11 Disorders of Calcium, Phosphorous, and Magnesium in the Newborn

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Disorders of Calcium, Phosphorous, and Magnesium in the Newborn

Calcium, phosphorous, and magnesium are stored mainly in the bone; hence these minerals are referred to as the "bone minerals." A portion of these minerals reside in the intracellular and extracellular spaces where they have important roles in critical physiological processes, including transport across cell membranes, enzyme activation and inhibition, regulation of intracellular metabolic pathways, and secretion and activity of hormones. These minerals are also involved in protein synthesis, maintaining membrane integrity, muscle contractility, neuromuscular excitation, nerve conduction, coagulation, and energy metabolism. Additionally, phosphorous is an important constituent of nucleic acids and cell membranes.

In the normal newborn nursery, symptoms of calcium, magnesium, and phosphorous abnormalities are relatively uncommon and often nonspecific. Awareness of these disorders facilitates early recognition and the institution of appropriate therapies. Failure to recognize the significance of symptomatic infants with these disorders can have dire consequences.

Case Presentation

A female infant is born at 37 4/7-week gestational age, with a birth weight of 4320 grams (9 pounds, 8 ounces). This is the first pregnancy for a 24-year-old mother whose blood type is A+. She had good prenatal care, and screening for group B streptococcus at 35-week gestation was negative. The pregnancy was complicated by maternal obesity (BMI 37) and gestational diabetes, with an abnormal oral glucose tolerance test and hemoglobin A1C level of 8.3% (desired value <6%). Onset of labor is spontaneous but ultimately results in caesarian section

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due to arrest of descent of the fetal head into the maternal pelvis. Rupture of membranes was 12 h prior to delivery. The infant is vigorous upon delivery, and no resuscitation is required beyond drying, bulb suction, and tactile stimulation. Apgar scores at 1 and 5 min are 9 and 9, respectively.

The infant is transferred to the newborn nursery at 1 h of life. She is doing well. She has attempted direct breastfeeding once and had a good latch and effective suck; however her mother's milk has not yet come in. At approximately 2 h of life, the infant is noted to be jittery.

What should you do?

1. Check blood glucose.
2. Check urine toxicology screen.
3. Check electrolytes including calcium and magnesium levels.
4. Draw blood culture and start antibiotics.

Given that this infant is large for gestational age, and the infant of a diabetic mother, the most likely cause of jitteriness and one that would require immediate attention, is hypoglycemia. Therefore, a reasonable first step would be to check a blood glucose level at the bedside.

Answer: 1

It would not be wrong, in the case of a jittery infant, to check a urine toxicology screen or electrolytes. However, in the case of the infant of a diabetic mother where neonatal hypoglycemia is the most common cause of jitteriness, this quick bedside point-of-care test is an appropriate first step.

Blood glucose checked and noted to be 25 mg/dL. The infant is fed, and blood glucose is checked again and is noted to be 32 mg/dL. Peripheral intravenous access is established, and the infant is given 2 ml/kg of 10% dextrose in water as an intravenous bolus, followed by the initiation of intravenous infusion of 10% dextrose in water at a glucose infusion rate (GIR) of 6 mg/kg/min. The blood glucose is checked again 10 min later and is now 70 mg/dL. On exam, however, the infant remains jittery.

Infants of diabetic mothers are at risk for hypoglycemia following delivery. This occurs as the result of fetal pancreatic islet cell hypertrophy in response to increased placental transfer of glucose from hyperglycemic mother to fetus. Maternal insulin is not transferred to the fetus across the placenta; therefore, in order to maintain euglycemia, the fetus increases endogenous production of insulin. At delivery, the placental transfer of glucose is abruptly discontinued, but the pancreatic islet cells continue to secrete insulin at the rate that was necessary for glucose metabolism during fetal life, placing the infant at risk for hyperinsulinemic hypoglycemia. Hypoglycemia is a common cause of jitteriness in an infant, but it is not the only cause.

What are your next steps?

1. Check electrolytes including calcium and magnesium.
2. EEG.
3. Give a second D10W IV bolus and recheck blood glucose level.
4. Increase GIR until jitteriness resolves.

The most recent blood glucose, taken when the infant was on a GIR of 6 mg/kg/min, is within normal limits. Since the infant remains on consistent GIR, and remains jittery, the next step is to evaluate for other causes of jitteriness, including electrolyte abnormalities.

Answer: 1

A set of electrolytes is sent to the lab for analysis and reveals the infant to have a total serum calcium level of 6.8 mg/dL with an ionized calcium level of 0.79 mmol/L.

What is/are the next step(s)?

