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Original Research

Calcium and Magnesium in Drinking Water as Risk Factors for Ischemic Heart Disease

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Abstract

The aim of this research was to determine the interdependence between calcium and magnesium in drinking water, and the morbidity from ischemic heart disease (IHD). A structured epidemiological questionnaire was used to collect information on the amount of drinking water consumed by 200 respondents in areas with the highest and lowest values of Ca and Mg. In addition, information on various risk factors for IHD (smoking, physical activity) was assembled for the same population group. In order to determine the average daily intake of Mg and Ca among the respondents, we ran a semi-quantitative questionnaire on frequency of food intake over the course of the previous year. The correlation between risk factors was assessed using linear regression and Pearson's coefficient of linear correlation. Finally, ROC analysis was employed to determine the minimal protective values for Mg and Ca. Despite the daily intake of drinking water in the respondents averaging less than 2l, a negative correlation between Ca and Mg from drinking water and risk factors for IHD were still observed. The analysis concluded that from the standpoint of preventing IHD, it would be necessary to have a daily intake of Ca and Mg of at least 75 mg Ca and 7 mg of Mg consumed through drinking water.

Keywords: calcium, magnesium, ischemic heart disease, drinking water

Introduction

Safe drinking water is one of the essentials of life; however, drinking water contains many constituents and contaminants that can also threaten our well-being. Water contains traces of many minerals that come from the rock and soils through which it passes. Most of these are present in trace quantities while some are present in much larger amounts, depending on the geological composition. In some instances, the small presence of calcium and magnesium in water could potentially have health benefits. Indeed, there is continuing interest in the possible negative correlation between hard water, including calcium and magnesium, and chronic heart disease.

Ischemic heart disease (IHD) is a major medical and socioeconomic problem in Serbia. Ischemic heart disease is the primary cause of morbidity in men, and a close second, after stroke, for women in the country. Similar to other Eastern European countries, mortality rates in Serbia have continued to increase. At present, approximately 53.3% of all deaths result from cardiovascular diseases [1].

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In addition to usual risk factors for ischemic heart disease such as age, gender, smoking, obesity, physical inactivity, and lipid status, some environmental factors may also play a role in its development following long-term exposure to them [2-5]. For instance, it has been previously suggested that hard drinking water – and in particular high magnesium intake – protect against cardiovascular disease (CVD) [6]. The role of water hardness has been widely studied and evaluated for many years in studies examining regional differences in the occurrence of cardiovascular diseases, depending on the hardness levels of the local drinking water [7, 8]. Geographical and regional distribution of hardness differ not only between countries but also within countries, highlighting the importance of the geomorphological characteristics of the soil from which they spring water and which conditions the high variability in mineral content of the water [9]. Also, amongst the population in a particular country, there are geographical variations in the incidence of ischemic heart disease [10, 11]. In Serbia, the mortality rate from ischemic heart disease is highest in Vojvodina, while in central Serbia it is somewhat lower than the national average. The existence of areas with high risk for IHD, especially for acute myocardial infarction (AMI), points to the fact that it is very likely that environmental factors are involved in the pathogenesis of cardiovascular disease, and therefore it is necessary to study them carefully [12]. Many authors believe the current evidence to be preliminary but promising, with an ongoing need to take on this issue[13]. There is generally a lack of epidemiological studies on the effects of drinking water hardness (in particular, the levels of magnesium and calcium in drinking water) as regards cardiovascular health of the Serbian population. We have therefore decided to undertake a study using national registry data on the occurrence of ischemic heart disease and split the population into two groups based on the level of hardness of the water they consume.

The aim of our research was to determine the interdependence between calcium and magnesium in drinking water and the morbidity from ischemic heart disease.

Material and Methods

Our research is based on the examined values of water hardness, and Ca and Mg in the drinking water within the Nis Water Supply System (NIVOS) during the period between 2000 and 2012 at four different measurement points which are representative of the four constituent parts of NIVOS: Moravian water supply system, Vinik, Studena, and Mediana (Table 1). Water sampling and analyses were performed at the laboratories of the public utility for water supply in Nis and at the Public Health Institute in Nis. Both laboratories are accredited to be compliant with ISO/IEC 17025 and ISO 9001 standards (SRPS ISO/IEC 17025:2006; ISO 9001:2000). Laboratory procedures for sample management, analytical methods, and quality control measures (accuracy, precision, and detection limits) are regulated by the relevant sections of Serbian law [14-16]. Current Serbian regulations limit calcium levels at 200 mg/l and magnesium at 50 mg/l [16]. Total amounts of calcium and magnesium in water as well as water hardness were determined using the titrimetric method with EDTA [17, 18].

