Magnesium in drinking water – a case for prevention?

Ragnar Rylander

ABSTRACT

Studies in many countries have demonstrated a relationship between drinking water mineral content and the risk of death in cardiovascular disease (CVD). Particularly strong relationships have been found for magnesium and it has been suggested that magnesium be added to drinking water. The aim of this article is to evaluate the validity of this suggestion by reviewing information on possible causative agents. Major epidemiological studies on the drinking water content of calcium, magnesium, and hardness were analysed regarding exposure specificity, confounding factors, dose-response relationships and biological plausibility. Intervention experiments were analysed. The risk of death in CVD was related to the content of Ca, Mg and HCO^{3-}. The data demonstrate that Ca and Mg need to be considered together, and that HCO^{3-} could play a role by intervening with the body acid load. There is no evidence to justify the addition of magnesium only to drinking water for preventive purposes. The data suggest that Ca and Mg could be administered together but no data are available regarding the relative proportions for an optimal effect.

Key words | acidity, calcium, hardness, magnesium

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INTRODUCTION

The relationship between drinking water and health has been known for thousands of years and became established in religious ceremonies like the offering of votives and coins in water springs. The real break-through in terms of prevention of disease did not, however, come until the discovery of bacteria. The health consequences of a microbiological contamination of drinking water have been known since the mid-1800s and were first applied to praxis in an epidemic of cholera in London, when John Snow turned off the famous water post in Broad Street in 1854.

Another component of drinking water that has attached attention for a long time is the content of minerals. Babylonian, Greek, and Roman elites believed in the healing resources of mineral wells. Although part of the improvement in health and well-being in spas was certainly attributable to general relaxation, intake of minerals could have contributed to the effect.

The aim of this article is to highlight the relationship between the mineral composition of drinking water and the risk of death in cardiovascular disease (CVD). Extensive reviews of the subject have been presented in previous publications (Rylander 1996; Catling *et al*. 2008; WHO 2009). This article will focus on the interpretation of the available data in view of epidemiological and biological principles, and present a conclusion regarding prevention by adding magnesium to drinking water.

DRINKING WATER CONSTITUENTS AND DISEASE

Hardness

The first epidemiological study on the relationship between minerals in drinking water and health was published in Japan (Kobayashi 1957). He noticed a high incidence of 'apoplexia' (cardiovascular disease) in areas with acidic drinking water. To help in further studies, assistance from the USA was called in but they had no methods to measure acidity and used hardness instead.

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Since then, more than 20 epidemiological studies on the relationship between hardness and CVD have been published. An inverse relationship between hardness and CVD was found in 11 of these. As an example, several studies from Finland demonstrated that the eastern part of the country with soft drinking water had a high incidence of CVD (Punsar & Karvonen 1979; Luoma *et al.* 1983). A Swedish study demonstrated that hardness was related to the risk of CVD in both genders but that the risk of ischemic heart disease was related to magnesium (Rylander *et al.* 1991).

Contrary to these findings, studies from the UK have not found a relationship between CVD and hardness (e.g. Morris *et al.* 2008; Lake *et al.* 2010). It has, however, been claimed that the use of phosphates to prevent sedimentation in water pipes, which is used extensively in the UK, leads to the formation of insoluble calcium-magnesium-phosphate salts and thus renders human exposure assessment impossible (Monarca *et al.* 2009).

Hardness of water is determined by the content of calcium (Ca) and magnesium (Mg) cations. The degree of hardness is measured using a number of different units, all including Ca and Mg. Hardness is not a precise exposure measure of either of these ions as the relative proportions may vary. In view of the limited information regarding a causative agent that is obtained from studies on hardness, the following will focus on the two major determinants of hardness – Ca and Mg.

Calcium

Ca in humans is almost exclusively found in bones and teeth. In body fluids it takes part in vascular contraction, blood clotting, muscle contraction, and nerve transmission. From a nutritional point of view Ca deficiency is uncommon as the ordinary diet, particularly dairy products, provides for an adequate intake. Regarding the risk of CVD, some studies have shown a relationship between urinary Ca excretion and blood pressure (Kesteloot *et al.* 2011). Intervention experiments with Ca have reduced blood pressure in some studies (Cappuccio *et al.* 1989; Bucher *et al.* 1996).

In drinking water, some studies show an inverse relationship between the content of Ca and CVD (Yang 1998; Yang & Chiu 1999) but others have not found a relationship.

