

# Morbid Hypocalcemia Associated With Phosphate Enema in a Six-Week-Old Infant

Dawn M. Walton, MD\*‡; David C. Thomas, MD\*‡; Hany Z. Aly, MD\*‡; and Billie L. Short, MD\*‡

**ABSTRACT.** A 6-week-old premature infant who was born at 29 weeks of gestation presented to the emergency department with a several-hour history of stiffness and increased alarms on his apnea monitor at home. On arrival he was noted to have generalized seizures, apnea, and bradycardia. He was intubated and required cardiopulmonary resuscitation including chest compressions and medications. After stabilization he was transferred to the neonatal intensive care unit for further management. His initial laboratory tests revealed a serum calcium level of 2.4 mg/dL (normal range: 8.4–10.2 mg/dL) and a serum phosphorus level of 28.5 mg/dL (normal range: 2.4–4.5 mg/dL). During the first week of admission, the infant's mother reported that she had administered a full pediatric Fleets enema (CB Fleet Company Inc, Lynchburg, VA) to him. The infant was discharged after 12 days of hospitalization.

Anticipatory guidance on the stool patterns and behavior of infants can prevent misconceptions about constipation that are especially prevalent in new parents. Proper management of constipation, should it arise, should be addressed with all parents at early well-child visits to avoid hazardous complications of treatments. *Pediatrics* 2000;106(3). URL: <http://www.pediatrics.org/cgi/content/full/106/3/e37>; hypocalcemia, seizures, premature infants, enema.

There have been a few historical reports of fatal electrolyte disturbances after the administration of enemas for constipation relief.<sup>1,2</sup> This article describes the first reported case of a former premature infant who presented with profound hypocalcemic seizures and cardiac arrest after the administration of a sodium phosphate Fleets enema at home.

## CASE REPORT

A 6-week-old premature infant who was born at 29 weeks' gestation presented to a community hospital emergency department with a several-hour history of stiffness and increased alarms on his apnea monitor at home. On arrival, he was noted to have generalized seizures, apnea, and bradycardia. He was intubated and required cardiopulmonary resuscitation, including chest compressions and 3 doses of epinephrine, before restoration of a normal heart rate. He also received 3 mEq/kg of sodium bicar-

bonate, 3 mL/kg D<sub>10</sub>%W, and 50 mg/kg of cefotaxime via bilateral intraosseous lines during the resuscitation. Phenobarbital was given in an attempt to stop the seizure activity, without success. After stabilization he was transferred to the neonatal intensive care unit at our institution for further management.

History obtained from the birth hospital revealed that he was born at 29 weeks of gestation to a 36-year-old, gravida 7, para 4 mother. Pregnancy was complicated by premature prolonged rupture of amniotic membranes for 3 days before delivery. Screening test for group B streptococcus was negative. His birth weight was only 992 g (<25%), which prompted a work-up for intrauterine growth restriction including a normal karyotype and negative screening tests for toxoplasmosis, cytomegalovirus, herpes simplex virus, and syphilis. Except for a few episodes of apnea, the postnatal course was uncomplicated and he was discharged from the hospital at 4 weeks old with an apnea monitor and no medications. A sleep study test was not available. He was discharged on the follow-up milk formula, Neocare (Ross Products Division, Abbott Laboratories, Columbus, OH), but his primary caretaker (a maternal aunt) was feeding him regular infant formula, Similac (Ross Products Division, Abbott Laboratories), for financial reasons. Proper preparation of formula was described on admission. His caretakers reported no events on the apnea monitor before the day of admission and no concerns except for constipation that was described as infrequent soft stools with apparent straining on defecation. At the time of admission they reported no use of constipation remedies or use of other formula, water, cow's milk, cereal, or juices. He had not seen a pediatrician since discharge.

Physical examination on arrival to the neonatal intensive care unit at the Children's National Medical Center was remarkable for a pale, lethargic, and intubated infant with frequent spasms of the extremities and slow jerking of the head to one side. Axillary temperature was 36.7°C, pulse rate was 148/minute, and mean arterial pressure was 40 mm Hg. He was breathing spontaneously on the ventilator. The anterior fontanel was open and flat. Pupils were equal and reactive. A bullous skin lesion with an erythematous base was present above the umbilicus, where a temperature probe had been placed during resuscitation. Cardiac examination revealed regular rate and rhythm with no murmurs. The capillary refill was 4 to 5 seconds, and all pulses were weak. Lungs were clear on auscultation with equally good air entry bilaterally. The abdomen was soft and nontender, but distended. Bowel sounds were absent. The infant's tone was generally poor with irregular movements as described above.

Initial laboratory data on admission are presented in Table 1. Chest radiogram revealed a left lower lobe opacity believed to be an infiltrate because no previous films were available for comparison. Head computed tomography scan was within normal limits for gestational age.

Because the serum phosphorus, calcium, and magnesium were grossly abnormal, serum parathyroid hormone level was measured. Intravenous boluses of magnesium and calcium were administered until normal serum levels of calcium, magnesium, and phosphorus were obtained by the fourth day of hospitalization. The infant was able to maintain normal serum minerals values as intravenous fluid was weaned off and feeding with the follow-up milk formula, EnfaCare-22 (Mead Johnson Nutritionals, Evansville, IN), was established (Table 1). Phenobarbital was discontinued, and no further seizure activity was noted. All cultures were negative and antibiotics were discontinued after 7 days. Intact serum parathyroid hormone level was 173 pg/mL (normal range: 12–72 pg/mL).

