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Role of Waterborne Magnesium in Preventing Chronic Diseases

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ABSTRACT

Low intake of dietary magnesium in typical western diet is associated with magnesium deficiency and its related diseases. Americans are falling short of dietary intake of magnesium by 27 and 52 mg / day for men and women respectively. Water supplies only 6-7 % of the daily requirement of magnesium. Magnesium deficiency is common in normal and hospitalized people (2% & 26% respectively); while critically sick patients have hypomagnesaemia up to 60 %. Hypomagnesaemia influence the prognosis of the disease resulting in high mortality in severely sick and hypomagnesaemic patients, as compared to other hospitalized patients. Magnesium in hard water is known for its cardio protective effect especially against sudden cardiac death by preventing malignant arrhythmias and coronary vasospasm. Waterborne magnesium is also known for its protective effect on diabetes, metabolic syndrome, hypertension, stroke, insulin resistance, preeclampsia, and other chronic diseases. It is so much effective that even a small amount (6 mg / 1) can prevent the cardiovascular mortality by 10% (a disproportionate response). Hard water supplies other micronutrients like, calcium, zinc, iodine etc. and it also protects the body against other harmful chemicals of water like, cadmium, aluminum, beryllium, mercury, and nickel. Demineralized water produced through reverse osmosis process remove 93-97% of calcium and magnesium. Such water is stripped of its beneficial elements and produce magnesium deficiency if consumed for prolonged period.

Keywords: Waterborne magnesium, Prevent chronic diseases. Cardio protective, demineralized water

Introduction

There are emerging evidences that habitually low intake of dietary magnesium is associated with magnesium deficit and its related diseases worldwide with the changes taken place in the food habits. The US Department of Agriculture Continuing Survey of Food Intake by Individuals (CSFII) in 1994, indicated that the mean daily intake of magnesium in males and females was 323 and 228 mg per day respectively.¹ against the recommended daily allowances for male of 350 mg/ day and for females 280 mg /day.² Thus a short fall of 27 and 52 mg/ day exist for males and females US population respectively and therefore, they are marginally deficient in magnesium intake. Magnesium deficiency can be strong risk factor for hypertension, cardiac arrhythmias, ischemic heart disease, atherogenesis and sudden cardiac death.³ There is an increasing level of evidence that drinking water hardness which has elevated concentration of magnesium may reduce the risk of cardiac death, in particular

the risk of sudden cardiac death.^{4, 5} In spite of this, magnesium hypothesis has yet to gain wide spread acceptance. Magnesium deficiency is very subtle and frequently overlooked by the clinicians.⁶

Sources of magnesium

Magnesium is widely distributed in plants and animal foods. Green Leafy vegetables are rich in magnesium. Foods such as unpolished cereals, legumes, pulses and nuts have high magnesium content. Magnesium is primarily found in bran and germ, 80% of which is removed from refined grains.² It is likely that an overall 'western' diet (lower in magnesium containing food but also high in refined grains, high fat dairy product) is associated with a pro-inflammatory pattern. While a diet rich in whole grain, leafy vegetables, legumes and nuts exert a beneficial effect at least in part through an anti- inflammatory effect.⁷ Because of change in food the Americans were eating in last 90 years, there has been a progressive fall in magnesium intake from 475-500 mg/day during 1900-1908 to only 225-318 mg/day during the years 1978-1985.³

Water is the only marginal and variable source Typically water with of magnesium. increased hardness has a higher concentration of magnesium salts.¹ Natural surface water sources typically containing concentration of up to 10mg/l, such sources rarely contain more than 100 mg of magnesium per liter, and hardness calcium it is usuallv that predominant. On the other hand ground waters contain more hardness and also the more concentration of magnesium.⁸ Water with 100 units of hardness contribute 6-7% of the daily total magnesium intake i.e. about 23 mg of magnesium per day, and water with 400 units of hardness, which is usually found in most of the drinking water sources contribute about 68 mg of additional magnesium per day, which may be critical to make up deficient

intake through food.⁹ There does not appear to be any convincing evidence that water hardness causes adverse health effect in human. In contrast, the result of a number of epidemiological studies have suggested that water hardness may protect against diseases.¹⁰ In North America mineral intake from tap water is low but important when drinking from mineral-rich sources. For half of the tap water sources, adult men may fulfill between magnesium 6% and 23% of dailv recommended intake and adult women may fulfill between 8% and 31% of their magnesium daily recommended intake by drinking 2 liters of water per day.¹¹

