

Fatal Hypermagnesemia in a Child Treated With Megavitamin/Megamineral Therapy

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ABSTRACT. We report a case of fatal hypermagnesemia resulting from the unsupervised use of high doses of magnesium oxide administered as part of a regimen of megavitamin and megamineral therapy to a child with mental retardation, spastic quadriplegia, and seizures. The treatment regimen was given at the recommendation of a dietician working as a private nutritional consultant without the involvement or notification of the child's pediatrician. Hypermagnesemia is an uncommon but serious side effect of the use of magnesium containing compounds. These compounds are widely used as laxatives and dietary supplements, and serious side effects are uncommon when used in appropriate dosages and with adequate supervision.

The use of alternative medical therapies, including megavitamin/megamineral therapy, is widespread. Many patients use alternative medicine or seek care from alternative medicine practitioners without the recommendation or knowledge of their primary physicians. Despite unproved benefit, many alternative therapies may be safe. However, unsupervised use of generally safe treatments can result in serious side effects. This case report serves to illustrate the characteristic pathophysiologic changes of severe hypermagnesemia, an entity rarely seen in pediatric practice, and more importantly, it alerts primary care and subspecialty pediatricians to be aware of and monitor the use of alternative medical therapies in their patients. *Pediatrics* 2000;105(2). URL: <http://www.pediatrics.org/cgi/content/full/105/2/e18>; *magnesium, alternative medicine, toxicity*.

The use of alternative medical therapies, including megavitamin therapy, is widespread.¹⁻³ Alternative medicine use in children was reported by 11% of parents in a pediatric survey.⁴ Many patients use alternative medicine or seek care from alternative medicine practitioners without the recommendation or knowledge of their primary physicians.^{1,3} Despite unproved benefit, many alternative therapies may be safe. However, unsupervised use of generally safe treatments may result in serious side

effects. We report a case of fatal hypermagnesemia resulting from the unsupervised use of high doses of magnesium oxide as part of a regimen of megavitamin and megamineral therapy, administered to a child with mental retardation and spastic quadriplegia.

Hypermagnesemia is an uncommon but serious side effect of the use of magnesium containing compounds. These compounds are widely used as laxatives and dietary supplements, and when used in appropriate dosages and with adequate supervision, are known to be safe. In our patient, megavitamin/megamineral therapy was given at the recommendation of a dietician working as a private nutritional consultant without the involvement or notification of the child's pediatrician. This case report serves to illustrate the characteristic pathophysiologic changes of severe hypermagnesemia, an entity rarely seen in pediatric practice. More importantly, it alerts primary care physicians to be aware of and to monitor the use of alternative medical therapies in their patients.

CASE REPORT

A 28-month-old boy presented to the emergency department with cardiopulmonary arrest. He had a history of severe mental retardation, spastic quadriplegia, and seizure disorder of unknown cause. He received nighttime mechanical ventilation via a tracheostomy tube for central hypoventilation and received all nutrition and medications via a gastrostomy tube. In the 3 weeks before presentation, his mother had been giving him high doses of vitamin and mineral supplements at the recommendation of a private nutritional consultant, without the knowledge of the patient's physician. The regimen included calcium carbonate, multivitamins, essential fatty acids, lactobacillus, bifidobacterium, and magnesium oxide, which the mother was told "would help relax his muscles and relieve his constipation." She had been instructed to give .5 teaspoons of magnesium oxide 4 times per day (800 mg) and to watch for loose stools. Several days before admission, she increased the dose to .5 tablespoon 4 times per day (2400 mg) because of continued constipation. Specific dosages of other components of the regimen could not reliably be ascertained. The mother reported that 2 days before presentation, he was drowsy and less arousable. The next day, she noticed that his heart rate was frequently 70 to 80 bpm. On the morning of admission, she found him unresponsive, unarousable, and with "big" pupils. Because of concern regarding the pupils, she disconnected him from his ventilator and brought him to the emergency department, approximately a 5-minute trip.