Magnesium

Mg is the second most abundant cation in intracellular fluid (Vormann 2003). It is a cofactor for more than 350 cellular enzymes, regulating energy metabolism, protein and nucleic acid synthesis, muscular tension, and insulin sensitivity. The uptake is via intake of food and drinking water. Magnesium deficiency is common in the Western population, due to inadequate intake of vegetables and the use of refined flour (Bates *et al.* 2001).

Magnesium homeostasis can be disturbed by an insufficient intake or an increased urinary excretion of Mg. This is induced by an increased acid load, following excessive exercise or the consumption of large amounts of proteins (Remer 2001; Rylander *et al.* 2006, 2009). An increased acid load will increase the acidity of the urine which decreases the reabsorption of Mg in the renal tubuli (Remer 1995). Figure 1 illustrates the influence of acidity on the regulation of magnesium homeostasis in the body.

Epidemiological investigations

Several studies from Canada, Finland, Italy, Spain, and Sweden have found relationships between the amounts of Ca and Mg in drinking water and the risk of cardiovascular mortality. In an extensive review of the epidemiological studies it was concluded that there was significant evidence of an inverse association between Mg levels in drinking water and cardiovascular mortality and that the evidence for Ca was unclear (Catling *et al.* 2008). In Finland a relationship was found between the ratio of Ca/Mg and acute myocardial infarction among males (Kousa *et al.* 2006) and

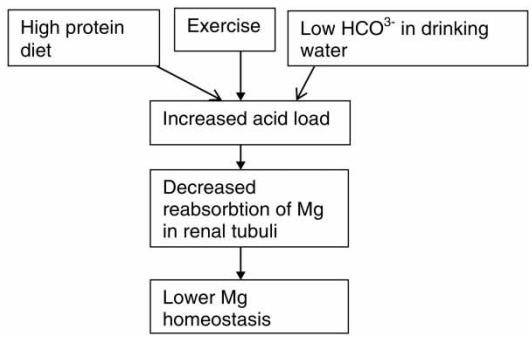

Figure 1 | Acid regulation of magnesium homeostasis in the body.

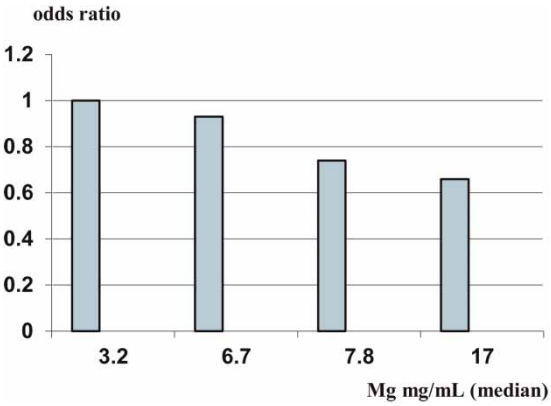

Figure 2 | Odds ratios for death in heart infarction among males with different amounts of magnesium in the drinking water (Rubenowitz *et al.* 1996).

between acute myocardial infarction among females and males (Kousa *et al.* 2008). One Swedish study reported a decrease in deaths due to heart infarction among men in areas where the content of Mg in the drinking water was higher (Rubenowitz *et al.* 1996), as illustrated in Figure 2.

The figure illustrates a dose-response relationship with a successively lower mortality in areas with a higher level of Mg in the drinking water. In a subsequent study of acute myocardial infarction among women, it was related to the content of Ca and to Mg in the drinking water (Rubenowitz *et al.* 1999). The figure also illustrates that studies in areas with a drinking water content of Mg at the lower end of the illustrated range do not have the power to test the relationship and thus cannot be used as evidence for an absence of an effect (Rosenlund *et al.* 2005).

Clinical investigations

A few studies have comprised clinical investigations of individuals from population samples. Subjects living in two Swedish cities with different levels of Mg in the drinking water were subjected to a muscle biopsy for determination of the Mg content (Landin *et al.* 1989). A questionnaire was used to assess the intake of Mg via food and water. There was a significantly higher intake of Mg via drinking water among the inhabitants in the city with a high level (5.7 mg/L as compared to the low level 1.7 mg/mL). The skeletal muscle content was higher among those in the city with a higher level of Mg in the drinking water (4.1 vs 3.9 mmol/100 g).

A study from Serbia examined population samples in three different locations with a varying content of calcium and magnesium in the drinking water (Rasic-Milutinovic *et al.* 2012). A significantly lower diastolic blood pressure and a higher serum magnesium level were found among inhabitants in the area with the highest total hardness. Persons in that area also had significantly lower levels of serum triglycerides and creatinine.