Magnesium Deficiency

Usually, overt magnesium deficiency may be absent but it may be present in sub clinical form. Such deficiency over a long period of time could result in significant problem, specially when some conditions in which tissue magnesium level comes down are super imposed e.g. alcoholism. diabetes. diarrhea, diuretic malabsorption, chronic medication, pregnancy, elderly, athletics and any kind of stress, may it be thermal, surgical or emotional, ^{12, 13} till the deficiency becomes moderately or severely of advanced stage. The increasing prevalence of older people raises prevalence of hypertension, cardiac diseases and the use of diuretics, which may increase urinary excretion of magnesium. These three conditions might contribute both to increase in obesity and insulin resistance as well as to magnesium deficiency. Low magnesium level is also associated with endothelial dysfunction, increased vascular reaction, elevated circulating level of C-reactive protein and decreased insulin sensitivity. Low magnesium status has been implicated in hypertension, coronary artery disease, type 2 diabetes and the metabolic syndrome.¹⁴

Magnesium is second most abundant intracellular cation take part in more than 300 enzymatic reactions and so it is impotent for the body metabolism Out of the total 24 gm of body magnesium, about half is in the bone and another half in the soft tissue, namely skeletal muscles, the nervous system and other organs with high metabolic rate, like the liver, myocardium, digestive tube, kidney etc. Serum magnesium account for only 1% of the total body magnesium. The normal serum concentration is 1.8-2.3 mg / dl.¹⁵ Deficiency magnesium is closely linked of to abnormalities in calcium and potassium metabolism. A fundamental inter action between magnesium and other ions seems to occur at the cellular level.¹⁶. Because of pivotal role of magnesium in electrolyte homeostasis, hypomagnesaemia is the common finding among the hospitalized patients and in general population. In general population hypomagnesaemia was estimated to be 2 %.¹⁷ Hypomagnesaemia was found more common in critically ill patients. It was higher, (about 60%) in patients admitted to post operative/intensive care units, as compared to only 26% in other hospitalized patients.^{3,18} Hypomagnesaemia was found types of electrolyte along with all disturbances, but, since magnesium and potassium work together at various cellular metabolic processes and so, it was the commonest among patients had hypokalaemia (38%) Than in hypokakaemic patients, 25 %. (P < 0.007). The disease out come has always been found unfavorable in the presence of hypomagnesaemia, as magnesium deficiency enhances the stress reaction.¹³ The mortality in acutely ill patients admitted in post operative / ICU was higher (41%) for those patients with hypomagnesaemia than those who were eumagnesaemic (13%) (P <0.02).¹⁹

Waterborne magnesium prevents diseases

There are no known harmful health effects in the general population associated with the consumption of calcium and magnesium within a large range (hard water) and the nutritional essentiality of calcium and magnesium is well known. There are emerging evidences that habitually low intake of magnesium and resulting abnormal magnesium metabolism are associated with etiological factors in various metabolic diseases.¹ Body's low magnesium status has been implicated in hypertension, coronary artery disease, type 2 diabetes, insulin resistance, metabolic syndrome, cardiac arrhythmias, preeclampsia, atherosclerosis and many more chronic disease conditions.¹⁴ In addition, limited but suggestive evidence exist for benefits associated with other diseases (stroke, renal stone formation, cognitive impairment in elderly, very low birth weight, bone fractures among children, pregnancy complications, and possibly some cancers.²⁰

