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Clinical paper

Magnesium and calcium in drinking water and cerebrovascular mortality in Taiwan

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Summary: The relationship between death from cerebrovascular disease and the levels of magnesium and calcium in drinking water was examined using an ecological design. The study area consisted of 227 municipalities in Taiwan. Data on the levels of magnesium and calcium in drinking water have been collected from the Taiwan Water Supply Corporation (TWSC). These levels of magnesium and calcium were compared using the standardized mortality ratios (SMRs) for cerebrovascular disease (1981–1990). A statistically significant inverse relationship was present between cerebrovascular mortality and levels of both magnesium and calcium after adjusting for urbanization index. After adjustment for calcium levels in drinking water and urbanization index, the weighted multivariate-adjusted regression coefficient indicated a decrease of 0.248 in the standardized mortality ratios (SMRs) for every 100 mg/L increase in magnesium levels in drinking water. The results from this study strengthen the hypothesis that magnesium in drinking water helps to prevent death from cerebrovascular disease.

Key words: Magnesium, calcium, drinking water, cerebrovascular mortality.

Introduction

The relationship between water hardness and mortality from cardiovascular disease has been studied for more than 40 years. The association was first described in Japan[1], where a significant correlation between drinking water quality and mortality from cerebrovascular disease was found. Subsequently, a number of studies conducted in various countries have demonstrated a negative association between cardiovascular diseases mortality and water hardness[2–11].

The hardness of drinking water is determined largely by its content of calcium and magnesium. It is expressed as the equivalent amount of calcium carbonate that could be formed from the calcium and magnesium in solution. Two theories have been offered concerning the causative agent for the relationship between death from cardiovascular disease and water hardness. Soft water is more corrosive than hard water, and promotes the dissolution of cadmium, lead and other toxic substances from the plumbing system into the drinking water[12]. Another theory is that there is a protective effect from the water content of magnesium[13–15].

The former hypothesis could not be tested in this study because the amounts of lead and cadmium levels in drinking water was not available. The aim of this study was to examine the relationship between the amounts of calcium and magnesium in drinking water and death from cerebrovascular mortality in 227 municipalities in Taiwan.

Methods

Study area

Taiwan is divided into 361 administrative districts, which will be referred herein to as municipalities. They are the units that will be subjected to statistical analysis. Out of these

361 municipalities, 30 aboriginal townships and nine islets were excluded from the analysis in order to reduce the variation which may result from their different lifestyles and living environments. In addition, 19 districts had changed administrative size during 1981–1990, and were excluded from analysis. The elimination of these unsuitable municipalities left 303 municipalities for this analysis.

Magnesium and calcium levels in drinking water

Information on levels of magnesium and calcium in each municipality's treated drinking water supply was obtained from the Taiwan Water Supply Corporation[16]. Among the 303 municipalities, 76 were excluded as they had more than one waterworks to supply the drinking water and the exact population served by each waterworks could not be determined. Their details are given in an earlier publication[10]. The final complete data consisted of hardness data from 227 municipalities. Hardness (calcium and magnesium) remains reasonably constant for long periods of time and is a quite stable characteristic of a municipality's water supply[17]. The levels of magnesium and calcium were defined as the annual mean level of $CaCO_3$ equivalent expressed as mg/L and were obtained from routine chemical analysis in 1990.

Mortality

Information concerning both the number of deaths and Taiwan's midyear population by sex, age, calendar year, and municipality from 1981–1990 was obtained from the Bureau of Vital Statistics of the Taiwan Provincial Department of Health which is in charge of the death registration system in Taiwan. In this report cerebrovascular mortality is that which is defined by the International Classification of Disease, Injury and Causes of Death (9th revision) (ICD-9 codes 430–438). Indirect standardization was applied to produce standardized mortality ratios (SMRs) for cerebrovascular disease. The standardized mortality ratio for a municipality is the ratio of the number of deaths occurring in the municipality to the number expected at standard rates in each sex and age group. The standard rates used were the rates for all of Taiwan. SMRs for cerebrovascular mortality were calculated for each of the 227 municipalities in Taiwan. Deaths for the years 1981–1990 were pooled and the SMRs were calculated using the central year, 1985, population estimates.

