CE 2.5 HOURS Continuing Education

Management of Hypotension in the Very Low-Birth-Weight Infant During the Golden Hour

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ABSTRACT

Primum non nocere, a saying in Latin that means "first, do no harm," is a phrase neonatal clinicians should keep in mind when initiating or suggesting treatment. In the "golden hour" of resuscitation of the very low-birth-weight infant, team members assess multiple parameters of the infant's vital signs, with a key one being that of the cardiovascular status, specifically blood pressure. Attempts to treat a number rather than after assessment and develop a sound plan of care based on findings, will affect both short- and long-term outcomes. By understanding what neonatal hypotension is and knowing when and how to treat it, the neonatal clinician honors this charge and can safely and effectively manage the very low-birth-weight infant with hypotension shortly after birth.

Key Words: golden hour, neonatal hypotension, neonatal resuscitation

During the stabilization period, immediately after birth, the neonatal resuscitation program recommends utilizing an ABC acronym to direct the sequence of neonatal resuscitation. The third letter, C for circulation, addresses not only immediate assessment and management of an adequate heart rate but also determination and maintenance of perfusion and appropriate blood pressure. However, what is considered an acceptable blood pressure in the very low-birth-weight (VLBW) neonate? The intent of this article is to define what is considered hypotension in the VLBW infant, evaluate the reliability of the accepted parameters, investigate treatment recommendations based on clinical scenario, and evaluate both the short- and long-term outcomes of those infants whether treated or not. At the completion of this review, it is hoped that the reader will be able to make a more informed decision as to whether treating a patient will improve outcome or may, in fact, initiate a cascade of events that will alter the infant's outcomes later in life.

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Definition

In a review of the literature, *neonatal hypotension* is defined as a mean arterial blood pressure less than the 10th percentile for gestational/birth weight and postnatal age or a mean arterial blood pressure less than gestational age in weeks.[1-7] For example, if an infant's gestational age is 24 weeks, the mean blood pressure should be at least 24 mm Hg. This determination is based more on "urban myth" than on evidence-based practice and may result in unnecessary or overtreatment of an otherwise hemodynamically stable infant, resulting in both short- and long-term morbidity. Early works[8] are commonly cited when asked to define the range of acceptable blood pressures in the neonate; however, these parameters were on infants who were both larger and more mature than the VLBW infant cared for during the "golden hour" period. Later, work was attempted to clarify what really were normal ranges for blood pressures in the VLBW infant in the first 24 hours of life.[9] By evaluating the blood pressures over the time during the first day of life, the authors were able to point out that the earlier defined ranges were perhaps inaccurate in these tiny immature infants and even the held practice of considering an infant to be hypotensive

when the mean blood pressure was less than the gestational age would result in treatment of more infants based on a number rather than the clinical picture. In all, the health care providers are cautioned not to simply "treat a number" but to consider all measurements of cardiovascular stability in determining whether an infant is hypotensive or not. Some of these other measurements would include heart rate, pulses, capillary refill time as an indicator of tissue perfusion, oxygenation, presence of acidosis, and urine output. During the flux of transition to life in the first hours after birth, these measurements are not always reliable as the infant's heart adapts, and other situations may mask the true cardiovascular status (ie, hypothermia). The challenge for the clinician is to take in all the considerations and use this comprehensive assessment quickly as the resuscitation team makes decisions regarding treatment.

