

5. MINERALS FROM DRINKING WATER: BIOAVAILABILITY FOR VARIOUS WORLD POPULATIONS AND HEALTH IMPLICATIONS

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I. INTRODUCTION

Low mineral intakes from foods and water are common in many parts of the world. Today, sub-clinical deficiencies of iron, zinc and calcium prevail in the developed and developing world. Although dozens of geographical studies have been conducted on minerals in drinking water and their relationships to various diseases, the daily intake and the status of deficiency as well as their health consequence are still largely unknown. Furthermore, mineral bioavailability may change due to different stage of growth and ageing. In this chapter the health implication of low mineral content in drinking water in different age groups and gender from various parts of the world is assessed. Studies from Asia, North America, Europe, Africa and Australia were reviewed with regard to minerals in drinking water and the health effects reported.

II. STUDIES IN ASIA

Soft water is commonly consumed in most parts of Asia. The levels of calcium, magnesium and zinc in drinking water are usually low. Several epidemiological investigations on the possible associations between the risk of esophageal, gastric, rectal and colon cancers and minerals in drinking water, in particular hardness have been reported in Taiwan. These case-control studies showed excess risk of several types of cancers in relation to the use of soft water. In one of their studies, Yang and his colleagues reported a 42% excess risk of mortality from esophageal cancer in relation to the use of soft water (1). For rectal cancer the odds ratio were 1.24 and 1.38 respectively, for exposure to moderately hard water and soft water compared with the use of hard water (2). The same group of researchers also showed that there was a significant negative relationship between drinking water hardness and colon cancer mortality, with odds ratio of 1.22 and 1.46, respectively, for exposure to moderately hard water and soft water compared with the use of hard water (3). Their earlier study also showed a significant negative relationship between drinking water hardness and gastric cancer mortality. The odds ratios were 1.16 and 1.65 respectively, for exposure to moderately hard water and soft water compared with the use of hard water (4).

In view of the limited data available from the Asian region on the daily intake of nutritionally essential trace elements, a recent study was undertaken to estimate the daily dietary intake and organ content of some selected trace elements. Nine Asian countries - Bangladesh, China, India, Indonesia, Japan, South Korea, Pakistan, Philippines, and Vietnam--which represented more than 50% of the world's population, participated in this study. Analysis of about 700 diet samples was carried out for four common (calcium, potassium, magnesium, and sodium) and eight trace (chromium, cobalt, copper, iron, iodine, manganese, selenium, and zinc) elements. These samples consisted of total cooked foods, market basket and 225 staple foods. The

maximum inter-country variation was observed for iodine intake (factor of more than 45), being highest for Japan and lowest for Pakistan. For iron, an important trace element, the variation between the intakes was a factor of four being lowest for Vietnam and highest for Pakistan (5). Overall data suggest that the intake of minerals from diet varied tremendously and residents in many of the studied countries have low intakes of various essential minerals.

A number of studies carried out in several Asian countries have shown negative correlations between coronary mortality and the presence of trace elements in water supplies. A cross-sectional survey was conducted in 20 randomly selected streets in North India to determine the association of magnesium with risk of coronary artery disease (CAD). The results suggest that magnesium intake and serum magnesium were inversely correlated with CAD. The odds ratio for dietary magnesium intake indicates a higher prevalence of CAD at lower intakes of magnesium in both rural (0.67) and urban (0.72) subjects. Multivariate regression analysis showed that serum and dietary magnesium, but not hypertension, were significantly associated with CAD (6,7). Data on water hardness throughout Taiwan have been collected to examine the ecological correlation between deaths from coronary disease (1981-1990) and total hardness in drinking water. Analysis demonstrates a significant negative association between drinking water hardness and coronary mortality. After adjustment for the urbanization index, coronary mortality in municipalities with soft water was estimated to be 9.6% higher than that in municipalities with hard water. The weighted multivariate-adjusted regression coefficient indicated a decrease of 0.053 in standardized mortality ratios (SMRs) for every 100 mg/L increase in total hardness in drinking water after allowing for the urbanization condition (8). The same group of researchers further examined specifically whether calcium and magnesium in drinking water are protective against cerebrovascular disease and the general finding suggests that there was a significant protective effect of magnesium intake from drinking water on the risk of cerebrovascular disease (9).

1. Hypertension

Hypertension is a complex, heterogeneous disorder whose exact etiology is unknown. The difficulty in ascribing an independent role to a single dietary constituent in blood pressure regulation may be due to interactions among nutrients that influence blood pressure. Several clinical, experimental and epidemiologic studies have supported the role of magnesium in hypertension, whereas a few studies negate this role. Magnesium deficiency can predispose to increased contractility of the arteries and its excess can modulate smooth muscle contractility caused by bradykinin, angiotensin II, serotonin, prostaglandins and catecholamines. The possible association of magnesium and hypertension was examined in a cross-sectional survey in two randomly selected villages in North India; the overall findings suggest that intake of magnesium, and also serum magnesium levels were inversely associated with the risk of hypertension (7).

