Magnesium

Magnesium		Women	Men	Children		
	mg/d			2-5 y	6-9 y	10-13 y
Recommended intake	RI	280	350	120	200	280
Average requirement	AR	-	-			
Lower level of intake	LI	-	-			
Upper level of intake	UL	-	-			

Introduction

Magnesium is a divalent ion and is involved in a range of biochemical reactions and cellular functions. The metabolism of and requirement for magnesium are still rather poorly understood.

Dietary sources and intake

Magnesium is found in abundance in green, leafy vegetables, legumes and whole grain cereals. Concentrations are especially high in dark chocolate, nuts and coffee. 'Hard' water contains more magnesium than 'soft' water and may contribute to total magnesium intake. The intake of magnesium according to the most recent dietary surveys in the Nordic countries can be seen in chapter XX Dietary intake in Nordic countries.

Physiology and metabolism

The body content of magnesium is regulated via absorption and excretion. At normal dietary intakes 20-60 % is absorbed, being inversely proportional to the amount of magnesium ingested (Lakshmanan et al 1984; Schwartz R et al 1984). It is uncertain to what degree the composition of the diet influences absorption (Coudray et al. 2003). Plasma concentrations are probably regulated via the kidneys and are kept within a narrow range (0.75-0.95 mmol/litre). At low magnesium intakes, kidney excretion is reduced.

A large number of biochemical and physiological processes are regulated by magnesium. Magnesium is necessary for energy dependent membrane transport, gene regulation, sustained electrical potential in nerves and cell membranes and for transmission of neuro-muscular impulses.

The total body content of magnesium in an adult is estimated to be 20-28 g, 40- 45 % being intracellular in muscles and soft tissue, 1 % extracellular and the rest in the skeleton. Although we do not have a true storage organ for magnesium, approximately one-third of

skeletal magnesium is in equilibrium with plasma levels and functions as a buffer to maintain extracellular magnesium concentrations.

Magnesium depletion is very unusual in the absence of dietary restriction or some disorder causing magnesium loss from the body. Magnesium depletion is usually secondary to another disease process or to a therapeutic agent. The physiological manifestations of severe magnesium depletion are the following: hypokalaemia and hypercalcaemia, neuromuscular hyperexcitability, electrocardiographic abnormalities and cardiac arrhythmias. Adverse heart rhythm changes where observed after 78 days of magnesium depletion with an intake of 101 mg magnesium/day (Nielsen et al. 2007).

Therapeutic use of magnesium in heart arrhythmia conditions (Kalus et al 2003 Dittrich et al 2003, Kiziltepe et al 2003) and to reduce the risk of eclampsia in women with pre-eclampsia (Duley et al 2003, Livingston et al 2003, Belfort et al 2003; Altman et al 2002) has received wide scientific attention in recent years. The neuroprotective role for antenatal magnesium sulphate therapy given to women at risk of preterm birth for the preterm foetus has also been established (Doyle et al. 2009). However, no studies have so far been conducted to show a preventive potential of high versus low-magnesium diets in relation to reducing the risk of these conditions in the general population.

Requirement and recommended intake

Magnesium research has for years been hampered by the lack of good biomarkers of body status (Witkowski et al. 2011). At present, useful data that could contribute to the development of evidence-based dietary recommendations is limited, especially for specific vulnerable population groups, such as infants, children and adolescents, pregnant women and the elderly (Witkowski et al. 2011). Epidemiological studies have reported a relationship between low magnesium intake and increased risk of cardiovascular disease, hypertension, stroke, colorectal tumor risk, obesity and type 2 diabetes (Zhang et al. 2012, Houston M 2011, Larson et al. 2012, Wark et al. 2012, Bo et al. 2006, Song et al. 2005, He et al. 2006, Ford et al. 2007, McKeown et al. 2008, Chacko et al. 2010, Larsson et al. 2007). However, at present the results are difficult to interpret as it is not possible to tell whether the observed associations are primarily attributable to magnesium intake itself or other constituents of magnesium-rich food, i.e. whole grains, beans, nuts and green leafy vegetables. High quality RCT's in the area are scarce (Witkowski et al. 2011).

