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Neonatal Glucose Management

2.00 Contact Hours

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Outcomes

≥90% of participants will understand how to provide evidence-based care for glucose management in the neonate.

Objectives

After completing this course, the learner will be able to complete the following objectives:

1. Discuss the process of glucose metabolism.
2. Describe the role of the following hormones in glucose regulation: insulin, glucagon, cortisol, and epinephrine.
3. Outline the concepts of maternal and fetal glucose metabolism.
4. Describe the transition of the fetus to extrauterine life in terms of glucose regulation.
5. Discuss risk factors, symptoms, and management of hypoglycemia.

Introduction

Nurses caring for high-risk neonates are often challenged to maintain glucose homeostasis. Many Maternal-Child Nurses consider neonatal hypoglycemia a mild complication of the neonatal period, and they tend to underestimate the potential risks and outcomes associated with this condition. Both hyperglycemia and hypoglycemia are serious and are significant risks for many newborns. Because the neonatal brain is glucose-dependent, a lack of circulating glucose can cause neuronal damage. Insufficient glucose in the brain may result in seizures and brain damage, leading to long-term consequences such as developmental delay and learning disabilities. The neonate with hypoglycemia may be asymptomatic or symptomatic. Those with symptomatic and recurrent hypoglycemia are more likely to have a poorer prognosis than those who are asymptomatic.

Nurses working with infants, whether in the Mother-Baby Unit or the Neonatal Intensive Care Unit, must be knowledgeable, competent, and skilled in the identification and management of hyperglycemia and hypoglycemia of the newborn to prevent morbidity and mortality. Nurses need to understand the physiologic processes that regulate glucose production and utilization. An understanding of the nursing interventions which may be employed to prevent or manage glucose instability is also important. This module discusses definitions, pathophysiology, recognition, prevention, and nursing management of neonatal hypoglycemia and hyperglycemia in newborns. Hypoglycemia is addressed in two states – excessive glucose utilization and insufficient supply of glucose.

Fetal glucose homeostasis predominately depends on the constant maternal supply of glucose. During the third trimester, the fetus prepares for extrauterine survival by increasing energy stores and developing metabolic processes for rapid glucose production and utilization. Key metabolic processes which influence glucose homeostasis are:

- **Glycolysis** – the conversion of glucose to lactate and pyruvate resulting in adenosine triphosphate (ATP) storage
- **Glycogenesis** – the release of glycogen from the liver to form glucose
- **Gluconeogenesis** – the production of glucose by the liver and kidneys from non-carbohydrate substrates like fatty acids and amino acids

The transition from intrauterine to extrauterine life involves many physiologic changes. The fetus receives a constant supply of glucose from the mother across the placenta. At delivery, termination of the maternal glucose supply results in a decrease in neonatal blood glucose values, which reach a nadir at one to three hours post-delivery. During the initial "starvation period," glycolysis, glycogenolysis, and gluconeogenesis are initiated. These processes are the major energy sources for the neonate in the first hours of life. An exogenous glucose supply becomes vital for continued homeostasis because liver glycogen stores are 90 percent diminished by three hours of age (De Leon-Crutchlow & Lord, 2019).

Successful activation of the metabolic processes regulating glucose homeostasis depends on an adequate supply of glycogen and fat and mature or intact hormonal regulatory mechanisms. Insulin and glucagon are important hormones for regulating glucose levels. As early as twelve weeks' gestation, the fetus can synthesize these hormones but has a limited ability to secrete them from the pancreas, even when challenged with a high glucose load. Insulin inhibits gluconeogenic enzyme induction and suppresses glucose production in the liver. Insulin also plays an important role in the growth of the fetus because it stimulates the growth of cardiac muscle and adipose, hepatic, connective, and skeletal tissue. This situation explains why infants of diabetic mothers are often macrosomic or large for gestational age, whereas infants with neonatal diabetes mellitus experience intrauterine growth retardation (De Leon-Crutchlow & Lord, 2019).

Definition

- **Hypoglycemia** – plasma glucose concentration < 40 mg/dl
- **Hyperglycemia** – plasma glucose concentration > 150 mg/dl
- **Gluconeogenesis** – formation of glucose from non-carbohydrate substances
- **Glycogen** – stored form of glucose
- **Glycogenesis** – the process of making glycogen from glucose
- **Glycogenolysis** – the breakdown via phosphorylation pathway
- **Glycolysis** – the breakdown of glucose to make adenosine triphosphate (ATP)

Glucose Metabolism

Neonatal glucose metabolism and deviations from normal represent complex physiology and pathophysiology. Glucose is the body's main substance to create ATP. Ninety percent of ingested carbohydrate is used to make ATP. The breakdown of glucose to make ATP is known as glycolysis and occurs in two ways depending upon the presence or absence of oxygen. In the presence of oxygen, aerobic metabolism breaks down glucose into ATP. When oxygen is absent, anaerobic metabolism is a less efficient glycolysis method. Both methods burn pyruvic acid, creating carbon dioxide and water as by-products (Thornton et al., 2015).

Most glucose comes from the diet as either carbohydrates or starches. Glucose can also be made from various body substrates. First, it can come from stored glucose, called glycogen, found in all cells. It is stored in the liver, skeletal and cardiac muscles, and the kidney, intestine, brain, and placenta. The liver stores the largest amount of glycogen. Glycogenesis is the process of making glycogen from glucose until the storage is full. The rest is stored as fat.