Socioeconomic factors

Each municipality in Taiwan was assigned to an urbanization category, 1–8, based on the urban-rural classification scheme of Tzeng and Wu[18], which takes into account variables such as population density, age composition, mobility, economic activity and family income, educational level, environmental, and health service related facilities. A municipality with the highest urbanization score, such as Taipei metropolitan area, was classified in category 1, while mountainous areas with the lowest score were assigned to category 8. In this study, the term urban areas, refers to those municipalities in categories 1–4, while rural areas, are those which fall into categories 5–8.

Statistics

In this analysis, the 227 municipalities were divided into quartiles according to the levels of magnesium and calcium in the drinking water. The risk ratios were calculated in relation to the group with the lowest exposure level. A weighted regression model was used to calculate the coefficients of SMR for every 100 mg/L increase in magnesium and calcium in drinking water after adjusting for the urbanization index. Since Taiwan municipalities vary greatly in size, the regression model used took into account the size of municipalities. For each municipality the weight was the reciprocal value of the estimated variances of the SMRs, i.e. $W_i = exp_i^2/obs_i$, where exp_i denotes the expected number of deaths in the municipality, and obs_i denotes the corresponding observed number[19].

Results

The levels of magnesium in the drinking water of the municipalities studied ranged from 1.5 to 41.3 mg/L and that of calcium from 4.0 to 81.0 mg/L. The correlation coefficient between magnesium and calcium in the drinking water was 0.50 ($p < 0.01$).

Table 1 shows the mean SMR for cerebrovascular mortality for municipalities grouped according to quartiles of calcium levels both with and without adjustments for the effect of urbanization index. The risk ratios for death from cerebrovascular disease were significantly lower for the three groups with high levels of calcium in the drinking water. Adjustments for the urbanization index only slightly altered the risk ratios. The adjusted risk ratios were 0.982 for the group with water calcium levels between 25.1 and 35.9 mg/L, 0.931 for the group with calcium levels betweeen 35.9 and 42.6 mg/L, and 0.949 for the group with calcium levels of 42.6 mg/L or more.

Table 2 shows the mean SMR for cerebrovascular mortality for municipalities grouped according to quartiles of magnesium levels both with and without adjustments for the effect of urbanization index. The risk ratios for death from cerebrovascular disease were significantly lower for the three groups with high levels of magnesium in the drinking water. Adjustments for the urbanization index only slightly altered the risk ratios. The adjusted risk ratios were 0.972 for the group with water magnesium levels between 7.0 and 9.3 mg/L, 0.958 for the group with magnesium levels betweeen 9.3 and 15.5 mg/L, and 0.937 for the group with magnesium levels of 15.5 mg/L or more.

Table 1. Risk ratio of mortality from cerebrovascular disease by calcium levels in drinking water in 227 Taiwan's municipalities, 1981–1990

		n	Estimated SMR (SE)[a]		Risk ratio	95% CI[b]
Unadjusted						
≤25.1	(16.5)[c]	55	1.0613	(0.0019)	1.000	Reference
25.1–35.9	(34.6)	60	1.0435	(0.0026)	0.983	0.975–0.991
35.9–42.6	(40.6)	53	0.9891	(0.0027)	0.932	0.924–0.940
42.6–81.0	(54.4)	59	1.0087	(0.0026)	0.950	0.942–0.958
Adjusted for urbanization						
≤25.1	(16.5)[c]	55	1.0562	(0.0031)	1.000	Reference
25.1–35.9	(34.6)	60	1.0371	(0.0027)	0.982	0.971–0.993
35.9–42.6	(40.6)	53	0.9830	(0.0027)	0.931	0.921–0.941
42.6–81.0	(54.4)	59	1.0025	(0.0027)	0.949	0.938–0.960

[a] SE: standared error.
[b] 95 % CI: 95% confidence interval.
[c] Referent group for risk ratio shown.