Table 1. Differences in water hardness, calcium, and magnesium among the various sources of the NIVOS system.

	Part of the NIVOS water supply system	Number of samples	AVG	MIN	MAX	F	p
The hardness of drinking water (^{0}dH)	Studena	58	9.3047	7.8	10.22	545.16	0.000*
	Moravian water supply	49	18.3014	16.3	22.2		
	Vinik	41	14.0837	11.4	16.3		
	Mediana	74	13.3536	10.3	16		
Ca (mg/l)	Studena	58	60.0526	49.4	69.2	145.56	0.000*
	Moravian water supply	49	104.752	71.8	146.4		
	Vinik	41	88.9276	62.5	107.3		
	Mediana	74	81.1353	38.2	99.8		
Mg (mg/l)	Studena	58	5.3714	2.4	6.90	35.92	0.000*
	Moravian water supply	49	9.6671	6.5	14.9		
	Vinik	41	6.7222	3.3	15.57		
	Mediana	74	7.7778	3.4	16.1		

*statistical significance

The basic pattern anamnestic research included 200 respondents of both sexes from Nis district in which the hardness testing system NIVOS established minimum and maximum values for magnesium and calcium. People living in this municipality share similar lifestyles, socioeconomic characteristics, and dietary habits. The study group consisted of patients selected by random sampling from the database (National Registry for Acute Coronary Syndrome) of the Public Health Institute Nis, with the diagnosis of acute myocardial infarction and unstable angina pectoris, from 2010 to 2012. The respondents were grouped as follows:

– A group of patients with IHD exposed to the risk factor of soft and medium-soft drinking water (AVG = 9.3 ^{0}dH); 60 subjects from the Niska Banja area and the surrounding settlements connected to the Studena water supply system (Fig. 1).
– Healthy group (control group) exposed to the risk factor of soft and medium-soft drinking water (AVG = 9.3 ^{0}dH); 60 subjects from the area of Niska Banja and the surrounding settlements connected to the Studena water supply system (Fig. 1).
– A group of patients with IHD and exposed protective factor of hard drinking water (AVG = 18.3 ^{0}dH); 20 subjects from the area of the villages connected to the Moravian water supply system (Fig. 1).
– A healthy group (control group) exposed to the protective factor of hard drinking water (AVG = 18.3 ^{0}dH); 60 subjects from the area of the villages connected to the Moravian water supply system (Fig. 1).

The control population group consisted of persons who are not diagnosed with ischemic heart disease, or other diagnosis of cardiovascular disease and diabetes, matched by gender and age (±3 years) with respondents from the group of patients who consume water from the same source of water supply and suffering from heart diseases. Among the control group population there were no drug users, psychiatric patients, or cancer patients. Five percent of the control group population had gallbladder disease, 15% had bone and joint system problems, and the rest were healthy or had minor health problems such as headaches or chronic fatigue. The section of the population that has lived less than 10 years at their current address was excluded as well as those who use bottled water for drinking, excluding the six subjects from the Moravian area water supply system who use their own wells for drinking water, and two subjects from the area of Niska Banja (Spa) who consume more than 1 liter of bottled water per day.

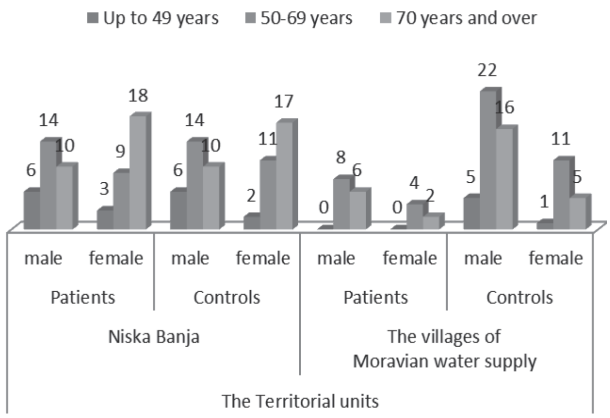

Fig. 1. Number of respondents by age in observed territorial units.

The respondents were previously familiar with the objectives of the research, and only a negligible proportion of the control group (less than 2%) refused to participate in the study. In fact, from the initial number of 212 subjects, eight were turned away and four refused to participate in the study.

The information on the drinking water amount entered and risk factors for IHD (smoking, physical activity) were collected through interviews using the original structured epidemiological questionnaire. The presence or lack of physical activity was assessed subjectively by the respondents. To determine the average daily intake of Mg and Ca in patients, we used the validated semi-quantitative questionnaire on frequency of food intake in the previous year, the Food Frequency Questionnaire (FFQ) [19, 20]. The average daily intake of Ca and Mg was calculated using the relevant food composition tables [21, 22]. Ca and Mg intake through drinking water was calculated based on the average daily water intake and average concentrations of Ca and Mg in the drinking water consumed by the respondent.

