PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "**Neonatal Hypoglycemia.**" These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Neonatal Hypoglycemia

Developed by Carina Lauzon and Dr. Marc-Antoine Landry for PedsCases.com.
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Introduction

Hi everyone, my name is Carina Lauzon and I am a second year medical student at the University of Alberta. This PedsCases podcast is designed to give an organized approach to neonatal hypoglycaemia, the most common metabolic problem in neonates and the leading cause of admissions to the neonatal intensive care unit. This podcast was created with Dr. Marc-Antoine Landry, a neonatologist at the Royal Alexandra Hospital in Edmonton, Alberta, Canada.

Clinical Case

Let's start with a clinical case: you are a third year medical student working on your pediatrics rotation. You are called to see baby Emma, who was born one hour ago, at 39 weeks gestation, to a mother with gestational diabetes. Emma's mother's pregnancy and Emma's birth were uneventful, but she now presents with irritability and jitteriness. Considering what you know about this patient, what should your next steps be? We will review the answer to this case at the end of the podcast.

Objectives

After listening to this podcast, the learner will be able to:

1. Recognize which infants are at risk for neonatal hypoglycaemia
2. Know the signs and symptoms of neonatal hypoglycaemia
3. Recognize which infants should be screened for neonatal hypoglycaemia and know how screening should be performed
4. Know how to diagnose and manage neonatal hypoglycaemia

Normal Glucose Homeostasis

We will start with an overview of normal glucose homeostasis. Maintaining appropriate blood glucose levels is extremely important. The brain uses glucose as its primary fuel to meet its metabolic needs and therefore, sustained hypoglycaemia or very low glucose levels can lead to brain damage.

The main hormones responsible for control of blood glucose are insulin and glucagon, but adrenaline, cortisol, and growth hormone also play a role in glucose homeostasis. In response to high blood glucose levels, insulin secretion from beta cells in the pancreas is increased and this stimulates the liver to store glucose as glycogen. When blood glucose levels are low, glucagon secretion from pancreatic alpha cells is increased and this stimulates glycogenolysis and gluconeogenesis, therefore increasing the release of glucose into the bloodstream. During times of starvation, amino acids from muscle stores can be used for

gluconeogenesis and fatty acids can be broken down to produce ketone bodies, an alternate fuel source for the tissues of the body, including the brain. Starvation also stimulates the sympathetic nervous system, thus causing the release of epinephrine from the adrenal glands, which increases the release of glucose from the liver. Finally, in periods of prolonged hypoglycaemia, the body secretes growth hormone and cortisol; these hormones reduce the rate at which the body utilizes its limited glucose supply.

In utero, the fetus receives a constant supply of glucose from its mother via facilitated diffusion through the placenta. The fetus produces its own insulin in order to maintain glucose homeostasis in the womb. After birth, the constant supply of glucose that the baby was receiving from its mother stops abruptly, and therefore, in order to prevent hypoglycaemia, neonatal secretion of insulin must be regulated. In the healthy newborn, serum glucose levels will drop in the first 2-3 hours of life, then will spontaneously increase and subsequently be maintained by regular feedings. It can be normal to see low blood glucose levels in the first 24-48 hours of life, as the baby adjusts to life outside the womb. This is called transitional hypoglycaemia and is seen in up to 10% of healthy term infants. In asymptomatic babies without risk factors for neonatal hypoglycaemia, which we will discuss next, these brief periods of low blood glucose are assumed to be benign.

Risk factors/Causes for Neonatal Hypoglycaemia

The most important risk factors for neonatal hypoglycaemia include being small for gestational age (SGA, <10th percentile) or large for gestational age (LGA, >90th percentile), intrauterine growth restriction (IUGR), being born prematurely (<37 weeks), and being the infant of a diabetic mother. Infants who suffer from sepsis and infants of mothers with eclampsia or chorioamnionitis are also at an increased risk for hypoglycaemia.

The two most common causes of neonatal hypoglycaemia are excess insulin production and inadequate glycogen stores: in both of these situations, gluconeogenesis is impaired.

