Magnesium

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Related nutrients/biomarkers: calcium, potassium, sodium, vitamin D

Importance of magnesium for health

Magnesium is an essential nutrient involved in many key physiological reactions. The typical adult body contains around 25 g magnesium, most of which is found in bone (50-60%), the remaining fraction in soft tissue of the skeleton, cardiac and smooth muscle (1, 2). One third of the fraction in bone is exchangeable and may provide a reservoir to maintain homeostasis of extracellular magnesium (3), which accounts for around 1% of total body magnesium (4, 5). Less than 0.3% of total body magnesium is present in serum (6). Serum magnesium is made up of three fractions: 5-15% in mineral complexes (phosphate, citrate, bicarbonate, sulphate), 20-30% bound to proteins, and 55-70% as free, ionised magnesium (6). Ionised magnesium has the greatest biological activity (3, 6), though it is not measured routinely.

Magnesium is a co-factor for over 300 enzyme reactions (2, 3, 6), including in key reactions of glycolysis, where it is required for the activity of hexokinase and the transfer of a phosphoryl group from ATP to a six-carbon sugar such as glucose, and directly as an enzyme activator (7).

Magnesium regulates the outward movement of potassium in myocardial cells (8); arrhythmias seen in magnesium deficiency may be due to a resulting dysfunction of this mechanism (5). Further, magnesium blocks the action of calcium in smooth muscle promoting its relaxation (9); thus conditions of magnesium depletion may result in coronary and cerebral vasospasms, myocardial infarction and hypertension (5, 6).

Dietary sources of magnesium

Magnesium is the central part of the chlorophyll molecule, and is thus present in green leafy vegetables. Other good sources of dietary magnesium include nuts, seeds and unprocessed cereals, whereas legumes, fruits, meat and fish supply intermediate levels of magnesium, and dairy foods are generally poor sources of dietary magnesium (10).

Magnesium is also present in drinking water in variable quantities, depending on the hardness of the water (11), with harder water having the higher concentration of dissolved magnesium salts (5). Omission of water magnesium content in intake estimations may lead to an underestimation in total magnesium intake (5).

Poor magnesium intakes are especially prevalent in elderly populations due to a lower calorific consumption and changes in magnesium metabolism with ageing (5). Furthermore, food processing reduces the integral magnesium content of a food (10) and with dietary changes in many populations shifting towards an increased consumption of processed foods, populations, or population sub-groups, may be at increased risk of the development of chronic latent deficiency (2, 3, 6, 12). Populations consuming a diet with a high phytic acid content may be at risk of a lower intake of magnesium due to the chelation of magnesium ions with phytate (13), though a deficiency in iron, calcium or zinc is more widely reported in the literature.

Public health risks associated with magnesium deficiency

Hypomagnesaemia, a deficiency in magnesium, is associated with an elevated risk for several non-communicable chronic diseases (NCDs) including metabolic syndrome, type II diabetes mellitus, atherosclerosis, hypertension, myocardial infarction, arrhythmia, hyperlipidaemia, premenstrual syndrome, osteoporosis (1, 5, 6, 9, 10, 14), and psychiatric disorders (6), including Alzheimer's disease and attention deficit hyperactivity disorder (ADHD) (15).

Approximately 40% of patients with hypomagnesaemia will have coexisting hypokalaemia (1), and hypocalcaemia may also be present (6).

Secondary data analysis of NHANES 2001-2010 data showed that a higher intake of magnesium (from diet and supplements) was associated with a significantly lower odds ratio for the development of metabolic syndrome, overweight and obesity, elevated systolic blood pressure, a

reduction in HDL cholesterol and an elevated C-reactive protein (16). Magnesium as a therapeutic agent has been described in pre-eclampsia and certain forms of arrhythmia (14), and in migraine headaches and asthma (15), though more data are needed to confirm clinical indication.

Magnesium in excess

Hypermagnesaemia is rare in healthy subjects, however may occur in hospitalised patients, usually with renal disease, or due to an error in total parenteral nutrition, or in elderly subjects with compromised renal function and a concomitant high magnesium intake (e.g. in laxatives or antacids) (6).

Human biomarkers of population magnesium intakes

Since almost all body magnesium is split between bone and soft tissue, magnesium status is physiologically difficult to measure. Possible methods for magnesium analysis have been described in several reviews: (12) (2) (17)

Serum magnesium

Serum magnesium is the most available and most commonly-used assay in clinical practice for the determination of magnesium status in normal subjects or those with pathologies that could lead to increased magnesium excretion (2, 5, 12). Serum magnesium can also be used to investigate hypermagnesaemia, however must be creatinine-corrected, thereby needing measurement of serum creatinine (for more information, see http://www.acb.org.uk/docs/default-source/committees/scientific/amalc/magnesium.pdf for more details).

Reference values for serum magnesium concentration have been determined for the US population using NHANES I data (5), however confounding factors may indicate that these reference values do not apply to other populations. For more information on confounding factors, see below.

Serum magnesium concentration is not considered as representative of true magnesium status (2, 3, 5, 6) due uncertainty over equilibration and homeostatic mechanisms regulating magnesium between body pools, thus serum magnesium may not reflect total body stores. Serum magnesium concentrations have been measured in previous national surveys, e.g. the US NHANES (NHANES I only) and UK NDNS publications.