Cardiovascular diseases

According to WHO, in 2002 there were 7.20 globally.²¹ million deaths from CHD cardiovascular diseases are the leading cause of death in western countries. Among all the disease cardiovascular risk factors. magnesium now assumed first place as judged by the epidemiological, pathophysiological, clinical, experimental and therapeutic data.²² Geographical variation in cardiovascular deaths has been correlated with hardness and magnesium content of drinking water in various studies. In a study by Rubinowitz cardiovascular mortality was found to inversely related with the deferent grades of magnesium in drinking water. The adjusted OR for age and calcium was 0.88 (95 % CI

0.66-1.16) for group with water magnesium levels between 3.6 and 6.8 mg / 1 and 0.70 9 (95 % CI 0.53 - 0.93), for group with magnesium levels between 6.9 and 9.7 mg / 1 the and OR was 0.65 (95 % CI 0.50 - 84)for group with water magnesium levels of 9.8 mg /l or more.²³ In an another study by Kousa et al, the age standardized incidence was highest, 622/100,000 / year, (95% CI, 591-649) in lowest tertile of magnesium <2.28 mg/ 1 of well water as compared with higher magnesium level of >3.12 / 1 i.e. 463 (95 % CI, 454 - 474).²⁴ Magnesium rather than calcium has been clearly demonstrated to be the critical" protective factor" in hard waters.²⁵ In studies carried out to quantify the effect of waterborne magnesium on human morbidity and mortality in several region of the world indicated a consistent pattern that. waterborne magnesium could be the critical protective "Water factor". In humans, there is evidence for an inverse (protective) relationship between magnesium and coronary heart disease. Magnesium is actively involved in the maintenance of normal cardiovascular functions as well as in the etiology of cardiovascular diseases.²⁶

Sudden cardiac death

Sudden death is a significant cause of cardiovascular death, and many of these deaths are related to arrhythmia and coronary artery vasospasm.⁴ Among 728,743 cardiac disease deaths that occurred during 1999 in U.S. a total of 462,340 (63.4%) were sudden cardiac deaths.²⁷ Most convincing findings to date have been the relationships between the occurrence of sudden cardiac death and deficient magnesium intake through food. The heart with its high metabolic activities is particularly vulnerable magnesium to and deficiency deficiency. magnesium interferes with potassium retention in heart muscles. Loss of myocardial potassium that magnesium deficiency from results contributes to electrophysiological changes

and produces malignant arrhythmias and sudden cardiac death.²⁵ Arrhythmias are more frequent, 47% in patients of AMI without magnesium therapy as compared to those with magnesium therapy, 21 % (P = 0.003).²⁸ Anderson et al in 1971 found the proportion of sudden cardiac deaths was higher by 20-30% in northern city of Port Arthur (soft water area) as compared to Southern city of Kichener (hard water area) of Ontario, Canada. (P < 0.05).²⁹ Further, Anderson et al in 1989 found in the province of Ontario as a whole the deaths rate due to sudden IHD was almost twice as high in soft water areas as to the hard water areas. In this study the evidence in favour of cause-and- effect relationship was reasonably strong and where the magnesium appeared to be the cause of such high cardiac Further a new finding with mortality.³⁰ magnesium deficiency reported was the provoked coronary artery spasm in more than half of the Japanese patients with a recent AMI, suggesting a closed association between magnesium deficiency and AMI.³¹

Autopsy studies

Study by Anderson et al in Ontario, Canada indicated that hearts of patients who died of accidental deaths from soft water areas exhibited 7% deficit of magnesium in myocardial cells as compared with those who lived in hard water areas and died (t=2.43, P < 0.01). The mean myocardial magnesium of those who died from IHD was 22% lower than age adjusted mean of those who died accidentally. Those who died from IHD were also characterized by relative low magnesium concentration in both the diaphragm and pectoris muscles.³⁰ In a case control study involving patients died of AMI and acute trauma, Speich et al reported a significantly lower potassium (P < 0.05) and magnesium (P < 0.01) concentration in necrosed tissue area of left ventricle than that of non necrosed tissue of left ventricle and that of those who died of acute trauma.⁶ An interesting finding was that on autopsy, the patients with history of angina exhibited both magnesium and potassium were significantly depressed (P < 0.05 and P < 0.025 respectively) whereas patient without history of angina appears to exhibit near normal myocardial magnesium content.³²

