Reducing Germinal Matrix-Intraventricular Hemorrhage: Perinatal and Delivery Room Factors

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Practice Gaps

Much research has gone into understanding the pathogenesis and prevention of germinal matrix hemorrhage–intraventricular hemorrhage (IVH). Based on the current evidence, it is widely accepted that antenatal corticosteroid administration has helped reduce the risk of IVH in preterm infants. With continued identification of maternal interventions that can be implemented during the perinatal period, we hope to see a reduction in IVH rates. Almost half of all IVH occurs within the first day after birth, so understanding delivery room interventions that reduce IVH risk will hopefully contribute to further the ongoing efforts on reduction. At this time, prevention of premature birth continues to have the single greatest impact on reducing the incidence of germinal matrix hemorrhage–IVH.

Abstract

Germinal matrix hemorrhage–intraventricular hemorrhage (IVH) is the most common form of brain injury in preterm infants. Although severe IVH has declined over the years, it still affects approximately 6% of infants born before 32 weeks of gestation. Most IVH cases are detectable by the first 24 hours after birth; therefore interventions to prevent IVH should focus on antenatal management for pregnant women and delivery room management. Obstetrical interventions, including antenatal corticosteroids, maternal rather than infant transport, and possibly elective cesarean delivery have been associated with a decreased risk of IVH. Neonatal interventions in the delivery room, including delayed cord clamping or umbilical cord milking, maintaining normothermia, avoiding fluctuations in cerebral blood flow, and optimal ventilation management are associated with a decreased risk of IVH. Multiple clinical trials are under way to further identify IVH risk factors, ability to monitor or predict IVH, and ideally prevent IVH altogether. This discussion will focus on reviewing current obstetric and neonatal management practices and their associations with germinal matrix hemorrhage–IVH.

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ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
CO_2	carbon dioxide
CS	cesarean section
DCC	delayed cord clamping
ELBW	extremely low birthweight
Fio_2	fraction of inspired oxygen
GMH	germinal matrix hemorrhage
ICC	immediate cord clamping
IVH	intraventricular hemorrhage
NICHD	National Institute of Child Health and Human Development
NIRS	near-infrared spectroscopy
NRN	Neonatal Research Network
SpO_2	oxygen saturation
UCM	umbilical cord milking
VLBW	very low birthweight

Objectives After completing this article, readers should be able to:

1. Describe the grading of intraventricular hemorrhage.
2. Identify the antenatal factors associated with decreased risk of intraventricular hemorrhage.
3. Identity delivery room management associated with decreased risk of intraventricular hemorrhage.

BACKGROUND

Germinal matrix hemorrhage (GMH)–intraventricular hemorrhage (IVH) is a well-described neonatal brain injury and is the most common form of intracranial hemorrhage in neonates. GMH occurs in the highly vascularized region in the developing brain known as the *subependymal germinal matrix*, an area from which precursor central nervous system cells originate. When bleeding from the subependymal region extends into the lateral ventricles, the bleeding is classified as IVH. The immature vascular network in the germinal matrix is most abundant in the fetal brain between 24 and 34 weeks' gestation. With increasing gestation, this region matures, and by term, this primitive collection of blood vessels involutes and is replaced by a mature capillary network. (1)(2)

GMH-IVH severity is graded using 1 of 2 published classification systems describing cranial ultrasonography findings. The Papile grading system was originally based on brain computed tomography images of IVH and was named according to the location and magnitude of hemorrhage. (3) As ultrasound technology improved and more cranial ultrasound scans were obtained, the Papile grading system became commonly used to also describe ultrasound images. (Fig 1). The Volpe grading system is the other major grading system and is based on cranial ultrasonography findings. (2) One main difference between the 2 systems is the definition of and pathophysiologic mechanism underlying what constitutes a grade 4 hemorrhage (Table 1).

It has been well reported that the incidence and severity of IVH increases with decreasing gestational age. The normal vascular physiology of the developing brain, as outlined earlier, provides context to help explain this decrease in incidence and severity of GMH-IVH seen with increasing gestational age. According to data from the Vermont Oxford Network, based on 247,392 very-low-birthweight (VLBW; birthweight <1,500 g) infants born between 2009 and 2013, the incidence of any grade IVH is 24% to 26%. (1) A National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN) study published in 2010 looked at data for 9,575 VLBW neonates born between 22 and 28 weeks' gestation and reported the incidence of IVH at approximately 20% to 25%. (4) Fortunately, the authors also saw a reduction in the incidence of severe IVH in VLBW infants from 19% in 1993 down to 15% in 2012. (5) Again, a decline in severe IVH was also reported in a 2018 study that examined data from over 44,000 infants born at less than 32 weeks' gestation over a 10-year period; severe IVH rates decreased from 9.7% in 2005 to 5.9% in 2015. (6)

In 2014, a systematic review and meta-analysis of IVH timing in preterm infants found that almost half of IVH cases occurred within the first 6 hours after birth while 38% of cases were diagnosed after 24 hours of age. (7) By day 4 after birth, almost 90% of IVH lesions are detectable. (2) Given the early timing at which most GMH-IVH occurs, implementation of perinatal and delivery room interventions that reduce IVH may be the most impactful. The following is a review of perinatal and immediate delivery room interventions that have been clearly shown to reduce the risk of GMH-IVH in preterm infants, factors that are linked to an increased risk of developing GMH-IVH, and those interventions for which the evidence is still unclear but current investigations are under way (Table 2) (Table 3).

