Detailed Report of Magnesium on Health

Overview

Magnesium plays a major role in biological functions within the body particularly in disease prevention and maintaining overall health. Several excellent reviews have been written on the role of Magnesium in health in disease and we recommend any interested reader to consult (Laires, Monteiro, and Bicho 2004) and (Musso 2009) for a general introduction to the topic. In brief, the academic literature broadly agrees on several clinical situations related to magnesium including: renal disease, hypertension, pre-eclampsia, diabetes mellitus, cardiac disease, and the administration of therapeutic drugs (Sanders, Huijgen HJ, and Sanders R 1999), though some specialists also include alcoholism, osteoporosis (Fatemi et al. 1991) atherosclerosis and asthma (Saris et al. 2000).

Acute Health Care
Magnesium enriched intravenous drips are widely used in acute clinical practice for its roles as a membrane stabilizer (making membranes less active) and as a muscle relaxant. In clinical settings, the onset of severe pre-eclampsia may be predicted by monitoring elevated ionized magnesium concentration. The Collaborative Eclampsia Trial provided compelling evidence in favor of the use of $MgSO_4$, rather than diazepam or phenytoin, in the treatment of eclampsia. Treatment of mothers with $MgSO_4$ before delivery may also reduce the risk of cerebral palsy and mental retardation in early preterm infants (Saris et al. 2000).

Chronic Conditions Effected by Magnesium

Magnesium deficiency is also associated with a number of chronic diseases. In renal disease moderate hypermagnesemia is often observed as the kidneys lower function reduces the bodies ability to control magnesium balance. In the case of high blood pressure and hypertension magnesium blood concentration may become lowered. Chronic low blood magnesium has an effect on the progression towards diabetes mellitus. Cardiac diseases are also generally correlated to diminished magnesium levels. For example serum magnesium levels drop during myocardial infarction heart attacks. There is a growing interest in studying the role of magnesium in colorectal disease and ostheoporosis.

Magnesium deficiency is not uncommon among the general population: its intake has decreased over the years especially in the western world (Saris et al. 2000). It is notable that the daily dietary intake of magnesium has decreased from an estimated 500 mg/d in the 1900s to 175 mg/d (below RDI). The decrease has been attributed to an increase in consumption of processed foods (Volpe 2013). A significant subclinical Magnesium deficiency has been widely reported many currently healthy elderly subjects (Gullestad et al.). Persons who live in soft water areas, who use diuretics, or who are predisposed to magnesium loss may require more dietary magnesium than would others (Klevay and Milne 2002).

In order to improve your daily intake of magnesium, good nutrition is important. Food sources rich in magnesium include unrefined whole grains, spinach, nuts, legumes, and white potatoes (Volpe 2013). Universal drinking water and beverages can contain moderate to high levels of magnesium (10–100 ppm) and it has been suggested that enhanced magnesium concentration is drinking water could potentially prevent 4.5 million heart disease and stroke deaths per year, worldwide (Rosanoff 2013). Among types of drinking water, mineral waters sourced in eastern Slovenia, around Rogaška Slatina, have long been known to contain significantly higher concentrations of Mg (1100 mg/L) than other mineral waters, making it one of, if not the most magnesium rich natural mineral water in the world.

Magnesium Adsorption

If mineral waters are considered as a potential source of Magnesium (Mg) Daily Recommended Intake (DRI), understanding of its adsorption from ingested solution is crucially important. Several scientific reports have focused on measuring the adsorption of Mg from mineral water, and though the conclusions are sometimes inconsistent, most agree that >40% of dissolved Mg content is adsorbed by the body. For example, in healthy young women, 50% of the magnesium from magnesium-rich mineral water was absorbed when consumed alone (Leskovar R. 1978). Magnesium bioavailability from mineral water is enhanced when the water is consumed with a meal, suggesting that not only the concentration of Mg, but also the overall diet and dietary habit affects Mg absorption. For example, high dietary fructose significantly increases magnesium balance during both low and high dietary magnesium intakes (Milne and Nielsen 2000). Magnesium retention is also significantly increased by consumption of the high protein diet, due to decreased fecal losses without being linked to changes in urinary excretion (Schwartz et al. 1973).

Another study further suggested that the consumption pattern, and the volume consumed per serving also influence Mg absorption. A study on the effect of serving volume and consumption pattern of artificial mineral water (AMW) and Mg concentration on Mg absorption concluded that Mg absorption from AMW decreases when the amount of Mg in each serving is increased. The authors suggest that frequent consumption is preferable for Mg rich mineral water when the total consumption of mineral water remains the same (Nakamura et al. 2012).