There were more cases of myocardial scaring (healed infarcts) more confluent atheroma and lumen stenoses in the young age of 30-44 years, who died in accident and lived in soft water area than in those who died in accidents and lived in hard water area (P < 0.02). Low concentration of calcium and magnesium in coronary arteries was found in area where disease appears earlier and is more lethal, but when the disease is established, the calcium gets precipitated and is deposited in the advanced lesion. In general population also, there were more cases of ischemic heart disease in soft water area than in hard water area.³³ multivariate analysis in a case control study of 120,852 men and women in Netherland. Leurs et al observed no relationship between tap water hardness and IHD mortality(hard vs. soft water hazard ratio (HR) = 1.03;95% confidence interval (CI), 0.85-1.28 for men and HR =0.93;95 % CI,0.71-1.21 and HR =0.86; 95% CI,0.62 -1.20, respectively). It was quiet interesting to note that for men with the 20% lowest dietary magnesium intake, an inverse association was observed between tap water intake and stroke mortality (HR) per one mg/l intake = 0.75; 95 % CI, 0.61 - 91), whereas for women with the 20 % lowest dietary magnesium intake the opposite was observed.³⁴

Quantification of effect of hard water on mortality

Many studies indicate that small increase in magnesium intake may result in reduced risk of sudden cardiac death. Therefore, it is possible that relatively modest increases in water magnesium levels might result in considerable benefits with minimum risk of

any adverse effect.⁴ Different workers attempted to quantify the effect of waterborne magnesium in preventing the cardiovascular mortality in different areas. Rubinowitz et al estimated that magnesium is as effective as 6 mg/l in decreasing ischemic heart disease mortality by approximately 10 percent, ²³ a disproportionate response. The estimation of incidence of myocardial infarction in study population is if everyone were to drink water containing magnesium 9.8mg /l or more, the decrease in mortality from AMI would be about 19%. The decrease in incidence of AMI magnesium one mg/l could per be approximately 10/100,000 population. While Kousa et al in their study in rural Finland found that with every one mg/l increment in magnesium level in drinking well water decreases the risk of AMI by 4.9%.²⁴ Marier & Neri have also quantified the effect of hard water and its magnesium concentration on the disease cardiovascular mortality. Thev concluded from the study by Schroeder who reported the chemical composition of drinking water throughout the continental USA, that total hardness of 100 containing magnesium at the level of 8.3% would confer 10% reduction in cardiovascular mortality. Similarly, on the basis of the study conducted in South Africa by Leary, they calculated that a 10% reduction in IHD mortality would be conferred by waterborne magnesium of approximately 6 mg/l^{35}

Diabetes mellitus

Magnesium plays an important role in glucose metabolism and in release of insulin, and therefore, there is a strong relationship between serum magnesium and diabetes. Low serum magnesium is one of the risk factors of diabetes mellitus and its complications, at the same time diabetes is one of the common causes of hypomagnesaemia.³⁶ Several studies have documented an inverse relationship

between magnesium intake and risk of developing type 2 diabetes, and development of insulin resistance.¹⁴ Hypomagnesaemia is a common feature in patients with type 2 diabetes and was reported to occur in 37.6% of patients, as compared to 10.9% of nondiabetic control subjects. (P < 0.001).³⁷ Again, magnesium intake was associated inversely, in a dose response manner, with the risk of incidence of metabolic syndrome magnesium intake associated inversely with incidence of metabolic syndrome. Risk was 31 % low in patients of highest quartile than those in lowest quartile (HR, 0.69 (95 % CI, 0.52-0.91; P < 0.001).In addition, magnesium intake was also inversely related to individual components of the metabolic syndrome and fasting insulin level (P for trend < 0.01).³⁸ It has been hypothesized by Takaya et al that infants with intrauterine growth retardation induced by magnesium deficiency are at higher risk for metabolic syndrome in childhood or adulthood.³⁹

