



Managing magnesium deficiency: Strategies for diagnosis and treatment

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Magnesium (Mg) plays a vital role in maintaining bodily functions; in consequence, its deficiency has been linked to various chronic diseases. Diagnosis of Mg deficiency is challenging due to the absence of specific symptoms and its impact on health. Raising awareness to healthcare professionals can facilitate accurate diagnosis and appropriate treatment. This review delves into the role of Mg in chronic diseases, examines the potential benefits of Mg supplementation and presents a tool to support diagnosis and management of Mg deficiency.

Magnesium (Mg) is a mineral that plays an essential role as a cofactor in around 300–600 biochemical reactions, which are responsible for regulating a wide range of fundamental cellular and physiological processes (e.g. cell cycle, channel regulation, apoptosis, membrane and nucleic acid stability, cofactor of hundreds of vital enzymes and in stress responses) [1, 2].

The daily requirement of Mg varies with an individual's age, sex and current health condition. For adults, the generally accepted daily requirement of Mg is around 300–400 mg. Main food groups that contribute to Mg intake are grains and grain-based products, milk and dairy products, as well as coffee, cocoa, tea and infusions [3, 4]. **Table 1** depicts the

recommended daily intake of Mg expressed as adequate intake (AI) for infants and other age groups [4].

Magnesium deficiency

Mg deficiency can lead to neuromuscular and cardiovascular disorders (CVDs) and may act as a risk factor for osteoporosis and impair insulin secretion, resulting in insulin resistance and type 2 diabetes. Several epidemiological studies demonstrate an inverse correlation between normal serum Mg levels and cardiovascular risk factors, such as arterial hypertension, type 2 diabetes and metabolic syndrome. Mg offers diverse cardioprotective benefits, including anti-hypertensive, anti-arrhythmic, anti-inflammatory and anti-platelet properties [3]. Low levels of Mg ions in blood (hypomagnesaemia) may interfere with the synthesis and secretion of parathormone, leading to hypocalcaemia.

There are numerous causes and possible consequences associated with Mg deficiency (**Fig. 1**). Mild hypomagnesaemia is usually asymptomatic, but severe Mg deficiency can manifest itself as persistent asthenia, tiredness, impaired concentration, increased susceptibility to infections, mental stress, hand tremor and tingling, eyelid and lip twitching, psychomotor agitation, anxiety and palpitations or tetany attacks [3].

The negative consequences of stress and hypomagnesaemia reinforce each other in a vicious circle; that is, mental stress could lead to increased Mg loss and mineral deficiency. Conversely, Mg deficiency could worsen the effects of mental stress (fatigue and insomnia, dizziness, headaches, palpitations, muscle cramps, eyelid twitching, tics and increased susceptibility to infections). Mg supplementation

Tab. 1. Summary of adequate intake for magnesium (Mg); adapted from EFSA NDA Panel (2015) [4].

Group	Age [Years]	Daily Mg requirement [mg]
Infants	7–11 months	80
Children and adolescents	1–<3	170
	3–<10	230
	10–<18 (male)	300
	10–<18 (female)	250
Adults	≥18 (male)	350
	≥18 (female)	300
Pregnancy	≥18	300
Lactation	≥18	300