Glycogenolysis is the breakdown of glycogen via a phosphorylation pathway. Glucose can also be made from non-carbohydrate substances through gluconeogenesis. Proteins, fats, and acids are key substrates for gluconeogenesis strongly affected by glucocorticoids and thyroid hormones. Whether ingested or made in the body, glucose in the bloodstream cannot be used as an energy source. To be utilized by the body, glucose must enter the cells. Because of its size, glucose cannot efficiently enter most cells. Insulin is required to get glucose into most cells, except the liver and brain (Thornton et al. 2015).

Fetal Glucose Homeostasis

Fetal glucose homeostasis predominately depends on a constant maternal glucose supply. Maternal glucose is the primary source of energy during fetal life. Maternal glucose crosses the placenta by carrier-mediated diffusion. The glucose concentration in the fetus is approximately 80 percent of that in maternal blood. Changes in maternal metabolism, including increased calorie intake and decreased sensitivity of the maternal tissues to insulin, provide additional substrates needed to meet the demands of the growing fetus.

As early as the third month of gestation, the human fetal liver has the enzymatic capacity for gluconeogenesis and glycogenolysis. If maternal nutrition and placental supply of glucose to the fetus are normal, there is no need for fetal gluconeogenesis. The fetus produces little, if any, glucose, although the enzymes for gluconeogenesis are present. Additional evidence suggests that the fetus relies on fuels other than glucose, such as lactate and amino acids, even in the basal state, to meet some of its energy demands. However, when the exogenous supply of glucose is limited, such as during maternal starvation, the fetus can augment the glucose supply endogenously through gluconeogenesis and glycogenolysis (Hay, 1998).

The fetus also has the potential to use beta-hydroxybutyrate as an energy substrate during periods of maternal starvation and glucose deprivation. Fetal hepatic glycogen stores have been identified by the ninth week of gestation, and fetal hepatic glycogen content increases linearly at this early gestational age when maternal nutrition is normal.

At term, these hepatic glycogen stores are three times greater than those of a well-fed adult. Skeletal muscles and cardiac muscles also contain several times greater glycogen concentrations at term than found in adults. During the last trimester, the fetus also stores energy in the form of triglycerides in fetal adipose tissue. Since the transfer of free fatty acids from the mother to the fetus is limited, this occurs primarily as a result of synthesis from glucose.

Insulin is considered a major stimulus for fetal growth. Insulin does not cross the placenta (Roberts & Myatt, 2019). By the eighth week of gestation, insulin is present in the plasma and pancreatic tissue of the fetus, suggesting that pancreatic beta-cell function is present. Fetal pancreatic alpha cells are present at eight to eleven weeks' gestation. Pancreatic insulin content increases in late gestation, exceeding adult levels when the infant reaches term.

This elevated insulin concentration increases both fetal glucose utilization and glucose oxygen consumption. Glucagon does not cross the placenta and is present in plasma by fifteen weeks' gestation, reaching peak concentrations by 24 to 26 weeks (Roberts & Myatt, 2019). In early

gestation, the fetal insulin response to maternal hyperglycemia is negligible. At term, the fetus is capable of significant response, but it is diminished, and there is a lag in the response. In maternal diabetes, the fetal beta-cell sensitivity is induced by repeated episodes of maternal hyperglycemia because of greater insulin response (Roberts & Myatt, 2019).

The fetus prepares for extrauterine life during the third trimester by increasing energy stores and developing metabolic processes for rapid glucose production and utilization. The glucose concentration in the umbilical vein is 70 percent to 80 percent of maternal glucose concentration. At delivery, the maternal supply of glucose to the infant ceases.

In the term infant, the blood glucose concentration falls to 50 to 60 mg/dl during the first four to six hours. By 72 hours, the blood glucose concentration stabilizes to 60 to 70 mg/dl in term infants and at lower levels in low birth weight infants.

Several hormonal and metabolic changes occur at birth, facilitating the adaptation necessary to maintain glucose homeostasis. Catecholamines increase dramatically at birth due to the decrease in environmental temperature and loss of the placenta. Increased glucagon and growth hormone levels and a relatively low plasma insulin level accompany the decrease in blood glucose following delivery. Elevated glucagon and norepinephrine levels activate hepatic glycogen phosphorylase, which induces glycogenolysis. Simultaneously, the falling glucose concentration and the perinatal surge in fetal cortisol secretion stimulate hepatic glucose-6-phosphatase activity, which results in increased hepatic gluconeogenesis.

Within minutes after birth, there is a rapid rise in plasma-free fatty acid and glycerol, evidence of intense lipid mobilization. Also, within a few hours after birth, there is an elevation of blood ketones that reaches its peak within two to three days due to increased oxidation of free fatty acids. These changes represent a change from predominantly glucose metabolism to predominantly fat metabolism. Increased use of fat for neonatal energy requirements allows the preferential sparing of glucose for the brain's metabolic needs (Rozance, 2020).

Glycogen stores in newborns are greater than in adults, but the newborn uses glucose twice that in adults. Within two to three hours after birth, the neonate begins to deplete the liver glycogen stores that remain low for several days and gradually increase to adult levels. Cardiac and skeletal muscle glycogen levels fall more slowly. Rapid depletion of glycogen stores occurs during asphyxia. Premature infants and small for gestational age infants have diminished glycogen reserves that may be rapidly depleted within twelve hours after birth.