Cerebrovascular disease

Annually 15 million people worldwide suffer from stroke. Of these 5 million die and another 5 million are left permanently disabled.40 In China alone there were 7.0 million cases of stroke in 2007 with a very high disability rate of 80 percent and recurrence rate of about 41 percent.⁴¹ Α significant negative correlation between mortality due to stroke with magnesium content of drinking water has reported the protective effect of waterborne magnesium on the risk of cerebrovascular disease.⁴² The adjusted odd ratio (95% confidence interval) were 0.75 (0.65 to 0.85) for the group with water magnesium levels between 7.4 and 13.4 mg/l and 0.60 (0.52 to 0.70) for the group with magnesium level of 13.5 mg / 1 and In another study in Spain, Ferrandiz more.⁴² studied the mortality due to et al

cerebrovascular disease and IHD separately for men and women at two different period e.g. 1991-94 and 1995-98 with two covariates calcium and magnesium. The relationship was stronger between cerebrovascular disease (all P < 0.001) than for IHD (all P values were between 0.001 and 0.05) and was more pronounced in women than in men and is more apparent with Magnesium than with calcium.⁴³

Hypertension

The estimated total number of adults with hypertension in 2000 was 972 million.⁴⁴ Magnesium deficiency has been implicated in the pathogenesis of hypertension. Some epidemiological and experimental studies demonstrating a negative correlation between blood pressure and serum magnesium level.¹⁴ The protective role of waterborne magnesium in reducing incidence of hypertension has been reported. Ragnar et al found that intake of mineral water among persons with low urinary excretion of magnesium may decrease the blood pressure significantly (P < 0.05).⁴⁵

Waterborne magnesium

Minerals are important parts of drinking water and are of both direct and indirect health significance. Sufficient evidence is now available to confirm that a certain minimum amount of mineral in water is desirable, since their deficiency have many negative health effects and possible aggression from toxic elements and bacteria.⁴⁶

Quantitatively, water provides magnesium and calcium both as nutrients, the water borne magnesium contribution may represent the amount of magnesium required to bring an insufficient dietary magnesium level to a correct level.²²

Qualitatively too, the contribution of water borne magnesium is also interesting. Study conducted by Lowik et al showed that magnesium in drinking water is 30 per cent better absorbed than dietary magnesium, possibly because of magnesium cations are in ionic form and so it is more available for quick absorption.47 The net absorption of dietary magnesium in a typical diet is approximately 50 percent.¹ Again higher bioavailability is observed when a given amount of magnesium is distributed over a day than been consumed in a single bolus.⁴⁸ Consequently а regular water intake distributed throughout the day would be expected to lead to a higher absorption of magnesium. Quickly and better absorbed water magnesium would avoid neuromagnesium endocrinal control of the homeostasis problems. It may also protect the nephrocardiovascular apparatus because of its qualitative mode of action.²² This particular bioavailability of magnesium might help to understand why an adequate water magnesium level may determine a better state of health, even without any deficiency.²⁵

The chemical substances in water that provides positive contribution to human health act mainly in two ways.⁴⁹

1. Nutritionally by supplying essential micro and macro elements that the diet may not provide e.g. Mn, Zn, I and,

2. Provide macro and micro elements that inhibit the absorption and/ or effect of toxic elements such as Hg, Pb, and Cd, Al, beryllium and nickel.