Excess insulin production, or hyperinsulinism, is the most common cause of neonatal hypoglycaemia. Hyperinsulinism frequently occurs in infants of diabetic mothers and in macrosomic infants (infants who weigh over 4kg at birth): these infants receive a large supply of glucose from their mothers in utero and therefore must produce a large amount of insulin in order to maintain glucose homeostasis. This can cause hypoglycaemia after birth, as the infant continues to produce large amounts of insulin in the absence of the large glucose supply. A more rare cause of hyperinsulinism is a congenital disorder called Persistant Hyperinsulinism Hypoglycaemia of Infancy (PHHI), in which the normal relationship between blood glucose levels and insulin secretion is disturbed and insulin is released even at low blood glucose levels. Other less common conditions such as Beckwith-Wiedemann syndrome and Sotos syndrome can also lead to hyperinsulinism.

Inadequate glycogen stores are another common cause of neonatal hypoglycaemia. Infants who are born prematurely (<37 weeks), are small for gestational age (SGA) or have intrauterine growth restriction may have low hepatic glycogen stores, low muscle stores, and low lipid stores to be used as substrates for gluconeogenesis and ketogenesis. Similarly, infants who experience perinatal asphyxia or starvation may deplete their glycogen stores and therefore be unable to produce glucose through gluconeogenesis.

Other less common causes of neonatal hypoglycaemia include increased glucose use (which can happen as a result of hypothermia, sepsis, polycythemia, growth hormone deficiency, or cortisol deficiency), inborn errors of metabolism, adrenal insufficiency, liver disease, poisonings or drugs, and systemic disease.

Signs and Symptoms

The clinical presentation of neonatal hypoglycaemia can range from a completely asymptomatic infant to severe central nervous system and cardiopulmonary disturbances.

There are two general categories of symptoms of neonatal hypoglycaemia: neurogenic symptoms and neuroglycopenic symptoms.

The neurogenic symptoms happen as a result of sympathetic nervous system stimulation in response to hypoglycaemia. They are the first symptoms to appear, occurring at higher blood glucose concentrations than the neuroglycopenic symptoms. The neurogenic symptoms include jitteriness, pallor, temperature instability, irritability, tachycardia, and vomiting.

The neuroglycopenic symptoms happen as a result of decreased glucose delivery to the brain and include apnea, episodes of cyanosis, hypotonia, unresponsiveness, lethargy, seizures, a weak or high-pitched cry, and coma that may lead to death if the hypoglycaemia is not corrected.

Severe, recurrent neonatal hypoglycaemia can cause permanent brain damage, which can lead to cognitive abnormalities, cerebral palsy, personality disorders, and occipital lobe epilepsy.

Screening

Because neonatal hypoglycaemia can lead to severe consequences, it is important to know which babies should be screened. It is not clear exactly what blood glucose level indicates neonatal hypoglycaemia, as a single number cannot be applicable to all infants and all situations. The blood glucose at which hypoglycaemia occurs depends on the infant's size, gestation, clinical condition, availability of energy sources and energy demand. For the purposes of screening, the Canadian Pediatric Society recommends using a cut-off of 2.6 mmol/L in at risk infants, as blood glucose levels below this are associated with adverse outcomes, especially if persistent or repeated.

During the first two hours of life, infants should not be screened for neonatal hypoglycaemia unless they are unwell. If they are unwell and have a blood glucose level of below 2.6 mmol/L, treatment should be considered.

After two hours of age, if the infant is well and is not at risk for neonatal hypoglycaemia, routine care should be given, including feeding on demand. The infant should not be tested unless they become unwell. In infants who are at risk for neonatal hypoglycaemia (SGA, LGA, IUGR, preterm, or infant of a diabetic mother), blood glucose levels should be checked at two hours of age, after at least one effective feed, and then every 3-6 hours after that, before feeds, provided that the infant remains well and glucose levels are stable.

In at risk infants, we aim for blood glucose levels above 2 mmol/L at 2 hours of age and above 2.6 mmol/L at subsequent checks. If the infant's glucose level is <1.8 mmol/L at 2 hours of age or <2 mmol/L at subsequent checks, treatment should be considered immediately. If the glucose level is between 1.8-2 mmol/L at 2 hours of age or 2-2.5 mmol/L at subsequent checks, the infant should receive another feeding and glucose levels should be checked again 1 hour later. If the glucose level remains < 2.6 mmol/L after feeding, treatment should be considered.

In infants of diabetic mothers or those who are large for gestational age, hypoglycaemia usually happens within the first 12 hours of life. Therefore, glucose testing can be stopped if levels have been consistently above 2.6 mmol/L at 12 hours of age. In infants who are small for gestational age or premature, hypoglycaemia usually happens within the first 36 hours of life. In these cases, testing can be discontinued if glucose levels are consistently above 2.6 mmol/L and regular feeds have been established by 36 hours of age.