The newborn infant has increased plasma levels of amino acids due to active placental transport, but gluconeogenesis is deficient. In both adults and newborns, many hormones regulate metabolism. There is a balance between those hormones and substances that lower and raise blood glucose.

The most important hormone is insulin. However, there are some differences. Insulin is not as affected by amino acids in newborns as in adults. Glucagon secretion is less affected by serum glucose levels in neonates than adults. Glucagon also induces phosphoenolpyruvate carboxykinase (PEPCK), the rate-limiting enzyme for gluconeogenesis. Glucocorticoids induce liver glycogen synthesis (which increases glycogen). The catecholamine effect is the same as in adults, but there may be a slower insulin response to hyperglycemia (Tas, 2020).

Maternal Concept

Pregnancy creates a diabetic-like state in all mothers due to the efforts of anti-insulin hormones such as human placental lactogen, progesterone, and estrogen. Glucose crosses the

placenta along a concentration gradient via carrier-mediated diffusion. Only 40 to 50 percent of glucose volume delivered to the placenta reaches the fetus. Insulin and glucagon do not cross the placenta (Rozance, 2020).

Altered maternal states, either hyperglycemia or hypoglycemia, can profoundly affect the fetus. Mild to moderate maternal hyperglycemia can cause fetal hypoxemia, hyperinsulinemia, increased oxygen consumption, CO₂ production, and glucose-lactate uptake. If hyperglycemia is severe, the effects can include further hypoxemia, hypoinsulinemia, increased erythropoietin levels, metabolic acidosis, decreased placental perfusion, and fetal demise.

The effects of maternal hypoglycemia on the fetus can also be significant. With a decrease in fetal blood sugar, there may be an increase in catecholamines and cortisol levels. Certain maternal states may predispose the fetus or infant to abnormal glucose environments. Maternal diabetes is a classic example of excessive substrate presented to the fetus. The increased circulating glucose crosses the placenta and causes fetal hyperglycemia.

When exposed to high maternal glucose levels, the fetus of a diabetic mother produces large amounts of insulin to maintain normoglycemia. Insulin suppresses glycogenolysis and lipolysis of adipose tissue, limiting the neonate's ability to use alternative sources of glucose supply that are eliminated at delivery, neonatal hyperinsulinemia continues, and the newborn becomes hypoglycemic within one to two hours of life. These infants can often achieve glucose homeostasis within 48 hours but may take up to five days to achieve normoglycemia (Rozance, 2020).

Maternal hypertensive states, especially pregnancy-induced hypertension, are the classic examples of reduced availability of substrates and fetal accretion of stores. Maternal drugs may result in hypoglycemia in the newborn. Oral beta-sympathomimetic tocolytic drugs cause sustained hypoglycemia and elevated cord blood insulin levels in infants delivered within two days of terminating tocolytic therapy. Tocolytic therapy, used to hold off preterm labor, has been shown to cause maternal hyperglycemia, thus leading to fetal hyperinsulinemia. Other maternal hyperglycemia causes include large infusions of intravenous glucose solutions before delivery (Rozance, 2020).

Fetal Concepts

Fetal glucose metabolism is characterized and influenced by the maternal environment, placental function, and inherent (developmental) capabilities. The fetal "diet" is high in carbohydrates and low in fat. This diet contrasts with post-natal life, where the diet is high in fat and lower in carbohydrates.

The brain, red blood cells, and renal medulla depend on glucose as the energy substrate. Fetal glucose levels and stores depend on the maternal pool. Fetal glucose production is usually very low because needs are generally met from maternal glucose transfer. However, the fetus can probably perform gluconeogenesis, and some limited amounts of glucose can be made from placental lactate in "stress" situations (Tas, 2020).

Most enzymes needed for gluconeogenesis are present, although amounts of PEPCK are limited or vary. PEPCK, the rate-limiting enzyme for gluconeogenesis, is stimulated by birth. The fetus can make and secrete insulin. Cortisol, growth hormone, and thyroxin are also produced. The fetus can mount a catecholamines response to stress. Glycogen, the stored form of glucose, is initially low. Major accumulation starts at about 36 weeks gestation.

Transfer to Extra-Uterine Life

At birth, the maternal glucose source is cut off. The infant needs to transition from a high-carbohydrate diet to a high-fat diet. The infant needs to survive until "food" is available. Glycogen stores are usually gone by three to twelve hours. Even if feeding occurs, the usual intake is limited, so the infant must initiate gluconeogenesis (Tas, 2020).

There are major changes in glucoregulatory hormones with birth. Epinephrine, norepinephrine, and glucagon levels increase. Insulin levels decrease. These changes result in the mobilization of glycogen stores and free fatty acids. The infant must perform glycogenolysis and gluconeogenesis to prevent hypoglycemia and survive. The liver production of glucose is 4 to 6 mg/kg/min. Total body basal glucose consumption is about 3.7 mg/kg/min. Though individual organ consumption of glucose varies, the brain uses it the most.