Demineralized water

Because of various sound reasons people all over the world are consuming water purified through reverse osmosis process. Such waters are generally demineralized (and not remineralized), and in all types of reverse osmosis process bulk of calcium and magnesium are removed to the extent of 93-97% during the purification process and are the poorest water sources of magnesium and calcium.⁵⁰ Such waters are commercially available as bottled water or through system installed at home. In India such purified bottled water supply magnesium in the range of only 1-5.5 mg/l.⁵¹

North American tap and bottle waters generally contain low mineral levels. European bottled water contains higher mineral levels than North American tap and bottled waters. Calcium and Magnesium levels are highest among moderate mineralized European waters, and sodium levels are highest among high mineralized European waters. In North America nearly 20% of households use bottled water for drinking purposes, all of which supply magnesium in the range of 0-10 mg/l except few selected brands, which supply higher magnesium content.¹¹

Drinking demineralized water for long time may create problems e.g. among Czech and Slovak population who started to use reverse osmosis based system for final treatment of drinking water at their home outlet in 2000-2002 and several weeks later reported different health complaints suggestive of acute magnesium deficiency. e.g. cardiovascular disorders, tiredness, weakness or muscular cramps.⁴⁶

Several authors have suggested that reduced cardiovascular mortality and other health benefits would be associated with minimum levels of approximately 20-30 mg/l calcium and 10 mg/l magnesium in drinking water.⁴⁶ The result of a number of epidemiological studies have suggested that water hardness may protect against diseases.¹⁰ A major benefit of drinking hard water is decrease risk of dying from cardiovascular diseases.⁴⁹

Conclusion

Drinking water containing magnesium is qualitatively and quantitatively useful and therefore, drinking and cooking water should not be softened .It is tempting to have it enriched in order to get 30 mg/l magnesium.

References

- Institute of Medicine, Washington (DC) Dietary reference intake for calcium, phosphorus, magnesium, vitamin D, and. Fluoride. Magnesium: background information. *National Academies press* (1997):190-228. http://www.nap.edu/openbook.php?record_id=5776
- 2. Institute of Medicine, Washington (DC). Recommended dietary allowances: Magnesium. 10 th Eds. *National Academies Press* 1989:187-194. http://books.nap.edu/openbools.php?record_id=1349 &page=187.
- 3. Altura BM, Altura BT. Cardiovascular risk factors and magnesium: relationship to atherosclerosis, ischemic heart disease and hypertension. *Magnes Trace Elem* 1991-92; 10:182-92.
- 4. Frost FJ. Studies of minerals and cardiac health in selected populations. In: Nutrients in drinking water. *Water, Sanitation and Health Protection and the Human Environment. WHO* 2005; 101-126. www.who.int/water_sanitation_health/dwq/nutrients indw.pdf.
- Anderson TW, Leriche WH, Hewitt D, Neri LC. Magnesium, water hardness, and heart disease. In: *Magnesium in health and disease*, Y Itokawa and J Durlach, eds; John Libbey Press, London, 1989:565-571.
- Speich M, Bousquet B, Nicolas G. Concentration of magnesium, calcium, potassium and sodium in human heart muscles after acute myocardial infarction. *Clin Chem* 1980; 26:1662-65.
- Esposito K, Giugliano D. Whole grain intake cool down inflammation. *Am J Clin Nutr* 2006; 83:1440-1.

- 8. Central Pollution Control Board, *Ministry of Environment & Forest, Government of India,* New Delhi. <u>www.cpcb.nic.in</u>
- Marier JR. Cardio- protective contribution of hard waters to magnesium in-take. In *Rev Can Biol.* 1978; 37:115-25. http://www.mgwater.com/durwater.shtml.
- 10. WHO Guidelines for Drinking water quality: Hardness in drinking water. *WHO Geneva*, 1996. WHO/SDE/WSH/03.04/06.
- 11. Azoulay A, Garzon P. Eisenberg MJ. Comparison of the mineral content of tap water and bottled waters. *J Gen Intern Med* 2001; 16:168-175.
- 12. Laires MJ, Monteiro CP, Bicho M. Role of cellular magnesium in health and human disease. *_Front Biosci.* 2004; 9:262-76.
- Mildred S Seelig. Consequences of magnesium deficiency on the enlargement of stress reaction; preventive and therapeutic implications (a review). In *J Am Coll Nutr* 1994; 13:429-46 <u>http://www.mgwater.com/durwater.shtml</u>.
- 14. WHO meeting of experts on the possible protective effect of hard water against cardiovascular disease. Washington DC, USA. 27-28 April 2006. *Public Health and Environment, WHO Geneva* 2006. WHO/SDE/WSH/06,06.
- 15. Elin JR. Assessment of magnesium status. Clin Chem 1987; 33:1965-70.
- 16. Hans CP, Sialy R, Bansal DD. Magnesium deficiency in diabetes mellitus. *Current Science* 2002; 83:1456-63.
- 17. Blaudemans B, Wijist JVD, Scola RH et al. A missence mutation in the Kv 1.1 voltage-gated potassium channel-encoging gene KCNAI is linked to human autosomal dominant hypomagnesemia. *Joun Clin Invest* 2009, 119:936-942.
- 18. Boyd JC, Bruns DE, Wills MR. Frequency of hypomagnesaemia in hypokalaemic states. *Clinical Chemistry* 1983; 29:178-9.
- Chernow B, Bamberger S, Stoiko M, Mills S, Hoellerich V, warshaw AL. Hypomagnesaemia in patients in post operative intensive care. *Chest*.1989; 95:391-7. [Free Chest article].