The need to treat hypotension immediately is based on the held belief that not doing so would result in decreased blood flow to essential organs such as the heart, brain, and kidneys. However, clinical studies disprove the correlation to end organ perfusion and hypotension.[4,10] In critically ill adults, left ventricular output is often used to measure systemic output. Using this known practice, blood pressure measurements and cardiac output in preterm infants were evaluated to see whether there were similar correlations.[11] In the VLBW infants, shunts across the patent foramen ovale or ductus would not provide reliable indicators of cerebral blood flow. However, when they monitored superior vena cava flow in the preterm infants, they could more accurately measure the amount of blood delivered to the upper body and brain. What was shown was a weak correlation using measurements between blood pressure and cardiac output in preterm infants, and it put in question our treatment of low blood pressures on the basis of this assumption.[11] In another study, questioning whether there is any relationship to blood pressure and extraction of oxygen in the preterm infant, near-infrared spectroscopy was used to measure the hemoglobin flow and venous saturation of blood flow in the upper arm of a hypotensive preterm infant, and oxygen delivery, consumption, and fractional oxygen extraction were calculated. What they found was that while there was lower peripheral consumption and delivery of oxygen to hypotensive infants, the extraction of oxygen was the same as in normotensive infants.[12] In infants who are normovolemic after birth, fetal hemoglobin, which has a higher affinity for the oxygen molecule, serves as almost a protective mechanism during transition to extrauterine life. In the presence of nonacidic conditions, the VLBW infant will perhaps be more tolerant of lower blood pressures because of this.

Causes

It is important for the clinician to remember that hypotension in itself is not a pathologic process.[2] However, there are situations in which intervention is necessary and should be immediate. Some of the causes of hypotension in the VLBW infant immediately after delivery include the following:

- hypovolemia from fetal-fetal transfusion, fetal-maternal transfusion, or cord accident;
- infection;
- alteration in cardiac output due to fetal arrhythmias;
- maternal anesthesia;
- pneumothorax; and
- asphyxia and resultant hypoxemia.

In cases such as arrhythmias and pneumothorax, treatment of the underlying condition may improve the blood pressure without any other intervention. In others, a comprehensive history will often provide the clinician with a starting point to move forward. If the infant is hypotensive and presents with clinical findings that support interventions, appropriate and timely treatment will need to be initiated to avoid the cascade of events that could lead to irreversible shock and resultant death.

Shock

Shock is defined as a clinical manifestation of hypotension and includes findings such as prolonged capillary refill time, tachycardia, cool mottled skin, decreased urine output, and acidosis.[13] Immediately after birth, it will be impossible to look at all of these markers with reliability, especially, because the VLBW infant is also at high risk for hypothermia, which could also alter tissue perfusion and capillary refill time. Shock can be described in 3 phases: compensated, where the perfusion to essential organs is maintained; uncompensated, when anaerobic metabolism increases as a result of the inability to deliver oxygenated blood to end organs; and irreversible shock that is where, despite all attempts, the body is unable to correct damage and the infant dies.[14]

In *compensated shock*, there may be minimal alteration in infant's vital signs. The perfusion to the vital organs remains preserved through initial attempts by the infant to correct an evolving cardiovascular picture through sympathetic reflexes.[7] Because of this, the clinician may miss subtle changes that would indicate impending difficulties. The infant may present with slight tachycardia that will continue to increase in an attempt to compensate for decreased oxygenation to the tissues. Over time, there may be prolonged capillary refill time and pallor.

Because the infant's body is unable to maintain homeostasis, the clinical picture will deteriorate,

and anaerobic metabolism begins to alter tissue oxygenation.

Uncompensated shock occurs at this time. The infant presents now with a clear-cut clinical picture of shock that includes tachycardia, tachypnea, pallor, and decreased pulses and capillary refill time, as well as low blood pressure.[7] With an increase in anaerobic metabolism, the infant is now more acidotic that results in impaired function of the myocardium, and decreased cardiac output. Left uncorrected, the dropping cardiac output continues with increasing acidosis, and efforts made by both the infant and the neonatal team will not be successful in breaking this cycle. Depending on the initial cause of shock (sepsis vs hypoxia), there is release of biochemicals such as cytokines, oxygen free radicals, and toxins that will have an effect on blood coagulation or shifting of intravascular fluid into the extra vascular space that magnifies the likelihood of hypotension.

Irreversible shock is often diagnosed at the time of death. Despite all efforts to correct metabolic and cardiovascular aberrations, the end organs have been so extensively damaged that restoration of function is impossible. This end is the one that clinicians seek to avoid by early and aggressive interventions.

