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 hypertension 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

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 hemorrhage.
rhage, and the initial electroencephalogram (EEG) was consistent with diffuse encephalopathy. Echo-
cardiography 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 dis-
charge 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
reated with procardia, 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 hypoten-
sive 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 doses of epinephrine within 48 hours of admission
and was transferred to our level III neonatal intensive care unit for further evaluation and manage-
ment. 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 broncho-
pulmonary 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 con-
duction, 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 com-
pounder. Physicians and pharmacists should be aware of this potentially fatal iatrogenic complica-
tion. 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 magne-
sium 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 hypermag-

nesemia may prevent or minimize life-threatening events; however, the vast majority of mild hyperma-
gnesemia 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, weak-
ness, 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 re-
moval of exogenous magnesium source, and the use
of intravenous calcium. The exact mechanism of
action of calcium is not known, but it causes dis-
placement 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 modal-
ities, but renal dialysis, either peritoneal or hemodi-
alysis is the treatment of choice in refractory hyper-
magnesemia.11–17

Both patients were followed at 4 and 8 months,
corrected age at the nursery follow-up clinic for de-
velopmental 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.

REFERENCES

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

Pediatrics 2003;112:e70

Updated Information & Services
including high resolution figures, can be found at:
/content/112/1/e70.full.html

References
This article cites 16 articles, 2 of which can be accessed free at:
/content/112/1/e70.full.html#ref-list-1

Citations
This article has been cited by 6 HighWire-hosted articles:
/content/112/1/e70.full.html#related-urls

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Infectious Disease
/cgi/collection/infectious_diseases_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2003 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.
Iatrogenic Acute Hypermagnesemia After Total Parenteral Nutrition Infusion Mimicking Septic Shock Syndrome: Two Case Reports

*Pediatrics* 2003;112;e70

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/112/1/e70.full.html