Treatment

Treatment methods for neonatal hypoglycaemia include increased breastfeeding frequency, supplementation with breast milk, formula, or 40% dextrose gel, IV glucose, and pharmacological intervention. Frequent breastfeeding on demand should be encouraged in at risk infants in an attempt to prevent neonatal hypoglycaemia. If mild hypoglycaemia occurs,

increased frequency of feeding plus or minus supplementation may be all that is needed to help the infant return to a euglycaemic state.

However, if hypoglycaemia is persistent or more severe, IV glucose therapy should be used. The Canadian Pediatric Society recommends starting with a 10% dextrose solution at 80 mL/kg/day. Blood glucose levels should be monitored 30 minutes after any change in therapy and therapy can be adjusted as needed to maintain blood glucose levels above 2.6 mmol/L. A single minibolus of 2mL/kg 10% dextrose solution can be used to reach target glucose levels more quickly, particularly when a baby is symptomatic. IV glucose therapy may be weaned when blood glucose levels have been stable for 12-24 hours, depending on the clinical stability of the child.

If rates of over 100 mL/kg/day of 12.5% dextrose are needed to maintain blood glucose levels above 2.6mmol/L, further investigations should be performed in order to identify a possible endocrine pathology or inborn error of metabolism. Referral to a specialist and pharmacological intervention in the form of IV glucagon should also be considered if the infusion rate is not sufficient to maintain adequate blood glucose levels. If glucagon is used, it should be given either by IV bolus at 0.1-0.3 mg/kg or by infusion at 10-20 ug/kg/h.

Conclusion: Return to clinical case

Now, back to baby Emma's case! Emma presented with jitteriness and irritability, which we now know are symptoms of neonatal hypoglycaemia. In addition, she is the infant of a gestational diabetic mother, a major risk factor for developing neonatal hypoglycaemia.

Because Emma is unwell, you decide to check her blood glucose level immediately, instead of waiting until 2 hours of age. Her blood glucose level is 1.7 mmol/L, so you treat Emma immediately with a 40% dextrose gel and encourage Emma's mother to breastfeed her child on demand. After treatment is administered, Emma's symptoms resolve quickly and her blood glucose level rises to 2.8 mmol/L. You continue to check Emma's blood glucose levels every 3 hours until she is 12 hours old. Her glucose levels remain stable and she is discharged the following morning!

Review main learning objectives

Thank you for listening to this PedsCases podcast on neonatal hypoglycaemia! Let's review our main learning objectives. You should now be able to:

1. Recognize which infants are at risk for neonatal hypoglycaemia
2. Know the signs and symptoms of neonatal hypoglycaemia
3. Recognize which infants should be screened for neonatal hypoglycaemia and know how screening should be performed
4. Know how to diagnose and manage neonatal hypoglycaemia

Take away points

1. The most important risk factors for neonatal hypoglycaemia are being small for gestational age, large for gestational age, intrauterine growth restriction, being born prematurely, and being the infant of a mother with gestational diabetes.
2. There are two main categories of symptoms of neonatal hypoglycaemia. The neurogenic symptoms include jitteriness, pallor, temperature instability, irritability, tachycardia, and vomiting. The neuroglycopenic symptoms include apnea, episodes of cyanosis, hypotonia, unresponsiveness, lethargy, seizures, a weak or high-pitched cry, and coma that may lead to death if the hypoglycaemia is not corrected.
3. Infants should be tested for neonatal hypoglycaemia if they are unwell. Infants with risk factors for neonatal hypoglycaemia should be screened at 2 hours of age and every 3-6

hours after that until 12 hours of age if LGA or infant of diabetic mother, or 36 hours if SGA, IUGR, or preterm.

4. If blood glucose levels are under 2.6 mmol/L despite feeding, treatment for neonatal hypoglycaemia should be considered. Initial treatment should include supplementation with formula and/or 40% dextrose gel. If this is not successful in raising blood glucose levels, IV glucose therapy should be considered. If IV glucose therapy is not successful, pharmacological intervention may be necessary.

We hope that this PedsCases podcast has been helpful. Stay tuned for more podcasts, and thanks for listening!

References

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