During the immediate post-natal period, there is a progressive refinement of the transition to self- "feeding." The ability to perform gluconeogenesis through increases in PEPCK improves. The balance between intake or stores and the utilization of these substrates also becomes more stable. Routine monitoring of blood glucose levels in healthy-term newborns is unnecessary unless high-risk conditions exist that indicate monitoring (Alsalem, 2019).

Blood Glucose Levels

Various hormones in both the adult and the neonate control glucose metabolism. The most important hormone is insulin. Insulin is made in the beta cells of the pancreas. Insulin enables glucose to get into the cells by changing wall permeability. This change lowers blood sugar and enables glucose to be used for fuel. Insulin also increases the phosphorylation enzyme systems and affects protein and fat transport into cells.

Glucagon, which is made in the alpha cells of the pancreas, has the opposite effect of insulin. Its main role is to increase blood glucose by increasing the breakdown of glycogen (glycogenolysis) and promoting glucose formation from non-carbohydrate substances (gluconeogenesis). Glucagon also causes free fatty acid release.

Glucocorticoids (mainly cortisol) also help maintain the blood glucose level. They are made in the adrenal cortex. It also increases amino acid mobilization and use. The release of cortisol can increase blood sugar by 50 percent. Growth hormone and thyroxine also have important roles in the use and availability of glucose for growth and development.

Epinephrine is also vital in the maintenance of blood glucose. It is made in the adrenal medulla. Its main roles include increasing glycogenolysis, gluconeogenesis, glucagon secretion and decreasing insulin secretion.

The blood glucose level is the dissolved glucose in the bloodstream. The level is always in flux and reflects the balance between intake or production of glucose and utilization for energy or storage. Various hormones modify the blood glucose level, with insulin the main blood glucose-lowering hormone. Glucagon, epinephrine, and cortisol are the main glucose-raising hormones.

Hypoglycemia can be defined as any plasma glucose level of less than 50 mg/dl with symptoms that resolve with glucose treatment. The blood glucose level in the newborn is a balance between the amount of glucose taken in and the amount used by the cells. The level drops to its lowest point (usually no lower than 40 mg/dL) by 2 hours of age. The depth and speed of the post-natal drop depend on the pre-birth insulin level. Hypothermia may result in hypoglycemia because the infant rapidly depletes body stores to increase heat production.

Neonates with cyanotic congenital heart disease may have lower blood glucose concentrations. Chronic hypoxia leading to a decrease in glycogen stores may be a factor. In all neonates during the first 24 hours, plasma glucose less than 40 mg/dl is defined as hypoglycemia. Beyond 24 hours, 40 – 50 mg/dl constitutes hypoglycemia.

The blood sample from which the level is determined greatly impacts the level. The level can be determined in both plasma and whole blood. In general, plasma is the preferred source because whole blood values can be 10 – 15 mg/dL less, especially with increased time from a blood draw to analysis. However, a skin puncture may be the preferred site for sampling for glucose testing. This preference is based on the potential risk of contamination of the blood sample with dextrose, which may be infused into an umbilical artery catheter used for sampling. A pre-sample specimen must be drawn to eliminate the contamination risk. The same contamination risk is present when blood is obtained from a vein that has a dextrose infusion occurring distal to the venipuncture site (Narvey & Marks, 2019).

Recognition of infants at risk for disturbances in glucose homeostasis is the most basic step in preventing hypoglycemia. In infants with conditions predisposing to hypoglycemia, glucose levels should always be assessed, screened, and appropriately and promptly treated. Related or influencing factors for neonatal hypoglycemia include (Narvey & Marks, 2019):

1. Decreased substrate (glycogen) availability secondary to:
 1. Prematurity
 2. Intrauterine growth retardation (IUGR) or (SGA)
 3. Glycogen storage disease
 4. Inborn errors of metabolism
2. Endocrine disturbances causing hyperinsulinemia secondary to:
 1. IDM
 2. Beckwith-Weidman syndrome
 3. Erythroblastosis fetalis due to Rh incompatibility
 4. Islet cell dysplasia, nesidioblastosis
 5. Maternal drugs (beta-sympathomimetics, beta-blockers, chlorpropamide), beta-agonist tocolytics
3. Endocrine disorders, such as:
 1. Hypopituitarism
 2. Hypothyroidism
 3. Adrenal insufficiency
4. Increased utilization of glucose secondary to:
 1. Perinatal asphyxia Apgar score 5
 2. True knots in the cord
 3. Nuchal cord
 4. Meconium aspiration
 5. Antepartal administration of IV glucose
 6. Hypothermia
5. Other causes such as:
 1. Sepsis
 2. Congenital heart disease
 3. Central nervous system abnormalities
 4. Exchange transfusion
 5. Infiltrated IV catheter

Successful activation of the newborn's metabolic processes is the key to regulating glucose homeostasis. This activation depends on an adequate supply of fetal glycogen and fat stores and

a mature and intact hormonal regulatory mechanism in the newborn. Preterm and small for gestational age infants lack adequate fat and glycogen stores. Similarly, post-term infants with depleted glycogen stores because of placental insufficiency are also at risk of developing hypoglycemia. These infants are most likely to experience hypoglycemia within the first six to twelve hours of life, particularly if oral or parenteral intake is inadequate.