2. Cognitive Function

The relation between trace element levels in drinking water and cognitive function was investigated in a population-based study of elderly residents (n = 1,016) in rural China. There was a significant quadratic effect for calcium and a significant zinc-cadmium interaction. Cognitive function increased with calcium level up to a certain point and then decreased as calcium in water continued to increase. In contrast, zinc showed a positive relation with cognitive function at low cadmium levels but a negative relation at high levels (10).

3. Fluoride

A large scale epidemiological study was conducted among 45,725 children in India exposed to high intake of endemic fluoride in the drinking water since their birth. Children with adequate (dietary calcium > 800 mg/d) and inadequate (dietary calcium < 300 mg/d) calcium nutrition and

with comparable intakes of fluoride (mean 9.5 +/- 1.9 mg/d) were compared. The toxic-effects of fluoride were severe and more complex and the incidence of metabolic bone disease (rickets, osteoporosis, and PTH bone disease) and bony leg deformities (genu valgum, genu varum, bowing, rotational and wind-swept) was greater (>90%) in children with calcium deficiency as compared to <25% in children with adequate calcium who largely had the osteosclerotic form of skeletal fluorosis with minimal secondary hyperparathyroidism. The findings suggest that children with calcium deficiency rickets reported in the literature should be re-investigated for possible fluoride interactions. Drinking water supply with fluoride <0.5 ppm and improvement of calcium nutrition provide protection against the toxic effects of fluoride and are recommended as the cost effective and practical public health measures for the prevention and control of endemic fluorosis (11).

4. Low Birth Weight

Magnesium is required in higher quantities, during the phase of rapid growth in children. Its level in the ground water in Kerala, India is low and is believed to cause magnesium deficiency, especially in children from the lower socio-economic groups who also suffer from nutritional insufficiency. Nair and colleagues (12) compared the serum and erythrocyte magnesium levels of school children from high and low socio-economic classes. The results showed that serum and erythrocyte magnesium levels were significantly lower in both boys and girls from low socio-economic groups who also consumed ground water and had lower body mass indices.

A few previous studies have looked at the relationship between pregnancy outcome and magnesium nutritional intake and found that magnesium supplementation could have beneficial effects on prenatal outcome. One study (13) examined the relationship between the levels of magnesium in drinking water and the risk of delivering a child of very low birth weight (birth weight less than 1500 g; VLBW). The study population comprised 1,781 women residing in 252 municipalities in Taiwan who had a first parity singleton birth during a five-year period, for whom complete information on maternal age, education, gestational age, birth weight, and sex of the baby were available. The results showed that there was a significant trend toward a decreased risk of having a child of VLBW with increasing magnesium levels in drinking water (14). It was hypothesized that calcium supplementation can reduce smooth muscle contractibility and tone and that this effect can be clinically manifested by a reduction in blood pressure and a reduction in the incidence of premature delivery. A study similar to that on magnesium was also conducted on the relationship between the levels of calcium in drinking water and the risk of delivering a child of very low birth weight (VLBW) in Taiwan. The study population comprised 1781 women residing in 252 municipalities in Taiwan who had a first-parity singlet birth between January 1, 1993 and December 31, 1997 and for whom complete information on maternal age, education, gestational age, birth weight, and sex of the baby were available. The results suggest a significant protective effect of calcium intake from drinking water on the risk of delivering a VLBW baby (14).

III. STUDIES IN PAN-AMERICA

Iron deficiency and related anemia are common in the developing world. Dutra-de-Oliveira and deAlmeida (15) evaluated the feasibility of iron fortification of domestic drinking water to prevent and control iron deficiency and iron-deficiency anemia. Twenty-one families representing 88 persons, including children, were selected to participate in this study. Iron-fortified drinking water increased hemoglobin. No significant changes in hemoglobin and ferritin were found in the placebo group after 4 months.

IV. STUDIES IN AFRICA

Similar to Latin America, relatively few studies have been conducted in Africa on minerals and water consumption. The mortality rates for acute myocardial infarction and ischemic heart disease (IHD) of white males and females in South Africa were noted to be much higher than those in the USA, Australia, England and Wales when individuals in the 15- to 64-year age group are considered. Magnesium levels in the drinking water of 12 South African districts and deaths due to IHD were assessed in white residents in the South Africa and a significant negative correlation was found between these two variables (16). An increased incidence of sudden death associated with ischemic heart disease has been found in some areas in South Africa which soil and drinking water lack magnesium. It was demonstrated experimentally that reduction of the plasma magnesium level is associated with arterial spasm (17).

V. STUDIES IN NORTH AMERICA

The US diet is low in magnesium, and with modern water systems, very little is ingested in the drinking water (18). Of major concern of this low intake of magnesium is the association between cardiovascular problems, such as myocardial infarction, hypertension, congestive heart failure, and hypomagnesaemia. In addition, evidence is mounting regarding the relationship between both types I and type II Diabetes Mellitus, and magnesium deficit.