By examining the state of nutrition in respondents, various anthropometric parameters (body height, body weight) were measured by standard procedures. Body weight was measured by a mobile medical scale with an accuracy of ±500 g and body height altimeter that can be fixed to the wall with an accuracy of ±0.5 cm. Persons with very significant changes in body weight in the past year (more than 5 kg) were not included in the research. Body mass index (BMI) was determined as the ratio of body weight in kilograms by height squared in meters (kg/m^2). Persons with BMI greater than or equal to 25 kg/m^2 were considered overweight, and those with a BMI of greater than or equal to 30 kg/m^2 were deemed obese.

Having examined the medical records of the respondents, important data on blood cholesterol, triglycerides, LDL cholesterol levels, and systolic and diastolic blood pressure were collected. The required laboratory analyses were performed at the Center for Medical Biochemistry, Clinical Center of Nis, the Biomechanical Laboratory of the Health Center Nis, and the Hematology Laboratories at the Biochemistry Institute of Occupational Health, Nis. We used the Colorenzymatic method to determine cholesterol and triglycerides, and LDL cholesterol was calculated according to Friedeald's formula. Approximately 45% of respondents did not give any information of LDL cholesterol. Lipid status is interpreted according to the recommendations of the Committee on lipids Endocrinology Section of the

Serbian Medical Society. Total cholesterol values of up to 5.2 mmol/l for LDL cholesterol up tp 3.4 mmol/l and triglycerides up to 1.7 mmol/l were considered normal.

The data are presented as mean values (and standard deviation for parametric data) or as relative numbers for non-parametric data. The homogeneity of the sample was analyzed using Student's t-test for parametric data and the chi-square (χ^2) test for non-parametric data.

SPSS software was used for all data analyses (Version 6, Stat Soft Inc., Tulsa, OK, USA). Differences in the mean values of Ca and Mg concentrations in drinking water from separate units of the NIVOS system were examined by analysis of variance (ANOVA).

To establish the correlation between risk factors we used the correlation analysis and Pearson's coefficient of linear correlation.

Using ROC analysis we determined the minimal protective value in patients.

Results and Discussion

This study has found that within NIVOS the water hardness was the highest in the Moravian water supply system and the lowest in Studena. The hardness of the water from the Mediana and Vinik water supply systems was in-between these two values. The differences were associated with various concentrations of minerals (calcium and magnesium) that contributed to the hardness of the drinking water. There is a statistically significant difference between these two parameters (ANOVA: F = 145.56, p = 0.000 for Ca; F = 35.92, p = 0.000 for Mg) (Table 1).

The results of the t-test indicated that different characteristics of the respondents from different regional areas (age, body weight, body mass index, and smoking) did not influence the differences in the incidence of diseases such as IHD. The t-test also led to a conclusion that there were no significant differences between respondents from different areas in age, body weight, and BMI, and these factors did not affect the differences in the incidence of diseases such as IBS. The examined population groups were statistically different only in body height (p = 0.044), which certainly could not influence the differences in the incidence of IHD in the observed territorial unit (Table 2). The χ^2 test helped identify the proportion of respondents in each area who are physically active (Table 2).

Ca and Mg in the water and food were concluded to be two factors that had significant impact on the difference in morbidity from IHD. In cases where the average daily water intake of the respondents was less than 2 liters, a statistically significant difference in the higher intake of calcium and magnesium through drinking water (p = 0.000) compared to the intake of these minerals in food (p = 0.008 for Mg and p = 0.043 for Ca) is present. Calcium and magnesium from food were examined in the following food sources: milk and dairy products, legumes (beans, peas, green beans), whole grains (integral cereals, integral bread), green leafy vegetables (spinach, broccoli, chard), sea fish (sardines, hake), walnuts, hazelnuts, and almonds.

