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Magnesium in developmental age. Principles of supplementation

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ABSTRACT

Magnesium is one of the mineral elements essential for proper growth and functioning of the human body. It participates in nerve and muscle function, cardiac excitability, maintenance of normal arterial blood pressure, bone integrity, and glucose–insulin metabolism. Magnesium deficiency is associated not only with disturbances in morphological growth and intellectual maturation of children and adolescents but also with later development of many chronic diseases, including migraine, cardiovascular events (myocardial infarction, stroke), arterial hypertension, type 2 diabetes, and increased susceptibility to the adverse effects of stress. States of normo-, hyper and hypomagnesemia were analyzed in the context of the above mentioned disease entities occurring in developmental age. Because meeting daily magnesium requirements from a typical European diet is often difficult, the rationale for supplementation with appropriate galenic forms of this mineral was considered. This applies to all age groups but primarily to children and adolescents during development, with regard to the physical and intellectual maturation noted above. The paper also reviews selected studies on magnesium and chronic diseases, dietary sources of magnesium and supplementation options. The expert analysis supports the conclusion that Mg supplementation is advisable, especially during developmental age.

KEY WORDS: magnesium, children, adolescents, adults, magnesium deficiency, supplementation.

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INTRODUCTION

This review, based on available literature, addresses magnesium – a natural and major mineral element in the body. Magnesium (Mg, Latin *magnesium*) is a divalent element from the alkaline-earth metals (group 2 of the periodic table). It is widespread in nature; three stable natural isotopes occur and radioactive isotopes also exist. Magnesium was first recognized as an element by Joseph Black (1755) and isolated in pure form in 1808 by Humphry Davy, who gave it its Latin name; the Polish name was proposed by Filip Neriusz Walter. In the earth's crust Mg occurs as magnesium oxide and ranks eighth among elements, while in seawater Mg occurs as salts and is the third most abundant element [1].

Mineral elements are exogenous elements that remain after tissue combustion and are essential nutrients that must be supplied regularly with food. An element is considered essential when deficiency symptoms appear

on a deficient diet or when its metabolic function is established. The human body comprises about 60 elements, which constitute roughly 4% of adult body mass. Depending on body content and recommended intake, minerals are classified as macro-, micro- and ultratrace elements. Macrominerals are present at > 0.01% of dry mass and have recommended intakes > 100 mg/person/day; these include Ca, P, Mg, Na, K (nutritionally important), S, Cl and the major elements C, H, O, N [2].

An adult contains approximately 20–35 g of magnesium, mostly deposited in bone (~60%) and in muscle and soft tissues (~39%); only about 1% is extracellular, including ~100 mg in blood. Therefore, low serum magnesium does not necessarily indicate whole-body deficiency, which may exist despite normal serum Mg. Normal serum magnesium is usually reported as 0.75–0.95 mmol/l (1.8–2.3 mg/dl) or in a wider range 0.65–1.25 mmol/l [3]. Approximately 55–70% of Mg is ionized; the remainder is

protein-bound (mainly to albumin). The ionized fraction constitutes the active, exchangeable pool.

ROLE OF MAGNESIUM IN THE BODY

Mg²⁺ is an essential mineral and, alongside potassium, the principal intracellular cation. As a cofactor for some 300 (by some estimates up to 600) enzymes, magnesium participates in numerous physiological processes: protein biosynthesis, nerve conduction, muscle contractility, thermoregulation, systemic and bone mineral metabolism, and regulation of arterial blood pressure [4]. Mg²⁺ ions regulate muscle contraction and neuromuscular transmission, acting antagonistically to calcium; as an ATP cofactor, magnesium is directly involved in ATP production and storage [5]. Severe or chronic magnesium deficiency is often associated with increased neuromuscular excitability (tremor, muscle cramps, tetany, generalized seizures) [5].

Magnesium slows aging processes, has anti-allergic properties and protects against eczematous skin lesions. It stabilizes cell membranes, reducing their propensity for inflammation, and participates in homeostasis of other minerals (Na, K, Ca). It is directly involved in ATP and glucose metabolism and, by forming complexes with membrane phospholipids, contributes to membrane stability and permeability. Even small changes in Mg²⁺ availability may disrupt intracellular signaling and membrane transport processes [6]. In children and adolescents (during growth) and in older adults (osteopenia, osteoporosis), magnesium stimulates osteoblast activity, activates phosphatases involved in bone formation and is incorporated into inorganic bone compounds that increase resistance to fracture [7]. Interventional data support beneficial effects of supplementation on bone mineral content and density: in a randomized, blinded trial of 120 girls aged 8-14 with baseline Mg intake < 220 mg/day, 300 mg/day oral Mg for one year increased bone mineral content (BMC) in hip, femoral neck and lumbar spine [8]. Stendig-Lindberg *et al.* [9] reported that 750 mg/day Mg for 6 months followed by 250 mg/day for 18 months increased bone mineral density (BMD) at 12 months in osteoporotic patients.

