

Magnesium in Drinking Water and Death from Acute Myocardial Infarction

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The relation between death from acute myocardial infarction and the level of magnesium in drinking water was examined using mortality registers and a case-control design. The study area comprised 17 municipalities in the southern part of Sweden that have different magnesium levels in the drinking water. Cases were men in the area who had died of acute myocardial infarction between ages 50 and 69 years during the period 1982–1989 ($n = 854$). The controls were men of the same age in the same area who had died from cancer during the same time period ($n = 989$). In both groups, only men who consumed water supplied from municipal waterworks were included in the study. The subjects were divided into quartiles according to the drinking water levels of magnesium and calcium and the quotient between magnesium and calcium. The odds ratios for death from acute myocardial infarction in the groups were inversely related to the amount of magnesium in drinking water. For the group with the highest levels of magnesium in drinking water, the odds ratio adjusted for age and calcium level was 0.65 (95 percent confidence interval 0.50–0.84). There was no such relation for calcium. For the magnesium/calcium quotient, the odds ratio was lower only for the group with the highest quotient. These data suggest that magnesium in drinking water is an important protective factor for death from acute myocardial infarction among males. *Am J Epidemiol* 1996;143:456–62.

calcium; coronary disease; drinking water; magnesium; myocardial infarction

An inverse relation between water hardness and death from cardiovascular disease has been observed in a number of studies (1–7). A major hypothesis that has emerged from studies in recent years is that magnesium, which together with calcium is the main determinant of water hardness, protects against death from ischemic heart disease. There are number of facts to support this hypothesis.

Magnesium is an enzyme activator, and is essential for neuromuscular excitability and cell permeability. It is an activator of sodium/potassium-adenosinetriphosphatase (Na/K-ATP-ase), an enzyme that is necessary for the transportation of sodium and potassium across cell membrane, and that is thus necessary for maintaining the intracellular concentrations of potassium (8, 9). It is also thought to function as a natural calcium antagonist (9–12). Magnesium deficiency can induce artery spasm, as has been shown in animal experiments (13–16), and it facilitates the develop-

ment of arrhythmias (9, 12, 17). Significantly lower magnesium levels have been found in the uninfarcted heart muscle of persons who died suddenly from ischemic heart disease compared with persons who died from other causes (18–23).

In the general population, the major portion of magnesium intake is via food, and to a lesser extent via drinking water (in Sweden, generally less than 5 percent). However, previous studies support the hypothesis that magnesium in drinking water can be critical for the magnesium content of the body. Relations have been shown between water magnesium and magnesium content in heart muscle (22), coronary arteries (24), and skeletal muscle (25).

In the modern-day world, intake of dietary magnesium is often lower than the recommended dietary amounts (6 mg/kg/day) (26). For individuals at the borderline of magnesium deficiency, waterborne magnesium can make an important contribution to the total daily intake. In addition, the loss of magnesium from food is lower when the food is cooked in magnesium-rich water. Another reason why magnesium in water can play a critical role is its higher bioavailability. Magnesium in water appears as hydrated ions, which are more easily absorbed than magnesium in food (27–29). The contribution of water magnesium among persons who use water with high magnesium levels

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Abbreviations: CI, confidence interval; ICD, *International Classification of Diseases*; pH, acidity as measured by hydrogen ion concentration.

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could thus be crucial in the prevention of magnesium deficiency.

The absorption of magnesium is affected by simultaneous intake of other nutrients. Examples of substances that can reduce the absorption of magnesium are saturated fats, sugar, phytates, proteins, phosphates, and calcium (26, 30). A quotient of 1/2 between magnesium and calcium has been suggested to be adequate in the diet (26).

Epidemiologic studies in the United States (2), Canada (31, 32), South Africa (33), Finland (34, 35), and Sweden (36) have shown an inverse correlation between magnesium in drinking water and mortality from ischemic heart disease. The relation has been observed primarily among men.

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, owing to an increased tendency to vasoconstriction (15, 16) or arrhythmias (12, 32, 37, 38).

In the above-mentioned epidemiologic studies, except for those done in Finland, the relation was studied on a group level and the individual magnesium exposure was not determined. The aim of this investigation was to study, on an individual level, the relation between the amount of magnesium in drinking water and death from myocardial infarction among males.