ANTENATAL GLUCOCORTICOIDS

There are clear perinatal interventions that help reduce the incidence of GMH-IVH. Because the greatest risk factor for GMH-IVH development is prematurity, interventions that reduce preterm birth will also indirectly help to reduce the incidence of hemorrhage. According to the American College of Obstetricians and Gynecologists (ACOG), women who are at risk for preterm delivery within 7 days should be given antenatal glucocorticoids for induction of fetal

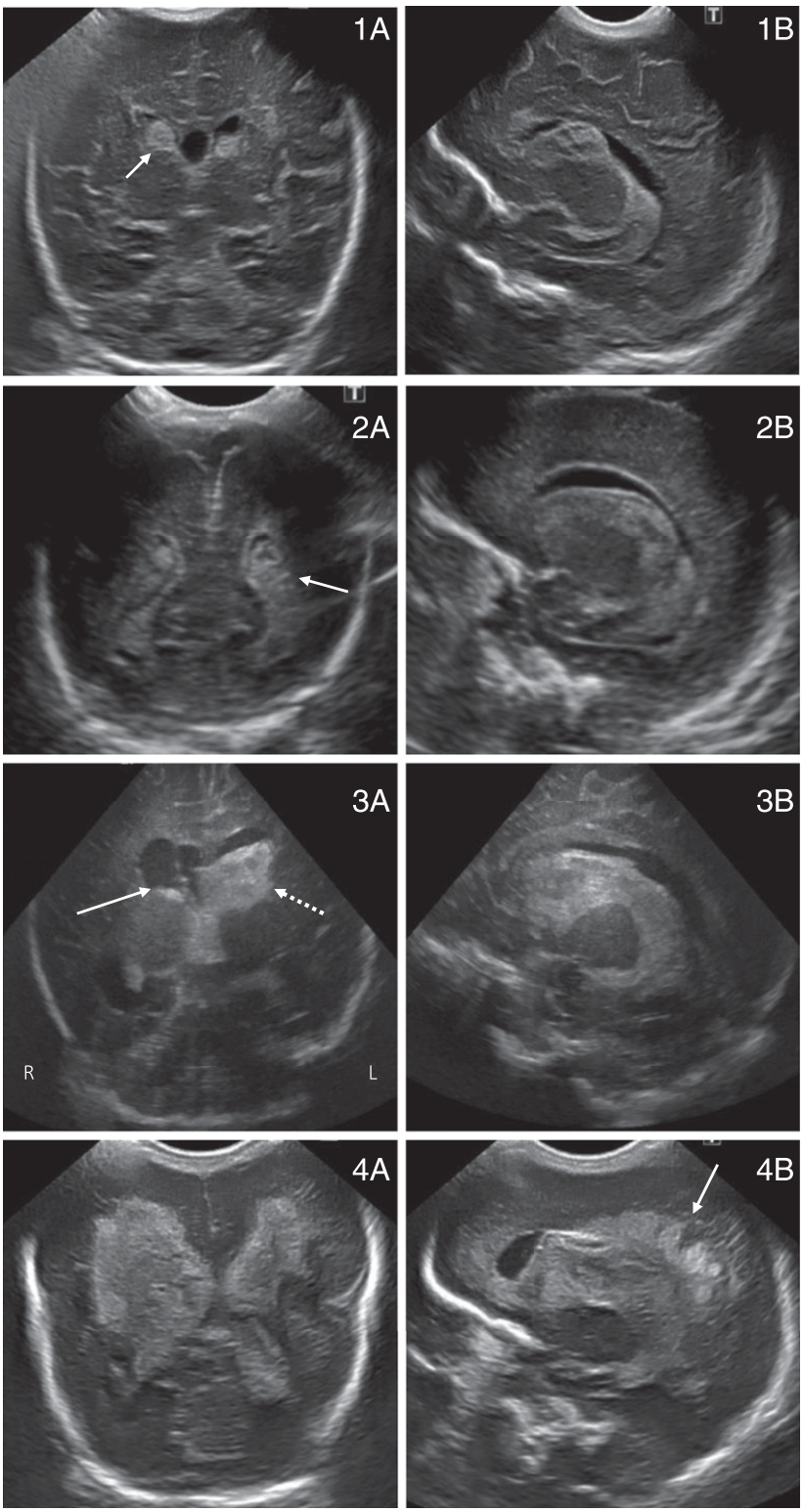

Figure 1. Cranial ultrasound images based on Papile grading system. 1A. Coronal image of bilateral grade 1 intraventricular hemorrhage with a solid arrow pointing at a germinal matrix hemorrhage. 1B. Sagittal image of grade 1 intraventricular hemorrhage. 2A. Coronal image of bilateral grade 2 intraventricular hemorrhage with a solid arrow pointing at a grade 2 intraventricular hemorrhage with blood in the ventricle and no ventricular dilation. 2B. Sagittal image of grade 2 intraventricular hemorrhage. 3A. Coronal image of left-sided grade 3 intraventricular hemorrhage and right-sided grade 2 intraventricular hemorrhage. Dashed arrow is pointing at a dilated ventricle filled with blood. Solid arrow is pointing at blood in the ventricle without ventricular dilation. 3B. Sagittal image of grade 3 intraventricular hemorrhage. 4A. Coronal image of bilateral grade 4 intraventricular hemorrhage with bleeding into the ventricles causing dilation and parenchymal hemorrhage. 4B. Sagittal image of grade 4 intraventricular hemorrhage with a solid arrow pointing at hemorrhage in the parenchyma.

maturity. (8) This practice has been shown to decrease overall neonatal mortality and morbidity. Antenatal steroid administration has also been shown to independently decrease IVH risk as well as the severity and frequency of respiratory distress syndrome, the need for respiratory support, the incidence of necrotizing enterocolitis, and

TABLE 1. **Comparison of Intraventricular Hemorrhage (IVH) Grading Systems**[a]

SEVERITY	PAPILE	VOLPE
Grade 1	Germinal matrix hemorrhage	Germinal matrix hemorrhage with or without IVH (< 10% of ventricle filled with blood)
Grade 2	IVH without ventricular dilation	IVH (10%–50% of ventricle filled with blood) typically without ventricular dilation
Grade 3	IVH with ventricular dilation	IVH (>50% of ventricle filled with blood) typically with ventricular dilation
Grade 4	IVH with ventricular dilation and parenchymal hemorrhage	Periventricular hemorrhagic infarction *Not an extension of IVH*

[a]*Mild IVH is generally defined as grade 1 or 2 and severe IVH is generally defined as grade 3 or 4.*

systemic infections in the first 48 hours after birth. (9) The maturational effect of antenatal steroids on a developing fetus' organs is complex and continues to be studied.

