Magnesium in Health and Disease: Y. Itokawa & J. Durlach, eds. © 1989 John Libbey & Co Ltd. pp 183-190.

Risk of myocardial infarction in relation to magnesium and calcium concentrations in drinking water, with some aspects on the magnesium vs. fluoride interactions

Heikki Luoma

Department of Preventive Dentistry and Cariology, University of Kuopio, Kuopio, Finland.

According to the letter of Dr. Itokawa, fall 1987, the organizing committee proposed me to present a paper on my own work on the risk of myocardial infarction in relation to magnesium and calcium concentration in drinking water. My presentation will meet this initial proposal. However, studies of my group on this topic were primarily initiated by need of learning more about the safety of the increased intake of fluoride for prevention of tooth decay. Therefore, fluoride became an essential part of our studies from the very beginning. For the same reason, the fluoride cannot entirely be excluded from this presentation either.

The basic hypothesis of our work was that increased intake of fluoride may possibly promote the prevalence of cardiovascular diseases, including myocardial infarction, among subjects who may otherwise be susceptible to them. If that hypothesis would be true, fluoride intake should be reduced, or perhaps the suitability of fluoride could be improved by other ions, such as magnesium.

In the early 1970'ies, several excellent epidemiolgical articles and reviews were available relating the prevalence of cardiovascular diseases to the quality of drinknig water or diet (Kobayashi, 1957; Schroeder, 1960; Seelig and Heggtveit, 1974), and especially to their magnesium content (Marier, 1968; Neri et al., 1975 and others).

As to Finland, who in the beginning of the 1970'ies was on top regarding the prevalence of cardiovascular diseases, the ischaemic heart disease was associated by Karppanen and Neuvonen (1973) in part tho the low soil magnesium and, further, to low Mg in drinking water. In fact, the relative age-adjusted death rate from coronary heart diseases in 1969 was highest in the easternmost Finland (Puska, 1972, Fig. 1), where largest areas of low-Mg soils exist (Kurki, 1972).

For us these data were enough to include magnesium as one of the elements of drinking waters, that we analyzed in our first field study (Luoma et al., 1973). In this study we compared the prevalence of cardiovascular diseases to the magnesium and fluoride content of drinking water among 300 men living in different rural districts of Finland and who had drank the same water for several years. Two of these districts were from areas, where the well waters had distinctly higher contents of many elements than the wells in rural Finland in general (Fig. 2).

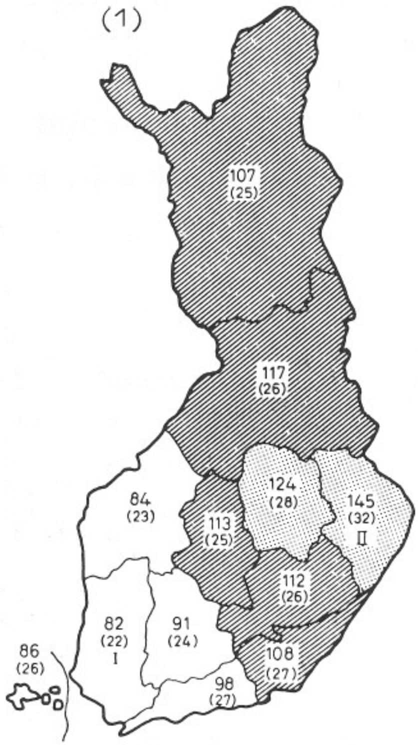

Fig. 1. Relative age-adjusted death rates from coronary heart diseases in Finland. Average mortality of the country = 100 (Puska, 1972).
Fig. 2 . Four sampling districts having drinking waters with high (dotted areas) and low (white areas) contents of most minerals (see Luoma et al., (1973) and Fig. 3).