MATERIALS AND METHODS

A survey was carried out of the magnesium content in drinking water in all Swedish municipalities. In part

of southern Sweden, it was found that, within a relatively small geographic area, the water magnesium levels were different *between* municipalities as well as *within* those municipalities. A questionnaire was sent to all 37 municipal offices in two of the counties in the area, Skåne and Blekinge (excluding the city of Malmö), asking about drinking water hardness, acidity (as measured by hydrogen ion concentration (pH)), and water treatment procedures.

Of these 37 municipalities, 17 were identified where the water quality concerning the above parameters and treatment had been basically unchanged (change of hardness <10 percent and pH <5 percent) during the last 10 years. Figure 1 shows the location of the 17 municipalities that comprised the study area.

Information on all men in the study area who had died between ages 50 and 69 years during the period 1982–1989 was obtained from the National Central Bureau of Statistics. Men with a diagnosis of acute myocardial infarction (*International Classification of Diseases* (ICD) code 410 (39)) as underlying cause of death were considered cases. Controls were men with the diagnosis of cancer (ICD codes 140–239) as the underlying cause of death. The median age of death was 64 years in both groups.

Parish population registers were used to obtain the addresses of the study subjects. Information on the waterworks that supplied the drinking water to each of the addresses, or the use of private wells, was obtained from the municipalities.

According to the criteria described, 1,237 cases and 1,381 controls were identified.

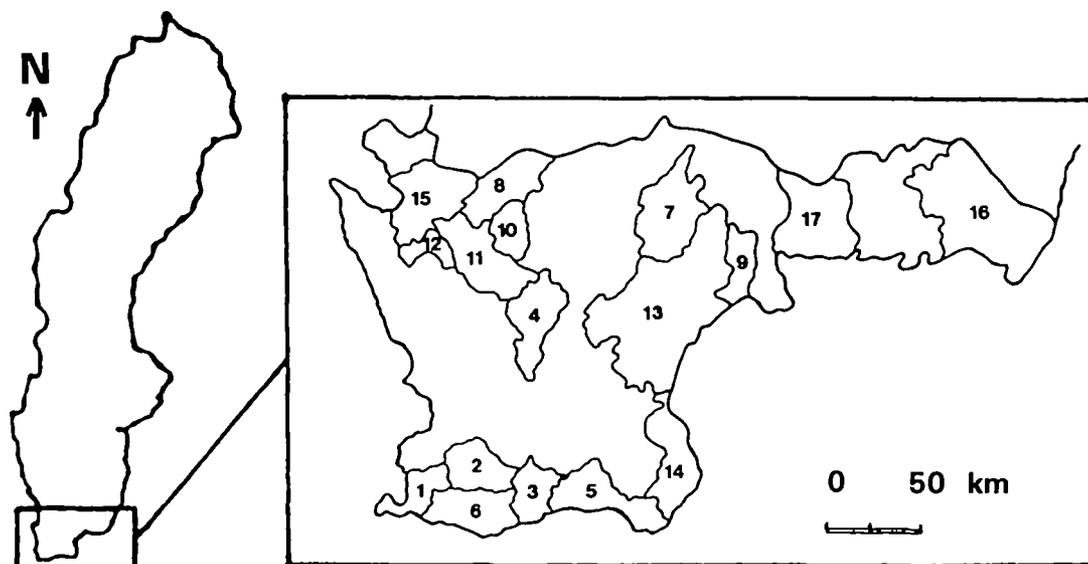


FIGURE 1. The country of Sweden, with Skåne and Blekinge counties enlarged. The 17 municipalities in the study are numbered corresponding to table 2, i.e., 1, Vellinge; 2, Svedala; 3, Skurup; 4, Höör; 5, Ystad; 6, Trelleborg; 7, Ö Gøinge; 8, Örkelljunga; 9, Bromölla; 10, Perstorp; 11, Klippan; 12, Åstorp; 13, Kristianstad; 14, Simrishamn; 15, Ängelholm; 16, Karlskrona; 17, Karlshamn.

The final numbers in the study were 854 cases and 989 controls. The numbers of persons excluded from the study and the reasons for their exclusion are shown in table 1. The persons excluded from the study were evenly distributed between cases and controls, and over the study area.