During the first week of admission, the biologic mother re-

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**TABLE 1.** Laboratory Values on Admission and at Discharge

Test Name	Admission	Discharge	Units
Blood count			
White count	7.3	10.7	10 <sup>3</sup> /mm <sup>3</sup>
Hemoglobin	6.3	12.4	g/dL
Hematocrit	18.8%	37.4	
Platelet	252	282	10 <sup>3</sup> /mm <sup>3</sup>
Differential			
Granulocyte	3%	31%	
Lymphocyte	74%	42%	
Monocyte	6%	16%	
Neutrophil band	16%	0%	
Arterial blood gas			
Ph	7.23		
Partial pressure of carbon dioxide, arterial	35		mm Hg
Partial pressure of oxygen, arterial	42		mm Hg
HCO <sub>3</sub> <sup>-</sup>	14		mmol/L
Base deficit	-12.5		mmol/L
Blood chemistry			
Sodium	145	140	mmol/L
Potassium	3.2	4.6	mmol/L
Chloride	102	112	mmol/L
Carbon dioxide	12	25	mmol/L
Blood urea nitrogen	2	2	mg/dL
Creatinine	.5	.3	mg/dL
Phosphorus	28.5*	5.7	mg/dL
Calcium	2.4†	9.4	mg/dL
Magnesium	1‡	2.3	mg/dL
Albumin	1.8	3.1	g/dL
Alkaline phosphatase	126	229	U/L

\* Normal range is 2.5 to 4.5 mg/dL.

† Normal range is 8.4 to 10.2 mg/dL.

‡ Normal range is 1.7 to 2.2 mg/dL.

ported that while under her care on the day before admission, she had administered a full pediatric Fleets enema to her infant. The infant was discharged from the hospital under the care of his aunt after 12 days of hospitalization. Follow-up with serum parathyroid hormone level was recommended to the primary pediatrician. Anticipatory guidance on infant stool patterns and the management of constipation were discussed. The infant was referred to the Women, Infant and Children program for formula supply.

## DISCUSSION

This is a case of a near fatal electrolyte disturbance caused by an over-the-counter remedy for constipation. Straining with defecation or changes in stool color or frequency can be a significant cause of concern for new parents. Well-meaning health care personnel may unnecessarily heighten this concern by providing parental education that overemphasizes monitoring infant defecation patterns.

Calcium and phosphorous are tightly regulated by the interdependent actions of parathyroid hormone, vitamin D, and calcitonin.<sup>3</sup> The fetal build-up for these minerals starts to increase at 24 weeks of gestation, and the peak accretion occurs at 34 to 36 weeks of gestation.<sup>4</sup> For this reason, along with a suboptimal intake of calcium and phosphorus, premature infants become deficient in these minerals after birth. The recommended daily allowance for these minerals is much higher for preterm infants compared with term infants.<sup>5,6</sup> This patient had normal serum calcium, phosphorous, and alkaline phosphatase enzyme levels at discharge from the birth

hospital but had been home on a less than optimal formula, in terms of mineral supply, for his gestational age. However, his serum alkaline phosphatase enzyme level on this admission was still within the normal range. The differential diagnosis of hypocalcemia can be classified by early versus late onset of the symptoms. Early-onset hypocalcemia usually presents in the first 48 hours of life and is frequently secondary to prematurity, perinatal asphyxia, maternal diabetes mellitus, or maternal use of anticonvulsants.<sup>7</sup> Late onset, as in this case, was historically associated with early use of cow milk-based formulas with a high phosphate load and a low calcium to phosphorous ratio. Infant formulas currently on the market have more favorable calcium to phosphorous ratios and, therefore, may reduce this problem. Other causes of late-onset hypocalcemia include phosphate loads from other sources, hypomagnesemia, and hypoparathyroidism. In this patient, the high phosphate load from the enema led to the severe hyperphosphatemia and hypocalcemia that resulted in seizure activity and cardiorespiratory arrest. The elevated parathyroid hormone is secondary to the state of severe hypocalcemia.

Sodium phosphate enemas, like many other over-the-counter medications, are not recommended for children <2 years of age. They do not require a prescription; however, they are kept behind the counter in many pharmacies so consumers can be instructed on the proper usage. A rectal dosage of a pediatric enema contains 11.4 mmol of dibasic sodium phosphorous and 39.7 mmol of monobasic sodium phosphorous. The recommended daily allowance for phosphorous in an infant is only 1 to 2 mmol/kg/day. In the past, many physicians would recommend enemas for infants with the belief that very little phosphorous is absorbed during rectal administration. There have been a few case reports of fatal poisoning and severe electrolyte disturbances after the administration of phosphate enemas in children of different ages. One fatal case resulted from enemas administered in the hospital before surgery.<sup>2</sup> This case led the authors to perform an experimental study with piglets to measure the absorption of electrolytes after different dosages of enemas. The administration of enema—even at a dose as low as 20 mL/kg—was fatal.<sup>2</sup> Although no longer recommended for infants' constipation, these products are still available for other uses such as preoperative bowel preparation.

Anticipatory guidance on the stool patterns and behavior of infants can prevent misconceptions about constipation that are especially prevalent in new parents. Proper management of constipation, should it arise, should be addressed with all parents at early well-child visits to avoid hazardous complications of treatments.

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