Turner et al (19) determined the nutrient intake from food across trimesters for middle-to upper-income pregnant women compared with estimated average requirements (EAR) to determine whether food intake exceeded the tolerable upper intake level (UL) for any nutrient. The findings suggest probabilities of usual nutrient intake from food being less than the EAR were highest for iron (0.91), magnesium (0.53), zinc (0.31), vitamin B6 (0.21), selenium (0.20), and vitamin C (0.12). In contrast, women were not at risk of exceeding the UL from food intake for any nutrient studied. These data provide evidence that the study participants did not consume adequate amounts of iron from food to meet the needs of pregnancy, and therefore the authors recommended iron supplementation for this population.

Annual mortality rates for 1968 of six types of cardiovascular diseases among persons over 45 years of age in 24 Texas communities were compared with respective community drinking water and urine metal levels of calcium, magnesium, potassium, lithium, strontium, and silicon. Numerous inverse correlations were found between mortality rates and the levels of various metals in both drinking water and urine. Positive correlations were also observed between several of the mortality rates and the ratio of the concentration of sodium to that of the other metals in both water and urine. Mean community urinary levels of lithium, magnesium, strontium, and silicon showed a direct correlation to the levels of exposure via the drinking water. The results of this study suggest that calcium, magnesium, lithium strontium, and silicon may protect against cardiovascular mortality; possibly, by competing with sodium and potassium for transport in the intestinal lumen, increasing excretion of sodium, or other mechanism (20). Another investigation was conducted in 1980 to evaluate the association of cardiovascular diseases and drinking water constituents. A sample of 4200 adults was randomly selected from 35 geographic areas to represent the civilian noninstitutionalized population of the contiguous United States. Each participant was interviewed and given a thorough physical examination and a tap water grab sample was collected from each participant's residence and analyzed for 80 inorganic chemical constituents. Hardness and calcium appeared to follow the normal trend of negative associations with the mortality rates for most groups of cardiovascular diseases, whereas the area means for copper and lead were positively associated. Zinc and cadmium associations were examined, but

the range of constituent levels in the sampled drinking waters was too small for meaningful interpretation of the results (21).

Bloom and Peric-Golia (22) searched for evidence of myocyte calcification in hearts of patients found to have AMI at autopsy in Salt Lake City, a region with a low myocardial infection death rate, and Washington, DC, a region with a high myocardial infection death rate. The basis of this difference in myocyte calcification is unknown, but it may be related to the fact that the Salt Lake City drinking water contains a higher level of magnesium, which is known to protect against soft tissue calcification, than does that of Washington, DC. This finding is consistent with the apparent protection that dietary magnesium exerts against myocardial infarction death.

In both humans and experimental animals, dietary induced magnesium deficiency is correlated with insulin resistance. A study was performed to determine whether dietary magnesium intake is associated with insulin sensitivity or blood pressure in a sample of nondiabetic, young adult black Americans. The authors (23) examined dietary calcium, potassium, and sodium intake of young adults and who had been followed longitudinally. Nutrient intake was assessed by obtaining a 24-hour recall interview of dietary intake. There was a significant negative correlation of total dietary magnesium intake with the sum of insulin levels measured during an oral glucose tolerance test. The results suggest a possible role for dietary magnesium in insulin resistance. Lower levels of dietary and serum magnesium have been associated with an increased prevalence of hypertension, insulin resistance, and diabetes. Studies suggest a greater prevalence of occult magnesium deficiency among African-Americans compared to other populations. This increased prevalence of hypomagnesaemia may contribute to increased insulin resistance leading to accelerated atherosclerosis and premature death (24).

Schwartz and colleagues (25) conducted a study to assess the impact of water hardness on urinary stone formation. Patients who form calcium stones ($n = 4833$) were identified geographically by their zip codes. Water hardness information from distinct geographic public water supplies was obtained, and 24-hour urine chemistries were evaluated. The calcium and magnesium levels in the drinking water were analyzed as independent variables. The results indicated that the number of total lifetime stone episodes was similar between patients residing in areas with soft public water and hard public water. Patients consuming the softest water decile formed 3.4 lifetime stones and those who consumed the hardest water developed 3.0 lifetime stones ($P=0.0017$). The 24-hour urine calcium, magnesium, and citrate levels increased directly with drinking water hardness, and no significant change was found in urinary oxalate, uric acid, pH, or volume. The impact of water hardness on urinary stone formation remains unclear, despite a weak correlation between water hardness and urinary calcium, magnesium, and citrate excretion. Tap water, however, can affect urinary electrolytes in patients who form calcium stones (25).