Table 2. Risk ratio of mortality from cerebrovascular disease by magnesium levels in drinking water in 227 Taiwan's municipalities, 1981–1990

		n	Estimated SMR (SE)[a]		Risk ratio	95% CI[b]
Unadjusted						
≤ 7.0	(3.7)[c]	55	1.0607	(0.0019)	1.000	Reference
7.0– 9.3	(9.1)	57	1.0303	(0.0026)	0.971	0.963–0.979
9.3–15.5	(11.8)	57	1.0186	(0.0026)	0.960	0.952–0.968
15.5–41.3	(18.1)	58	0.9962	(0.0026)	0.939	0.931–0.947
Adjusted for urbanization						
≤ 7.0	(3.7)[c]	55	1.0500	(0.0034)	1.000	Reference
7.0– 9.3	(9.1)	57	1.0211	(0.0027)	0.972	0.961–0.983
9.3–15.5	(11.8)	57	1.0063	(0.0027)	0.958	0.947–0.961
15.5–41.3	(18.1)	58	0.9835	(0.0027)	0.937	0.926–0.948

[a] SE: standard error.
[b] 95% CI: 95% confidence interval.
[c] Referent group for risk shown.

Results of the univariate and multiple regression analyses were similar and only the multiple regression analysis is shown in Table 3. In the multiple regression analysis, the weighted regression coefficient for magnesium is significant and indicates a decrease of 0.248 in SMR for every 100 mg/L increase in magnesium levels in drinking water after adjusting for the calcium and urbanization index.

Table 3. Weighted multiple regression analysis of SMRs from cerebrovascular disease in relation to calcium and magnesium levels in drinking water in 227 Taiwan's municipalities, 1981–1990

Independent variable	B[a]	SE	*p* value
Calcium	-0.042	0.069	0.537
Magnesium	-0.248	0.135	0.016
Urbanization[b]	0.031	0.021	0.147

[a] B, regression coefficient indicating a decrease in SMR for every 100 mg/L increase in calcium and magnesium of drinking water after adjusting for urbanization condition.
[b] Rural municipalities were the reference.

Discussion

These results show that, after adjusting for calcium levels in drinking water and urbanization condition, a significant negative association remained between levels of magnesium in drinking water and cerebrovascular mortality. The results from this study strengthen the hypothesis that magnesium in drinking water helps to prevent death from cerebrovascular disease.

In contrast to other studies, which only considered cities or townships in some regions, our study which was a nationwide survey also included rural municipalities. This study was more extensive than previous studies and the results reconfirm the previously observed inverse relationships between mortality from cerebrovascular disease and water hardness (particular magnesium content in drinking water).

Despite their inherent limitations[20] studies on the ecological correlation between mortality and environmental exposures have been used widely to generate or discredit epidemiological hypotheses. The completeness and accuracy of a death registration system should be evaluated before any conclusion based on the mortality analysis is made. Since it is mandatory to register death certificates at local household registration offices and since the household registration information is verified annually through a door-to-door survey, the death registration in Taiwan is very complete. Although causes of death may be misdiagnosed and/or misclassified, the problem has been minimized through the improvement in the verification and classification of causes of death in Taiwan since 1972. Furthermore, Taiwan is a small island with a convenient communication network, and the accessibility of medical service facilities is comparable among study municipalities. Mortality data differences between the units in this study do not appear to result from systematic differences in recording and codification.

To detect correlation between specific environmental exposures and mortality rates the environmental indicators under study must differ among the geographic units considered. In this study, there are considerable differences in levels of magnesium and calcium in drinking water among the examined municipalities. Information on levels of magnesium and calcium in drinking water were supplied by Water Quality Research Center of Taiwan Water Supply Corporation, which conducts routine water analyses to assess the suitability of water for drinking from both the source and at various points in the distribution system. Also, the waterworks in each municipality received a questionnaire requesting information on whether any changes had occurred in the water source, quality and treatment during the period 1981–1990. No municipality was excluded because of changes in water quality, e.g. use of water softening had occurred during that period. It was felt that the calcium and magnesium levels have remained reasonably constant in drinking water. We therefore made the assumption that the magnesium and calcium levels in 1990 were about the same as during the period when the mortality data were collected (1981–1990).