Table 2. Baseline characteristics of the respondents

The Territorial units			
	Niska Banja	The villages of Moravian water supply	p
Age (years) AVG	64.78	65.99	0.471
Body mass index (kg/m^2) AVG	26.39	26.42	0.948
Body weight (kg) AVG	73.83	76.06	0.143
Body height (cm) AVG	167.14	169,21	0.044*
Smoking (number of years) AVG	6.65	6.23	0.800
Physical activity (number of respondents No/Yes)	65/54	50/30	0.270

*statistically significant

Table 3 shows the relationship among these risks factors, including the static ones (age and gender) using linear regression and Pearson correlation coefficient. Based on the correlation analysis, we conclude that:

– BMI and longer smoking history were positively correlated with the observed risk factors, but gender and physical activity did not show a significant correlation with morbidity of IHD and values of observed risk factors.
– The amount of Ca and Mg consumed through water was negatively correlated to the observed risk factors. Consequently, smaller values of Ca and Mg in drinking water may cause diseases such as IHD and elevated systolic and diastolic blood pressure, triglycerides, and total and LDL cholesterol.
– Ca and Mg from food were negatively correlated to IHD, and systolic and diastolic blood pressure, while it had no impact on the levels of triglycerides. Ca from food did not affect levels of total and LDL cholesterol.

Results of this study are consistent with the results of many other published studies in which the inverse relationship between water hardness and cardiovascular morbidity and mortality was established [23-25]. Persons who consumed medium hard drinking water had a significantly higher rate of incidence of IHD compared to people of the same sex and age who consume hard drinking water.

A similar study conducted in three cities of Serbia with different hardness of drinking water, showed that in areas with a water hardness above 20 ^{0}dH (Pozarevac) where the concentration of Mg is high (greater than 42 mg/l), there

Table 3. Correlation between different risk factors for IHD.

		Age (years)	BMI (kg/m^2)	Gender	Physical activity	Smoking	Ca from food (mg)	Mg from food (mg)	Ca from the taken water (mg)	Mg from the taken water (mg)
IHD	Pearson									
	R	-.005	.238**	.083	-.090	.376**	-.257**	-.551**	-.360**	-.358**
	p	.943	.001	.241	.204	.000	.000	.000	.000	.000
Systolic blood pressure	Pearson									
	R	.067	.328**	.092	.110	.250**	-.271**	-.410**	-.256**	-.254**
	p	.344	.000	.197	.122	.000	.000	.000	.000	.000
Diastolic blood pressure	Pearson									
	R	.008	.274**	.040	.056	.273**	-.231**	-.340**	-.264**	-.262**
	p	.914	.000	.575	.430	.000	.001	.000	.000	.000
Triglycerides mmol/l	Pearson									
	R	-.262**	.283**	-.075	-.078	.306**	.050	-.072	-.196**	-.196**
	p	.000	.000	.289	.275	.000	.485	.311	.005	.005
Total cholesterol mmo/l	Pearson									
	R	-.010	.369**	.060	-.100	.188**	-.023	-.224**	-.160*	-.158*
	p	.883	.000	.395	.162	.008	.746	.001	.024	.025
LDL cholesterol mmol/l	Pearson									
	R	-.098	.331**	-.013	-.029	.147*	-.012	-.191**	-.188**	-.191**
	p	.174	.000	.853	.692	.040	.868	.008	.008	.008

* smaller statistical significance
** higher statistical significance

is a significantly lower diastolic blood pressure in subjects in relation to the city (Grocka) where the hardness of the water around 11.15 ^{0}dH and content of Mg in the water of about 11 mg/l. Serum Mg was highest among respondents from Pozarevac after adjustment for age, sex, and BMI, and only total cholesterol and mean serum Mg levels were dependent predictors of diastolic blood pressure in all the investigated municipalities [26]. Studies in healthy respondents, free of cardiovascular disease, reported that magnesium intake was inversely associated with arterial calcification, which may play a contributing role in magnesium's protective associations in coronary heart disease [27].

Research done in Bosnia and Herzegovina showed significant correlation between the prevalence of CVD in the population group who drink soft water (the value of the relative risk (RR) is 1.127) [28].

The research also included an entry of Ca and Mg through food in patients and healthy respondents. Data from the literature confirm this statement, stating that patients with ischemic heart disease had much lower intake of foods rich in magnesium, such as vegetables, whole grains, and nuts [29, 30]. Meta analysis of prospective studies on the impact of dietary Mg circulating and the risk of CVD has confirmed the importance of a diet rich in Mg in the prevention of CVD disease, especially ischemic heart disease, highlighting the non-linear inverse association between dietary intake of Mg and mortality as IBS [31]. The study conducted in Nis (Serbia) shows an inverse correlation between nutritional intake of magnesium and the risk of coronary heart disease [32].

The protective amount of Mg and Ca from the water and the food for the development of IHD was determined on the basis of ROC analysis (Fig. 2). Research has shown that in respondents, the daily minimum protective amount Ca in food for IHD was 802.86 mg and 75.7 mg of the water, while the minimum protective Mg the daily amount of food amounted to 260.33 mg and 6.87 mg of water (surface area under the curve, p = 0.000). ROC analysis revealed a protective minimum daily amount of magnesium and calcium from drinking water (more than 7 mg of magnesium and more than 70 mg Ca) in accordance with the results of other studies [33] and can be used for the final conclusion on the minimum concentrations of these minerals drinking water in order to prevent IHD.