Management/Treatment

Treatment of neonatal hypotension is multifactorial. In the golden hour, it must be effective to allow progression of care and ultimate transfer to the NICU. In all scenarios, the first line of treatment will be dependent on both the history and clinical presentation and should minimize deleterious effect. The 3 areas of treatment to be discussed include fluid resuscitation, vasopressor use, and supportive therapies. There are many "rabbit trails" a clinician could pursue when deciding a course of therapy for managing neonatal hypotension; for the purposes of this article, treatment modalities discussed will be those that achieve a positive response in a short period of time.

Fluid Resuscitation

Treating the VLBW infant who presents with low blood pressure within the first hours of life can be a decision-making challenge. Whether to treat the number in absence of any history of blood loss or other clinical signs of hypotension (tachycardia, decreased capillary refill time, etc), or watch and wait that can cause angst among those in the stabilization unit. When this scenario is encountered, the clinician needs to use a comprehensive view of whether, in fact, there has been blood loss and what type of hypovolemia may be occurring (cord accident, placental abruption, etc), and then decide what type and how much of volume to administer. There should also be awareness of why in some cases treatment may not be the best choice.

Historically, a low blood pressure was treated with volume. This was done, because the thought was that when acutely ill, cardiac output and cerebral blood flow were impaired, and fluid resuscitation would ensure that the neonate did not suffer ill effects. Numerous studies conducted examined the benefits of colloid (albumin) versus crystalloid (normal saline) to treat hypotension.[2,15] The studies found that there was no benefit to using colloid instead of normal saline and in fact there was additional expense, risk, and consequences to its use. But, there is "nothing normal in normal saline," and the use of this in absence of known fluid loss could serve to set the infant up later on for potential problems including patent ductus arteriosus, chronic lung disease, or necrotizing enterocolitis.[16-18]

Long-term follow-up in VLBW neonates who were treated in the first 72 hours of life versus those who were not should make us reconsider our decision to treat.[16-18] Neonates who were treated for hypotension on the basis of commonly accepted practices of treating blood pressure when the mean was less than gestational age or less than the 10th percentile in light of any other symptoms or with a history of acute blood loss versus those who were not treated with the same findings were more likely to have worse outcomes. In one analysis,[18] it was found that infants born at 27 to 29 weeks' gestation who received more than 30 mL/kg of volume in the first 48 hours of life were more likely to die than those who received less than 30mL/kg during the same time. Many of the complications that caused the deaths in those who received larger volumes could be attributed to large fluid boluses (massive pulmonary hemorrhage, massive intracranial hemorrhage, or unexplained cardiorespiratory collapse).[17,18] Several retrospective studies[5,16,17] evaluated VLBW infants who were treated for hypotension versus those who were not with relation to the short- and long-term outcomes. In separate studies, it was found that infants who received volume for hypotension in the first hours of life had more long-term morbidities (delayed motor development, hearing loss, and increased severity of intraventricular hemorrhage).[17] Two other studies[5,19] examined same defined patient population–infants with hypotension without any other symptoms of cardiovascular instability who were not treated–and found that they had similar outcomes when compared with normotensive infants of similar gestation and birth weight.

Vasopressors

While commonly found in the arsenal of medications called on to assist in treating hypotension, there is little evidence-based research to support the use of

inotropic agents in the VLBW infant. However, if there is persistent hypotension with other symptoms of cardiovascular instability, the clinician may utilize these medications to assist in stabilizing the VLBW infant in the first hours of life. The medications most frequently used of this drug class would be dopamine and dobutamine. The end result, improving hypotension, is the same, but the actions in the body and the side effects on the infant are very different.

Dopamine (dopamine hydrochloride) is a sympatheomimetic amine that exerts its cardiovascular effects through dopaminergic and α- and β-adrenergic receptors. It is thought to exert up to 50% of its inotropic effect through an indirect action on β-2 adrenoceptors, stimulating the release of endogenous norepinephrine.[7,14] Dose range will determine the effect on infant. In low doses of 0.5 to 2 μg/kg/min, there will be vasodilatation in the renal, mesenteric, coronary, and intracerebral vascular beds through stimulation of dopaminergic receptors. Mid range doses of 2 to 10 μg/kg/min dopamine stimulate the β-1 adrenoceptors causing improvement in myocardial contractility and cardiac output. There is some stimulation of the β-2 adrenoceptors that results in peripheral vasodilatation. At intermediate rates of infusion, total peripheral resistance is usually unchanged. At high rates of infusion, 10 to 20 μg/kg/min, dopamine stimulates α-receptors, causing peripheral vasoconstriction and increasing blood pressure. Vasoconstriction occurs first in skeletal muscle vascular beds, but with increasing doses, vasoconstriction is evident in renal and mesenteric vessels.