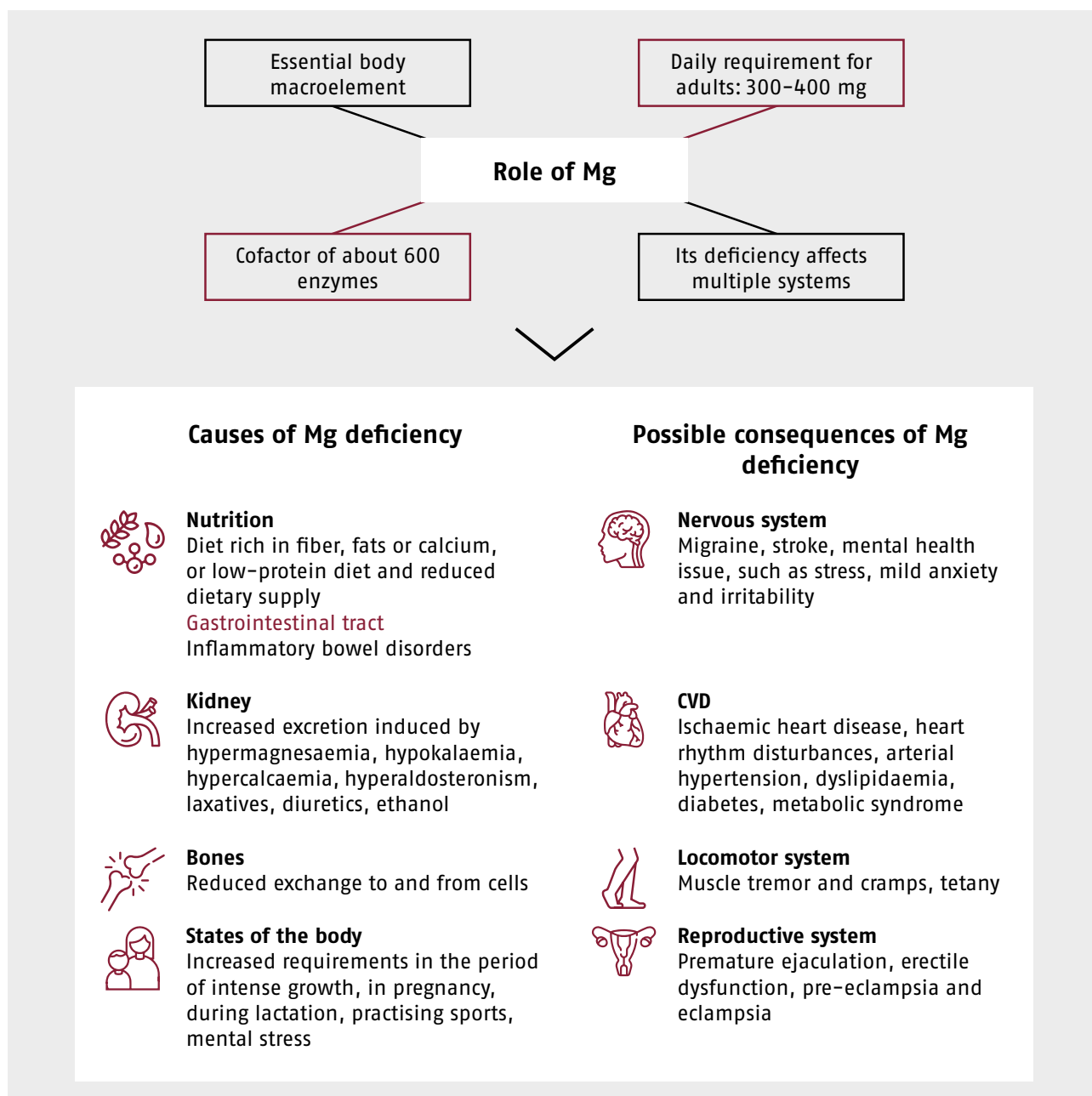


Fig. 1. Pathophysiology of Mg deficiency. Adapted from Jędrzejek et al. (2021) [3]. CVD: cardiovascular disease; Mg: magnesium

reduces stress, anxiety and serum cortisol and increases Mg levels in the serum and erythrocytes [5].

Moreover, symptoms of Mg deficiency can also arise with normal levels of Mg in the body due to the pathological transfer of Mg into the bones, which can affect overall balance [3]. Diagnosis of Mg deficiency based on the symptoms alone is challenging as they are not specific in nature. Additionally, only 1% of Mg is present in blood, and there are multiple risk factors that can contribute to the development of Mg deficiency. Routine assessment of Mg in blood has a limited diagnostic value since it does not correlate with its contents in the tissue [3].

Proper usage of Mg products

Mg deficiency is common in growing children, pregnant/lactating women, people under chronic stress or those

practicing professional sports. The primary care physician should assess the patient for symptoms of Mg deficiency and provide adequate supplementation if needed [3, 5].