VI. STUDIES IN EUROPE

The role of water hardness as a risk factor for cardiovascular disease has been widely investigated and evaluated with regard to regional differences in Europe. Water constituents like magnesium, calcium, etc. were found to be usually negatively associated with cardiovascular diseases in a study of more than 600 water supply areas in the Federal Republic of Germany (26). To study the influence of drinking water composition on the risk of myocardial infarction a study was conducted in 1983 on men 30-64 years of age who had been discharged with a first acute myocardial infarction (AMI) in a hospital in Finland. Results were consistent with the hypothesis that both low fluoride and a low Mg intake are conducive to atherosclerosis leading to AMI (27).

Ischemic heart disease (IHD) is a major public health problem in most industrialized countries. In the death rates from IHD, marked differences exist between various countries and also between different areas of individual countries. Unfavorable dietary factors appear to play an important role in the etiology of IHD, and thus differences in dietary habits and the quality of food may be mainly responsible for the geographic differences in the prevalence of IHD. Reduced intakes of potassium and magnesium may increase the death rate from IHD by predisposing the heart to fatal arrhythmias, and also by other mechanisms. The likelihood of magnesium deficiency also appears to be influenced by the area of residence. Karppanen (28) claimed that the higher-than-average death rates from IHD in the North Karala area in eastern Finland and in some other areas with exceptionally high death rates from this disease may be at least partly due to the very low levels of magnesium in the soil and drinking water. He concluded that electrolyte disturbances have important implications in the etiology and pathogenesis of IHD. Leoni et al (29) studied the pattern of mortality resulting from cardiovascular diseases, ischemic heart diseases, and cerebrovascular diseases in the region of Abruzzo, Italy, which has a population of 594,323. These variables were then correlated with mortality rate and water hardness. An inverse correlation was observed between drinking water hardness and mortality due to cardiovascular disease, for individuals aged 45-64 yr. The incidence of sudden cardiac death among the population of the Media Valle del Serchio area in Italy, which made up of 35,000 residents, was found to be twice that of the European average (9 per 10,000 in the examined year). The high incidence of sudden cardiac death among the residents correlated with water that was of very low total hardness (30).

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. 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. 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. Magnesium in drinking water correlated as an important protective factor for death from acute myocardial infarction among males (31).

To examine whether higher concentrations of magnesium in drinking water supplies are associated with lower mortality from acute myocardial infarction a geographical study using 13,794 census enumeration districts was studied. Water constituent concentrations (magnesium, calcium, fluoride, lead) were measured according to water supply zones in North England. The relative risk of mortality from acute myocardial infarction for a quadrupling of magnesium concentrations in drinking water (for example, 20 mg/l vs 5 mg/l) was 1.01. There was no evidence of a protective effect for acute myocardial infarction even among age, sex, and deprivation groups that were likely to be relatively magnesium deficient. For ischemic heart disease mortality, however, there was an apparent protective effect of magnesium and calcium (with calcium predominating in the joint model), but these were no longer significant when the geographical trends were incorporated. The authors suggested that there was no evidence of an association between magnesium concentrations in drinking water supplies and mortality from acute myocardial infarction. The main finding of this study does not support the hypothesis that magnesium is the key water factor in relation to mortality from heart disease (32). In another case-control study, Rubenowitz and his colleagues 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). The results suggest that magnesium and calcium in drinking water are important protective factors for death from acute myocardial infarction among women (33). Rubenowitz *et al* (34) further 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. They classified subjects by quartile of water magnesium or calcium levels. The risk of death was 7.6% lower in the quartile with high magnesium levels ($> \text{ or } = 8.3 \text{ mg/liter}$). The odds ratio for death from acute myocardial infarction in relation to water magnesium was 0.64 for the highest quartile relative to the three lower ones. Multivariate analyses showed that other risk factors were not important confounders. These data suggested that magnesium in drinking water is associated with lower mortality from acute myocardial infarction (34).

Drinking water could be an important source of calcium in the elderly particularly because of increased needs and decreased consumption of dairy products. Information about all deaths (14,311) occurring in 69 parishes of the South-West of France for a seven-year study period from 1990 to 1996) were investigated. A significant relationship was observed between calcium and cardiovascular mortality with a relative risk, RR: 0.90 for non-cerebrovascular causes and RR: 0.86 for cerebrovascular. There was a protective correlational effect of magnesium concentrations between 4 and 11 mg/l with a RR: 0.92 for non-cerebrovascular and RR: 0.7 for cerebrovascular mortality, as compared to concentrations lower than 4 mg/l. These findings suggest a potential protective dose-effect relation between calcium in drinking water and some CVD. However, for magnesium, a U-shape effect is possible, especially for cerebrovascular mortality (35).