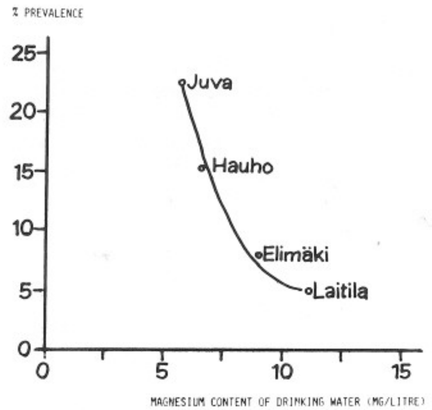

Fig 3. Prevalence of cardiovascular diseases among 300 men living in 4 districts of Finland with different magnesium content in drinking water (Luoma et al. 1973).

According to Fig. 3, the percentage prevalence of all cardiovascular diseases was four times higher in the district of Juva with the average Mg-concentration of 5.8 ppm in drinking water, as compared to the CV-prevalence in the district of Laitila, where the average water Mg- content was 11.0 ppm. The percentage prevalence of ischaemic heart disease in the respective extreme districts were 8.6 (Juva) and 1.1 (Laitila). The mean serum cholesterol values were 286 and 272 mg/100 ml, serum potassium 5.43 and 4.61 mM/l, and water F-contents 0.05 and 2.57 ppm, respectively.

Ten years later we published another field study, also of a pilot nature, on the possible association of magnesium, calcium, and fluoride content of drinking water to the risk of myocardial infarction among Finnish men (Luoma et al. 1983). The final group of infarction cases contained 30 - 64 -year-old men that had been treated in the Central Hospital of Town of Kotka (in South-Eastern Finland) for their first myocardial infarction. The hospital control group contained men who had been treated surgically in the same hospital during the same year as the cases. As the population control group we had men selected from the population register of the same area and who were not hospitalized. After several exlusions were made on the basis of additional informations, we finally had 50 case-hospital control pairs and 50 case-population control pairs. Table 1 shows that the increasing magnesium concentration of the drinking water was associated with decreasing relative risk of infarction in each comparison. Fluoride exhibited a similar relationship, especially in the case/hospital control comparison. There was a trend of increasing risk with the increase in water calcium content.

Table 1. Decreasing relative risk (RR) of acute myocardial infarction along with increasing magnesium (and fluoride) level in drinking water (Luoma et al. 1983).

Element in water	Concentr. cut-off limit (ppm)	Case/hosp.control RR	Case/popul.control RR
Mg	1.2	2.00	4.67
	1.5	1.11	2.29
	3.0	1.00	1.63
F	0.1	3.00	4.40
	0.3	2.17	6.33
	0.5	1.63	6.33
	1.0	0.91	2.33
Ca	16	0.73	0.56
	18	0.77	1.07
	20	0.91	1.64

The results of these two field studies were consistent with the widely accepted view, that low magnesium intake is associated with increased risk of cardiovascular diseases, including myocardial infarction. The results on fluoride support a hypothesis on a similar association, earlier suggested by Bernstein et al. (1966). The data on coronary heart disease and constituents of drinking water in East- and West-Finland (Punsar et al., 1975), were in line with the Mg-and F-data of both of our studies.

In the early 1970'ies, some evidence had accumulated concerning the reduction by magnesium of arteriosclerotic calfications or even myocardial infarctoid changes or necroses of experimental animals, as shown by Selye (1958a), Rigo and coworkers (1963) and Savoie (1972) and reviewed by Pyke (1973).

We also had to perform animal experimentations on the effect of magnesium and fluoride intake on the cardiovascular health, partly to justify our clinical field studies, mentioned above.

In the attempts to produce myocardial infarctions in rats we only could confirm the previous information (Selye, 1958a; Mishra, 1960; Seta et al. 1965) that infarctions only occur in the inner layers of rat myocardium. We considered this model less suitable for further experimentation. Therefore, we preferred to quantify the possible modification of the pathologic calcium salt accumulation in the cardiovascular system of rats by elevated dietary Mg and F.