Although a number of relationships have been found between drinking water charateristics and CVD, these relationships are not a proof of causality. In the following the data on drinking water minerals and CVD will be analysed against the criteria required for causality.

CRITERIA FOR CAUSALITY

Exposure specificity

Exposure specificity means that the agent chosen to describe the exposure is unrelated to any other agent in the environment. In nature most of the exposures involve many agents. Depending on which agent is chosen, dose-relationships for CVD may be present but this could also be present for a variety of other agents that co-vary with the original agent tested. In the previously mentioned Finnish study, the ground water also contained Fe, Zn, Al, and Cu (Kousa *et al.* 2004). A slightly increased risk (not significant) of myocardial infarction was found for Fe and Cu. In a Swedish study the content of Mg co-varied with the concentration of hydrogen carbonate (Rylander 2008). This could potentially reduce the acid load and prevent the loss of magnesium in urine. Thus measurements of only calcium or magnesium in drinking water do not meet the requirement of exposure specificity.

Confounding factors

The risk of CVD is not related to one specific agent but to a number of factors such as diet, smoking, genetic predisposition, and exercise. Most of the studies on the relationship between drinking water quality and CVD have been of an ecological nature. This implies that there might be other risk factors for the disease, which could influence the results if they are unevenly distributed in the populations studied.

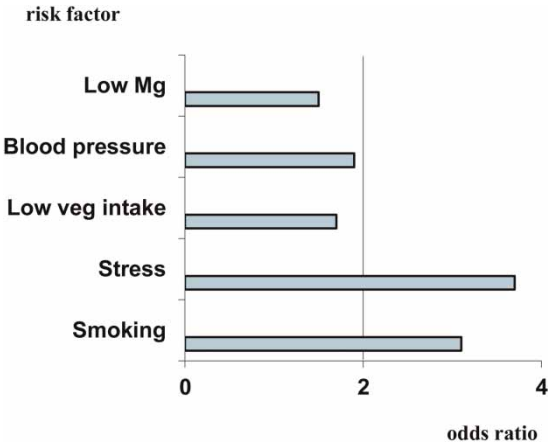

Figure 3 | Odds ratios for heart infarction for common risk factors and for magnesium in drinking water (Rubenowitz *et al*. 2000).

This concept is illustrated by studies from Sweden and the Netherlands. In the Swedish study interviews were performed to assess the presence of risk factors for CVD in general (Rubenowitz *et al.* 2000). Figure 3 demonstrates the relative importance of such factors for the risk.

The figure demonstrates that the odds ratio was higher among those with a low level of Mg in the drinking water. Higher odds ratios were, however, also related to other risk factors for CVD such as blood pressure, stress, and smoking. The figure very clearly illustrates the need to take several risk factors into consideration when assessing causality for drinking water Mg and death in CVD.

The consumption of vegetables and fruit is a risk factor for Mg-deficiency. In a study from the Netherlands (Leurs *et al.* 2009) an extensive dietary investigation was performed, in addition to calculating the amount of Mg in the drinking water. Although the study has some weaknesses as the consumption of drinking water from the tap is limited in the Netherlands, the results demonstrated a relationship between Mg in drinking water and stroke mortality, but only in a group of males with insufficient intake of dietary Mg. The presence of such risk groups may vary depending on the characteristics of the population studied and thus introduce methodological errors.

Dose–response relationships

One of the prerequisites for conclusions on causality is the presence of dose–response relationships. These are found in many of the studies on Ca, Mg and hardness. As other agents may co-vary (absence of exposure specificity) with the agent studied, the mere presence of a dose–response relationship is not a strong support for causality.

Biological plausability

A relationship found in epidemiological studies needs to be ascertained by knowledge about the biological mechanisms involved. Regarding Mg and Ca, the biological plausability for effects on the cardiovascular system and CVD is very high. In a prospective cohort of women in the USA, higher plasma concentrations and dietary magnesium intakes were associated with a lower risk of sudden cardiac death (Chiuve *et al.* 2010). In a study on 45–64-year-old subjects in the USA, the highest quartile of serum Mg had a significantly lower risk of sudden cardiac death (Peacock *et al.* 2010). In a five-year follow-up population study in Germany, low serum Mg levels were associated with a higher mortality in CVD (Reffelmann *et al.* 2011). A Swedish population study could not find a relationship between magnesium intake determined from questionnaires but no blood samples were taken (Kaluza *et al.* 2010). There was, however, a relationship between a low Ca intake and CVD mortality.

