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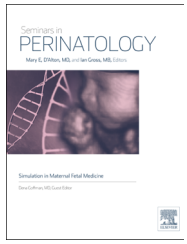

Initial resuscitation and stabilization of the periviable neonate: The Golden-Hour approach

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ABSTRACT

There is a paucity of data to support recommendations for stabilization and resuscitation of the periviable neonate in the delivery room. The importance of delivery at a tertiary center with adequate experience, resuscitation team composition, and training for a periviable birth is reviewed. Evidence for delayed cord clamping, delivery room temperature stabilization, strategies to establish functional residual capacity, and adequate ventilation as well as oxygen use in the delivery room is generally based on expert consensus, physiologic plausibility, as well as data from slightly more mature extremely low gestational-age neonates. Little is known about optimal care in the delivery room of these most fragile infants, and thus the need for research remains critical.

The impending birth of a periviable infant is associated with immense anxiety for family members and the medical care teams for mother and baby as well. Many complex decisions regarding maternal management and counseling of the family regarding the risks and benefits of a trial of intensive care for the infant must be made, often in a relatively short time period. Collaboration based in excellent communication between the obstetrical, anesthesia, neonatology, and family support services is vital. Once a decision has been made to proceed with a trial of resuscitation and intensive care for the periviable neonate, there is much to prepare and consider for the coming first hour of life, known as the "Golden Hour."

1. Golden-Hour strategies

A Golden-Hour strategy is a philosophical approach that reinforces communication and collaboration (inter- and intra-team) using evidence-based protocols and procedures that standardize as many elements as possible for delivery and initial management of a very preterm birth. Golden-Hour strategies lay out how the neonatal team will receive notification from the obstetrical service of an impending periviable birth and stress the importance of collaborative counseling of the family. Pre-resuscitation check lists are used for briefing the care team to the equipment that they will need to prepare both in the delivery room and neonatal intensive care unit (NICU) in the form of standardized check lists. Personnel have clearly assigned roles and responsibilities, and the work flow of the carefully choreographed and timed events that will need to occur is reviewed. This promotes training and adherence to the American Academy of Pediatrics/American Heart Association Neonatal Resuscitation Program (NRP) algorithm[1] and provides a framework for later debriefing in which the care teams can reflect on what went well and what factors could be changed to improve care for the next patient.

2. Periviable neonates can be difficult to stabilize in the delivery room

Periviable neonates are notoriously fragile and have many features that increase the difficulty of stabilization

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immediately following birth. They can quickly become hypothermic due to extremely immature skin with a minimally developed epidermal barrier that allows evaporative heat loss. They have minimal fat deposition that normally occurs during the last trimester, increased body-surface area to mass ratio, and ineffective non-shivering thermogenesis all of which puts them at risk for detrimental hypothermia.[2] In addition, periviable neonates have poor energy stores, immature tissues that may be damaged more easily by oxygen, weak chest muscles that can limit adequate ventilation, immature nervous systems that may lead to poor respiratory drive, surfactant deficiency that can contribute to poor lung expansion and difficulties with gas exchange. Periviable neonates are at an increased risk for infection due to their underdeveloped immune systems. They have fragile capillaries within the immature brain, which can rupture, and small total blood volumes that make them more susceptible to hypovolemic effects of blood loss. Caregivers must take all these things into consideration and at the same time offer compassionate support to highly stressed parents.

Given the rarity and complexity of the situation, it is essential that whenever possible, all efforts are made to deliver a periviable neonate at a tertiary care center with equipment, training, and experience for the care of such mothers and periviable neonates. Multiple studies demonstrate improved outcomes for very low-birth-weight (VLBW) infants born in tertiary care centers versus outborn infants who are subsequently transferred.[3–5] Binder et al.[3] recently reported odd ratios and 95% Confidence intervals of 3.86 (2.21–6.76) for death/major morbidity, 2.41 (1.49–3.90) for mortality, and 3.44 (2.09–5.68) for 500–999 g infants born at non-tertiary versus tertiary maternity hospitals in a large cohort of infants in Cincinatti. Reasons for the improved outcomes in tertiary care centers could be due to better maternal antepartum care (such as steroids and antibiotics), the presence of experienced neonatal resuscitation teams in the delivery room to initiate appropriate resuscitation, and improved resources for multidisciplinary care in the NICU.