Nursing Management

Nurses providing ongoing care at the bedside are often the first to identify an infant at risk for developing hypoglycemia. Prophylactic care for any infant assessed to be at risk for hypoglycemia includes (Narvey & Marks, 2019):

1. Early enteral feeding, if appropriate, or IV infusion of D10W
2. Maintenance of a neutral thermal environment
3. Correction or treatment of other problems that increase energy requirements

When a newborn arrives in the nursery, a protocol that includes head-to-toe assessment and gestational age assessment of predisposing risk factors should be followed. A nurse's recognition of hypoglycemia begins with the nursing process.

Steps of the Nursing Process	Examples
Assessment	• Identification of infants at risk • Pertinent history and current condition of infants • Observing for signs and symptoms of hypoglycemia • Interpreting laboratory values • Family dynamics related to hypoglycemia such as fear, anxiety, and guilt
Diagnosis	• Alteration in glucose metabolism • Risk for hypoglycemia
Goals	• Infant will maintain normal glucose values • Infant will exhibit adequate growth and weight gain • Family will verbalize an understanding of hypoglycemia and its treatment • Family will demonstrate the ability to care for infant independently
Implementation	• Initiation of treatment • Correction and treatment of other problems that may increase energy expenditure • Maintenance of a neutral thermal environment • Early Enteral feedings • Ongoing glucose monitoring • Use of proper IV glucose solution • Maintenance of IV patency • Medication administration such as antibiotics for sepsis, glucagon (to promote release of glycogen from hepatic stores)

Steps of the Nursing Process	Examples
	• Weaning of infant from IV glucose to oral feedings (breast or formula) while maintaining normal glucose levels • Parental education
Evaluation	• Infant maintains a normal glucose state • Family demonstrates the ability to feed the infant and monitor for signs of hypoglycemia • Review and revise nursing care based on changes in newborn condition

Nurses who care for newborns should assess the infant for signs and symptoms of hypoglycemia on an ongoing basis. These symptoms are often subtle, nonspecific, and extremely variable. They include (Rozance, 2020):

- Abnormal cry
- Poor feeding
- Vomiting
- Hypothermia and diaphoresis
- Neurologic instability
 - Tremors
 - Jitteriness
 - Hypotonia
 - Irritability
 - Lethargy
 - Seizures
 - Abnormal eye movements
- Cardio-respiratory disturbances
 - Cyanosis
 - Pallor
 - Tachypnea
 - Periodic breathing
 - Apnea
 - Congestive heart failure
 - Cardio-respiratory arrest
- Abnormal or high-pitched cry
- Hypothermia
- Diaphoresis
- Poor feeding

When hypoglycemia is suspected, the plasma glucose concentration must be determined. Ideally, this determination should be made using laboratory chemical analysis; however, even when ordered STAT, laboratory analysis takes a minimum of up to one hour to obtain.

Hypoglycemia in breastfed newborns can be prevented or greatly reduced by hospital policies that support breastfeeding:

- Breastfeeding within an hour of birth

- Skin-to-skin contact between mother and newborn to prevent cold stress and use of glucose stores
- Breastfeeding eight to twelve times per day
- Feeding in response to readiness cries, not on a schedule
- Not letting the newborn get to the point of crying (i.e., crying depletes glycogen stores rapidly and can contribute to a steep decline in blood sugar levels)
- Pump or hand expressing colostrum into a spoon or cup for the newborn that is reluctant to suckle at the breast and feed the newborn colostrum several times per hour until he can feed adequately at the breast

Blood Glucose Measurement

Blood glucose sampling techniques and analysis methods may significantly affect the blood glucose level. Bedside glucose monitoring using glucose monitoring devices has become the standard of care. Although these devices provide rapid, accurate results and are relatively easy to use, the operators must follow a standard procedure, understand how the instrument functions, calibrate the device and perform quality control measures. Using glucose monitoring devices allows blood glucose screening results to be obtained within minutes and promotes early treatment of hypoglycemia, but they should be used with caution. Because these are whole blood measurements, underestimating the actual glucose level may occur. Procedural variability can significantly alter results, including pressure applied during blotting or wiping, handling of test strips, and the date of strips. Bedside glucose testing should be used primarily as a screening method. They have been shown to vary considerably from actual blood glucose levels, especially for blood glucose levels less than 50 mg/dL. One reason for the variance is the source of the blood used for testing. Another potential variance in values is contamination with isopropyl alcohol, which falsely elevates glucose results. Isopropyl alcohol should be allowed to dry thoroughly before the skin is punctured, and the first drop of blood should be wiped away before the drop is placed on the test strip to increase the accuracy of blood glucose determinations. If the test requires color matching, it has been recommended that color blindness testing be done on all staff that routinely performs glucose measurements read by eye and compared with a color chart. Laboratory confirmation of serum glucose values should be performed when test strip values are abnormal or suspicious. Because of the significant risk to the patient, if treatment is delayed, interventions should be initiated if test strips or clinical symptoms suspect hypoglycemia, even if the laboratory confirmation is not available. The following information is important to keep in mind when drawing blood samples for glucose analysis:

1. Whole blood glucose concentrations are approximately fifteen percent lower than plasma glucose concentrations because the erythrocytes will continue to metabolize the glucose in the sample. The higher the hematocrit, the greater the difference between the whole blood and the plasma values.
2. Venous blood glucose concentrations are approximately ten to fifteen percent lower than arterial blood glucose concentrations that are approximately ten percent less than capillary specimens because the venous blood returns from the tissues where glucose has been extracted from the arterial supply and utilized.
3. Blood samples should be put immediately on ice to slow glucose metabolism in the sample. The glucose concentration may fall as much as 18 mg/dl/hour when allowed to remain unanalyzed at room temperature.
4. The infant's heel should be warmed before drawing capillary samples, as venous stasis may cause an underestimation of actual blood glucose value.