1. Add oral calcium supplementation to enteral feeds.
2. Add calcium gluconate to IV fluid infusion.
3. Give calcium bolus.
4. Check magnesium.

Because the infant is symptomatic, IV calcium gluconate is added to continuous IV fluids

with dextrose. The infant's jitteriness resolves. Upon recheck, total serum calcium concentration is 8.8 mg/dL, and ionized calcium level is 1.2 mmol/L. As the infant begins to feed, she is able to be weaned off of continuous infusion of dextrose and calcium, and neither hypoglycemia nor hypocalcemia recur.

Answer: 2

Neonatal Hypocalcemia

Neonatal hypocalcemia is defined as a serum calcium concentration of less than 2 mmol/L (8 mg/dL) or an ionized calcium concentration of less than 1.1 mmol/L (4.8 mg/dL). The interruption of the placental calcium supply at the time of birth is associated with a physiologic drop in the serum calcium concentration. The infant normally maintains serum calcium homeostasis by reabsorption of calcium stored in the bones and from enteral nutrition.

Hypocalcemia may be associated with?

1. Prematurity.
2. Maternal diabetes.
3. Perinatal asphyxia.
4. Intrauterine growth restriction.
5. All of the above.

The most common causes of hypocalcemia in the newborn (1–4 days of life) include prematurity, maternal diabetes, perinatal stress/asphyxia, and intrauterine growth restriction. Symptoms are nonspecific and may include jitteriness, apnea, cyanosis, or seizures.

Answer: 5

Infants of diabetic mothers (IDM) have an exaggerated drop in serum calcium concentration. IDMs are also at increased risk of being born prematurely and of perinatal stress/asphyxia, both of which are independent risk factors for hypocalcemia and further increase the risk for an infant of a diabetic mother. Hypocalcemia in an IDM may be related to maternal hypomagnesemia which is caused by increased urinary excretion of magnesium. This can result in fetal and neonatal hypoparathyroidism and will make it difficult to correct the serum calcium concentration until the serum magnesium concentration is replete. The degree of hypocalcemia in an IDM is correlated with the severity of maternal diabetes during the pregnancy.

When an infant has symptoms associated with hypocalcemia, it is important to determine the concentrations of total serum calcium as well as the ionized portion. It is important to consider the ionized portion in addition to the total blood calcium concentration, as calcium is highly bound to albumin. It is the ionized portion of calcium that is physiologically active. Newborns often have relatively low levels of blood albumin; therefore, their total blood calcium concentration may be proportionally lower than their ionized calcium concentration. When this is the case, the infant is generally not symptomatic, as the physiologically active ionized portion may be within normal limits. It is also important to check serum albumin, a blood gas (acidosis will displace calcium from albumin, allowing for a relatively increased ionized portion of total serum calcium), and urine concentrations of calcium, magnesium, and phosphorous. If hypocalcemia is refractory to treatment with calcium supplementation, it may be accompanied by concurrent hypomagnesemia. If the cause remains undetermined, the next steps may be to perform a thorough physical exam including a cardiac exam, check parathyroid hormone and calcitonin levels, obtain a radiograph of the chest looking for absence of the thymus, and obtain genetic studies to evaluate for DiGeorge syndrome.

The treatment for hypocalcemia is to provide supplemental calcium. In most cases, asymptomatic neonatal hypocalcemia will resolve spontaneously with enteral nutrition, and many providers will choose to monitor without treatment. Symptomatic hypocalcemia, on the other hand, is treated with administration of calcium salts, usually intravenously. In cases of hypocalcemic seizure, tetany, or apnea, an intravenous bolus of a calcium salt should be given, usually in an intensive care setting. First choice is usually calcium gluconate, but calcium chloride may be more readily available and may be

used in an emergency. A bolus of 1–2 ml/kg of 10% calcium gluconate (approximately 9–18 mg/kg elemental calcium) may be administered intravenously over 10 min. This must be done while an infant is on a continuous heart rate monitor, as it can be accompanied by bradycardia. Following a bolus, or to correct more slowly in cases of lower urgency, IV calcium replacement may be given as a continuous infusion at a rate of up to 75 mg/kg/day of elemental calcium until serum calcium levels normalize and then should be weaned slowly over a period of approximately 8–24 h. Calcium levels should be monitored closely during the period of replacement and for at least 1–2 days following discontinuation of therapy. Alternatively, if an infant is tolerating oral feeds, enteral calcium preparations may be used to provide calcium supplementation, but this should also be done with caution, as all calcium preparations are hypertonic and are accompanied by a theoretical risk of necrotizing enterocolitis. Infants requiring calcium replacement for symptomatic hypocalcemia should generally be transferred to a tertiary care setting for close monitoring during replacement.

