

Iatrogenic Acute Hypermagnesemia After Total Parenteral Nutrition Infusion Mimicking Septic Shock Syndrome: Two Case Reports

Ayoob Ali, MD; Corinne Walentik, MD; Gregory J. Mantych, MD; H. Farouk Sadiq, MD; William J. Keenan, MD; and Akhihiko Noguchi, MD

ABSTRACT. Two premature newborn infants developed extreme magnesium toxicity while receiving total parenteral nutrition (TPN) infusion. Both patients exhibited acute hypotonia, apnea, hypotension, and refractory bradycardia mimicking septic shock syndrome. The complete blood count was normal, and blood cultures were negative. Serum magnesium concentration in 1 patient was 43.1 mEq/L and in the other patient was 45 mEq/L (normal values for serum magnesium being 1.6–2.1 mEq/L). Hypermagnesemia resulted from malfunction of an automated TPN mixing device. Unexplained sudden onset of apnea, refractory bradycardia, and hypotension should raise suspicions of hypermagnesemia, a reversible condition if identified and treated early. *Pediatrics* 2003;112:e70–e72. URL: <http://www.pediatrics.org/cgi/content/full/112/1/e70>; total parenteral nutrition, hypermagnesemia.

ABBREVIATIONS. TPN, total parenteral nutrition; EEG, electroencephalogram.

Magnesium is the second most common intracellular cation and a natural calcium channel blocker. High magnesium concentration competitively inhibits several calcium-dependent reactions, resulting in muscle paralysis and dilatation of resistance vessels. Studies have shown that magnesium administered to the mother will cross the placenta to the fetus. Approximately 70% to 80% of serum magnesium is ionized and diffusible, while the remainder is bound to protein. Magnesium ions are reabsorbed by all portions of the renal tubules, and it is the distal tubules and collecting ducts that regulate urinary excretion of magnesium. Magnesium is required as a catalyst for many intracellular enzymatic reactions, particularly those relating to glycolysis, energy metabolism, and ion transport. The normal serum concentration of magnesium lies between 1.6 mEq/L and 2.1 mEq/L. Impaired renal function is the most common cause of hypermagnesemia in children.^{1–5}

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CASE REPORTS

Case 1

This 1605-g male was born at 29 weeks gestation to a 17-year-old gravida 1, para 0 mother. Pregnancy was complicated by preterm labor, tobacco use, and marijuana abuse. Two doses of betamethasone were administered before delivery. The infant was delivered by spontaneous vaginal delivery with Apgar scores of 9 at 1 and 5 minutes. Resuscitation consisted of bulb suction and bag mask ventilation. The infant required 5 cm of nasal continuous positive airway pressure and was weaned to room air within 24 hours. Intravenous fluids were started at birth. On the second day of life, nasogastric feeding with breast milk was initiated, and intravenous fluids were changed to total parenteral nutrition (TPN). On the 10th day of life, while on nasogastric feedings of ~120 mL/kg/day and TPN of 40 mL/kg/day, the infant was noted to have hypotonia, temperature instability, and lethargy. Blood was drawn for a complete blood count and blood culture, spinal tap and urine culture were collected, and intravenous antibiotics were started. Initial arterial blood gases were consistent with severe metabolic acidosis; the infant developed hypotension, bradycardia, and apnea. He was intubated, and received multiple boluses of Ringer's lactate with dopamine, dobutamine, and epinephrine infusions. Acidosis was corrected with bicarbonate without any improvement in hypotension and bradycardia, so the patient was transferred to our level III newborn intensive care unit for further evaluation and management. On admission he had refractory bradycardia with heart rate of 80 to 100 beats per minute, systolic blood pressure of 42 to 48 mm Hg by Doppler, serum creatinine of 0.9 mg/dL, ionized calcium of 1.6 mmol/L, and total calcium of 11.2 mg/dL. The patient received multiple doses of epinephrine through the endotracheal tube and intravenously and continued on intravenous infusions of epinephrine, dopamine, and dobutamine for hypotension. Serum magnesium was 7.4 mEq/L when checked ~24 hours after the episode. Retrospective serum magnesium level checked—from a blood sample, drawn on admission and saved in the laboratory—revealed a serum magnesium level of 43.1 mEq/L. Liver enzymes, serum osmolality, and urine osmolality were within normal limits. The infant was stabilized with mechanical ventilation. An electrocardiogram was consistent with sinus bradycardia, head ultrasound was negative for hemor-

rhage, and the initial electroencephalogram (EEG) was consistent with diffuse encephalopathy. Echocardiography revealed a patent foramen ovale without any structural anomalies. Nerve conduction studies showed neuromuscular junction blockade. The serum magnesium level was monitored closely along with serum electrolytes. Our patient weaned quickly from the ventilator, as serum magnesium level returned to normal, and he was extubated to room air on the 15th day after admission. Nasogastric feeding was started on the seventh day after admission when serum magnesium level was within normal limits and repeat EEG and nerve conduction velocity were normal. The infant continued to do well, and he was discharged on the 53rd day of life with adjusted gestational age of 36 weeks. On discharge he weighed 2680 g, was on room air, and was taking feedings well.