5. Ideally, a sample tube containing a glycolytic inhibitor should be used to prevent erythrocytes in the sample from continuing to metabolize glucose and falsely reducing the glucose level. If tubes containing glycolytic inhibitors are not available, the sample should be transported on ice and analyzed quickly.

Treatment of neonatal hypoglycemia begins with anticipation and prevention. Early identification of the infant at risk for developing hypoglycemia and the institution of prophylactic measures to prevent the occurrence constitutes the best treatment plan. In those infants who become hypoglycemic, the treatment goals are twofold:

- Return the glucose level to normal levels
- Maintain glucose within the normal range

In the infant who is at risk for or has hypoglycemia secondary to increased utilization (such as IDM), early feedings may be all that is needed for prevention or treatment. Other infants may require more complex care. Maintaining a neutral thermal environment is important to prevent increased metabolic demands due to hypothermia. Providing long periods of uninterrupted rest can also conserve energy.

Often hypoglycemia may be prevented in the NICU through intravenous dextrose infusions. For hypoglycemia requiring treatment, the general practice is to give a bolus of 2 ml/kg of D10W, followed by an infusion of 6 – 8 mg/kg/minute (Cranmer, 2018). The glucose load may need to be increased to as high as 15 mg/ml/minute. Hypertonic glucose solutions may be required to prevent fluid overload. A central line may need to be placed to reduce the risk (especially skin sloughs) associated with a hypertonic infusion.

Blood glucose needs to be monitored every 30 minutes to one hour to prevent hyperglycemia during the acute phase of treatment. Steroids and glucagon may be used to increase blood glucose if intravenous glucose fails to correct hypoglycemia. An endocrine consultation should be considered for persistent hypoglycemia.

Glucose Dosing or Intake: How to Figure It Out

How much glucose is there in these dextrose solutions D10W and D25W?

The percent value of the dextrose solution tells you how many grams of glucose are dissolved in 100 ml of the solution. So:

- D10 has 10 gm glucose in 100 ml or 100 mg in 1 ml
- D25 has 25 gm glucose in 100 ml or 250 mg in 1 ml

How much glucose is the baby getting?

To calculate the intake, you need to know:

- The dextrose concentration of the IV fluid
- The number of mg of dextrose in each ml of IV fluid
- The hourly IV rate
- The baby's weight in kg

To calculate the total hourly dextrose intake:

- Multiply mg dextrose/ml by the hourly IV rate
- Divide the result by the baby's weight

Then to get mg/kg/minute

- Divide hourly intake by 60

If the infant is on more than one dextrose solution, repeat the calculation for each solution and add the results.

Example: An infant weighing 1 kg is getting D10W at 4 ml/hour. What is the glucose intake?

- In D10W, each ml contains 100 mg of glucose
- At an infusion rate of 4 ml/hour, 400 mg of glucose is infused each hour
- Dividing by the 1 kg weight gives 400 mg/kg
- Dividing by 60 gives an intake of 6.6 mg/kg/minute

The outcome for infants with neonatal hypoglycemia is directly related to the hypoglycemia's duration, severity, and underlying etiology. Infants with asymptomatic hypoglycemia usually have a normal developmental outcome, although minor abnormalities (such as learning disabilities and abnormal EEGs without seizure disorders) have been reported in long-term follow-up.

Symptomatic infants have a poorer prognosis, with abnormalities ranging from learning disabilities to cerebral palsy and seizure disorders and mental retardation of varying degrees (Rozance, 2020b). Prompt initiation of treatment is associated with positive outcomes.

Neonatal Hyperglycemia

Hyperglycemia is another problem that may be encountered in the NICU. Hyperglycemia is usually defined as a 150 mg/dl plasma glucose concentration or whole blood glucose value of 125 mg/dl (Stark & Simmons, 2019). Hyperglycemia is often asymptomatic and is frequently diagnosed on routine screening of an infant at risk. Signs and symptoms that may occur include polyuria, glycosuria, and dry, hot, flushed skin.

The major hyperglycemia causes are stress, sepsis, and transient diabetes mellitus. Some commonly used medications, such as methylxanthines and corticosteroids, may also contribute to hyperglycemia. Preterm infants, especially those under 30 weeks gestation and 1000 grams are likely to experience hyperglycemia because of immature regulatory mechanisms (Stark & Simmons, 2019). These infants have a limited ability to secrete insulin from the pancreas, a decreased sensitivity to the insulin that is secreted, and an inability to suppress endogenous glucose production even when they receive an adequate exogenous supply. In general, the smaller the infant, the less likely he or she can tolerate maintenance rates of exogenous glucose. Critically ill infants, especially those with respiratory distress, hypoxia, or pain, are also at risk for hyperglycemia because these conditions cause increases in circulating catecholamine levels. Catecholamines cause increased lipolysis and glycogenolysis and antagonize the action of insulin.