- 20. WHO. Potential Health consequences of long term consumption of demineralized, remineralized and altered mineral content of drinking water. Nutrients in Drinking water-Chapter 1. *WHO* Geneva, 2005.
- 21. Atlas of heart disease and stroke: Deaths from coronary heart disease. *WHO* Sept, 2004. http://www.who.int/cardiovascular_diseases/en/cvd _atlas_13_coronaryHD.pdf
- 22. Durlach J, Bara M, Guiet-Bara A. Magnesium level in drinking water: its importance in cardiovascular risk. In: *Magnesium in Health and Disease*. Y Itokawa and J Durlach eds. John Libbey Press London, 1989; 173-82. <u>http://www.mgwater.com/durwater.shtml</u>.
- Rubenowitz E, Axelsson G, Rylander R. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 1996; 143: 456-62. [Free PMC article].
- Kousa A, Havulinna AS, Moltchanova E, Taskinen O, Nikkarinen M, Eriksson J et al. Calcium:magnesium ratio in local ground water and incidence of acute myocardial infarction in rural Finland. *Environ Health Perspective*. 2006; 114:730-34.
- 25. Durlach J, Bara M, Guiet-Bara A. Magnesium level in drinking water and cardiovascular risk factor: a hypothesis. *Magnes* 1985; 4:5-15. <u>http://www.mgwater.com/durwater.shtml</u>.
- 26. Altura BM, Altura BT. Magnesium and cardiovascular biology: an important link between cardiovascular risk factors and atherogenesis. *Cell Mol Biol Res* 1995; 41:347-59.
- Centers for Disease Control and Prevention. State– specific mortality from sudden cardiac death– United States. MMWR Morb Mortal Wkly Rep, 2002 / 51(06); 123-6. Available from www.cdc.gov/mmwr/preview/mmwrhtml/mm5106 a3.html last accessed 2010 May1
- 28. Mitchell C. Magnesium and acute myocardial infarction. *West J Med* 1991; 155:285. [Free PMC letter].
- 29. Anderson W, leRiche W H. Sudden death from ischemic heart disease in Ontario and its correlation with water hardness and other factors. *CMA journal* 1971; 105:155-160.