Information on levels of magnesium and calcium in tap water was obtained from each waterworks. Table 2 shows the number of waterworks, the range of magnesium in drinking water, and the amount of magnesium in water supplied to the most densely populated area in each municipality. Within the municipalities, the number of waterworks engaged in the study varied between 1 and 15, and the total number was 78. The amount of magnesium in the drinking water in the municipalities varied between 1.3 and 20.0 mg/liter, and the amount of calcium ranged from 22 to 225 mg/liter. There was no correlation between magnesium and calcium in the drinking water ($r_{xy} = 0.056$). Water magnesium in the most densely populated area varied between 1.3 and 20.0 mg/liter.

A measure of validity of the data for the water magnesium content was made. One sample of tap water, taken at the municipality office, was obtained from the main waterworks of each municipality. The sample was analyzed with atomic absorption spectrophotometry at the Chalmers University of Technology, Göteborg, Sweden. There was a strong correlation between the values of magnesium and calcium in these analyses and the values we obtained from the waterworks (magnesium: $r_{xy} = 0.96$, $p < 0.001$; calcium: $r_{xy} = 0.97$, $p < 0.001$). This demonstrated that the content of magnesium in the water did not change on the way from the waterworks to the households.

Logistic regression models were fitted to the data with the EGRET software package (SERC, Seattle, Washington) for unconditional maximum likelihood estimation of the regression parameters. In the analyses, the subjects were divided into quartiles according

TABLE 1. Sample of myocardial infarction cases and controls, and the losses according to exclusion criteria, in 17 municipalities, southern Sweden, 1982–1989

	No. of cases	No. of controls*
Initial sample	1,237	1,381
Insufficient information on addresses or waterworks	129	117
Less than one year at the last address	36	64
Used own well	218	211
Final sample	854	989

* Controls were men of the same age (50–69 years) in the same study area as the cases and who had died of cancer.

TABLE 2. Number of waterworks, the range of magnesium in drinking water, and the amount of magnesium in water supplied to the most densely populated areas of 17 municipalities, southern Sweden, 1982–1989

Municipality no.*	No. of waterworks in the study	Range of magnesium in water (mg/liter)	Water magnesium (mg/liter) in the most densely populated area
1	2	5.9–10.0	10.0
2	2	6.8–20.0	20.0
3	4	2.6–10.0	9.0
4	2	8.8–13.0	8.8
5	5	5.1–11.9	7.5
6	4	6.5–18.0	16.0
7	9	3.3–13.5	5.0
8	3	3.0–6.9	6.9
9	5	1.3–7.6	1.3
10	2	4.0–9.0	9.0
11	2	5.5–9.0	8.0
12	1	10.0	10.0
13	15	1.3–14.4	6.7
14	9	3.8–13.4	9.7
15	2	7.0–11.0	11.0
16	9	2.0–13.0	2.0
17	2	1.9–5.0	2.0

* Municipality numbers correspond to figure 1.

to the levels of magnesium, calcium, and magnesium/calcium ratio in the drinking water. Odds ratios were calculated in relation to the group with the lowest exposure. In addition, trend analyses with $2 \times K$ tables were made. Adjustments for age were made in all analyses. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Table 3 shows the numbers of cases and controls and odds ratios in relation to the magnesium content in drinking water.

The odds ratios for death from acute myocardial infarction were significantly lower for the two groups with high levels of magnesium in the drinking water. Adjustments for the amount of calcium in drinking water only slightly altered the odds ratios. The adjusted odds ratio (95 percent confidence interval (CI)) was 0.88 (0.66–1.16) for the group with water magnesium levels between 3.6 and 6.8 mg/liter, 0.70 (0.53–0.93) for the group with magnesium levels between 6.9 and 9.7 mg/liter, and 0.65 (0.50–0.84) for the group with magnesium levels of 9.8 mg/liter or more. Trend analyses showed statistical significance for magnesium adjusted for calcium.

Odds ratios in relation to calcium levels showed slightly lower values with higher calcium levels, but when adjusted for magnesium there was no difference between the groups with different levels of calcium

TABLE 3. Magnesium in drinking water in relation to numbers of myocardial infarction cases and controls and odds ratios with 95% confidence intervals (CI) for death from myocardial infarction among men in 17 municipalities, southern Sweden, 1982–1989

	Magnesium, mg/liter (median)			
	≤3.5 (3.15)	3.6–6.8 (6.7)	6.9–9.7 (7.8)	≥9.8 (17)
No. of cases	243	223	202	186
No. of controls	233	228	262	266
Odds ratio adjusted for age	1.0	0.93 (0.72–1.20)*	0.74 (0.57–0.95)	0.66 (0.51–0.86)
Odds ratio adjusted for age and calcium in drinking water	1.0	0.88 (0.66–1.16)	0.70 (0.53–0.93)	0.65 (0.50–0.84)

* 95% CI in parentheses.