A study was performed to evaluate the relation between calcium and magnesium in drinking water and diet and risk factors for cardiovascular disease in individuals living in hard and soft water areas with considerable differences in cardiovascular mortality in Sweden. Intake of magnesium and calcium was calculated from the diet questionnaire with special consideration to the use of local water. Household water samples were analyzed for magnesium and calcium. No correlation was seen with magnesium content in household water to any of the risk factors. Magnesium in diet was positively correlated to diastolic blood pressure (DBP). This study of individuals living in soft and hard water areas showed significant correlations between the content of calcium in water and major cardiovascular risk factors. Regression analyses indicated that calcium content in water could be a factor in the complexity of relationships and importance of cardiovascular risk factors. However, based on these results the authors were unable to conclude any definite causal relation and suggest that further research is needed (36).

Calcium and magnesium deficiencies in particular have been considered as risk factors for elderly people and have been implicated in the aging process. Their deficiencies in the elderly can occur due to inadequate nutrient intakes from food and water, multiple drug use, or altered gastrointestinal function. It is not known to what extent suboptimal intakes of trace elements such as calcium and magnesium may affect the aging process; however, magnesium-deficient conditions have been associated with neuromuscular and cardiovascular disorders, endocrine disturbances and insulin resistance. Data presented in a review by Costello and Moser-Veillon suggest that there was a decreased availability of magnesium in the food supply, lower intakes of magnesium by elderly people, and widespread supplementation practices (37).

Gullestad *et al* (38) studied magnesium status among healthy elderly subjects. A study was thus carried out on 36 healthy elderly subjects and their magnesium status was assessed by serum Mg, basal urinary Mg output, and with a Mg loading test, and compared with 53 healthy younger subjects. Their dietary intake was assessed by a quantified food frequency questionnaire. Basal

urinary Mg excretion was 3.3 +/- 1.1 mmol/day and 24-hour Mg retention after a Mg load was 28 +/- 16% compared to 6 +/- 11% in younger controls, suggesting Mg deficiency in the elderly. Their study also found a significant sub-clinical Mg deficit, not detected by serum Mg, in many healthy elderly subjects. The data further indicated that Mg supplementation improved Mg status and renal function.

A study aimed to examine the relationship between nitrate, zinc and magnesium in drinking water and the risk of childhood-onset Type 1 diabetes mellitus was conducted by Zhao *et al.* (39) in the far south-west of England. Five hundred and seventeen children, aged 0-15 years, diagnosed with Type 1 diabetes mellitus between 1975 and 1996, were identified for inclusion in the study. Poisson regression analyses showed that only zinc and magnesium were significant factors. The data suggest that the incidence rate of childhood diabetes is significantly lower when the concentrations of zinc and magnesium in the domestic drinking water are in the range 22.27-27.00 microgram/l, 0.76) and greater than 2.61 mg/l, 0.72; respectively. Their findings suggest evidence of a possible association between zinc and magnesium in the domestic drinking water and childhood diabetes. However, these possible protective effects of zinc and magnesium in domestic drinking water warrant further confirmation (39).

The role of calcium in the formation of kidney stones is controversial. Both amount and timing of dietary calcium intake influence the recurrence of renal calcium stones. Bellizzi *et al* (40) evaluated whether the hardness of drinking water modified the risk for calcium stones. The urinary levels of calcium, oxalate and citrate, i.e., the main urinary risk factors for calcium stones, were measured in 18 patients with idiopathic nephrolithiasis, in a double-blind randomized, crossover fashion. As compared with both tap and soft water, hard water was associated with a significant (50%) increase of the urinary calcium concentration in the absence of changes of oxalate excretion; the calcium-citrate index revealed a significant three fold increase during ingestion of hard water as compared with respect to soft water. This study suggests that, in the preventive approach to calcium nephrolithiasis, the intake of soft water is may be preferable to hard water, since it was associated with a lower risk for recurrence of calcium stones (40).

VII. STUDIES IN THE WESTERN PACIFIC REGION

An attempt was made to determine whether an association existed between hardness of water and certain cardiovascular diseases in primitive population groups who drink untreated water collected directly from rivers. Blood pressure was measured in persons living in villages along the banks of the Wogupmeri River in New Guinea. The water was analyzed for calcium content. Trace element concentrations were also determined in toenails from the same subjects to see whether a correlation existed (41). Calcium content of the river water decreased as the river flows downstream, while blood pressure of the villagers living along this river increased. The trace element analysis of toenails revealed strong correlations between aluminum and vanadium. The concentrations of these two elements decrease with age. This association was present in both sexes, in adults and in children. A similarly strong correlation also existed between these two elements in staple food. This investigation tended to confirm the findings of earlier studies indicating an apparently beneficial effect of relatively hard water on cardiovascular parameters.

VIII. CONCLUSION

This chapter has highlighted some recent studies on minerals in drinking water and their relationship with various diseases. Most of these studies were conducted in Europe, Asia and the US and the common minerals studied were calcium and/or magnesium. Among various diseases studied, the cardiovascular system attracted the most attention. The relationship between the

cardiovascular mortality and the mineral content of drinking water was first described by Kobayashi (42) in Japan and Schoeder (43) in the US. Since then many studies have shown an inverse relationship between cardiovascular disease (CVD) and the water hardness, especially the magnesium content of the drinking water. Most of the investigations before 1980 were with ecological design and geographical areas defined. Often, the mineral content of drinking water was determined at the time of study after the time of the CVD events and thus the results could not reflect the exact quality of water the persons have ingested before their death or were exposed to. Furthermore, in most of these earlier studies the relationship between CVD mortality and drinking water hardness was tested by simple regression analysis, without considering potential confounding factors.

