

# Therapeutic Uses of Magnesium

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Magnesium is an essential mineral for optimal metabolic function. Research has shown that the mineral content of magnesium in food sources is declining, and that magnesium depletion has been detected in persons with some chronic diseases. This has led to an increased awareness of proper magnesium intake and its potential therapeutic role in a number of medical conditions. Studies have shown the effectiveness of magnesium in eclampsia and preeclampsia, arrhythmia, severe asthma, and migraine. Other areas that have shown promising results include lowering the risk of metabolic syndrome, improving glucose and insulin metabolism, relieving symptoms of dysmenorrhea, and alleviating leg cramps in women who are pregnant. The use of magnesium for constipation and dyspepsia are accepted as standard care despite limited evidence. Although it is safe in selected patients at appropriate dosages, magnesium may cause adverse effects or death at high dosages. Because magnesium is excreted renally, it should be used with caution in patients with kidney disease. Food sources of magnesium include green leafy vegetables, nuts, legumes, and whole grains. (*Am Fam Physician*. 2009;80(2):157-162. Copyright © 2009 American Academy of Family Physicians.)

**M**agnesium is the fourth most abundant essential mineral in the body. It is distributed approximately one half in the bone and one half in the muscle and other soft tissues; less than one percent is in the blood.<sup>1</sup> Studies estimate that 75 percent of Americans do not meet the recommended dietary allowance of magnesium,<sup>2</sup> which has raised concern about the health effects of magnesium deficiency. Lifestyle factors (e.g., poor nutrition, excess alcohol intake), some medications (e.g., diuretics), and lower mineral content in commonly eaten foods (e.g., fruit, vegetables) have led to an increase in studies evaluating the potential link of magnesium deficiency to a number of diverse medical conditions, and magnesium's possible effectiveness in supplementation.<sup>3-5</sup>

Early signs of magnesium deficiency include loss of appetite, nausea, vomiting, fatigue, and weakness. Persons may experience numbness, tingling, muscle contractions and cramps, seizures, personality changes, abnormal heart rhythms, and coronary spasms as magnesium levels decrease. Severe deficiency may lead to hypocalcemia and hypokalemia.<sup>1</sup> Conditions that may lead to hypomagnesemia include poorly-controlled diabetes mellitus; chronic malabsorptive problems (e.g., Crohn disease, gluten-sensitive enteropathy, regional enteritis); medication

use (e.g., diuretics, antibiotics); alcoholism; and older age (e.g., decreased absorption of magnesium, increased renal exertion).<sup>1</sup>

There are challenges in diagnosing magnesium deficiency because of its distribution in the body. Magnesium is an intracellular cation and its blood concentrations may not accurately mirror magnesium status.<sup>6</sup> However, reductions in normal serum magnesium concentrations (1.8 to 2.3 mg per dL [0.74 to 0.95 mmol per L]) signify deficiency. Therefore, serum magnesium concentrations are specific, but not sensitive, to magnesium deficiency.<sup>7</sup> Magnesium homeostasis is related to calcium and potassium status, and should be evaluated in combination with these two cations.<sup>7</sup> There are other methods to assess magnesium status, but the serum level is the most common and practical test in the clinical setting.<sup>8</sup>

## Pharmacology

Magnesium is the second most abundant intracellular divalent cation and is a cofactor for more than 300 metabolic reactions in the body.<sup>9,10</sup> These processes include protein synthesis, cellular energy production and storage, cell growth and reproduction, DNA and RNA synthesis, and stabilization of mitochondrial membranes.<sup>11-14</sup> Magnesium is one of the minerals responsible for managing bone metabolism, nerve transmission, cardiac excitability, neuromuscular

## SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Magnesium is effective for treating eclampsia and preeclampsia.	A	20-25
Intravenous magnesium is effective for treating torsade de pointes and managing rapid atrial fibrillation.	A	26, 27
In severe acute asthma, parenteral magnesium supplementation improves peak expiratory flow rate and forced expiratory volume in one second, and reduces hospital admissions.	B	29, 32
Oral and parenteral magnesium is possibly effective in improving symptoms of migraine.	B	33-37
Magnesium is a widely accepted and effective approach to treat dyspepsia.	B	38
Magnesium is accepted as a standard treatment for constipation, but there are few rigorous studies to prove its effectiveness.	B	40

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

conduction, muscular contraction, vasomotor tone, and blood pressure.<sup>11-14</sup> Magnesium also plays a significant role in glucose and insulin metabolism, mainly through its impact on tyrosine kinase activity, phosphorylase b kinase activity, and glucose transporter protein activity.<sup>15-19</sup> Because of these vital roles, magnesium levels may be affected by stressors to the body, such as in certain disease states. Supplementation with magnesium may have therapeutic effects in these situations.