Smoking habits represent a possibly important confounder, but any correlation between the extent of smoking in different municipalities and the magnesium or content of the water is not likely[9]. There is also no reason to believe that there would be any correlation

between other traditional risk factors, such as fat consumption and stress and the level of magnesium in drinking water in study areas. Nevertheless, the problem of possible confounding factors should be evaluated. It has been suggested that socioeconomic factors have an independent association with cardiovascular mortality[21-22]. In this study, we used an integrated indicator urbanization index to adjust for possible confounding resulting from the different socioeconomic characteristics in municipalities.

Most studies have reported only correlation coefficients and not risk estimates as a function of exposure. So far there has been little reported work on risk estimation[11,23]. The risk ratios for death from cerebrovascular disease were inversely related to the amount of magnesium in drinking water. The risk ratio estimates were 0.972, 0.958, and 0.937 for death from cerebrovascular disease in municipalities with increasingly higher levels of magnesium in their drinking water. A similar relationship was also found for calcium. However, the calcium level in drinking water was not found to be a significant predictor of cerebrovascular mortality when weighted multiple regression analysis was used. Since magnesium levels and calcium levels are significantly correlated, controlling for magnesium levels eliminates the perceived effect of calcium levels on cerebrovascular mortality. The present study has found a decrease of 24.8 per cent in SMRs for every 100 mg/L increase in magnesium levels in drinking water. This is an lower decrease than Marier and Neri[23] estimated. They estimated that an increase in water magnesium level of 6 mg/L would decrease ischaemic heart disease mortality by approximately 10 per cent.

The significant association between mortality from cerebrovascular disease and the amount of magnesium in the water is supported by a knowledge of the function of magnesium. Its pathophysiological and clinical importance in cardiovascular risk has been reviewed by Durlach[15]. Of particular concern is how the relatively small intake of magnesium via drinking water can have such a critical impact. In the modern-day world, intake of dietary magnesium is often lower than the recommended dietary amounts (6 mg/Kg/day)[24]. For individuals at the borderline of magnesium deficiency, magnesium via drinking water can be 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[25]. Another reason why magnesium in water can play a critical role is its higher bioavailability. Magnesium in water is more easily absorbed than magnesium in food[15,26]. The contribution of water magnesium to the diet of persons who use water with high magnesium levels could thus be crucial in the prevention of magnesium deficiency[11].

Conclusions

In summary, the present study suggests that mortality from cerebrovascular disease can be related to the amount of magnesium levels in drinking water. The observed inverse relationship was statistically significant, but the evidence presented here does not establish conclusively that magnesium in drinking water prevents cerebrovascular disease. The problem of possible confounding factors should be evaluated further. Future studies on the estimation of individual intake of magnesium, both via food and drinking water are needed.

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Magnésium et calcium de l'eau de boisson et mortalité cardiovasculaire à Taïwan

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Résumé: Les interrelations entre maladie cérébrovasculaire et taux de magnésium et calcium dans l'eau de boisson ont été étudiées sur le plan écologique. Les zones étudiées représentent 227 municipalités à TAIWAN. Les données sur les taux de magnésium et calcium de l'eau de boisson ont été collectées par la corporation de fourniture d'eau de Taiwan. Ces taux ont été comparés aux rapports de mortalité standardisés (SMRs) pour la maladie cardiovasculaire (1981–1990). Il existe, après ajustement par rapport à l'index d'urbanisation, une corrélation inverse statistiquement significative entre mortalité cardiovasculaire et les taux tant de magnésium que de calcium. Après ajustement par rapport aux taux de calcium dans l'eau de boisson et à l'index d'urbanisation, le coefficient de régression multivarié indique une diminution des rapports de mortalité standardisés (SMRs) de 0.248 par chaque augmentation de 100 mg/l. du taux de magnésium dans l'eau de boisson. Les résultats de cette étude étayent l'hypotèse selon laquelle le magnésium de l'eau de boisson aide à prévenir la mort par maladie cérébrovasculaire.

Mots clés: Magnésium, calcium, eau de boisson, mortalité cérébrovasculaire.

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