- 30. Shozo S, Hiroshi F, Kouki W et al. Magnesium deficiency in patients with recent myocardial infarction and coronary artery spasm. *Jpn Circ* J 2001; 65:643-48.
- Anderson TW, Neri LC, Schreiber GB, Talbot FDF, Zdrojewski A. Ischemic heart disease, water hardness and myocardial magnesium. C M A Journal 1975; 113:199-203. [Free PMC letter].
- 32. Johnson CJ, Peterson DR, Smith EK. Myocardial tissue concentration of magnesium and potassium in men dying suddenly from ischemic heart disease. *Am J Clin Nutr* 1979; 32: 967-70.
- Crawford T, Crawford M D. Prevalence and pathological changes of ischemic heart disease in hard water and in a soft water area. *The Lancet* 1967: 289:229-232. [Free PMC article].
- 34. Leurs LJ, Schouten LJ, Mons MN, Goldbohm RA, van den Brandt PA. Relation ship between tap water hardness and calcium concentration and mortality due to ischemic heart disease or stroke in the Netherlands. *Environ Health Perspect* 2010; 118:414-420.
- Marier JR, Neri LC. Quantifying the role of magnesium in the interrelationship between human mortality/morbidity and water hardness. *Magnes* 1985; 4:53-59. http://www.mgwater.com/quantif.shtml.
- 36. Haque WMM, Khan AR, Nazimuddin K, Musa AKM, Ahmad AKMS, Sarker RSC. Frequency of hypomagnesaemia in hospitalized diabetic hypokalaemic patients. *Journal Bangladesh College Physician Surgeon*. 2008; 26:15-18.
- 37. Walti MK, Zimmermann MB, Spinas GA, Hurrell RF. Low plasma magnesium in type 2 diabetes. *Swiss Med Wkly* 2003; 133:289-92. [Free Swiss Med Wkly article].
- 38. He K, Liu K, Daviglus ML et al. Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation* 2006; 113:1675-82 [Free Circulation article].
- 39. Takaya J, Yamato F, Kaneko K. Possible relationship between low birth weight and magnesium status: from the stand point of "fetal origin" hypothesis. *Magnes Res* 2006; 19:63-9.
- 40. Atlas of heart disease and stroke, Global burden of stroke. *WHO* Sept, 2004.

www.thefreelibrary.com/The+Atlas+of+heart+dise ase+and+stroke(HealthWatch)-a0133372976

- 41. Huang Y, Ren J. Cost benefit analysis of a community based stroke prevention program in Bao Shan District, Shanghai, China. *IJCRIMPH* 2010; 2:307-16.
- 42. Yang CY. Calcium and magnesium in drinking water and risk of death from cerebrovascular disease. *Stroke* 1998; 29:411-4. [Free Stroke article].
- 43. Ferrandez J, Abellan JJ, Gomez-Rubio V et al. Spatial analysis of the relationship between mortality from cardiovascular and cerebrovascular disease and drinking water hardness. *Environmental Health Perspective* 2004; 112:1037-44.
- 44. Kearney PM, Whlton M, Raynold K, Munther P, Whelton P, He Jiang. Global burden of hypertension: analysis world wide data. www.thelancet.com 2005; 365:217-22
- 45. Ragnar R, Arnaud. MJ. Mineral water intake reduces blood pressure among subjects with low urinary magnesium and calcium. *BMC Pub Health* 2004; 4: 56. [Free PMC article].
- 46. Kozisek F. Health significance of drinking water calcium and magnesium. National Institute of Public Health 2003; Prague; Czech Republic. www.midasspringwater.com/typed%20documents/ HealthSignificance.pdf
- 47. Lowik MRH, Groot EH, Binnerts WT. Magnesium and public health: the impact of drinking water. Annu Symp Proc Univ of Missouri. *Trace Substances in Environ Health* 1982; 16:189-95. <u>http://www.mgwater.com/quantif.shtml</u>.
- Fine KD, Santa ACA, Porter JL, Fordtran JS.. Intestinal absorption of magnesium from food and supplements. *J Clin Invest* 1991; 88:396-402. [Free JCI Article].
- 49. Hopps HC, Feder GL. Chemical qualities of water that contribute to human in a positive way. *The Science of the Total Environment* 1986; 54:207-16.
- 50. The process of Reverse Osmosis: Drinking water quality guidelines, <u>http://watertiger.net/RO/how_ro_works.htm</u>. Access on July3, 2010.

 Babaji I, Shashikiran NN, Reddy SVV. Comparative evaluation of trace elements and residual bacterial content of different brands of bottled waters. *Ind Soc Pedo Prev Dent* 2004; 22:201-4. ISSN0970-4388.