### Uses and Effectiveness

Magnesium has been used for numerous conditions. The most common indications are discussed here in order of most supported to least supported in the literature.

#### ECLAMPSIA AND PREECLAMPSIA

Magnesium sulfate (intravenous and intramuscular) has been shown to be relatively effective for treating eclampsia and preeclampsia, although it has been considered the standard of care for decades.<sup>20</sup> In 2003, two Cochrane reviews showed that magnesium use in patients with eclampsia was superior to that of phenytoin (Dilantin) and lytic cocktail,<sup>21,22</sup> with another study showing magnesium to be more effective than nimodipine (Nimotop).<sup>23</sup> A different 2003 Cochrane review showed that 1 to 2 g of intravenous magnesium sulfate per hour reduced the risk of eclampsia in patients with preeclampsia by more than one half.<sup>24</sup> The use of magnesium does not appear to have harmful effects on the mother or infant in the short term.<sup>25</sup>

#### ARRHYTHMIA

A well-known use of intravenous magnesium is for correcting the uncommon ventricular tachycardia of torsade de pointes.<sup>26</sup> Results of a meta-analysis suggest that 1.2 to 10 g of intravenous magnesium sulfate is also a safe and effective strategy for the acute management of rapid atrial fibrillation.<sup>27</sup> A six-week randomized, double-blind crossover trial showed that oral magnesium supplementation reduced the frequency of asymptomatic

ventricular arrhythmia in patients with stable congestive heart failure secondary to coronary artery disease.<sup>28</sup>

#### ASTHMA

A 2000 Cochrane review of magnesium sulfate for exacerbations of acute asthma in the emergency department found that evidence does not support routine use of intravenous magnesium in all patients with acute asthma; however, it appears safe and beneficial for severe acute asthma by improving peak expiratory flow rate and forced expiratory volume in one second.<sup>29</sup> In a meta-analysis of acute asthma in children, intravenous magnesium demonstrated probable benefit in moderate to severe asthma in conjunction with standard bronchodilators and steroids<sup>30</sup>; however, a randomized controlled trial showed that oral magnesium added no clinical benefit to standard outpatient therapy for chronic stable asthma in adults.<sup>31</sup> In a 2005 Cochrane review of inhaled magnesium sulfate in acute asthma, nebulized magnesium in addition to a beta<sub>2</sub> agonist were shown to improve pulmonary function and trend toward benefit in fewer hospital admissions.<sup>32</sup>

#### HEADACHE

Studies have found that patients with cluster headaches and classic or common migraine, especially menstrual migraine, have low levels of magnesium.<sup>33,34</sup> A prospective, multicenter, double-blind randomized study conducted in Germany showed that a single daily dosage of 600 mg oral trimagnesium dicitrate significantly reduced the frequency of migraine compared with placebo, whereas a lower twice daily dosage was found ineffective.<sup>35,36</sup> For acute treatment of migraine, intravenous magnesium sulfate showed a statistically significant improvement in the treatment of all symptoms in patients with aura, or as an adjuvant therapy for associated symptoms in patients without aura.<sup>37</sup>

#### DYSPEPSIA

Another common condition with several self-treatment options is dyspepsia, a key symptom of gastroesophageal reflux disease (GERD). Antacids are widely used

**Table 1. Selected Food Sources of Magnesium**

Food	Magnesium (in mg)
Halibut, cooked, 3 oz	90
Almonds, dry roasted, 1 oz	80
Cashews, dry roasted, 1 oz	75
Spinach, frozen or cooked, one half cup	75
Cereal, shredded wheat, two rectangular biscuits	55
Oatmeal, instant, fortified, prepared with water, 1 cup	55
Potato, baked with skin, one medium	50
Peanuts, dry roasted, 1 oz	50
Wheat bran, crude, 2 tablespoons	45
Yogurt, plain, skim milk, 8 fl oz	45
Bran flakes, three fourths cup	40
Rice, brown, long-grained, cooked, one half cup	40
Avocado, California, one half cup pureed	35
Kidney beans, canned, one half cup	35
Banana, raw, one medium	30
Milk, reduced fat (2%) or fat free, 1 cup	27
Bread, whole wheat, commercially prepared, one slice	25
Raisins, seedless, one fourth cup packed	25
Whole milk, 1 cup	24

NOTE: There is no upper intake level for dietary magnesium.