RECOMMENDED INTAKE BY AGE AND SPECIAL CONDITIONS

Daily magnesium requirements depend on age, sex and health status. Example ranges: infants and children 30-410 mg/day; adults – women 310-320 mg/day, men 400-420 mg/day. Intake standards were established as adequate intake (AI) for infants and as estimated average requirement (EAR) and recommended dietary allowance (RDA) for other age groups.

Selected intake standards [10]:

Neonates and infants (AI): 0-0.5 year – 30 mg; 0.5-1 year – 70 mg.

Population surveys indicate widespread inadequate intake: up to 75% of US residents consume insufficient

magnesium [11]. French studies from 1997 and 2019 reported high proportions with inadequate intake (1997: 77% women, 72% men; 2019: 52% women, 53% men), [12]. The WOBASZ II study found adequate Mg intake in only 28.8% of Poles, with particularly low intake among women aged 20-34 [13]. French population data (*n* = 2,373, ages 4-92) showed insufficient Mg intake in 71.7% of men (15-92) and 82.5% of women (10-90) [14]. Pediatric data are fewer: in a Polish survey of 1,241 children, the lowest prevalence of Mg-deficient diets was among 7-9-year-olds (13% boys, 19% girls), while in 10-12-year-olds insufficient intake affected 56% of boys and 74% of girls [15].

Studies of Polish high-school students (16-18 years) and adolescents (13-15 years) confirmed substantial magnesium deficits in many cases, with some reports indicating that daily requirements were met in only ~30% of participants and that up to 90% consumed Mg below EAR [16]. Cross-sectional US data in 7,250 children aged 2-18 suggest that micronutrient intakes (including Mg) can be so low that only supplementation ensures adequate coverage in some children [17].

DIETARY SOURCES AND REASONS FOR INADEQUATE INTAKE

Rich dietary sources include seeds and kernels, nuts, whole grains, legumes, certain vegetables and fruits, bran, buckwheat, oilseed plant seeds, cocoa, dark chocolate, fish, bananas, spinach and drinking water (especially hard water) [18]. Representative Mg content per 100 g (snacks) includes: pumpkin seeds 540 mg; sunflower seeds 359 mg; almonds 269 mg; buckwheat 218 mg; bean seeds 169 mg; bananas 33 mg; dried apricots 42 mg; cocoa (16%) 420 mg [19].

Despite availability, modern child diets often lack these foods; filtered water, cocoa-flavored milk drinks (rather than real cocoa), and widespread consumption of calcium-fortified products (which can reduce Mg absorption) contribute to inadequate intake [20]. Agricultural practices and food processing have also reduced Mg content in foods, further contributing to deficiency risk.

ABSORPTION AND REGULATION

In adults and children, magnesium is absorbed from the gastrointestinal tract in proportion to intake, with absorption rates around 15-36% (commonly ~30%). Absorption occurs via passive diffusion and active transport (TRPM6 and TRPM7 proteins). Diets high in calcium (> 2000 mg/day), high in fat, low in protein (< 30 g/day), high in fiber or rich in phytates and phosphates impair Mg absorption. The distal jejunum is a major absorption site. Kidneys maintain Mg homeostasis through filtration and reabsorption, while bone serves as a reservoir [21]; during active bone formation or low bone mineral density, skeletal deposition of Mg increases [22].

Magnesium homeostasis depends on coordinated function of intestines (absorption), bone (storage) and

kidneys (urinary excretion). Malabsorption syndromes (e.g., celiac disease, short bowel syndrome) and inflammatory bowel disease can impair Mg uptake [23]. Increased urinary losses may result from hypermagnesemia, hypercalcemia, hypokalemia, hyperaldosteronism, ketoacidosis, laxative use, diuretics and ethanol; certain diseases and medications are also associated with Mg deficiency [24].

MAGNESIUM DEFICIENCY – CLINICAL FEATURES AND IMPLICATIONS

Magnesium deficiency causes neuromuscular and cardiovascular disturbances, may increase osteoporosis risk and contribute to insulin resistance and impaired insulin secretion [21, 24]. Hypomagnesemia can impair parathyroid hormone (PTH) synthesis and secretion, leading to hypocalcemia, and may predispose to calcium kidney stones. Epidemiological and meta-analytic evidence links higher dietary Mg with reduced risk of some cancers and metabolic complications [25].