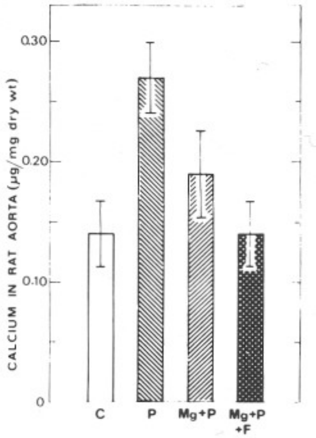

Fig. 4. Elevation by orthophosphate feeding of the calcium content of aorta in rats fed a low-Mg basic diet and the inhibition exerted by magnesium and fluoride additions in diet (Luoma et al., 1976).

Figure 4 shows the results of our first rat experiment (Luoma et al. 1976). In rats fed a low Mg diet (0.046 % Mg) an orthophosphate addition (2 % $NaH_2PO_4 \cdot H_2O$ to the diet doubled the aortic calcium. Magnesium added with phosphate (40 ppm Mg) prevented in part the calcium accumulation in the aorta, while magnesium plus fluoride (15 ppm F) in whole diet, added with phosphate and magnesium, could completely prevent the effect caused by phosphate addition alone.

Four animal studies published by our groups so far (Luoma et al., 1976; Luoma and Nuuja, 1977; Luoma et al., 1981 and Ericsson, Luoma and Ekberg, 1987) demonstrated the effectiveness of increased magnesium intake in reduction of calcium accumulation in aorta or heart muscle.

In the last animal study (Ericsson, Luoma and Ekberg, 1987) we had seven groups of rats (Table 2). There was a basal group (B) with normal diet. The rest of groups had an imbalanced diet (I) with low calcium and magnesium and high phosphorus contents. In the drinking water of the 5 imbalance groups, calcium, magnesium or fluoride or their combinations were added.

Table 3 shows that in the imbalance group having no additions in the drinking water, plasma calcium and magnesium were slightly reduced, aortic calcium was reduced by one fourth and aortic magnesium as well as heart magnesium slightly.

Table 2. Composition of the different diets and drinking water of rats for observations on the effects of drinking water additives on the calcium, magnesium and fluoride content of plasma and the cardiovascular system. (Ericsson, Luoma and Ekberg, 1987).

Group, designation	Solid diet (analyzed) Ca	P	Mg	K	Drinking water (calculated)
	%		ppm	%	
B, balanced	0.43	0.43	485	0.48	Distilled water
I, imbalanced	0.12	0.82	98	0.19	Distilled water
I + Ca	0.12	0.82	98	0.19	Distilled water with 0.2 % Ca as gluconate
I + Mg	0.12	0.82	98	0.19	Distilled water with 200 ppm Mg as sulfate
I + F	0.12	0.82	98	0.19	Distilled water with 30 ppm F as Na_2PO_3F (MFP)
I + Ca + F	0.12	0.82	98	0.19	Distilled water with additives as in group I + Ca + group I + F
I + Mg + F	0.12	0.82	98	0.19	Distilled water with additives as in group I + Mg + group I + F

Table 3. Parameters of plasma, aorta, heart and kidneys in different dietary groups, see Table 2. (From Ericsson, Luoma, Ekberg, 1987).

Parameter	Dietary group B	I	I + Ca	I + Mg	I + F	I + Ca + F	I + Mg + F
Plasma Ca, ug/ml	85.2	54.4	82.4	59.6	49.6	90.0	54.4
Plasma Mg, ug/ml	18.2	14.7	6.0	21.9	14.2	6.3	23.5
Plasma F^-, ug/L	6	6	6	7	249	171	255
Aorta Ca, ug/g	371	297	452	430	352	452	343
Aorta Mg, ug/g	266	235	227	240	218	241	248
Heart Ca, ug/g	102	85	113	67	65	96	64
Heart Mg, ug/g	1059	1012	1018	1042	1017	1013	1085

Plasma values are means of 7 - 11 rats per group. Other values are means of 14 - 16 rats per group.

Calcium addition to drinking water of the imbalanced group reduced plasma magnesium further, elevated the calcium of the aorta and heart above the level of the basal group. Magnesium addition to the water of the imbalanced rats surprisingly elevated the aortic calcium also above the level of the basal group, but reduced heart Ca further and restored the heart magnesium to the level found in the basal group. Fluoride addition to drinking water of these imbalanced rats elevated noticeably only plasma fluoride and slightly the aortic calcium, but tended to reduce the calcium content of the heart further.