Adapted from the National Institutes of Health Office of Dietary Supplements. Magnesium. <http://ods.od.nih.gov/factsheets/magnesium.asp>. Accessed January 12, 2009.

for dyspepsia; however, studies comparing antacids with histamine H<sub>2</sub> receptor antagonists (H<sub>2</sub> blockers) have been limited. A randomized, double-blind, crossover study showed that on-demand treatment with the antacid hydrotalcite (aluminum hydroxide, magnesium hydroxide, carbonate, and water) was more effective than famotidine (Pepcid) or placebo.<sup>38</sup> An editorial on these findings questioned the standard use of H<sub>2</sub> blockers, and recommended shifting to more individualized treatment of mild or intermittent GERD.<sup>39</sup>

#### CONSTIPATION

Patients often self-treat constipation with over-the-counter products, such as magnesium hydroxide (Milk of Magnesia) or magnesium citrate. However, there are few studies demonstrating effectiveness, as shown in a systematic review of chronic constipation.<sup>40</sup> Despite this, many physicians and patients have found these treatments helpful, which indicates that a lack of evidence is not necessarily synonymous with a lack of effect.<sup>41</sup>

#### OTHER

Magnesium is associated with maintaining or improving bone mineral density as a dietary component in

combination with potassium, fruits, and vegetables, or as an oral supplement.<sup>42,43</sup> One study suggested that adults 18 to 30 years of age with higher magnesium intake have a lower risk of developing metabolic syndrome.<sup>44</sup> Another study demonstrated a positive association between hypomagnesemia and metabolic syndrome in adults.<sup>45</sup> A 2002 Cochrane review showed that magnesium lactate or citrate twice a day was effective for leg cramps in pregnant women.<sup>46</sup> A 2001 Cochrane review of three small trials showed that in patients with dysmenorrhea, magnesium was more effective than placebo for pain relief and the need for additional medication was less.<sup>47</sup> Studies have linked magnesium deficiency to myocardial infarction, congestive heart failure, primary hypertension, and angina pectoris,<sup>48</sup> but evidence is still limited to recommend its use for these conditions.

#### Contraindications, Adverse Effects, and Interactions

Although oral magnesium supplementation is well-tolerated, magnesium can cause gastrointestinal symptoms, including nausea, vomiting, and diarrhea.<sup>49</sup> Overdose of magnesium may cause thirst, hypotension, drowsiness, muscle weakness, respiratory depression, cardiac arrhythmia, coma, and death.<sup>49</sup>

Concomitant use of magnesium and urinary excretion-reducing drugs, such as calcitonin, glucagon (Glucagen), and potassium-sparing diuretics, may increase serum magnesium levels, as may doxercalciferol (Hectorol).<sup>50</sup> Concomitant oral intake of magnesium may influence the absorption of fluoroquinolones, aminoglycosides, bisphosphonates, calcium channel blockers, tetracyclines, and skeletal muscle relaxants. Because of this, concomitant use should be monitored or avoided when possible.<sup>51</sup>

Additionally, because magnesium is cleared renally, patients with renal insufficiency (creatinine clearance of less than 30 mL per minute [0.50 mL per second]) may be at increased risk of heart block or hypermagnesemia; therefore, magnesium levels should be monitored. As with any dietary supplement, the quality of the product is important. Some magnesium products were found to contain lead.<sup>52</sup>

#### Dosages

Oral magnesium supplementation is safe in adults when used in dosages below the upper intake level of 350 mg per day (elemental magnesium).<sup>51</sup> However, higher dosages have been studied and may be used for specific medical problems. *Table 1* provides selected food sources of magnesium and the amount of magnesium per serving<sup>1</sup>; there is no upper intake level for dietary magnesium.

## Magnesium

Magnesium is safe in children when used in dosages below the tolerable upper intake level of 65 mg per day for children one to three years of age, 110 mg per day for children four to eight years of age, and 350 mg per day for children older than eight years.<sup>8</sup> Table 2 lists some common forms and dosages of magnesium.