Case 2

This patient B was a 1080-g male infant born at 28 weeks of gestation to a 17-year-old gravida 3, para 2 mother, whose pregnancy was complicated by no prenatal care and preterm labor. The mother was treated with procordia, magnesium sulfate, antibiotics, and betamethasone before delivery. The infant, delivered by cesarean section attributable to breech presentation, had Apgar scores of 6 at 1 minute and 7 at 5 minutes. The infant required manual ventilation at birth and was intubated secondary to poor respiratory effort. He received 1 dose of surfactant for hyaline membrane disease and was extubated to nasal continuous positive airway pressure within 48 hours. He was started on intravenous fluids at birth, and on the second day of life he began TPN and nasogastric feeding, which advanced slowly. On the 12th day of life our patient had increased episodes of apnea and bradycardia and rapidly became hypotensive and hypotonic. Blood was drawn for a complete blood count and blood culture, and the infant was started on intravenous antibiotics after obtaining urinary and cerebral spinal fluid cultures. The infant was intubated because of apnea, and received multiple boluses of normal saline and Ringer's lactate, and was started on dopamine and dobutamine drips without improvement in heart rate and blood pressure. Multiple doses of epinephrine were administered, followed by initiation of continuous epinephrine infusion, and he was transferred to our level III neonatal intensive care unit for further evaluation and management. On admission his serum magnesium level was 45 mEq/L, serum creatinine of 1.2 mg/dL, ionized calcium of 1.44 mmol/L, and total serum calcium was 12.6 mg/dL. A calcium gluconate infusion was begun, and he underwent exchange transfusion within a few hours after transfer to the intensive care unit. An electrocardiogram showed sinus bradycardia with a prolonged QT-interval. Ultrasound of the head was normal. EEG and nerve conduction velocity studies were done within 24 hours of admission and were normal for age. Infant serum magnesium and electrolytes were monitored, and the infant's heart rate and blood pressure normalized after exchange transfusion. Neurologically,

the patient showed progressive improvement as the serum magnesium level declined. The infant was weaned from mechanical ventilation and was extubated on the 18th day after admission but still required oxygen. Nasogastric feedings were resumed after the magnesium level normalized. The boy was discharged from the nursery on the 48th day of life at 37 weeks postconceptional age. Discharge weight was 1910 g. He was feeding well orally, and required nasal cannula oxygen during feeding for bronchopulmonary dysplasia.

DISCUSSION

These case reports present the highest recorded level of magnesium toxicity in infants and neonates. Hypermagnesemia causes parasympathetic blockade—including cutaneous flushing, hypotension, prolonged QT-interval, delayed intraventricular conduction, respiratory depression, neuromuscular blockade, and coma—and clinically mimics a central brainstem herniation syndrome. In both cases, the infants received erroneously prepared TPN, which contained excess amounts of magnesium sulfate attributable to maloperation of an automatic TPN compounding. Physicians and pharmacists should be aware of this potentially fatal iatrogenic complication. Unexplained sudden onset of apnea, refractory bradycardia, and refractory hypotension should raise suspicion of hypermagnesemia, which is reversible if identified and treated early. Iatrogenic hypermagnesemia has been reported from administration of parenteral magnesium, excessive magnesium in dialysate solution, and multiple doses of cathartic therapy given in conjunction with charcoal. The second case above occurred ~2 weeks after the first case, came from the same referring institution, and had a similar presentation. Therefore, suspicion for hypermagnesemia was high from the beginning. Early recognition and treatment of hypermagnesemia may prevent or minimize life-threatening events; however, the vast majority of mild hypermagnesemia patients may be missed.^{6–10}

Hypotension, electrocardiographic changes, and evidence of sedation appear at serum magnesium concentrations of 3 to 8 mEq/L. Disappearance of deep tendon reflexes, respiratory depression, weakness, and coma are reported at magnesium levels of 5 to 15 mEq/L; cardiac arrest is reported at serum magnesium levels of 20 to 30 mEq/L. Appropriate initial treatment of hypermagnesemia involves removal of exogenous magnesium source, and the use of intravenous calcium. The exact mechanism of action of calcium is not known, but it causes displacement of magnesium from the cell membrane, which results in transient reversal of symptoms of hypermagnesemia. Intravenous infusion of glucose and saline are also conservative treatment modalities, but renal dialysis, either peritoneal or hemodialysis is the treatment of choice in refractory hypermagnesemia.^{11–17}

Both patients were followed at 4 and 8 months, corrected age at the nursery follow-up clinic for developmental assessment. The first patient was found to be normal developmentally for corrected age, and

the second patient was found to have mild gross motor developmental delay.

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