It has been clearly demonstrated by three studies in adults, reviewed (Ekmekcioglu C 2000), that Mg absorption is load-dependent. Thus, for the higher and lower Mg loads tested in those three studies, that is, 47, 41.7, 40.1 and 1.9, 0.3, 1.5 mmol; absorption was 23.7, 14, 11 and 75.8, 70, 65%, respectively (Graham LA, Ceasar JJ, and Burgen AS 1960; Roth P and Werner E 1979; Fine KD et al. 1991). Using a different method, a lower value of Mg absorption (45.7±4.6%) was found from an Mg-rich mineral water. (Sabatier M et al. 2002). It is notable that Mg absorption is also heavily dependent on the counter-ion used for administration and it has been demonstrated that organic salts of Mg have higher bioavailability than inorganic salts.

The current health authority recommendations for adult daily consumption of Mg specify the following RDI:

Age	Male	Female
19-30 years	400 mg	310 mg
31-50 years	420 mg	320 mg
51+ years	420 mg	320 mg

Magnesium intake correlates significantly with Magnesium balance. In order to reach zero balance, men must ingest 4.078 mg/Kg and women 4.287 mg/kg of a given BW/d (Body Weight/Day) (Nishimuta M et al. 2006). Interestingly, in 2006, another study suggested that neutral magnesium balance may still be achieved at intakes of 165 mg/d (Hunt and Johnson 2006). Others agree with the recommended dietary allowance of 320 mg/d and consider 130 mg too little (Klevay and Milne 2002). One should also be aware of calls to increase Mg intake to 6-10 mg/kg/day for young adults, and to twice that much for those undergoing active anabolism, or under stress (Seelig 1982), however no pubic health authority has not yet endorsed such a claim.

Other dietary components may also affect the dosage of minerals matabolised. It was found that even with a diet at moderate levels of refined cellulose resulted in increased excretion of both Calcium and Magnesium. (Slavin and Marlett 1980)

Magnesium in Health and Disease

In the following section a summary of key research findings on the effect of magnesium on promoting healthy living and disease prevention are summarized. While not exhaustive of the academic literature available, it is a tailored selection providing the salient components of healthcare practitioners current understanding of the benefits of a magnesium rich diet, in particular one supplemented with the regular drinking of magnesium rich mineral water.

Metabolic Syndrome

Metabolic syndrome diagnosis is a cluster of the most dangerous heart attack risk factors: diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure, which combined show a pattern of metabolic disorder.

Dietary magnesium intake is inversely associated with the prevalence of metabolic syndrome.(Dibaba et al. 2014) The meta-regression model showed a generally linear, inverse relationship between magnesium intake (mg/day) and metabolic syndrome. This dose-response meta-analysis indicates that dietary magnesium intake is significantly and inversely associated with the risk of metabolic syndrome. Treatment with magnesium supplementation (mean dose, 410 mg) was reported to significantly decrease blood pressure by 3–4 mmHg for systolic pressure and 2–3 mmHg for diastolic pressure, which is more evident at the higher dose (≥370 mg/day) (Ju et al. 2014).

Heart Disease (CVD)

A large meta-analysis of clinical studies report that there is a statistically significant correlation between increased dietary magnesium intake and a reduction in total Cardiovascular Disease (CVD) event risks (Xinhua Qu et al. 2013). Blood serum magnesium concentrations are linearly and inversely associated with the risk of total CVD events and the greatest risk reduction occurs when intake is increased from 150 to 400 mg/d (Xinhua Qu et al. 2013). Dietary magnesium intake is inversely associated with fatal Coronary Heart Disease (CHD) (Chiuve et al. 2013) and circulating and dietary magnesium are inversely associated with CVD risk (Del Gobbo et al. 2013). A different study in community-dwelling participants free of cardiovascular disease, self-reported magnesium intake (estimated by food frequency questionnaire) was inversely associated with arterial calcification, which may play a contributing role in magnesium's protective associations in stroke and fatal coronary heart disease (Hruby et al. 2014).

Lower blood serum magnesium levels, but not necessarily dietary magnesium is associated with a higher Atrial Fibrillation (AF) risk (Misialek et al. 2013). Higher magnesium intake is associated with reduced risk of total and ischaemic stroke (Nie et al. 2013) Although studies of the effects of magnesium on blood pressure are not always in agreement. For example, one study detected dose-dependent BP reductions from magnesium supplementation, namely for each 10 mmol/day increase in magnesium dose, reductions of 4.3 mm Hg systolic BP and of 2.3 mm Hg diastolic BP were observed (Jee et al. 2002), corroborated with results of Kass who reported a decrease in SBP of 3 - 4 mm Hg and DBP of 2 - 3 mm Hg,

which further increased with crossover designed trials and a dietary Mg intake of >370 mg/day. (Kass, Weekes, and Carpenter 2012). A study by Mizushima confirms these findings (Mizushima et al. 1998). Indeed, many patients with high blood pressure will be treated with agents that cause hypomagnesemia due to increased urinary loss (loop and thiazide diuretics). Most of the clinical situations show hypomagnesemia due to renal loss, with the exception of renal disease (Sanders, Huijgen HJ, and Sanders R 1999).