Symptoms of Mg deficiency are diverse and often non-specific: mild hypomagnesemia is frequently asymptomatic, while more severe deficits produce persistent weakness, fatigue, concentration problems, increased infection susceptibility, heightened stress sensitivity, tremor and paresthesias, eyelid and lip twitching, psychomotor hyperactivity, anxiety, palpitations and tetany [21]. Because Mg redistributes between cells and bone, deficiency symptoms may occur despite normal or elevated total body Mg; thus routine serum Mg measurement has limited diagnostic value and should not delay therapeutic decisions when clinical suspicion is high. More precise assessments include erythrocyte Mg concentration or the magnesium retention test (intravenous Mg with subsequent urinary excretion measurement), but these are mainly research tools or impractical in routine care.

Clinically, Mg deficiency most often results from inadequate dietary intake, chronic diarrhea or specific diseases (e.g., diabetes). Symptoms include neuromuscular hyperactivity (tremor, cramps, seizures), arrhythmias, apathy, depression and nystagmus. Elevated thyroid hormones during stress increase urinary Mg loss [26]. Low serum calcium may be an early sign of Mg deficiency; in such cases Mg supplementation (pharmacological or dietary, e.g., Mg-fortified milk) is indicated.

RISK OF DEFICIENCY AND POPULATION STUDIES IN CHILDREN

US CSF II data estimated mean daily Mg intake for males ≥ 9 years at 323 mg/day (range 177–516) and for females at 228 mg/day (134–342) [46]. NHANES III found similar patterns with variation by ethnicity and age; in 5,007 children aged 6–17 those consuming $< 75\%$ RDA for Mg had higher serum CRP (0.38 mg/dl) than those with adequate intake (0.25 mg/dl). Japanese children aged 3–5 showed hypomagnesemia risk in Goshima *et al.* [27].

Dong *et al.* [28] in 766 adolescents (14–18 years) confirmed associations between low dietary Mg, higher CRP and lower muscle mass. A Polish study [29] of 4,000 healthy children aged 1–10 using hair Mg found no deficiency in that cohort.

MAGNESIUM AND CHRONIC PEDIATRIC CONDITIONS – SELECTED EVIDENCE

A Spanish study of 78 children/adolescents with chronic diseases (chronic kidney disease, sickle cell anemia, autism spectrum disorders, cystic fibrosis, diabetes) assessed anthropometry, serum Ca and Mg, dietary intake (72-hour diary), body composition and bone densitometry [30]. Mean serum Ca was 9.9 mg/dl and Mg 2.08 mg/dl; dietary DRI for Ca and Mg were met at 102% and 105%, respectively. Nevertheless, 45% had hypomagnesemia, 12% hypermagnesemia; 26% had insufficient and 24% excessive Mg intake. Elevated serum Ca/Mg ratio (> 4.70) and low dietary Ca/Mg ratio (< 1.70) were common and associated with risk of chronic conditions (cardiovascular disease, type 2 diabetes, metabolic syndrome, neoplasia). Authors concluded that 79% of participants were at increased risk of abnormal Mg status and related chronic disease development.

Shahbah *et al.* [31] evaluated serum Mg in 71 children with type 1 diabetes (mean age 9.68 ± 3.99 years) and its relation to glycemic control and lipid profile. Hypomagnesemia (< 1.7 mg/dl) occurred in 28.2%; those with low Mg received 300 mg MgO for 3 months. Serum Mg correlated positively with HDL, mean corpuscular volume and platelet count, and negatively with age, HbA_{1c}, triglycerides, total cholesterol, LDL and diabetes duration ($p < 0.001$). Supplementation was associated with significant HbA_{1c} reduction; correcting hypomagnesemia improved glycemic control and reduced atherogenic lipid fractions while increasing protective HDL.

Guerrero-Romero *et al.* [32] studied 3,954 healthy Mexican children and found hypomagnesemia (serum Mg < 1.8 mg/dl) associated with prehypertension and hypertension: prehypertension/hypertension prevalence was 12.2%/6.4% (ages 6–10) and 13.9%/10.6% (ages 11–15); hypomagnesemia was more frequent among children with elevated blood pressure, suggesting a link between low Mg and pediatric hypertension risk.

MAGNESIUM AND THE DEVELOPING NERVOUS SYSTEM

Research indicates neuroprotective effects of Mg (e.g., NMDA receptor blockade) [5]. Tissue Mg²⁺ deficiency may play a role in ADHD pathophysiology; two Polish studies reported lower Mg in children with ADHD [33]. Supplementation with magnesium plus vitamin B₆ (6 mg/kg/day and 0.6 mg/kg/day, respectively) reduced hyperreactivity and aggression and improved attention in some trials, with symptom recurrence after cessation [34].

MAGNESIUM AND SKIN HEALTH

Blach *et al.* [35] examined Mg deficiency's impact on skin lesions accompanied by increased neutrophils and eosinophils, elevated IgE, histamine and proinflammatory cytokines, resembling allergic skin disease. Proksch *et al.* [36] demonstrated that Mg supplements reduce inflammation, enhance epidermal proliferation and differentiation, improve skin hydration and barrier function; Mg combined with ceramides benefited mild-moderate atopic dermatitis.