(table 4). Trend analyses showed no statistical significance for calcium.

The odds ratios in relation to magnesium/calcium quotient are shown in table 5. The group with the highest quotient (≥ 0.22) had a significantly lower odds ratio (0.70, 95 percent CI 0.53–0.93). Odds ratios for the other groups were not significantly lower. The quotient for magnesium/calcium in water showed a trend similar to that seen for magnesium alone ($p < 0.05$). Adjustments for age, which were made in all analyses, only affected the odds ratios slightly.

DISCUSSION

Epidemiologic studies on the group level involve several methodological difficulties, particularly the description of the dose. In contrast to several previous investigations, this study determined the source of drinking water on the individual level, taking into account the fact that many municipalities were using several different waterworks, and avoiding the possible interference of private wells.

Most of the waterworks had information on magnesium levels only for the most recent years (1990–1991). Because only those municipalities were chosen where the water source, quality, and treatment had been stable for the last 10 years, we made the assumption that the magnesium levels in 1990–1991 were

about the same as during the period when the mortality data were collected (1982–1989). The assumption is supported by the fact that calcium levels, which had been registered for a longer time, had been stable over the time period. In the analyses, we used the values of calcium observed during the same period as that of the magnesium values.

Although the study offered an increase in precision in regard to the exposure to magnesium on the individual level, we were unable to calculate the exact amount of magnesium taken in from water, because the amounts of water consumed at home or at other places and the use of water filters could not be determined. The data on individual exposure were thus still characterized by a lack of precision.

As with all retrospective register studies, this study suffers from some uncertainty regarding the accuracy of diagnosis. In the study, death certificates formed the basis for the diagnosis. Autopsies were carried out in 40.6 percent of cases and in 23.6 percent of controls, and hospital examination before death in 50.1 percent and 75.4 percent, and medical examination outside hospital before death or examination after death in 9.3 percent and 1.0 percent, respectively. This allowed some validation of diagnosis. The autopsy frequency was nearly the same over the study area and in the four quartiles of magnesium in water (cases, 43, 37, 41, and

TABLE 4. Calcium in drinking water in relation to numbers of myocardial infarction cases and controls and odds ratios with 95% confidence intervals (CI) for death from myocardial infarction among men in 17 municipalities, southern Sweden, 1982–1989

	Calcium, mg/liter (median)			
	≤33 (28)	34–45 (40)	46–81 (66)	≥82 (82)
No. of cases	258	200	184	212
No. of controls	263	274	240	212
Odds ratio adjusted for age	1.0	0.74 (0.57–0.95)*	0.78 (0.60–1.01)	1.01 (0.78–1.31)
Odds ratio adjusted for age and magnesium in drinking water	1.0	0.88 (0.65–1.19)	0.84 (0.64–1.10)	1.06 (0.82–1.38)

* 95% CI in parentheses.

TABLE 5. Magnesium/calcium in drinking water in relation to numbers of myocardial infarction cases and controls and odds ratios with 95% confidence intervals (CI) for death from myocardial infarction among men in 17 municipalities, southern Sweden, 1982–1989

	Magnesium/calcium*			
	≤0.07	0.08–0.11	0.12–0.21	≥0.22
No. of cases	153	246	245	210
No. of controls	159	285	234	311
Odds ratio	1.0	0.90 (0.68–1.19)†	0.99 (0.75–1.31)	0.70 (0.53–0.93)

* Magnesium/calcium is shown as a quotient calculated as follows: magnesium (mg/liter)/calcium (mg/liter).
 † 95% CI in parentheses.

42 percent, respectively; controls, 25, 25, 24, and 21 percent, respectively).

We only included those persons who had lived at their address for at least a year at the time of death. Some investigators have found an influence of magnesium on the extent of atherosclerosis (37) and, if that is so, the exposure of water magnesium further back in time would be of interest. However, Crawford and Crawford (24) could not detect any difference in the prevalence of atherosclerosis between residents of hard-water and soft-water areas, although the levels of magnesium were lower in coronary arteries among persons in soft-water areas. The possible role of magnesium in preventing atherosclerosis is probably of minor importance in comparison to the predominant effect—the prevention of sudden death from ischemic heart disease, owing to its influence on blood vessel contraction and arrhythmia, which is related to the current magnesium status. A one-year exposure period would thus be relevant for this type of study because it is well sufficient for an adaptation to the local water magnesium level (26).