Adults. In the absence of functional indicators of magnesium status, the only basis we have for evaluating requirements are balance studies. As absorption of magnesium varies with the dietary intake and it seems possible to adapt to a low intake through more effective absorption. The USA Food and Nutrition Board (1997) set an Estimated Average Requirement (EAR) for magnesium of 255 mg/day for women and 330 mg/day for men aged 19-30 years. RDA (Recommended Dietary Allowance) is accordingly 310 and 400 mg/day for women and men respectively. The values are slightly higher for the age group 31-70 years: RDA for women is set at 320 mg/day and for men 420 mg/day.
Data from 27 balance studies where pooled by Hunt and Johnson in 2006 at the US department of Agriculture, and they suggested that the previously estimated EAR by the USA Food and Nutrition Board might have been too high. Neutral magnesium balance was predicted at a magnesium intake of 165 mg/day. Neither age nor sex affected the relation between magnesium intake and output (Hunt & Johnson 2006). Data were reported for adults only.

The EU Scientific Committee for Food (1993) considered 150-500 mg/d to an acceptable range of magnesium intake, based on observed intakes.

The Nordic Recommendations of 2004 recommended 350 and 280 mg magnesium/day for men and women (including pregnant and lactating women) respectively. There are no substantial new data since then indicating that these values should be changed (Hunt & Johnson 2006, Witkowski et al. 2011, Brown et al. 2012).

Infants and children. The magnesium content in human milk is 23-47 mg/L (Brown et al 2012). The concentration of magnesium in human milk is relatively constant the first 12 months of lactation (Dorea 2000). For children the RI values from 2004 are maintained (NNR2004).

Upper intake levels and toxicity

An excessive magnesium intake (0.5-5 g) gives diarrhoea, but otherwise no negative symptoms when kidney function is normal.

The USA Food and Nutrition Board (1997) has set a Tolerable Upper Intake level of 350 mg/day from supplements. This level is based on lowest observed adverse effect levels. The EU Scientific Committee for Food (2001) has derived a level of 250 mg magnesium per day based on similar data. The UL does not include magnesium normally present in foods and beverages.

References

Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, Smith D; Magpie Trial Collaboration Group: Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002; 359: 1877-90.

Belfort MA, Anthony J, Saade GR et al. A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. N Engl J Med 2003; 348: 304-11.

Bo S, Durazzo M, Guidi S, Carello M, Sacerdote C, Silli B, Rosato R, Cassader M, Gentile L, Pagano G. Dietary magnesium and fiber intakes and inflammatory and metabolic indicators in middle-aged subjects from a population-based cohort. Am J Clin Nutr 2006; 84: 1062-9.

Brown T, Mullee A, Collings R, Harvey L, Hooper L, Fairweather-Trait S. Literature search and review related to specific preparatory work in the establishment of Dietary Reference Values. Preparation of an evidence report identifying health outcomes upon which Dietary Reference Values could potentially be based for magnesium, potassium and fluoride. Scientific report submitted to EFSA 2012.

Chacko SA, Song Y, Nathan L, Tinker L, de Boer IH, Tylavsky F, Wallace R, Liu S. Relations of dietary magnesium intake to biomarkers of inflammation and endothelial dysfunction in an ethnically diverse cohort of postmenopausal women. Diabetes Care 2010; 33: 304-10.

Coudray C, Demigné C, Rayssiguier Y.Effects of dietary fibers on magnesium absorption in animals and humans. J Nutr. 2003 Jan;133(1):1-4.

Dittrich S, Germanakis J, Dahnert I et al. Randomised trial on the influence of continuous magnesium infusion on arrhythmias following cardiopulmonary bypass surgery for congenital heart disease. Intensive Care Med 2003; 29: 1141-4.

Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D.Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD004661.

Dorea JG. Magnesium in human milk. J Am Coll Nutr 2000; 19: 210-9.

Duley L, Gulmezoglu AM, Henderson-Smart DJ. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database Syst Rev 2003; CD000025.

Food and Nutrition Board, Institute of Medicine. Dietary reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington DC: National Academy Press, 1997.

Ford ES, Li C, McGuire LC, Mokdad AH, Liu S. Intake of dietary magnesium and the prevalence of the metabolic syndrome among U.S. adults. Obesity (Silver Spring) 2007; 15: 1139-46.

He K, Liu K, Daviglus ML, Morris SJ, Loria CM, Van Horn L, Jacobs Jr. DR, Savage PJ. Magnesium intake and incidence of metabolic syndrome among young adults. Circulation 2006; 113: 1675-82.

Houston M. The role of magnesium in hypertension and cardiovascular disease. J Clin Hypertens (Greenwich). 2011 Nov;13(11):843-7.
http://www.ncbi.nlm.nih.gov/pubmed/22051430

Kalus JS, Spencer AP, Tsikouris JP et al. Impact of prophylactic i.v. magnesium on the efficacy of ibutilide for conversion of atrial fibrillation or flutter. Am J Health Syst Pharm 2003; 60: 2308-12.

Kiziltepe U, Eyileten ZB, Sirlak M et al. Antiarrhythmic effect of magnesium sulfate after open heart surgery: effect of blood levels. Int J Cardiol 2003; 89: 153-8.

Lakshmanan FL, Rao RB, Kim WW et al. Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. Am J Clin Nutr 1984; 40: 1380-9.

Larsson, S. C. and A. Wolk (2007). "Magnesium intake and risk of type 2 diabetes: a meta-analysis." J Intern Med **262**(2): 208-214.

Larsson SC, Orsini N, Wolk A. Dietary magnesium intake and risk of stroke: a meta-analysis of prospective studies. Am J Clin Nutr. 2012 Feb;95(2):362-6.
http://www.ncbi.nlm.nih.gov/pubmed/22205313

Livingston JC, Livingston LW, Ramsey R et al. Magnesium sulfate in women with mild preeclampsia: a randomized controlled trial. Obstet Gynecol 2003; 101: 217-20.

McKeown NM, Jacques PF, Zhang XL, Juan W, Sahyoun NR. Dietary magnesium intake is related to metabolic syndrome in older Americans. Eur J Nutr 2008; 47: 210-6.

Nielsen FH, Milne DB, Klevay LM, Gallagher S, Johnson L. Dietary magnesium deficiency induces heart rhythm changes, impairs glucose tolerance, and decreases serum cholesterol in post menopausal women. J Am Coll Nutr 2007; 26: 121-32.

Reports of the Scientific Committee for Food. Nutrient and energy intakes for the European Community. Luxembourg: Commission of the European Communities, 1993.

Schwartz R, Spencer H, Welsh JJ. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable 26Mg. Am J Clin Nutr 1984; 39: 571-6

Scientific Committee on Food. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Magnesium. Expressed on 26 September 2001

Song Y, Ridker PM, Manson JE, Cook NR, Buring JE, Liu S. Magnesium intake, C-reactive protein, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. Diabetes Care 2005; 28: 1438-44.

Wark et al. Magnesium intake and colorectal tumor risk: a case-control study and meta-analysis. Am J Clin Nutr 2012
http://www.ajcn.org/content/96/3/622.abstract?sid=7e9af939-308b-4d65-82a5-78ed2dd0d2aa

Zhang W, Iso H, Ohira T, Date C, Tamakoshi A; JACC Study Group. Associations of dietary magnesium intake with mortality from cardiovascular disease: the JACC study. Atherosclerosis. 2012 Apr;221(2):587-95. http://www.ncbi.nlm.nih.gov/pubmed/22341866