MAGNESIUM IN NEONATES AND INFANTS

Caddell [37] considered Mg's role in necrotizing enterocolitis (NEC), noting that Mg deficiency increases synthesis of inflammatory mediators (IL-1, IL-6, TNF, TXA₂, endothelin, free radicals) that can damage intestinal tissues. A Taiwanese ecological study (1988-1997) [38] found lower SIDS incidence with increasing water hardness (implying higher Mg).

Mg deficiency is common in life-threatening illnesses requiring ICU admission. Dandinavar *et al.* [39] reported among 343 children (1 month – 12 years) that 28% had hypomagnesemia, 7.3% hypermagnesemia and 64.7% normomagnesemia; hypomagnesemia was more frequent in neurological disorders, associated with longer PICU stay ($p = 0.031$) and higher mortality (30.2% vs. 22.1% in normomagnesemia), supporting routine Mg monitoring in critically ill children.

MAGNESIUM AND STRESS IN CHILDREN AND ADOLESCENTS

Magnesium plays an important role in mitigating the effects of stress by influencing its different phases (eustress, distress, etc.). For many children, stress triggers include school, home, peer interactions, and social media ("instastress"). In the initial stage (mobilization phase), intracellular magnesium is released to reduce negative effects such as excessive cortisol and catecholamine secretion and oxidative stress [40]. Magnesium helps regulate nervous excitability by inhibiting catecholamine release (via NMDA receptor blockade, GABA receptor activation, and serotonin system stimulation) and modulating the hypothalamic-pituitary-adrenal axis (reducing ACTH release and adrenal sensitivity) [40].

Prolonged stress leads to magnesium depletion, creating a vicious cycle: magnesium deficiency increases stress susceptibility, and stress further depletes magnesium. Symptoms include fatigue, insomnia, headaches, palpitations, muscle cramps, eyelid twitching, and increased infection risk. Studies show magnesium supplementation reduces perceived stress and anxiety, lowers cortisol levels, and improves magnesium status in serum and erythrocytes. Adequate magnesium supports CNS functions, including concentration, memory, learning, and healthy sleep [41].

MAGNESIUM AND OTHER CHILDHOOD DISEASES

Research comparing magnesium levels in healthy children and those with pneumonia or obstructive bronchitis found lower intra- and extracellular magnesium and higher urinary excretion in sick children, both before and after treatment [42]. Magnesium absorption disorders also occur in celiac disease due to intestinal mucosal dysfunction [43]. Magnesium deficiency is observed in about 20% of untreated celiac patients and may persist even after inflammation subsides [23]. Since gluten-free products contain less magnesium, a magnesium-rich diet is recommended. A Polish study confirmed similar findings: magnesium deficiency occurred in 19.6% of treated and 21.4% of untreated children with celiac disease.

HYPERMAGNESEMIA AND SAFETY

Clinically relevant hypermagnesemia typically results from overdose or renal failure and may cause weakness, respiratory depression, altered consciousness and ECG changes; levels > 1.5 mmol/l are clinically significant [24, 44, 45]. Caution is required in renal impairment; proton-pump inhibitors may increase hypomagnesemia risk in some patients, and Mg can interact with certain antibiotics (e.g., tetracyclines), necessitating dosing intervals [46, 47].

SUPPLEMENTATION – INDICATIONS AND PRACTICAL GUIDANCE

Given frequent dietary insufficiency and increased needs during growth, controlled oral Mg supplementation is reasonable for children with inadequate intake, chronic disease or increased losses. Weight-based dosing (e.g., 4-6 mg/kg/day) is a practical approach. Organic salts (citrate, lactate) are preferred for bioavailability and tolerability. Monitor renal function (avoid in severe renal impairment, e.g., creatinine clearance < 30 ml/min) and consider drug interactions; do not rely solely on serum Mg to guide therapy [10, 21, 38, 48].

CONCLUSIONS AND PRACTICAL RECOMMENDATIONS

Magnesium is essential for neuromuscular, metabolic and skeletal health; tissue deficiency may exist despite normal serum levels [49, 50].

Dietary Mg intake is insufficient in many pediatric populations; targeted dietary assessment and selective supplementation are warranted.

Clinicians should prefer registered preparations with well-absorbed Mg salts, tailor dosing to age/weight and renal function, and monitor clinical response rather than serum Mg alone.

Overall, controlled magnesium supplementation during developmental age is often justified, particularly when diet is inadequate or disease-related losses occur.

DISCLOSURE

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AUTHORS' CONTRIBUTIONS

WC, AW prepared the concept and wrote the first version of the manuscript. WC revised the manuscript. Both authors contributed to the revised version and approved the final manuscript.