The benefits of an experienced neonatal resuscitation team to initiate appropriate resuscitation and stabilization cannot be over-emphasized. Every baby needs at least one person immediately available to focus solely on the newborn to assess the need for and offer initiation of resuscitation interventions after birth; however, a periviable birth is best served by an entire neonatal resuscitation team. Prior to birth, the team needs to prepare the delivery room by increasing the environmental temperature, making sure warming devices are available and prepared, pulse oximetry and blended oxygen are available, ventilation devices with the ability to provide continuous positive airway pressure (CPAP) and positive end expiratory pressure (PEEP) are ready in addition to appropriately sized supplies for possible intubation. In the early minutes of life, the baby will need to be gently handled, delayed cord clamping may be considered, multiple temperature stabilization techniques implemented, functional residual capacity established along with effective ventilation, oxygen levels monitored and adjusted on a minute-by-minute basis, possibly receive the surfactant (depending on the team's Golden-Hour strategy), and decisions made about the appropriateness of more intensive cardiopulmonary resuscitation if the infant does not respond to initial ventilation. The actions taken and infant's responses need to be carefully documented in real time (either through video recording or minute-by-minute documentation of a team member). The family needs to be kept apprised of the situation and supported emotionally. Each hospital may develop a unique team that works together to accomplish these complex tasks, but as an example in an academic setting such a team might include a neonatal attending/neonatal fellow to serve as the team leader, a neonatal nurse practitioner to help with any procedures, a neonatal nurse for assessing the neonate's responses to resuscitation, a neonatal respiratory therapist to focus on effective ventilation and oxygen management, an obstetrical circulating nurse to serve as recorder, and a family support nurse to help with communication and emotional support of the family. The important thing is that each team member precisely knows their role, has frequent opportunity to practice through simulation and debriefing, consistent delivery experience, and that the team constantly reflects on their performance and how to improve (thus the need for video or careful real-time documentation of the events).

3. Delivery room resuscitation of the periviable neonate

Resuscitation should be done in accordance with the recommendations of the Neonatal Resuscitation Program.[1] The following are some steps specific to prematurity for which there is some evidence, although in general, few periviable infants were included in the study populations.

Delayed cord clamping

The question of the optimal time to clamp the umbilical cord after delivery is controversial. There are several small RCTs that have compared early (<20 s) to late (>30 s) cord clamping following preterm birth as well as several prospective observational studies.[6] Systematic reviews of the trials suggest that for the otherwise uncomplicated preterm birth, delaying cord clamping for 30–180 s following delivery improves blood pressure and decreases IVH and the need for blood transfusions.[7] However, there are limited data regarding the hazards or benefits of delayed cord clamping in the non-vigorous infant, and almost no data regarding the periviable neonate. Cord milking has been suggested as more rapid method to influence placental transfusion if the medical providers feel that resuscitation efforts should not be delayed.[8,9] Recently, elegant preterm lamb studies at the time of birth examined the effects of early versus late cord clamping on transitional hemodynamics.[10] These studies demonstrate that early cord clamping leads to a rapid decrease in preload to the heart that results in bradycardia and decreased cerebral perfusion, unless there is prior establishment of increased pulmonary blood flow via sufficient inflation and ventilation of the lung. Ventilation prior to cord clamping markedly improved cardiovascular function by increasing pulmonary blood flow before the cord was clamped in the late clamping group, which further stabilized

the cerebral hemodynamic transition.[10] This might be the physiologic reason that delayed cord clamping benefits blood pressure and decreases risk of intraventricular hemorrhage. The investigators suggest that for compromised infants, delaying cord clamping until after ventilation onset might lead to a smoother transition to newborn life.[10] Further studies are needed, and solutions to the ergonomic difficulties of providing effective ventilation while attached to the placenta need exploration.