Based on epidemiological and clinical observations Marier and Neri (44) carried out a study in 1985 to quantify the effect of waterborne magnesium on human mortality/morbidity in several regions of the world. A consistent pattern emerged, indicating a global phenomenon that waterborne magnesium could play an important role in protecting against cardiovascular trauma and other ailments. The finding also attests to the inadequate magnesium status, especially of those who reside in ultra-soft-water areas. A more recent comprehensive review was conducted by Sauvant and Pepin (45) and arrived with a similar conclusion. The authors however cautioned that although there is a relationship between drinking water and CVD mortality, based on over 30 ecological and geographical investigations, its causality is still not proven, but there are many supporting arguments. Although there appears to be a close association of magnesium and cardiovascular disease, it seems unlikely that this relationship can only be attributed to a deficiency of calcium and magnesium in drinking water, because only 10-20% of the total daily intake of calcium and magnesium is derived from drinking water, unless that marginal contribution were significant to deficient diets. In some geographical areas, the magnesium content of drinking water may provide 20-40% of a person's daily requirement. For example, a liter of water with 100 mg/liter of magnesium could make up 25% or more of the daily magnesium requirement of 300 – 400 mg per day. A liter of water that is low in magnesium (<10 mg /liter) provides less than 3% of the daily requirement. It is true that the contribution of magnesium in water to the total intake may be small, compared to the amount ingested in food. On the other hand, the speciation of magnesium could explain its high bioavailability from water, rather than from food (46). Because of this the magnesium supplementation of drinking water has been suggested to reduce the incidence of some types of cardiovascular disease (47).

Calcium is found predominantly in milk, milk products and in hard water. The bioavailability of this mineral in water is believed to be at least as high as that of milk and milk products (48). Finnish women, with the highest daily consumption of calcium (1,300 mg/day) had the lowest frequency of fractures. In comparison, Japanese women, with the lowest calcium intake (400 mg/day) had the greatest frequency of fractures (49). Significant subgroups in most European populations have intake below the RDAs – below 10 to 40% of the RDA in zinc, iron, calcium and magnesium (50). The intake of calcium either from diet or water among Asians are known to be low because of soft water supply, dietary habits and cost. Recent studies have shown that the intakes of calcium, zinc, magnesium, potassium and other essential minerals were insufficient, and are a traditional problem in the Chinese diet (51).

A study conducted by Haring *et al* (52) investigated changes in the mineral composition of food when cooked in waters of different hardness. The most significant differences were found for calcium; the concentration of this element in potatoes and vegetables usually increased when cooked in hard-water, while a decrease was noted when soft water was used. This finding suggests that water used for cooking could indirectly affect the dietary intake of various trace elements (52).

Several studies have been conducted in Asia focusing on use of soft water and cancers, in particular in southern Taiwan. This region is supplied by both soft and hard water. The authors reported excess risks of several types of gastrointestinal cancers including esophageal, gastric, pancreatic colon and rectum (1-4). Based on empirical material from the Polish Cancer Registry a recent study in Poland also suggested the hypothesis that there is a possible association between drinking water composition and an increase of liver cancer (53), although the status of hepatitis and exposure to hepatotoxicants have not been investigated. Consumption of soft waters, especially those low in calcium and magnesium, has also been associated with very low birth weight, suggesting that the use of water with low mineral content may affect fetal growth (13,14). However, no other similar studies have been conducted in other parts of the world.