Correction and prevention of Mg deficiency usually involves oral supplementation with Mg products. There are numerous products in the market that contain different Mg compounds. It is noteworthy that among the abundant Mg products in the pharmaceutical market, approved Mg products with thorough chemical, pharmacological and clinical documentation are accessible (Fig. 2) [3]. The key factor in determining their efficacy is the type of salt used, which influences the absorption of Mg ions. Inorganic salts, such as oxides and chlorides, have a significantly lower absorption rate (around 10%–16%) than more commonly used organic salts, such as citrate, gluconate, lactate and aspartate that may enhance Mg absorption.

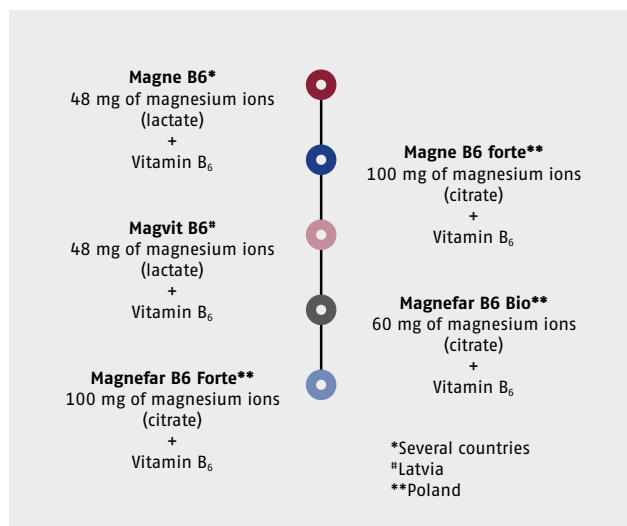


Fig. 2. Approved medicinal products containing magnesium (Mg). Adapted from Jędrzejek et al. (2021) [3].

Product selection also depends on the condition of the gastrointestinal tract; organic salts (citrate, lactate and aspartate) resembling Mg compounds in daily foods are recommended when the stomach and intestines are functioning properly. In patients with hyperacidity and gastritis, Mg oxide is better tolerated but with a low bioavailability. Mg chloride is recommended for patients with hypochlorhydria as it delivers chloride ions as an additional benefit. In case of peptic ulcers, enteric-coated formulation of Mg is recommended; however, bioavailability is a limitation. It is recommended to take Mg products with food and plenty of water for optimal absorption [4].

Treatment recommendations for Mg deficiency

Considering that the symptoms of Mg deficiency are not specific and there are several risk factors that can contribute to the development of this mineral deficiency, diagnosis of Mg deficiency can be challenging. To educate healthcare professionals (HCPs) on accurate diagnosis of Mg deficiency