The controls were men who had died from cancer. To our knowledge, there are no data which suggest that magnesium could influence the risk of death from cancer. However, for several other common diseases, such as cerebrovascular and respiratory disease, there are data showing a possible relation with magnesium (2, 40). Accidental death is not a suitable reference diagnosis, because in such cases of death alcohol is often involved, and it is known that alcohol affects the magnesium status (41).

Chlorinated surface water has been associated with cancers of the bladder and pancreas (42, 43). Among the 989 controls in the study, bladder and pancreatic cancers were the underlying cause of death among 28 and 66 controls, respectively.

Only three waterworks of 78 in the study supplied chlorinated surface water. Nine waterworks supplied chlorinated ground water. The magnesium levels in the water from the waterworks with chlorinated water ranged between 2.2 and 13.0 mg/liter, thus represent-

ing all quartiles. There is thus no reason to believe that this would be a confounding factor.

The strong negative relation found in this study, between death from myocardial infarction and drinking water magnesium, supports the results of several previous studies (2, 31–36). A few studies have reported contradictory results. Shaper et al. (44) found no relation between magnesium and cardiovascular mortality in Great Britain, although a significant relation was found for water hardness. However, their study included all cardiovascular diseases and did not distinguish between ischemic heart disease and stroke. As discussed above, it is death from ischemic heart disease that is of interest in regard to magnesium, and, furthermore, an inverse relation between calcium and cerebrovascular disease has been shown in previous studies (36).

Nerbrand et al. (7) studied water quality in 76 municipalities in Sweden in relation to cardiovascular mortality in 1969–1983. Water hardness was measured in 1980 and correlated negatively to ischemic heart disease mortality. Magnesium was measured 10 years later, in 1990, and no relation to magnesium was found. However, only average values of water magnesium in the municipalities were used, instead of considering the value from each waterworks, and those municipalities where water quality and treatment had been changed since 1980 were not excluded.

Biörk et al. (45) found a relation between water hardness and mortality from “arteriosclerotic heart disease” and “other degenerative heart diseases” but no relation to magnesium. In that study, however, magnesium data were available only from 14 of the 34 cities from which the populations were selected. Moreover, the largest cities in Sweden were included, and cardiovascular deaths in large cities involve a complex interaction in which life-style factors play a large role.

Thus, in our view, these studies with contradictory findings have important shortcomings in study design that make the conclusions less reliable.

In this study, the municipalities that were included were all middle-sized, and the area is geographically and culturally homogeneous. There is thus no reason to believe that there would be any correlation between such risk factors as smoking, fat consumption, and stress and the level of magnesium in drinking water in the study area, especially since the levels of magnesium varied within the municipalities as well as between them (table 2). Besides, the magnesium levels in the most densely populated area in the municipalities represented the whole range of levels (table 2).

The results show that magnesium alone was more important for the risk of having an acute myocardial infarction than was the magnesium/calcium quotient. The quotient of 1/2 discussed above in regard to food seemed to be less important in drinking water.

The results from this study strengthen the hypothesis that magnesium in drinking water helps to prevent death from myocardial infarction. An attempt to quantify the importance of magnesium has been made by Marier and Neri (46), using a number of the above-mentioned epidemiologic studies. They estimated that an increase in water magnesium level of 6 mg/liter would decrease ischemic heart disease mortality by approximately 10 percent.

The data from this study could be used to estimate the impact of magnesium on the incidence of myocardial infarction in the study population. If everyone were to drink water from the highest quartile (≥ 9.8 mg/liter), the decrease in mortality from acute myocardial infarction would be about 19 percent. This means that the age-specific incidence of death from myocardial infarction in the study area would change from about 350/100,000 to 285/100,000. The incidence decrease per mg/liter magnesium could be calculated to be approximately 10/100,000, which is an even larger decrease than Marier and Neri (46) estimated.

Future studies should increase the precision of the estimation of the individual's intake of magnesium, both via food and water, and control for confounding factors. This could be done in prospective studies on cases of non-fatal myocardial infarction. In such studies, it would also be possible to investigate whether magnesium in drinking water is important for people in general, or if there are certain risk groups that benefit from high magnesium levels in drinking water.

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