Interestingly, a different set of studies found no direct beneficial effect of magnesium supplements on blood pressure (E. Cosaro et al. 2014), which was confirmed by another study which reported that "the evidence in favour of a causal association between magnesium supplementation and blood pressure reduction is weak" (Dickinson et al. 2006). Further studies on causal links between magnesium blood serum levels and dietary intake may clarify the nature of correlations reported elsewhere.

Type 2 Diabetes (Diabetes Mellitus)

Diabetes is an important part of the metabolic syndrome. Magnesium deficiency has been associated with chronic diseases, amongst them, diabetes mellitus. Epidemiological studies have shown low levels of magnesium ingestion in the general population, as well as a relation between the ingestion of food rich in magnesium and the reduction of diabetes installation and its complications (Sales and Pedrosa 2006). Hypomagnesemia is frequently present in diabetic patients, however there is not an exact elucidation of the mechanism of magnesium deficiency in diabetes mellitus. Supplementation with magnesium has been suggested in patients with diabetes mellitus who have proven hypomagnesemia (Sales and Pedrosa 2006).

Increased magnesium intake has been found to be statistically significantly correlated with a reduced risk of type 2 diabetes in a dose-response manner.(Wysham and Kirkman 2011) That is to say, the greater your magnesium dietary intake above peer group, the less likely you are to be afflicted by Type 2 diabetes. The fact that magnesium intake reduced diabetes risk and, may be due to its strong correlation with fiber, which may explain the protective effect of fiber.(Hopping et al. 2009) Dietary intake of magnesium was associated with a reduced risk of type 2 diabetes in Japanese populations, also known for high fiber.(Kirii et al. 2010) Although a small effect cannot be excluded, another study reported only a small effect in more target group of Japanese men at risk of type II diabetes.(Nanri et al. 2010) Magnesium intake was inversely associated with incidence of diabetes. The potential beneficial effects of magnesium intake on the risk of diabetes may be explained by the favorable effects of magnesium on systemic inflammation and insulin resistance.(Kim et al. 2010) In a more recent study Hruby and co-workers reported, consistent with other studies, a higher magnesium intake was associated with lower fasting glucose and insulin.(Hruby et al. 2013) Findings support a protective role of higher intake of magnesium (430 mg/day) in reducing the risk of developing type 2 diabetes, especially in overweight women (Song et al. 2004).

In conclusion, consumption of magnesium-rich foods such as whole grains, beans, nuts, and green leafy vegetables may reduce the risk of type 2 diabetes. (Larsson and Wolk

2007)(Lopez-Ridaura et al. 2004) In particular, Magnesium supplementation or increased intake of magnesium-rich foods and water may be an important tool in the prevention of type 2 diabetes in obese children (Dickerson et al. 2004).

Obesity

Dietary magnesium intake has been favorably associated with better metabolic outcomes in overweight individuals. Chacko and co-workers set out to examined the effects of oral magnesium supplementation on metabolic biomarkers and global genomic and proteomic profiling in observational studies. They undertook a randomized, crossover, pilot trial in 14 healthy, overweight volunteers who were randomly assigned to receive magnesium citrate (500 mg elemental Mg/d) or a placebo for a 4 week period. Biochemical assays were conducted on blood and urine specimens. They observed that magnesium treatment significantly decreased fasting C-peptide concentrations and appeared to decrease fasting insulin concentrations, however no consistent patterns were observed across inflammatory biomarkers. Gene expression profiling revealed up-regulation of 24 genes and down-regulation of 36 genes including genes related to metabolic and inflammatory pathways such as C1q and tumor necrosis factor-related protein 9 (C1QTNF9) and pro-platelet basic protein (PPBP). It was concluded that magnesium supplementation over a four week period in overweight individuals led to distinct changes in gene expression and proteomic profiling when compared to a placebo group indicating favorable effects of magnesium supplementation on several metabolic pathways (Chacko et al. 2011).

Colorectal disease

Daily consumption of a natural mineral water rich in magnesium sulphate and sodium sulphate improved bowel movement frequency and stool consistency in subjects with functional constipation. Moreover, the subjects' health-related quality of life improved. (Bothe, Coh, and Auinger 2015). Excess magnesium is not associated with other health risks as it is most commonly excreted by the kidneys (Musso 2009) however higher intakes of magnesium mineral salts in the digestive tract stimulate gastric mobility by promoting osmotic activity, having a diuretic effect on the bowels, which may lead to diarrea or other laxative effects.