References

1. Yang CY, Chiu HF, Cheng MF, Tsai SS, Hung CF, Lin MC. Esophageal cancer mortality and total hardness levels in Taiwan's drinking water. *Environ Res* 1999; 81:302-8.
2. Yang CY, Tsai SS, Lai TC, Hung CF, Chiu HF. Rectal cancer mortality and total hardness levels in Taiwan's drinking water. *Environ Res* 1999; 80:311-6.
3. Yang CY, Hung CF. Colon cancer mortality and total hardness levels in Taiwan's drinking water. *Arch Environ Contam Toxicol* 1998 ; 35:148-51.
4. Yang CY, Chiu HF, Chiu JF, Cheng MF, Kao WY. Gastric cancer mortality and drinking water qualities in Taiwan. *Arch Environ Contam Toxicol* 1997; 33:336-40.
5. Iyengar GV, Kawamura H, Parr RM, Miah FK, Wang JX, Dang HS, Djojosebroto H, Cho SY, Akher P, Natera ES, Nguy MS. Dietary intake of essential minor and trace elements. *Asian Diets Food Nutr Bull* 2002; 23:124-8.
6. Singh RB, Niaz MA, Ghosh S, Rastogi V, Raghuvanshi RS, Moshiri M. Epidemiological study of magnesium status and risk of coronary artery disease in elderly rural and urban populations of north India. *Magnes Res* 1996; 9:165-72.
7. Singh RB, Rastogi V, Niaz MA, Sharma JP, Raghuvanshi R, Moshira M. Epidemiological study of magnesium status and risk of hypertension in a rural population of north India. *Magnes Res* 1996; 9:173-81.
8. Yang CY, Chiu JF, Chiu HF, Wang TN, Lee CH, Ko YC. Relationship between water hardness and coronary mortality in Taiwan. *J Toxicol Environ Health* 1996; 49:1-9.
9. Yang CY. Calcium and magnesium in drinking water and risk of death from cerebrovascular disease. *Stroke* 1998; 29:411-4.
10. Emsley CL, Gao S, Li Y, Liang C, Ji R, Hall KS, Cao J, Ma F, Wu Y, Ying P, Zhang Y, Sun S, Unverzagt FW, Slemenda CW, Hendrie HC. Trace element levels in drinking water and cognitive function among elderly Chinese. *Am J Epidemiol* 2000; 151:913-20.
11. Teotia M, Teotia SP, Singh KP. Endemic chronic fluoride toxicity and dietary calcium deficiency interaction syndromes of metabolic bone disease and deformities in India: year 2000. *Indian J Pediatr* 1998; 65:371-81.
12. Nair RR, Eapen JT, Radhakumary C, Rajasree S. Magnesium levels in serum and erythrocytes of children from Kerala. *Natl Med J India* 1995; 8:118-20.
13. Yang CY, Chiu HF, Tsai SS, Chang CC, Sung FC. Magnesium in drinking water and the risk of delivering a child of very low birth Weight. *Magnes Res* 2002; 15 :207-13
14. Yang CY, Chiu HF, Chang CC, Wu TN, Sung FC. Association of very low birth weight with calcium levels in drinking water. *Environ Res* 2002 ;89:189-94.
15. Dutra-de-Oliveira JE, de Almeida CA. Domestic drinking water--an effective way to prevent anemia among low socioeconomic families in Brazil. *Food Nutr Bull* 2002; :213-6.
16. Leary WP. Content of magnesium in drinking water and deaths from ischaemic heart disease in white South Africans. *Magnesium* 1986; 5:150-3.
17. Leary WP, Reyes AJ. Magnesium and sudden death. *S Afr Med J.* ; 1983; 64:697-8. 18.

18. Innerarity S. Hypomagnesemia in acute and chronic illness. *Crit Care Nurs Q* 2000; 23:1-19.
19. Turner RE, Langkamp-Henken B, Littell RC, Lukowski MJ, Suarez MF. Comparing nutrient intake from food to the estimated average requirements shows middle- to upper-income pregnant women lack iron and possibly magnesium. *J Am Diet Assoc* 2003; 103:461-6.
20. Dawson EB, Frey MJ, Moore TD, McGanity WJ. Relationship of metal metabolism to vascular disease mortality rates in Texas. *Am J Clin Nutr* 1978; 31:1188-97.
21. Greathouse DG, Osborne RH. Preliminary report on nationwide study of drinking water and cardiovascular diseases. *J Environ Pathol Toxicol* 1980; 4:65-76.
22. Bloom S, Peric-Golia L. Geographic variation in the incidence of myocardial calcification associated with acute myocardial infarction. *Hum Pathol* 1989; 20:726-31.
23. Humphries S, Kushner H, Falkner B. Low dietary magnesium is associated with insulin resistance in a sample of young, nondiabetic Black Americans. *Am J Hypertens* 1999; 12:747-56
24. Fox CH, Mahoney MC, Ramsoomair D, Carter CA. Magnesium deficiency in African-Americans: does it contribute to increased cardiovascular risk factors? *J Natl Med Assoc* 2003; 95:257-62.
25. Schwartz BF, Schenkman NS, Bruce JE, Leslie SW, Stoller ML. Calcium nephrolithiasis: effect of water hardness on urinary electrolytes. *Urology* 2002; 60:23-7.
26. Sonneborn M, Mandelkow J. German studies on health effects of inorganic drinking water constituents. *Sci Total Environ* 1981; 18:47-60.
27. Luoma H, Aromaa A, Helminen S, Murtomaa H, Kiviluoto L, Punsar, S, Knekt P. Risk of myocardial infarction in Finnish men in relation to fluoride, magnesium and calcium concentration in drinking water. *Acta Med Scand* 1983; 213:171-6.
28. Karppanen H. Ischaemic heart disease. An epidemiological perspective with special reference to electrolytes. *Drugs* 1984; 28, Suppl 1:17-27.
29. Leoni V, Fabiani L, Ticchiarelli L. Water hardness and cardiovascular mortality rate in Abruzzo, Italy. *Arch Environ Health* 1985; 40:274-8.
30. Bernardi D, Dini FL, Azzarelli A, Giaconi A, Volterrani C, Lunardi M. Sudden cardiac death rate in an area characterized by high incidence of coronary artery disease and low hardness of drinking water. *Angiology* 1995; 46:145-9.
31. Rubenowitz E, Axelsson G, Rylander R. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 1996; 143:456-62.
32. Maheswaran R, Morris S, Falconer S, Grossinho A, Perry I, Wakefield J, Elliott P. Magnesium in drinking water supplies and mortality from acute myocardial infarction in north west England. *Heart* 1999; 82:455-60.
33. Rubenowitz E, Axelsson G, Rylander R. Magnesium and calcium in drinking water and death from acute myocardial infarction in women. *Epidemiology* 1999; 10:31-6.
34. Rubenowitz E, Molin I, Axelsson G, Rylander R. Magnesium in drinking water in relation to morbidity and mortality from acute myocardial infarction. *Epidemiology* 2000; 11:416-21.