### Bottom Line

Magnesium is an essential mineral with evidence of effectiveness in treating eclampsia and preeclampsia, arrhythmia, severe asthma, and migraine (Table 3). The National Center for Complementary and Alternative Medicine is currently investigating the role of magnesium supplementation in mild to moderate persistent asthma.<sup>53</sup> There are few studies to support wide use of

magnesium for treating constipation and dyspepsia. Some of the potential indications that require further investigation include lowering the risk of metabolic syndrome, treating leg cramps in pregnant women, preventing osteoporosis, and alleviating dysmenorrhea. Diagnosis of mild to moderate magnesium deficiency is challenging because patients may be asymptomatic, and usual diagnostic testing is specific but not sensitive. Magnesium testing and supplementation should be considered in at-risk patients, especially those on diuretics, with poor nutritional intake, or with malabsorptive states. Supplementation of magnesium should generally not exceed the age-adjusted tolerable upper intake level and should be used with caution in patients with kidney dysfunction or in those taking certain medications.

**Table 2. Common Magnesium Formulations and Dosages**

Supplement	Elemental magnesium content	Dosage schedule for adults*
Magnesium oxide (MagOx)	61% elemental magnesium 242 mg in 400-mg tablet	Two tablets per day with food
Magnesium hydroxide (Milk of Magnesia)	42% elemental magnesium 167 mg in 400 mg per 5 mL oral suspension	5 to 15 mL as needed up to four times per day
Magnesium citrate	16% elemental magnesium 48 mg elemental magnesium and 13 mg potassium in 290 mg per 5 mL oral solution	One half to one full bottle (120 to 300 mL)
Magnesium gluconate (Mag-G)	5% elemental magnesium 27 mg in 500-mg tablet	One or two divided tablets per day
Magnesium chloride (Mag-SR)	12% elemental magnesium 64 mg in 535-mg tablet	Two tablets once per day
Magnesium sulfate	10% elemental magnesium 1 g per 100 mL solution for injection	Atrial fibrillation: IV 1.2 to 5 g initial dose over one to 30 minutes Asthma: IV 25 to 75 mg per kg single dose (study of children younger than 18 years) Eclampsia, preeclampsia: IV 4 to 6 g over 15 to 20 minutes, then 1 to 2 g per hour
Magnesium sulfate (Epsom salts)	10% elemental magnesium 98.6 mg in 1 g salts	Cathartic: mix 2 to 4 teaspoons in 8 oz water; take up to twice per day
Magnesium lactate (Mag-Tab SR)	12% elemental magnesium 84 mg in 84 mg tablet	One to two tablets every 12 hours
Magnesium aspartate hydrochloride (Maginex DS)	10% elemental magnesium 122 mg in 1,230 mg dietary supplement granules	Mix in 4 oz water; take up to three times per day

IV = intravenous.

\*—Recommended dietary allowance for adults 19 to 30 years of age: 310 mg per day for women and 400 mg per day for men; for adults older than 30 years: 320 mg per day for women and 420 mg per day for men.

**Table 3. Key Points About Magnesium**

Effectiveness	Effective: eclampsia and preeclampsia, arrhythmia, severe asthma, migraine, dyspepsia, constipation Possibly effective: lowering risk of metabolic syndrome, improving glucose and insulin metabolism, preventing osteoporosis, improving symptoms of leg cramps in pregnant women, dysmenorrhea
Adverse effects	Oral supplementation generally is safe and well-tolerated; some reports of nausea, vomiting, diarrhea; overdose may lead to hypotension, muscle weakness, and coma
Contraindications	Patients with renal impairment (creatinine clearance of less than 30 mL per minute [0.5 mL per second]) may be at risk of heart block or hypermagnesemia
Oral dosage and tolerable upper intake level	Adults: 350 mg per day of elemental magnesium Children: 65 mg per day for children one to three years of age; 110 mg per day for children four to eight years of age; 350 mg per day for children older than eight years
Cost	Less than \$20 for 30 tablets
Food sources	Green leafy vegetables, fish, almonds, legumes, whole grains (see Table 1)

Members of various family medicine departments develop articles for "Complementary and Alternative Medicine." This is one in a series coordinated by Sumi Sexton, MD, and Benjamin Kligler, MD, MPH.

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