A higher magnesium intake seems to be associated with a modest reduction in the risk of some cancers, in particular, colon cancer.(Chen, Pang, and Liu 2012) Qu and co-workers report that dietary magnesium intake has a statistically significant nonlinear correlation with reduced risk of colorectal cancer. The greatest reduction for magnesium intake was found above 200-270 mg/day (X Qu et al. 2013).

Bone Mineralization

Bone mineralization is the human bodies natural process to maintain the strength and hardness of the skeleton. It is a carefully controlled process which can be effected by poor nutrition, in particular if there is an excess or lack of mineral nutrients including calcium and magnesium. A reduced magnesium intake (<206.5 mg Mg/d) was found to be associated

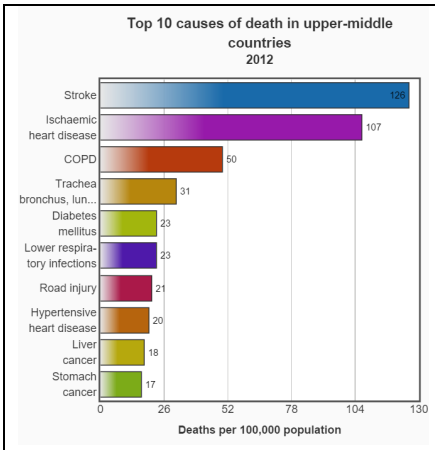
with a lower bone mineral density (BMD) of the hip and whole body compared to high intake (>422.5 mg/d), but this result does not translate into increased risk of fractures. (Orchard et al. 2014) The effect of an increased magnesium intake appears to depend on the person taking it. Ryder and co-workers reported that higher magnesium intake was shown to be correlated with a higher BMD in both men and women. (Ryder et al. 2005) However and earlier studies have shown that increasing the mean magnesium intake in healthy young adults above the usual dietary intake does not affect blood pressure or the rate of bone turnover, (Doyle, Flynn, and Cashman 1999) perhaps due to efficient renal excretion. Doubling magnesium intake increased urinary excretion of Mg by 36% and erythrocyte Mg content by 5% but had no effect on serum Mg, Ca, or bone-specific alkaline phosphatase biomarkers of bone formation, urinary pyridinium crosslinks of collagen biomarkers of bone reabsorption, or on blood pressure. (Doyle, Flynn, and Cashman 1999) It is possible that the form of Mg salt ingested gives rise to this study dependant results. For example magnesium oxide (MgO) treatment (with 300 mg elemental Mg per day in two divided doses) showed a positive effect on integrated hip bone mineral content on a children's growth study conducted in healthy young girls (8-14 years) (Carpenter et al. 2006)

Sport enhancement

An update on the relationship between magnesium and exercise has been provided by Nielsen and co-workers.(Nielsen and Lukaski 2006) At 27 degrees C, sweat sodium, potassium, calcium, magnesium (1265 ng/mL), and copper remained similar to baseline over 7 h of exercise-heat stress (Montain, Cheuvront SN, and Lukaski HC 2007).

Conclusions

According to the World Health Organization the top ten causes of human mortality are diseases which have a causal correlation to magnesium deficiency in both the diet and blood serum levels. Maintaining a healthy magnesium balance, particular through ensuring that daily recommended intakes of magnesium are achieved may have a significant impact on human health outcomes. Drinking magnesium rich mineral water provides an easy solution to ensure adequate nutritional load of magnesium for a healthy life. Although a number of studies have already demonstrated the correlation between a healthy daily intake of magnesium, further studies are warranted to expand the knowledge base and broaden the impact of magnesium on health.



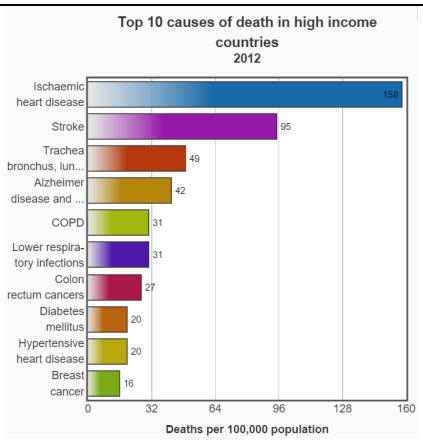


Figure 1: The 10 leading causes of death by* country *income group (for 2012), as reported by World Health Organization. Source: http://www.who.int/mediacentre/factsheets