When calcium plus fluoride were added to the drinking water, the plasma magnesium was again reduced further (see group I). Plasma F was not increased as much as in the former group, but calcium in the aorta was elevated more than with the calcium addition alone. Finally, the magnesium plus fluoride additions in drinking water elevated plasma fluoride as much as did the fluoride addition alone. The aortic calcium was not elevated as much as by the magnesium addition alone. The magnesium of the aorta in this group was highest among the imbalanced groups. In the heart, the calcium content was lowest and the magnesium content highest of all the seven groups. Thus the heart Mg/Ca ratio was the highest in this group.

In our four animal studies, in which attempts were made to modify the calcium content of the arteriae, we never found any atherosclerotic plaques. The calcium changes were generally observable only by chemical means. In some rat series, where dietary magnesium was very low, phosphorus and sodium high and some cholesterol added, calcifications in the coronary ateries of some rats could be demonstrated also by histopathological methods (Fig.5). Calcium accumulations appeared in the Lamina elastica that seemed to be fragmentary thus resembling the figures shown by Selye (1958b) and Hungerford and Bernick (1980). There was no proliferation of cells of the artery wall as shown by Bloom (1988) in hamsters and Yamori et al. (1982) in rats. These observations, however, are still continued.

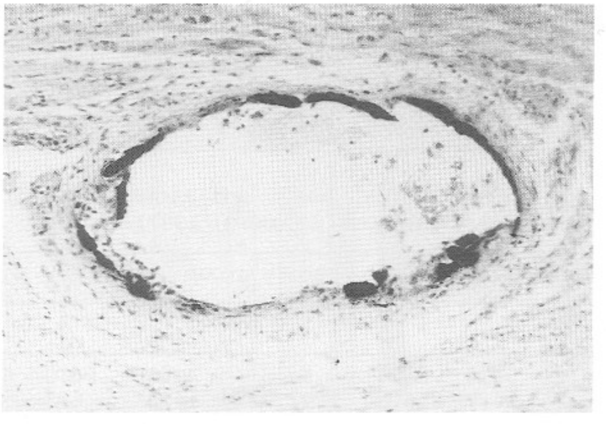

Fig. 5. Calcific deposits along Lamina elastica of a coronary artery in a 6 week-old rat fed a low-magnesium, high-phosphorus high-sodium, high vitamin D diet with added cholestrol. von Kossa staining. (Luoma, H. and Seppä, A. Unpublished).

In conclusion, with some exceptions these epidemiological and experimental data collectively support the concept of the protective action of magnesium of drinking water or of food against the degenerative changes of the cardio-vascular system, including the myocardial infarction. They are in a fair accordance with the many recent review articles or books on the cardio-protective function of magnesium written eg. by Szelenyi (1973); Altura (1979); Marier et al. (1979); Durlach et al. (1980); Seelig (1980); Karppanen (1981) and by many speakers in this symposium.

In view of the well known high consumption of animal fats and sodium by the Finnish people, the marginally safe daily intake of magnesium from food by the Finns (Varo and Koivistoinen, 1980) and the probably indirect reduction of its utilization by dietary calcium and phosphorus (Seelig, 1980), which are high in the average Finnish food (1.5 and 2.0 g/day, respectively) (Varo and Koivistoinen, 1980), the magnesium in most of our drinking waters seems insufficient essentially to contribute to the safe total Mg-intake in all population subgroups. Thus the need of further research and the present endeavours to increase the magnesium intake by our people, as proposed by Karppanen (1981), seem justified.