Intervention

Intervention is a critical tool for assessment of causality. Regarding Mg in general, intervention experiments to prevent CVD have yielded contradictory results. In a review it was concluded that there was a suggestion of a dose-dependent reduction in blood pressure from Mg intervention but that the relationship should be confirmed in larger studies, using higher doses (Jee *et al.* 2002).

Only a few, small studies have been performed on Mg and Ca in drinking water. In one study healthy volunteers were given drinking water with 25 mg Mg/L for 6 weeks (Rubenowitz *et al.* 1998). The urinary excretion of Mg was measured after a loading test (575 mg Mg) before and after the drinking water supply. There was a 14% increase in the Mg/creatinine excretion at the end, suggesting that a drinking water supply of Mg could influence the body Mg homeostasis.

In an intervention study using waters that contained Mg only, or a number of naturally occurring minerals, people

consuming the water containing Mg had an increased secretion of magnesium in the urine (Rylander & Arnaud 2004). A reduced blood pressure was found in the group consuming water with several minerals but not in the group consuming water with Mg only.

In another study subjects received mineral water with 74 mg Mg, 30 mg Ca, and 0.3 mg K (Rylander *et al.* 2012). There was a significant relationship between the acidity of the urine, measured as urea, and the excretion of Mg, Ca, and K. Among persons with a high excretion of urea, there was an inverse relationship between the excretion of Mg and systolic blood pressure. After intervention with the mineral water, there was a strong tendency for a decrease in systolic blood pressure among those with an initial high excretion of urea and a low excretion of Mg, reflecting an Mg deficiency.

Synthesis

The analysis of causality supports the hypothesis that minerals in drinking water are of importance for the risk of mortality in CVD, and particularly heart infarction. For Ca and Mg, physiological and cell function data document their importance in muscular contraction, muscle excitability and strength. The few intervention studies available support the hypothesis that minerals in the drinking water may influence the body homeostasis. A model for the relationship between drinking water constituents and mortality in CVD is presented in Figure 4.

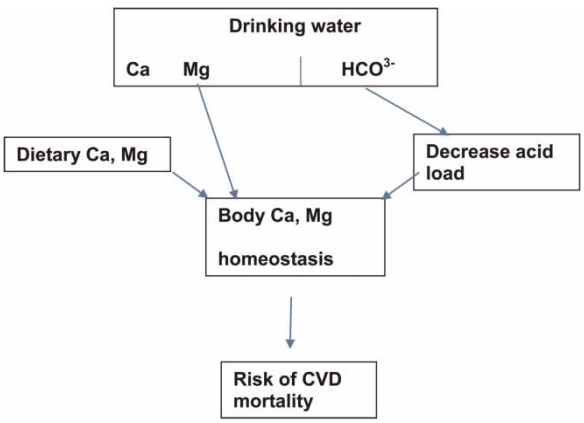

Figure 4 | A model for drinking water constituents and mortality in cardiovascular disease.

It is not possible, however, to gain support for a hypothesis regarding a single, causative mineral. On the contrary, the evidence suggests that Ca and Mg in combination, as they appear in nature, reduce the risk of mortality in CVD (Rylander *et al.* 1991; Kousa *et al.* 2006; Rasic-Milutinovic *et al.* 2012). This suggests that an intervention using a mixture of minerals is the most powerful tool for prevention. There are, however, no data available to suggest the optimal concentration of and relationship between Ca and Mg.

PREVENTION

A prerequisite for any kind of prevention on a population basis is well established evidence for causality. The data presented for drinking water and CVD and the model for interaction (Figure 4) suggest that this is not the case, neither for Mg, nor for Ca when given as single agents. On the other hand the concept of an intervention that mimics the real-life situation in terms of several minerals together has considerable support.

Owing to the lack of compelling evidence for the role of magnesium as a single contributory element in relation to CVD mortality there is little support for the concept of adding Mg to drinking water for preventive purposes on a population scale. The data suggest that a mixture of Ca and Mg is the appropriate measure but the exact proportion of the different minerals to be used is not known.

CONCLUSIONS

In summary, the review demonstrates the following:

1. Drinking water composition in terms of calcium, magnesium, and potassium is related to the risk of cardiovascular disease.
2. The available evidence is not sufficient to recommend addition of magnesium to drinking water on a population basis.
3. Intervention studies to assess requirements for intervention and control of calcium and magnesium in drinking water are required. In view of the potential importance from a public health point of view, such studies have a high priority.

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