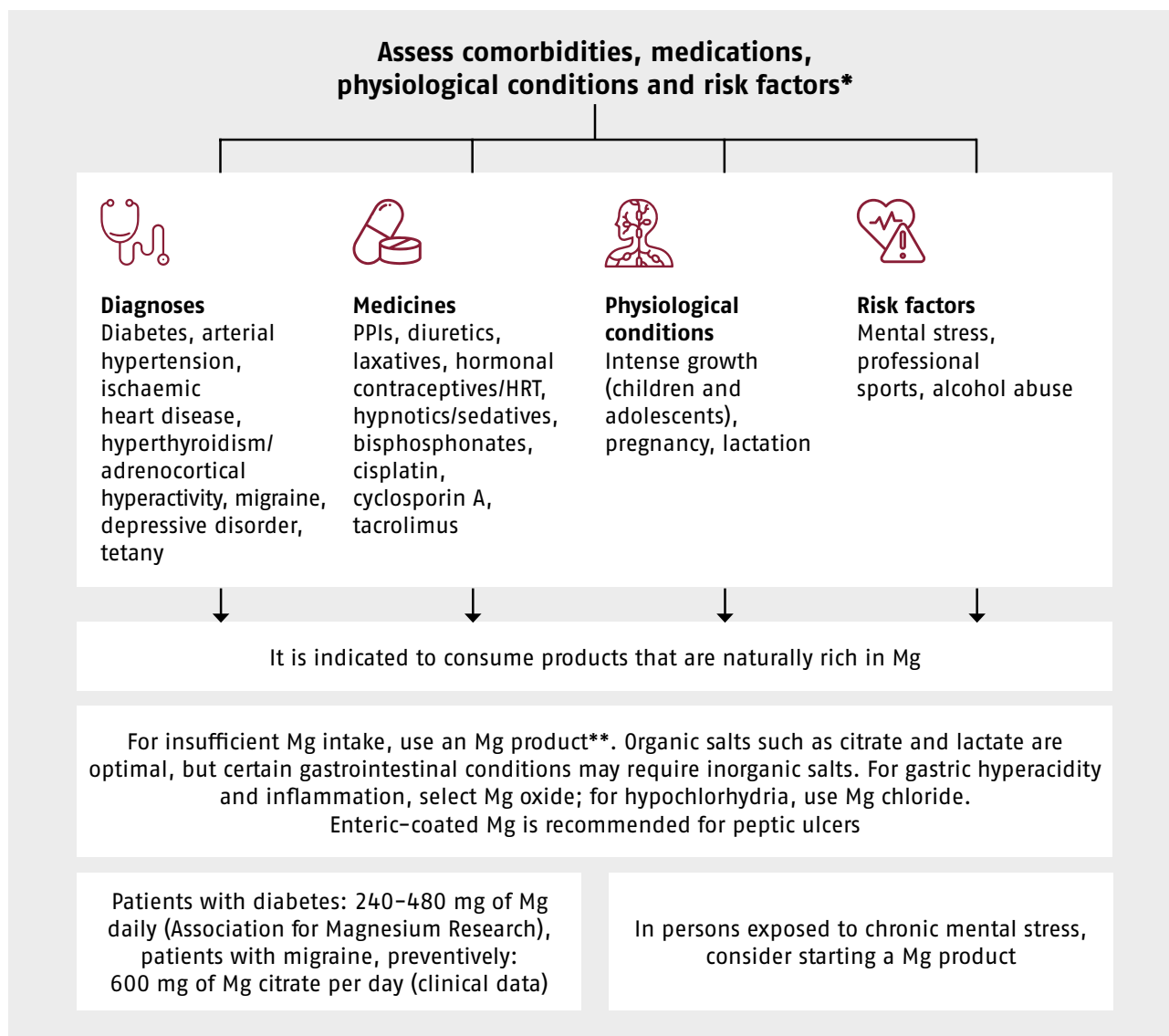


Fig. 3. Recommended strategies for integrating Mg-based products; adapted from Jędrzejek et al. (2021) [3].

*These recommendations do not consider the assessment of magnesemia, because clinical assessment and potential assessment of tissue Mg stores have a higher diagnostic value than the assessment of plasma Mg levels. The above-listed disorders and conditions are a sufficient basis for starting Mg drugs or supplements. **Contraindicated in patients with eGFR <30 mL/min. HRT: hormone replacement therapy; Mg: magnesium; PPI: proton pump inhibitor.

and recommend appropriate treatment, an algorithm was developed as a valuable tool [3], which:

- Contains lists of common risk factors for Mg deficiency, such as diseases, medicines and physiological conditions;
- Specifies the choice of Mg treatment, dosage and time frame;
- Facilitates and expedites HCP recommendation on Mg products based on evidence-based medicine.

The family physician's practice algorithm for using Mg products is presented in **Figure 3**. Patient eligibility for Mg treatment is determined based on pathophysiological considerations. The algorithm does not require testing blood Mg levels, and it underlines a need for the systematic and chronic use of Mg products. Treatment or prevention of Mg deficiency involves oral supplementation with approved medicinal products [3].

Summary

Mg is a macroelement essential for the normal functioning of the body. It plays a vital role in maintaining overall human health. Inadequate dietary intake of Mg may directly contribute to the development of numerous diseases of affluence, such as CVDs, type 2 diabetes, cancer, depression and other metabolic disorders. It is essential to have Mg deficiency tracking tools in place for effective treatment and prevention. A recent publication proposed a tool that can be easily incorporated in HCPs' practice to support the diagnosis and help determine the best course of action for managing Mg deficiency in their patients.

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