Complications of IV calcium infusions include:

1. Cardiac arrhythmias.
2. Cardiac arrest.
3. Nephrolithiasis.
4. Skin necrosis.
5. All of the above.

IV infusion of calcium has a number of potential complications. The cardiac rhythm may be affected, most commonly as bradycardia, but other arrhythmias may occur as well. For this reason, IV calcium boluses should be administered slowly in a controlled setting with continuous cardiac monitor. Nephrolithiasis is another possible complication of IV calcium administration. Additionally, intravenous calcium can extravasate from the vein into the soft tissues, causing calcium deposition into the tissues and sometimes even tissue necrosis.

Answer: 5

Neonatal Hypercalcemia

Neonatal hypercalcemia is defined as a serum calcium concentration of greater than 2.75 mmol/L (11 mg/dL) or an ionized calcium concentration of greater than 1.35 mmol/L (5.4 mg/dL). It is generally caused by excess administration of calcium or vitamin D_3, although there can be other causes. Thiazide diuretics, for example, cause the kidney to retain calcium and can lead to hypercalcemia. Other potential causes include hyperparathyroidism (maternal or neonatal), vitamin A toxicity, and hypophosphatemia. Signs are nonspecific, including poor feeding, vomiting, constipation, and hypotonia. Treatment will depend in part on the etiology but in general involves intravenous hydration and loop diuretics to increase calcium excretion.

Case Presentation

A 27-year-old G2 P1001 woman is admitted to labor and delivery at 36 6/7-week gestation for severe headaches and is found to have a blood pressure of 180/100 and proteinuria. She is diagnosed with severe preeclampsia and started on IV blood pressure medication and IV magnesium sulfate (initial loading dose of 4 g, followed by IV infusion of 1 g/h) for seizure prophylaxis. Her blood pressure proves difficult to control on IV antihypertensive medication and magnesium sulfate, and the decision is made to induce labor. Thirty six hours later, she delivers a female infant with a birth weight of 2270 grams (5 pounds). At the time of delivery, the infant has spontaneous respiratory effort and a heart rate of 130 but is noted to have low tone. Apgar scores are 6, 7, and 8 at 1, 5, and 10 min, respectively. She is transferred to the normal nursery. On your exam 2 h later, you notice significant hypotonia and decreased respiratory drive with shallow breathing.

What is the most likely cause of the infant's condition?

1. Prematurity.
2. Hypermagnesemia.

3. Spinal muscular atrophy.
4. Perinatal asphyxia.

In light of the prolonged exposure to high-dose intravenous magnesium sulfate, the most likely diagnosis for this infant is hypermagnesemia. The infant is late preterm, and this degree of hypotonia and shallow breathing is out of proportion for what would be expected of a late preterm infant. Spinal Muscular atrophy is characterized by severe hypotonia as well as tongue fasiculations, which are absent in this infant. The Apgar scores were not compatible with perinatal asphyxia. A set of electrolytes is sent, including a magnesium level, which was 3.4 mg/dL. Hypermagnesemia is defined as a serum magnesium concentration greater than 1.15 mmol/L (2.8 mg/dL).

Answer: 2

Neonatal Hypermagnesemia

Question: Neonatal hypermagnesemia is usually caused by?

1. Maternal hyperparathyroidism.
2. Hypercalcemia.
3. Renal impairment of magnesium excretion.
4. Exogenous administration of magnesium.

In the fetus and newborn, hypermagnesemia is always the result of exogenous magnesium sources, including intrapartum magnesium sulfate, gastric acid suppressive medications taken during pregnancy, neonatal parenteral nutrition, or magnesium administered to critically ill infants as therapy for such conditions as persistent pulmonary hypertension of the newborn.

Answer: 4

Magnesium sulfate is frequently given intravenously intrapartum as a prophylactic measure in women with preeclampsia to prevent the development of seizures and progression to eclampsia. In the case of threatened or impending preterm delivery, magnesium sulfate infusion is also used for prevention of cerebral palsy in the fetus. However, maternal hypermagnesemia and fetal/neonatal hypermagnesemia may be induced by the infusion. In the scenario of intrapartum magnesium exposure, the serum magnesium concentration in the neonate will usually spontaneously return to normal over a period of hours to a few days.

Hypotonia is the most common symptom seen in neonatal hypermagnesemia, but infants can also exhibit respiratory depression as seen in the vignette, neuromuscular depression, hypotension, and urinary retention.

