myocardial infarction,[28] but for women a low level of calcium was a risk factor. There is evidence that calcium deficiency can cause hypertension.[43–45] Low serum concentrations of ionized calcium have been measured in patients with hypertension.[46] Several studies have shown an inverse relation between dietary calcium intake and blood pressure. In a meta-analysis comprising 38,950 persons, Cappuccio *et al* showed that a high calcium intake lowered both systolic and diastolic blood pressure.[47]

A low intake of calcium is common among the elderly, especially women. The absorption and renal conservation of calcium decreases with age. The absorption of calcium from food varies between 15 and 75%,[48] but among menopausal women only about 20–30% is absorbed.[49] Exacerbating this reduced absorption is a decreased calcium intake among the elderly.[50,51] The recommended dietary amount of calcium for adult women in Sweden is 800 mg/day. A study comprising 61,000 women of ages 40–76 showed that the calcium intake decreased with age, and that a majority of postmenopausal women had deficient calcium intake.[52] Several studies from the United States have also shown an intake lower than recommended, especially among women.[53-55] For those with an initial deficiency, the additional calcium from water could be crucial to prevent deficiency.

There are several possible mechanisms that could explain the blood pressure-lowering effect of calcium. One mechanism could be that hypocalcemia inhibits calcium-ATPase activity, leading to an increase in free intracellular calcium and contraction of vascular smooth muscles.[56] Calcium supplementation has been shown to be efficacious especially among salt-sensitive hypertensive patients with a deficient basal calcium intake.[57] These individuals often have increased levels of the calcium-regulatory hormones parathyroid hormone and active vitamin D (1,25-$(OH)_2$-D), which can cause increased peripheral resistance. Dietary calcium suppresses these hormones, with a blood pressure-lowering effect. Calcium and calcium-regulatory hormones may also influence blood pressure regulation via the central nervous system.[58] Another blood pressure-lowering property of calcium is to induce natriuresis, which has been shown in postmenopausal hypertensive women.[59]

In summary, our findings indicate that both magnesium and calcium in drinking water may prevent death from acute myocardial infarction among women, and the effect might be more pronounced for lower age groups.

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