3.2. *Strategies to stabilize the temperature in the delivery room*

Unless significant preventative efforts are made, periviable newborns will quickly lose heat in the delivery room by evaporation of amniotic fluid from the baby's body, by conduction of heat from the body touching cooler surfaces, by convection to cooler surrounding air, and by radiation to cooler objects in the vicinity. For every 1°C below 36°C on admission temperature, mortality increases by 28%.[11] One of the first important interventions is to increase the ambient temperature of the delivery room or operating room to 77°F (25°C) before the delivery occurs. A recent randomized controlled trial demonstrated that warming the delivery environment to this level can decrease rates of moderate hypothermia upon NICU admission in preterm infants.[12] Given the mean gestational age of ~30 weeks for the study subjects, it is unlikely that any were in the periviable range.

The periviable infant should be placed in a high diathermancy food-grade polyethylene bag or wrap without initial drying up to the level of the shoulders.[13–15] This allows radiant heat from the warmer to pass through to the infant while stopping almost all evaporative losses. All subsequent resuscitation interventions can be done with the polyethylene wrap in place. Multiple studies have shown that plastic bags and wraps improve temperature upon admission to the NICU, but as of yet there are no studies powered for important clinical outcomes, such as mortality or long-term neurodevelopmental outcomes. It is important to note that although helpful, use of polyethylene bags does not prevent all hypothermia and thus additional strategies may be needed. Preterm infants can be placed on a chemically activated thermal mattress that also improves temperature stabilization.[16,17] A few studies have examined the use of wrap and thermal mattresses in combination and note that although hypothermia may be further reduced, caution must be taken to prevent hyperthermia.[16,18]

The head of the periviable infant should be covered by a hat. There is evidence to support the use of either a polyethylene plastic cap[19,20] or woolen caps,[21,22] but not the stockinette caps that are frequently used. Monitoring the infant's temperature while in the delivery room to guide further interventions and to prevent iatrogenic hyperthermia is useful.[23] Perinatal hyperthermia is associated with respiratory depression,[23] and newly born preterm lambs exposed to initial hyperthermia have worse lung injury, acidosis, premature death, pneumothoraces, impaired lung function, and increased inflammatory mRNAexpression compared to normothermic animals.[13,24] The challenging goal is to achieve normothermia and avoid both hypothermia and hyperthermia.

3.3. *Respiratory support in the delivery room*

The goals of delivery room respiratory support for the periviable neonate are to achieve adequate minute ventilation by improving lung compliance, decreasing work of breathing, avoiding apnea, and providing assisted ventilation as needed. In order to achieve sufficient oxygenation, functional residual capacity must be established and maintained, which will lead to increased pulmonary blood. FiO_2 is adjusted to meet the goal saturations per minute of life of healthy term babies[25] as recommended by NRP.[1] The trickier part is to avoid iatrogenic complications using the least invasive, most gentle approach to which the infant responds. This means avoiding intubation unless necessary for apnea, inadequate heart rate, or for surfactant administration if surfactant deficiency is severe. Excessive tidal volumes must be avoided, which can be challenging in a tiny periviable neonate. At present, none of the positive pressure devices used in the delivery room actually measure tidal volume. It is recommended that all such devices use pressure monitoring, including self-inflating bags in order to limit excessive damage to the fragile lung.[1]

3.3.1. *Sustained inflation*

In animal models, prolonged initial sustained inflations of 10–20 s have been shown to achieve functional residual capacity faster and to improve lung function without adverse circulatory effects.[26,27] Small clinical trials suggest that initial sustained inflations may reduce the need for intubation and development of bronchopulmonary dysplasia.[28,29] More trials are needed to determine the optimal time of a sustained inflation and its safety regarding risk of pneumothorax before such practice becomes routine.