On arrival, he was pulseless, without respiration, and unresponsive to stimulation. His pupils were 5 mm and nonreactive, and his tone was flaccid. He was warm centrally with cool extremities. Cardiopulmonary resuscitation was initiated. Epinephrine was administered with a return of heart rate at 70 bpm, with palpable pulses and a systolic blood pressure of 110 mm Hg. The cardiac monitor rhythm suggested third-degree heart block. Atropine was administered without an increase in heart rate. Calcium

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chloride was given, and epinephrine and isoproterenol infusions were initiated.

Initial laboratory data obtained after the initial resuscitation revealed a serum magnesium level of 20.3 mg/dL (8.4 mmol/L). Other results included: serum sodium, 120 meq/L (120 mmol/L); serum potassium, 3.1 meq/L (3.1 mmol/L); serum chloride, 76 meq/L (76 mmol/L); carbon dioxide content, 26 meq/L (26 mmol/L); blood urea nitrogen, 52 mg/dL (18.6 mmol/L); creatinine, 2.2 mg/dL (190 μ mol/L); serum glucose, 187 mg/dL (10.4 mmol/L); serum albumin, 2.2 g/dL (22 g/L); ionized calcium, .90 mmol/L; arterial blood pH, 7.36; P_{aCO_2} , 63 mm Hg; P_{O_2} , 268 mm Hg; and base excess, +12 mmol/L. The electrocardiogram showed absence of p-waves with a junctional rhythm and a ventricular rate of 60 bpm with isolated premature ventricular complexes. An echocardiogram revealed marked depression of cardiac contractility.

Transesophageal pacing was instituted at a rate of 110 bpm, which resulted in 1:1 atrioventricular conduction and an adequate blood pressure. Emergent hemodialysis reduced the serum magnesium level to 7.6 mg/dL (3.1 mmol/L) and was followed by continuous veno-venous hemofiltration to further reduce the magnesium load. Despite the prompt correction of biochemical abnormalities and aggressive cardiopulmonary support, the patient expired 20 hours after admission from refractory cardiac dysrhythmias and profound cardiac dysfunction.

Postmortem examination showed subendocardial and subepicardial ischemic changes, acute interstitial pneumonia, early coagulation necrosis of the small and large bowel, and marked congestion of the kidneys. The stomach and small bowel contained a soft "chalk-like" material, and the stomach contained a 1.8-cm diameter calcium carbonate stone. A review of past medical records demonstrated documentation of previously normal renal function as assessed by normal blood urea nitrogen, creatinine, and urinalysis.

DISCUSSION

Uncommon or particularly profound pathophysiologic abnormalities should alert the physician to the possibility of side effects of alternative medical therapies. In our patient, the rarely seen condition of severe hypermagnesemia resulted from the overdose of an otherwise safe compound, magnesium oxide. We believe that this case demonstrates why pediatricians must incorporate inquiry regarding use of alternative medicine into the medical history.

Hypermagnesemia has been rarely reported in pediatric practice.⁵⁻⁷ Cases in adults usually result from large intravenous doses of magnesium or from excessive oral intake of magnesium-containing cathartics by patients with renal insufficiency.^{8,9} However, several cases of hypermagnesemia from enteral magnesium intake in patients with normal renal function have been reported.^{10,11} Magnesium is primarily absorbed in the small intestine, and with normal renal function, excess magnesium is efficiently eliminated in the urine.¹² Clinically significant hypermagnesemia occurs when the capacity for renal magnesium elimination is exceeded.

Excess magnesium is known to have direct and indirect cardiovascular effects.⁹ Magnesium has been described as "nature's physiologic calcium blocker,"¹³ and cardiovascular effects seen in hypermagnesemia may be caused by disruption of calcium action. Electrocardiographic observations in humans and animals have shown an increase in the P-R interval at concentrations of 6 to 12 mg/dL (2.5-5 mmol/L), which may progress to heart block and asystole at levels greater than 18 mg/dL (7.5 mmol/L).⁹ Hypotension is variably observed in mild hypermagnesemia and is consistently seen at higher blood concentrations. Mechanisms include decreased vas-

cular smooth muscle contraction and peripheral sympathetic blockade. Bradycardia may, in part, be a result of sympathetic blockade.⁹ Although direct myocardial depression has not been consistently observed in experimental models, our patient had severely decreased myocardial contractility. This finding may have been secondary to the cardiorespiratory arrest, direct magnesium toxicity, or both.