35. Marque S, Jacqmin-Gadda H, Dartigues JF, Commenges D. Cardiovascular mortality and calcium and magnesium in drinking water: an ecological study in elderly people. *Eur J Epidemiol* 2003; 18:305-9.
36. Nerbrand C, Agreus L, Lenner RA, Nyberg P, Svardsudd K. The influence of calcium and magnesium in drinking water and diet on cardiovascular risk factors in individuals living in hard and soft water areas with differences in cardiovascular mortality. *BMC Public Health* 2003; 18: 3-21.
37. Costello RB, Moser-Veillon PB. A review of magnesium intake in the elderly. A cause for concern? *Magnes Res* 1992; 5:61-7.
38. Gullestad L, Nes M, Ronneberg R, Midtvedt K, Falch D, Kjekshus J. Magnesium status in healthy free-living elderly Norwegians. *J Am Coll Nutr* 1994 13:45-50.
39. Zhao HX, Mold MD, Stenhouse EA, Bird SC, Wright DE, Demaine AG, Millward BA. Drinking water composition and childhood-onset Type 1 diabetes mellitus in Devon and Cornwall, England. *Diabet Med* 2001;18:709-17.
40. Bellizzi V, De Nicola L, Minutolo R, Russo D, Cianciaruso B, Andreucci M, Conte G, Andreucci VE. Effects of water hardness on urinary risk factors for kidney stones in patients with idiopathic nephrolithiasis. *Nephron* 1999; 81 Suppl 1:66-70.
41. Masironi R, Koirtiyohann SR, Pierce JO, Schamschula RG. Calcium content of river water, trace element concentrations in toenails, and blood pressure in village populations in New Guinea. *Sci Total Environ* ; 1976; 6:41-53.
42. Kobayashi Y. Geographical relationship between the chemical nature of river water and death rate from apoplexy. *Okayama University* 1957; 11: 12-21.
43. Schoeder HA. Relation between mortality from cardiovascular disease and treated water supplies. *J. Am. Med. Assoc.* 1960; 172: 98-10454. Tukiendorf, A., Krasowski, G., Rybak, Z Thyroid cancer morbidity in Opole province, Poland, after Czernobyl disaster. *Eur J Public Health* .2003; 11:98-101.
44. Marier JR, Neri LC. Quantifying the role of magnesium in the interrelationship between human mortality. *Magnesium* 1985; 4:53-9.
45. Sauvant MP, Pepin D. Drinking water and cardiovascular disease. *Food Chem Toxicol* 2002; 40:1311-25.
46. Durlach J, Bara M, Guiet-Bara A.. Magnesium level in drinking water and cardiovascular risk factor: a hypothesis. *Magnesium* 1985; 4:5-15.
47. Eisenberg MJ. Magnesium deficiency and sudden death. *Am Heart J* 1992; 124:544-9.
48. Heaney RP. Quantifying human calcium absorption using pharmacokinetic methods. *J Nutr* 2003; 133:1224-6.
49. Heaney RP, Dowell MS. Absorbability of the calcium in a high-calcium mineral water. *Osteoporos Int* 1994;. 4:323-4.
50. Flynn A, Moreiras O, Stehle P, Fletcher RJ, Muller DJ, Rolland V. Vitamins and minerals: A model for safe addition to foods. *Eur J Nutr* 2003; 42:118-30.
51. Chen J, Gao J. The Chinese total diet study in 1990. Part II. Nutrients. *JAOAC Int* 1993; 76:1206-13.

52. Haring BS, Van Delft W. Changes in the mineral composition of food as a result of cooking in "hard" and "soft" waters. *Arch Environ Health* 1981; 36:33-5.
53. Tukiendorf A, Krasowski G, Rybak Z. Thyroid cancer morbidity in Opole province, Poland, after the Chernobyl disaster. *Eur J Public Health* 2003; 11:98-101.