3.3.2. *CPAP*

Immediate application of CPAP to prevent collapse of the often surfactant-deficient preterm lung reduces the need for intubation, exogenous surfactant administration, and ventilator days, but not rates of bronchopulmonary dysplasia or death.[30,31] CPAP levels of 8 but not 5 cm H_2O[30,31] in the delivery room increased the risk for pneumothorax. Although CPAP may help establish and maintain a functional residual capacity in a stiff non-compliant lung, thus improving respiratory distress, it should never be used in place of positive pressure ventilation when respiratory effort is poor or absent.[13,32] Flow-inflating bags and T-piece resuscitators are needed to deliver CPAP in the delivery room. Self-inflating bags cannot deliver CPAP, even with a PEEP valve attached.

3.3.3. *Intubation*

It is quite possible that the periviable infant will need effective positive pressure ventilation and intubation for stabilization. Finer et al.[33] demonstrated that although about half of 24-wks GA infants can be stabilized on CPAP in the delivery room, very few infants of less than 24-wks GA avoided delivery room intubation. This may change as other non-invasive ventilation strategies are explored. If a

periviable infant is intubated, early use of surfactant may be beneficial.[34] Some may choose to do this in the delivery room and others will wait until just after admission to the NICU.

3.4. *Oxygen use in the delivery room*

3.4.1. *Oxygen concentrations*

Avoidance of hypo- and hyperoxemia during resuscitation of preterm infants in the delivery room is critical. Preterm infants are relatively deficient in anti-oxidant protection and oxygen toxicity may exacerbate morbidities, such as chronic lung disease, retinopathy of prematurity, intraventricular hemorrhage, and necrotizing enterocolitis. Pure oxygen is rarely needed for successful resuscitation of the ELBW infant, although many need some O_2 supplementation at least transiently in the delivery room.[35–38] No specific starting concentration recommendation is made for preterm infants but ranges between 21% and 40% are not uncommon.[39] The important thing is titrate the oxygen in order to limit hyperoxygenation and hypo-oxygenation. The optimal starting concentration of oxygen for resuscitation of preterm infants is an active area of current research.

3.4.2. *Pulse oximetry, blended oxygen, and goal saturations*

Blended oxygen and pulse oximetry must be available at every delivery of a periviable neonate. The pulse oximeter sensor should be placed on the right hand or wrist and subsequently connected to the monitor for the quickest, most accurate signal.[40] Optimal goal saturations per minute of life have not been determined for ELBW or periviable neonates. The current recommendation is to use the interquartile range of oxygen saturations of healthy term infants as the goal.[6,25]

3.5. *Cardiac compressions and medications warrant caution*

When initial resuscitative efforts focus on establishing effective ventilation, cardiac compressions and medications are rarely needed. For ELBW infants, compressions and medications are prognostic markers for adverse neurodevelopmental outcomes.[41,42] ELBW infants who receive cardiac compressions and medications in the delivery room and have a 5-min Apgar score <2 have only a 14% chance of disability-free survival.[41] Prolonged compressions and medications in such infants should be viewed with caution. Given the high rates of poor outcomes, families may decide in counseling before birth that they prefer to forego trials of compressions and medications if initial ventilator support fails to stabilize the heart rate of their periviable neonate.

4. Conclusion

An immense number of complex decisions and tasks must be accomplished in a short period of time following the birth of a periviable infant. A standardized approach, using the best possible evidence should be used, which allows for individual variation in the response of the neonate. An important goal is to provide the least invasive support needed while always being prepared for the worst. Strong communication, teamwork, medical knowledge, and clinical skills are essential.

5. Research directions

The need for research specific to the periviable neonate in the delivery room is broad. Examination of each step of the NRP alogorithm in the context of the periviable neonate is warranted.

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