The effects of magnesium on the peripheral and autonomic nervous systems may explain the decreased arousability, apparent drowsiness, and mydriasis in our patient. Magnesium blocks the neuromuscular junction by antagonizing calcium effects, suppressing acetylcholine release, and diminishing postsynaptic membrane responsiveness. Deep tendon reflexes are depressed at serum magnesium levels above 6 mg/dL (2.5 mmol/L) and are absent at levels above 12 mg/dL (5 mmol/L). Severe muscle weakness is seen at levels greater than 12 mg/dL (5 mmol/L) with the potential for respiratory muscle paralysis.^{9,14} Autonomic sympathetic blockade is manifested clinically as cutaneous flushing, dry mouth, pupillary dilatation, urinary retention, and hypotension. Magnesium is not an anesthetic or central nervous system depressant.⁹

The electrolyte and metabolic abnormalities seen in our patient can be attributed to altered renal handling of sodium and calcium induced by excess magnesium. Urinary magnesium excretion can be markedly increased in hypermagnesemia. This is associated with a natriuresis and calciuria attributable to inhibition of tubular resorption of these cations. Hypermagnesemia inhibits parathyroid hormone secretion, which may further exacerbate calcium loss, because parathyroid hormone enhances tubular resorption of calcium.¹² Alternatively, the effects on calcium metabolism may involve effects of elevated serum magnesium on the calcium sensing receptor present on the parathyroid gland and on the ascending limb of the loop of Henle. Magnesium may bind these receptors and lead to an inhibition of tubular resorption of calcium and magnesium, as well as inhibition of resorption of sodium and chloride.¹⁵ An acute rise in serum magnesium levels likely resulted from continued magnesium-dosing in the setting of impaired renal function.

The treatment for severe hypermagnesemia is aggressive supportive care, including airway protection and mechanical ventilation if needed. Maintenance of intravascular volume and cessation of magnesium administration are essential. Intravenous calcium administration may be beneficial, although the mechanism of action has not been fully elucidated. For life-threatening hypermagnesemia, definitive therapy is the removal of excess magnesium with peritoneal or hemodialysis.¹²

Although most alternative medicine therapies are of unproved benefit, they may be relatively safe, if appropriately monitored and supervised. Primary care and subspecialty pediatricians are in an ideal position to ask about the use of these therapies and to provide insight and education regarding potential risks and side effects. Unless specifically questioned, patients and parents may not voluntarily disclose

their usage of dietary supplements or other therapies. In fact, many patients do not view dietary supplements as “drugs” or therapies.¹⁶ Because most patients using alternative medicine use it in conjunction with, not instead of, conventional therapy,^{1,2} if essential medical therapy is maintained and appropriate monitoring provided, discontinuation of the alternative therapy may not be necessary. We suggest that a nonconfrontational and nonjudgmental approach will encourage more honest responses and provide an opportunity for discussion and education.

Several studies have evaluated the use of megavitamin therapy for the treatment of behavior and developmental delay without evidence of demonstrated benefit.^{17,18} Conventional therapy for chronic neurological conditions is often unsatisfactory, and frustrated parents and patients may seek alternative therapy. An understanding of the reasons for seeking alternative care may provide additional opportunities for education and support in caring for children with chronic problems.

Pediatricians need not become familiar with all the alternative therapies available but should rather support open discussion and appropriate understanding regarding the potential for adverse effects. Adequate supervision and monitoring of potentially dangerous alternative therapies may help prevent the development of serious or life-threatening side effects.

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