For most infants, treatment of hypermagnesemia is simply close monitoring and supportive care, while the excess magnesium is eliminated by the body by urinary excretion. This may include support of respiration until enough excess magnesium has been eliminated to allow for resolution of CNS depression. Intravenous fluids may be given to optimize hydration and increase urinary flow rate, or loop diuretics may be given to aid in renal elimination of excess magnesium. In acute cases, intravenous calcium may be given as a direct inhibitor magnesium.

Neonatal Hypomagnesemia

While the definition of hypomagnesemia is a serum magnesium concentration below 0.66 mmol/L (1.6 mg/dL), clinical signs are not seen until the level is less than 0.49 mmol/L (1.2 mg/dL). The two main causes are decreased magnesium supply (IUGR, malabsorption syndromes, intestinal magnesium transport defects) or increased urinary magnesium losses (maternal diabetes, hypoparathyroidism, renal tubular defects). Because magnesium influences parathyroid hormone secretion, severe hypomagnesemia may lead to hypoparathyroidism and resultant hypocalcemia. Signs of hypomagnesemia include hyperexcitability, irritability, tremors, and seizures. If the neonate has hypocalcemic seizures that do not respond to calcium infusion and anti-seizure medications, hypomagnesemia should be considered. Treatment is with magnesium salts, which should be given in an intensive care unit or other location with appropriate monitoring, as intravenous magnesium infusion can lead to hypotension and arrhythmias.

Neonatal Phosphorous Metabolism

Phosphorous has an important role and is found throughout the body, as opposed to calcium which is primarily stored in the bone. Given the critical role of phosphorous in multiple areas, phosphate deficiency can lead to a number of problems, including muscle weakness, poor immune system function, and abnormal bone metabolism. Hypophosphatemia is seen with high parathyroid hormone levels leading to increased renal phosphate excretion or with poor phosphate intake. The American Academy of Pediatrics recommends 100 mg/day of phosphorous in the first 6 months of life. Hyperphosphatemia can be seen with impaired phosphate excretion by the kidneys due to renal failure or low parathyroid hormone levels (Tables 11.1, 11.2, and 11.3).

Table 11.1 Normal values of calcium, magnesium, and phosphorous in the serum

Normal concentration in serum	mmol/L	mg/dL
Total calcium	2–2.75	8–11
Ionized calcium	1.1–1.35	4.28–5.4
Magnesium	0.66–1.15	1.6–2.8
Phosphorous	1.62–2.52	4.3–7.1

Derived from Abrams and Tiosano [1]; Kubicka and Little [4]

Table 11.2 Causes, signs, and evaluation of early neonatal hypocalcemia

Early hypocalcemia	
Causes	Prematurity
	Infant of a diabetic mother
	Perinatal stress and/or asphyxia
	Intrauterine growth restriction
	Maternal medications
Signs	Jitteriness
	Apnea
	Cyanosis
	Seizures Tetany
Evaluation	Total and ionized serum calcium concentrations
	Serum magnesium level
	Serum phosphorous level
	Blood glucose testing
	Acid/base balance (blood gas)
	Chest radiograph (thymic shadow)
	Urine calcium, magnesium, and phosphorous levels

Derived from Abrams and Tiosano [1]

Table 11.3 Causes, signs, evaluation, and treatment of neonatal hypermagnesemia

Hypermagnesemia	
Causes	Perinatal magnesium sulfate therapy
(All relate to increased supply)	Neonatal magnesium therapy
	Parenteral nutrition
	Acid suppressive medications
	Enemas
Signs	Birth depression in infants of mothers treated with perinatal magnesium
	Hypotonia
	Neuromuscular depression
	Hypotension
	Urinary retention
	Respiratory depression
Evaluation	Serum magnesium level
Treatment	Supportive
	IV calcium therapy in extreme cases
	Hydration therapy
	Loop diuretics

Derived from Abrams and Tiosano [1]

Clinical Pearls

1. Hypoglycemia is a common cause of jitteriness in a neonate, but it is not the only possible cause.
2. Neonatal hypocalcemia is strongly associated with gestational diabetes, and the degree of hypocalcemia correlates to the severity of gestational diabetes.
3. Intravenous calcium administration, be it bolus doses or continuous infusions, should always be given with caution and while on continuous cardiac monitor.
4. Asymptomatic neonatal hypocalcemia will likely resolve with good enteral nutrition alone.
5. Neonatal hypermagnesemia is always the result of exogenous administration.
6. Hypotonia is the most common symptom of neonatal hypermagnesemia, but hypermagnesemia can also cause respiratory depression which may require support of respiration while awaiting urinary excretion of excess magnesium.
7. Because magnesium levels affect parathyroid function, it can be difficult to correct hypocalcemia in the face of concurrent hypomagnesemia.

Further Reading

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