Neonatal diabetes mellitus is "a rare disorder characterized by hypoinsulinism, progressive wasting, polyuria, and glycosuria during the neonatal period. It may be caused by deficiencies in insulin receptors or the synthesis of abnormal, poorly functioning insulin molecules (Stark & Simmons, 2019). Neonatal diabetes mellitus is usually transient. In contrast to insulin, glucagon stimulates gluconeogenic enzymes. A delicate balance must exist between glucagon and insulin to achieve glucose homeostasis.

The incidence of hyperglycemia varies depending on birth weight, gestational age, the severity of illness, and the glucose concentrations being infused. An estimated five and one-half percent of all infants receiving IV D10W experience hyperglycemia. The incidence in premature infants is markedly increased. Neonatal hyperglycemia can have undesirable consequences. For

example, hyperglycemia has been associated with increased intraventricular hemorrhage, particularly in premature preterm infants. This hyperglycemia may occur because of changes in osmolality that result in fluid shifts within the germinal matrix.

Additionally, hyperglycemia can result in glycosuria and osmotic diuresis. Dehydration and electrolyte imbalance may also occur. A particular concern is hypokalemia because it may cause fetal cardiac arrhythmia.

Premature infants may develop hyperglycemia related to group B strep or E-coli sepsis. Some infants with early sepsis have an increased need for glucose. Depression of insulin secretion and end-organ receptor response may be important etiologies of hyperglycemia as the sepsis progresses. Thus infants with either hyperglycemia or a progressive need for increased glucose intake preceding hyperglycemia should be evaluated for infection (Stark & Simmons, 2019).

Certain factors involved in the care of sick newborns can cause hyperglycemia. Many infants are treated with theophylline or caffeine for apnea of prematurity or are on steroids for respiratory disease. These medications may cause an increase in blood glucose. Any stress, such as surgery, pain, or sepsis, may increase circulating catecholamines, which will result in hyperglycemia (Stark & Simmons, 2019). Serum glucose over 150 mg/dl indicates hyperglycemia, generally asymptomatic but may have serious complications. Hyperglycemia may cause an osmotic diuresis, which draws the fluid from the intracellular to the extracellular space and leads to dehydration. These fluid shifts may be a risk factor for intraventricular hemorrhage.

Glucose requirements depend on metabolic rate: the higher the metabolic rate, the higher the glucose requirement. The large energy requirement of the brain affects the metabolic rate, increasing the glucose needed as the ratio of brain mass to body mass increases. Premature infants have a higher brain-to-body mass ratio than term infants, requiring more glucose. Unfortunately, because of the immature regulatory mechanisms, few infants who weigh less than 1,000 grams tolerate maintenance amounts of glucose, especially in the first week of life.

Infants generally require a minimum of 5 – 6 mg/kg/minute of glucose to maintain homeostasis. Infants not receiving enteral feedings should receive IV fluids with ten percent dextrose concentration on the first day of life with an infusion rate of 4 – 6 mg/kg/minute of glucose. Most full-term infants will initially tolerate 8 – 10 mg/kg/minute. The rate or concentration should be increased gradually (by 1 – 2 mg/kg/minute/day) so that by day two or three of life, glucose intake is at least 6.5 mg/kg/minute for preterm infants and 8 – 10 mg/kg/minute for term infants (Stark & Simmons, 2019). Whether to increase the rate of infusion or concentration of glucose will depend on the fluid requirements of the infant and the route of administration (peripheral vs. central). Too rapid an increase in glucose intake may exceed an infant's carbohydrate tolerance and result in hyperglycemia.

Despite slow incremental increases in glucose intake, most infants 800gm and 40 percent of infants between 800 gm and one kg become hyperglycemic between the fifth and seventh day of life if full caloric intake is attempted. All infants at risk for hyperglycemia should be closely assessed for signs of the condition. Glucose levels should be assessed every four to eight hours. Urine output, urine glucose, and urine specific gravity should be assessed at least every eight hours. Normal urine output should be 1 – 3 mL/kg/hr. Urine output 5 mL/kg/hr, urine glucose 2+, or specific gravity 1.010 may indicate glucose intolerance and osmotic diuresis. Blood glucose levels may need to be assessed as often as every two hours if any signs are present. Weight should be monitored daily as it is a sensitive indicator of fluid balance. Serum electrolyte levels should be checked daily until stable, especially for extremely low birth weight infants.

In many cases, decreasing the amount of glucose in the intravenous solution will be sufficient to correct hyperglycemia. This decrease may not be a desirable long-term treatment because adequate calories may not be provided. If hyperglycemia occurs in the range of 150 – 200 mg/dl, and if the infant is not experiencing osmotic diuresis, glucose infusions may be decreased to maintain blood sugars between 50 and 150 mg/dl between 50 mg/dl and that level where glycosuria is 2+. Glucose infusions should not be decreased to levels that compromise nutritional and growth requirements for an extended period. The low birth weight infant has only a few days of stored calories and depends on increasing caloric intake. Glucose infusions of 50 kcal/kg/day will result in inadequate caloric intake and subsequent negative nitrogen balance and tissue catabolism. Glucose concentrations should not be decreased to five percent or less because the solution will be hypotonic, which should be avoided to prevent problems with hypo-osmolality. Other osmoles, such as sodium chloride, need to be added to produce an isotonic solution, and the additional sodium may adversely affect fluid and electrolyte balance. Lipid infusions also cause an increase in serum glucose levels. The lipid dose may have to be reduced or discontinued.