The findings that small elevations of fluoride alone or especially with magnesium in food or drinking water were also protective, were in agreement with the review

Marier,J.R.(1968): The importance of dietary magnesium with particular reference to humans. Z.Vitalstoffe Zivilizationskrankheiten 13, 144-149
Marier,J.R.; Neri,L.C.; Anderson,T.W.(1979): Water hardness, human health and the importance of magnesium. pp. 1-119 Ottawa: National Research Coundil Canada
Marier, J.R.(1980): Observations and implications of the Mg-vs-F in interrelations in biosystems. A review. Proc.Finn.Dent.Soc. 76, 93-102
Mishra,R.K.(1960): Studies on the experimental magnesium deficiency in the albino rat. 1. Functional and morphologic changes associated with low intake of magnesium. Rev.Can.Biol. 19, 122-135
Neri,L.C.; Hewitt,D.; Schreiber,G.B.; Anderson,T.W.; Mandel,J.S.; Zdrojewsky,A. (1975): Health aspects of hard and soft waters. J.Amer.Water Works Assoc. 67, 403-409
Punsar,S.; Erämetsä,O.; Karvonen,M.; Ryhänen,A.; Hilska,P.; Vornamo,H.(1975): Coronary heart disease and drinking water. A search in two Finnish male cohorts for epidemiologic evidence of a water factor. J.Chron.Dis. 28, 259-287
Puska,P.(1972): Sydän- ja verisuonisairauksien aiheuttaman kuolleisuuden alueelliset erot. Tilanne vuoden 1969 tietojen valossa (Regional differences in the mortality from cardiovascular diseases. The situation in the light of 1969 data) Suom.Lääk.l. 27, 3071-3075
Pyke,R.E.(1973): Relationships of calcium, phosphorus, magnesium and fluoride in hard- and soft- tissue calcification. In Biological mineralization, ed Zipkin, I. pp. 463-485, New York, John Wiley & Sons
Rigo,J.; Simon,G.; Hegyvari,C.; Sos,J.(1963): Effect of magnesium on dietary infarctoid changes in the heart. Acta Med.Acad.Sci Hung. 19, 231-236
Savoie,L.L.(1972): Role du magnésium, du potassium, d'antikaliurétiques, et d'hypo-cholesterolémiants dans le dévelopement de lésions cardiaques chez le rat nourri avec un régime thrombogéne et le Na_2HPO_4, Pathol.Biol. 20, 751-756
Schroeder,H.A.(1960): Relations between mortality from cardiovascular disease and treated water supplies. J.Amer.Med.Assoc. 172, 1902-1908
Selye,H.(1958a): On the site of interaction between NaH_2PO_4 and $MgCl_2$ or KCl in the prevention of phosphate-steroid cardiopathy. Acta Endocrinol. 28, 273-278
Selye,H.(1958b): Prophylactic treatment of experimental arteriosclerosis with magnesium and potassium salts. Amer.Heart J. 55, 805-809
Seta,K.; Hellerstein,E.; Vitale,J.J.(1965): Myocardium and plasma electrolytes in dietary magnesium and potassium deficiency in the rat. J.Nutr. 87, 179-188
Seelig,M.S.(1980) Magnesium deficiency in the pathogenesis of disease. pp. 141-264. New York, Plenum Medical Book Co
Seelig,M.S.; Heggtweit,H.A.(1974): Magnesium interrelationships in ischemic heart disease: A review. Am.J.Clin.Nutr. 24, 59-79
Szelenyi,I.(1973): Magnesium and its significance in cardiovascular and gastrointestinal disorders. World Rev.Nutr.Dietet. 17, 189-221
Varo,P.; Koivistoinen,P.(1980): Mineral element composition of Finnish Foods. XII General discussion and nutritional evaluation, in mineral element composition of Finnish Foods: N, K, Ca, Mg, P, S, Fe, Cu, Mn, Zn, Mo, Co, Ni, Cr, F, Se, Si, Rb, Al, B, Br, Hg, As, Cd, P and ash. ed P. Koivistoinen pp. 165-171 Acta Agricult. Scand. Stockholm, Suppl. 22
Yamori,Y.; Kihara,M.; Nara,Y.; Horie,R.(1982): Myocardial ischemic rats (MIR). Coronary vascular alteration induced by a lipid-rich diet. Atherosclerosis 42, 15-20