Schimatschek in their study indicated that even a relatively low intake of Mg and Ca from drinking water may be of importance for the prevention of Mg and Ca deficiencies [34], which was confirmed by this study – even in cases when the average intake of water is less than 2 l. Durlach [35] has repeatedly stressed the so-called qualitative significance elements, in particular Mg from

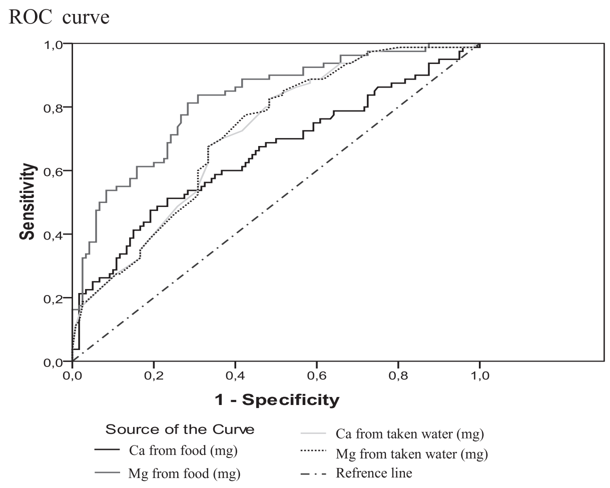

Fig. 2. The protective amount of Mg and Ca from water and food for IHD:

Test results	Surface area under the curve	SD	p	Limit (IHD positive if ≤)
Ca from food (mg)	.653	.041	.000	802.86
Mg from food (mg)	.820	.030	.000	260.33
Ca from taken water (mg)	.715	.036	.000	75.70
Mg from taken water (mg)	.716	.036	.000	6.87

drinking water. Specifically, its higher bioavailability in water than in food results in greater gastrointestinal absorption and is coupled with other biological benefits from Mg in water (hexa-hydrated ion) [36]. On the other hand, it has been proven that soft water can significantly reduce the content of different elements (including Mg and Ca) in food when used for cooking vegetables, meat, and cereals [37]. The statistical t-test used in this study has proven that the intake of Ca and Mg through water is one of the most important risk factors that influence differences in the incidence of IHD among the observed areas of the Nis region (p = 0.000). The importance of intake of these minerals through drinking water in the prevention of IHD has been confirmed in numerous studies [38]. Evidence from a meta analysis conducted in 2015 suggested that the highest level of calcium in drinking water versus the lowest level was significantly associated with reducing the risk of coronary heart disease mortality (RR = 0.88, 95% CI = 0.79-0.97, I^2 = 84.0%) [39]. Similar studies have revealed an inverse association between drinking water magnesium levels and coronary heart disease mortality (RR = 0.89, 95% CI = 0.79 – 0.99, I^2 = 70.6) [40]. A systematic review with meta-analysis included studies of the case-control type and confirmed a protective effect of the ions on CVD prevention, with an effect-size (ES) of 0.82 (95% CI = 0.70-0.95, p-value = 0.008) for calcium, and ES = 0.75 (95% CI = 0.66-0.86, p-value = 0.000) for magnesium [41].

The latest research shows that drinking water containing moderate to high levels of Mg (10-100 mg/l) has the potential to prevent 4.5 million deaths annually from heart disease worldwide [42]. This potential number is calculated on the basis of global mortality from 2010, combined with the recent quantification reverse association between magnesium from the water and heart disease. This is of particular importance in areas with prevailing inadequate magnesium intake with food.

Although many studies have favored Mg as the main protective mineral hard water for CVD [43], in its latest study Rylander nevertheless concludes that the Mg and Ca must be considered together, because the analysis of many epidemiological and experimental studies have shown that the risk of death from CVD was associated with a composition with the content of Mg and Ca [44].

Conclusions

Drinking water from the Nis water system varies in terms of hardness and values of Ca and Mg depending on the source of water supply, which can affect the health of the population.

Although the daily intake of drinking water was less than 2 liters, the effects on human health have been registered with the tested population.

Low levels of calcium and magnesium in drinking water are factors independent of significant impact on the increase in the total cholesterol, triglyceride, and LDL-cholesterol levels, and systolic and diastolic blood pressure, which indirectly increases the risk of IHD.

From the standpoint of preventing IHD, it is necessary to have at least 75 mg of calcium and 7 mg of magnesium in the daily intake of drinking water.

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