It must be stressed that there have been no studies in sick neonates who actually have hypotension and the actual dose response. These responses will be dependent on how well multiple organ systems such as the thyroid and adrenals are functioning. In a VLBW infant who may also have adrenal insufficiency, the adrenergic receptors may be stunted and therefore higher doses may be needed to achieve desired effect.[1] However, dopamine has a quick action time and may, in fact, achieve a normal blood pressure quicker than fluid boluses.

Dobutamine (dobutamine hydrochloride) is a synthetic catecholamine and a direct-acting inotropic agent. It stimulates the β-receptors of the heart, which improves myocardial function and cardiac output. Dose range is 2 to 20 μg/kg/min with titration of dose to achieve the desired effect.[1,14] If the infant is experiencing septic shock and resultant myocardial dysfunction, this may be the drug of choice. As a first-line drug in the period immediately after birth, dobutamine may not be the best vasopressor to choose. A meta-analysis that examined the effectiveness of dopamine over dobutamine in the hypotensive preterm infant verified that dopamine is significantly more effective in the short-term treatment of hypotension. It was also found that there were less treatment failures when dopamine was used and no difference in tachycardia between the two.[20]

Supportive Therapies

Following immediate measures to address the hypotensive infant, the clinician will need to further explore the underlying cause and institute treatment to support the neonate. Determining the reason for delivery at this gestational age will help in formulating a plan of care. When preterm labor occurs spontaneously and without a known cause, the clinician should consider infection, specifically, chorioamnionitis as a strong possibility. Initiation of antibiotic therapy based on the unit's policies ensures quick intervention and prevention of further damage to the neonate. However, the clinician should be mindful that if there is an actual bacteremia, the bactericidal actions of the antibiotics will increase the release of cytotoxins into the infant's blood stream and set off a cascade of events that could possibly result in hypotension.[21] Additional therapies to support the VLBW during the golden hour will include respiratory support, temperature stabilization, and initiation of appropriate fluids to ensure euglycemia.

Conclusion

The intent of this review is not to address all the treatment modalities of neonatal hypotension, because there have been many left undisclosed. Rather, it is to offer information to assist in making a more informed decision of whether to treat a low blood pressure during the golden hours immediately following birth prior to admission to the NICU. What occurs during this time has a major impact on the neonatal course and outcome of all care that follows. The question of whether to initiate treatment for hypotension in the VLBW infant during the golden hour remains unanswered. We have increasing sophistication of equipment immediately after delivery that allows us to see the vital signs of our patient rapidly and prompts us to respond. First response may be to treat a specific number that we see based on the past practices that we are familiar with. However, with an increasing desire to provide care that is evidence based rather than based on legacy, we need to take pause to ask whether the treatment is beneficial in both the short term and long term. In determining a course of treatment for this vulnerable patient, we need to utilize all our senses to assess and not simply rely on a number on a monitor.

Hypotension in the VLBW infant at birth can be real if there is known blood loss through a maternal or fetal event, and these require rapid response with appropriate volume. But in a large number of these infants, hypotension may be a reflection of a

physiologic adaptation to extrauterine life and may not require intervention. In treating, we now know that we may actually impact outcomes in a negative manner. Assessment of factors such as oxygenation and temperature in the period immediately after delivery may provide the clinician with assurance that no intervention is necessary at the moment for a "low number" on the monitor. It will also be important to know that volume alone does not always resolve a low blood pressure, and the VLBW infant may benefit more from institution of vasopressors such as dopamine or dobutamine. The most imperative time to "first do no harm" is during a neonates first hour of life. The challenge is yours.

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