If severe hyperglycemia persists despite a reduction in glucose infusion or if nutrition and growth are being compromised by trying to maintain normoglycemia, insulin administration should be considered. Insulin is also indicated for infants with neonatal diabetes. There is some controversy regarding the blood glucose level at which treatment should begin. One rationale for the early use of insulin is that it will allow the infant to tolerate higher glucose infusions, which will help to meet calories for growth. Insulin may be administered subcutaneously (rarely used in neonates) or IV routes. A continuous infusion of 0.05 to 0.1 units/kg/hour of recombinant human-derived regular insulin (Humulin) is suggested (Stark & Simmons, 2019). An initial IV dose of 0.1 to 0.5 units/kg may be given before continuous infusion. Insulin requirements vary greatly in small infants. A rule of thumb for initiating insulin infusions is 1 unit 10 gm of glucose.

Insulin may bind to the polyvinyl IV tubing, causing fluctuations in the amount of insulin delivered, despite constant flow rates. Interventions to decrease the amount of insulin that binds to the IV tubing include flushing the tubing with the insulin solution and using special IV tubing. The most cost-effective method of administration is to use small-volume tubing, flush the tubing with the insulin solution, and administer via a syringe pump.

Insulin is compatible with saline solution and dextrose solution, including total parenteral nutrition (TPN). Although insulin may be added to most maintenance fluids, a separate IV line should be used whenever possible to titrate dosage. It is best to calculate dosages to give the insulin in as little fluid as possible. A more dilute solution will allow the administration of smaller doses and facilitate weaning the insulin infusion in small doses to avoid rebound hyperglycemia. Glucose levels should be monitored every one to two hours during an insulin infusion. Serum potassium and phosphate levels should also be followed daily. Insulin facilitates an extracellular-to-intracellular shift of potassium and phosphate and may lead to hypokalemia and hypophosphatemia. Urine output should be closely monitored and assessed for the presence of glucose or elevated specific gravity (1.010).

Conclusion

Monitoring glucose balance is a challenge for the neonatal nurse. Neonates may be at risk for alteration in glucose homeostasis for various reasons. Laboratory values and clinical signs and symptoms indicative of hyperglycemia or hypoglycemia are frequent findings in high-risk infants. Careful clinical observation and assessment aimed at identifying those infants at risk

and intervening to prevent the complications associated with hypoglycemia or hyperglycemia will decrease neonatal morbidity and mortality. The accuracy of test results depends on various clinical and technical factors. This variance may require that abnormal results be confirmed with a second sample. However, treatment should not be delayed during this confirmation process.

Insulin is a larger molecule than glucose, and it does not cross the placenta, so maternal glucose levels are mirrored in the neonatal system and amniotic fluid. This maternal hyperglycemia leads to fetal hyperglycemia. Because maternal insulin does not cross the placenta, elevated glucose levels stimulate the fetal pancreas to secrete insulin. This stimulation also leads to hyperplasia of the beta cells and increased insulin production, which continues after delivery. Insulin is the main growth hormone for the fetus, so this hyperinsulinemia leads to fat accumulation and macrosomia. Because of this hyperinsulinism and the loss of maternal glucose at delivery, the infant can become hypoglycemic within a few hours of delivery and must be monitored closely.

The neonatal nurse cares for many patients daily who have the potential for abnormal blood glucose levels. Recognizing infants at risk can facilitate timely and appropriate interventions. The quality of the information received from tests and observation depends on decisions made by the nurse. Therefore, knowledge of glucose kinetics and monitoring techniques is essential.

Case Study

You are caring for baby Emma, 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 Emma now presents with irritability and jitteriness. Considering what you know about this patient, what should your next steps be?

Because Emma is symptomatic, you follow your hospital policy and check her blood glucose level immediately instead of waiting until 2 hours of age. Her blood glucose level is 31 mg/dL, so you treat Emma immediately with a 40% dextrose gel per hospital protocol 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 50 mg/dL. You check Emma's blood glucose levels every 3 hours until she is 12 hours old. Her glucose levels remained stable, and she was discharged the following morning.

Implicit Bias Statement

CEUFast, Inc. is committed to furthering diversity, equity, and inclusion (DEI). While reflecting on this course content, CEUFast, Inc. would like you to consider your individual perspective and question your own biases. Remember, implicit bias is a form of bias that impacts our practice as healthcare professionals. Implicit bias occurs when we have automatic prejudices, judgments, and/or a general attitude towards a person or a group of people based on associated stereotypes we have formed over time. These automatic thoughts occur without our conscious knowledge and without our intentional desire to discriminate. The concern with implicit bias is that this can impact our actions and decisions with our workplace leadership, colleagues, and even our patients. While it is our universal goal to treat everyone equally, our implicit biases can influence our interactions, assessments, communication, prioritization, and decision-making concerning patients, which can ultimately adversely impact health outcomes. It is important to keep this in mind in order to intentionally work to self-identify our own risk areas where our implicit biases might influence our behaviors. Together, we can cease perpetuating stereotypes

and remind each other to remain mindful to help avoid reacting according to biases that are contrary to our conscious beliefs and values.

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