Method

The reference method for magnesium assessment is Atomic Absorption Spectrometry (AAS).

Urine / Serum / Plasma are routinely measured photometrically in the clinical setting using automated clinical chemistry analysers. Reagents contain a metalochromatic indicator such as; calmagite, xylidil blue or magon, chlorophosphonazo III and arsenazol.

Inductively-coupled plasma mass spectrometry (ICP-MS) and inductively-coupled plasma optical emission spectroscopy (ICP-OES) methods have also been developed (18, 19), including measurement from dried blood spots (18).

Considerations for serum/plasma magnesium assessment from the Association for Clinical Biochemistry (http://www.acb.org.uk), are available to download here: http://www.acb.org.uk/docs/default-source/committees/scientific/amalc/magnesium.pdf

Other methods

Erythrocyte magnesium

The concentration of magnesium in erthyocytes is approximately three-fold that of serum. The measurement of erythrocyte magnesium may better reflect longer term magnesium status due to the lifespan of erthrocytes in the circulation.

24 h urine magnesium excretion

This assay measures magnesium wasting via the kidney. This assay is not strictly an assessment of magnesium intake or status (2), rather, it is used to assess the effects of medication, physiological status or disease on magnesium status (6) (see confounding factors). A 24 h sample is critical for this assay due to the circadian rhythm of magnesium excretion (maximal excretion occurs at night) (6). A high concentration of excreted magnesium indicates that a patient is losing magnesium via the kidney, whereas a low excretion suggests an inadequate intake or absorption. It is recommended that urine samples are acidified to prevent precipitation of magnesium complexes.

Flame AAS on hair or nails

Hair and nail magnesium has been measured in some studies (e.g. (20-22), though this method and guidelines on interpretation of results require further validation (12).

ICP-AES has also been used to measure metals, including magnesium, in nail samples in workers with routine exposure to metals. See the SOP from CDC for more details.

https://www.cdc.gov/niosh/docs/2014-151/pdfs/methods/8200.pdf

Magnesium retention test

Magnesium retention test or loading test, is considered by some as the best assessment of individual magnesium status (12). It involves the oral or intravenous administration of magnesium and the measurement of magnesium excretion in the urine. If bone magnesium stores are normal, the individual being tested will not retain a significant amount of the administered magnesium. On the other hand, if the individual is magnesium-deficient, and bone stores are inadequate, part of the administered magnesium will be retained and not excreted. This technique is restricted to a clinical or research setting, and requires trained staff and controlled conditions (12). The test also assumes normal kidney function and is not suitable for use in children.

Ionized serum magnesium

Ionized serum magnesium is the active fraction of circulating magnesium, and can be assessed by ion-selective electrode. However, the clinical value of this assay is not established (1), and is reserved for a research setting.

Quality Control and Technical Assistance

Quality Control

The National Institute of Standards and Technology produces Standard Reference Material (SRM) for magnesium assessment.

Sample stability

Blood samples should be collected in metal-free blood collection tubes. Serum is preferred over zinc-free heparinised plasma but all other anti-coagulants should be avoided. High concentrations of magnesium are found in RBCs therefore blood samples should be centrifuged within an hour to avoid artificially increasing magnesium concentration via cellular leakage. Haemolysed samples may give rise to falsely elevated readings for the same reason.

Magnesium in serum is stable for several days if refrigerated (23).

Confounding factors

Though malnutrition is a primary cause of hypomagnesaemia, certain pathologies or lifestyles can influence population survey results. By affecting the absorption of magnesium from the gastrointestinal tract, such conditions increase the probability for magnesium wasting via the kidney (excretion in urine). In turn, this promotes a loss of magnesium from bone to maintain the serum magnesium concentration. Under these conditions, the serum magnesium concentration may give a false indication of magnesium status. Such conditions include chronic diarrhoea and other malabsorption disorders e.g. Crohn's disease (12), diabetes mellitus, chronic alcoholism, renal tube disorders, hypercalcaemia, hyperthyroidism (6, 10) or genetic disorders (4). Severe illness may also cause altered magnesium compartmentalisation between body pools, thereby influencing magnesium excretion (6, 10) and older subjects are at a higher risk of inadequate magnesium intakes (12), due to a lower intake than the general population, and a decreased absorption seen with age (5), which may influence population data. Persons with extreme levels of activity, such as athletes, may show abnormal values of magnesium, depending on the assay used (5).

Further, certain drugs that can influence magnesium excretion, including aminoglycosides (e.g. streptomycin, gentamycin), cisplatin, digoxin, loop diuretics (e.g. furosemide), omeprazole, amphotericin B and cyclosporine (6). In population studies, individuals under therapy with such agents should not be sampled.

Laboratory accreditation

For laboratory accreditation, validation and details on availability of proficiency testing, please see the OpeN-Global page on Laboratory accreditation.

Technical assistance

For questions on methods of magnesium assessment or for technical assistance, please contact the OpeN-Global team at https://open-global.kcl.ac.uk/contact/

Useful links

US Institute of Medicine. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride: https://www.ncbi.nlm.nih.gov/books/NBK109816/

NIH Factsheet for Health Professionals: Magnesium: https://ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/

Further reading

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