It has become standard of care that expectant women at risk of imminent preterm delivery be given either betamethasone or dexamethasone. Both steroids have the ability to cross the placenta and have been well-studied. A recent Cochrane systematic review of over 30 studies comparing these 2 steroid regimens revealed possible increased reduction of IVH in neonates whose mothers received dexamethasone compared with betamethasone. (10) However, an NICHD NRN study of 3,600 VLBW infants who received antenatal betamethasone versus dexamethasone found that both steroids equally reduced the risk of IVH, while betamethasone further reduced the risk of neonatal death and severe retinopathy of prematurity. (11) A follow-up NICHD NRN study comparing extremely low-birthweight (ELBW <1,000 g) infants exposed to prenatal dexamethasone versus betamethasone found that at 18 to 22 months' corrected age, ELBW infants exposed to dexamethasone were more likely to have neurodevelopmental and hearing impairments compared with those exposed to betamethasone. (12) Given these results, based on the current available evidence it is most prudent to administer antenatal betamethasone over dexamethasone to expectant women in preterm labor.

TABLE 2. **Perinatal Factors Associated with Intraventricular Hemorrhage (IVH) in Preterm Infants**

Increased IVH Risk
• Maternal inflammatory conditions (ie, chorioamnionitis)
• Placental abruption
Decreased IVH Risk
• Antenatal glucocorticoids
• Maternal medications
◦ Tocolytics in setting of preterm labor, specifically nifedipine or atosiban
◦ Antibiotics in setting of chorioamnionitis
Possible Impact on IVH Risk
• Maternal transport before delivery
• Delivery mode and timing
• Preeclampsia

MATERNAL TRANSPORT

Evidence from a large multicenter retrospective study of nearly 67,600 VLBW infants demonstrated that interhospital transport within the first 48 hours after birth was an independent risk factor for IVH development. (13) Furthermore, it has been reported that the longer the duration of transport (>60 minutes), the higher was the rate of neonatal death. (14) However, a recent single-center study, which controlled for an even larger number of maternal and birth variables than the previous study, reexamined the postulated association between IVH and interhospital transport of VLBW infants and concluded that based on their findings, interhospital transport is not an independent risk factor for IVH as previously reported. (15) Thus, it is evident that further research must be done in this area to better understand the true risk of IVH associated with neonatal transport. If in fact transport does contribute to the development of IVH, it is reasonable to assume that the cause is

TABLE 3. **Delivery Room Factors Associated with Intraventricular Hemorrhage (IVH) in Preterm Infants**

Increased IVH RIsk
• Hypothermia (moderate or severe)
• Factors that decrease cerebral blood flow
◦ Hypoxemia
◦ Hypotension (with signs of poor perfusion)
◦ Hypercapnia
• Multiple intubation attempts (in VLBW infants)
Decreased IVH Risk
• Delayed cord clamping (no benefit found in preventing severe IVH)
• Umbilical cord milking (no benefit found in preventing severe IVH)

multifactorial, including underlying maternal processes, degree of prematurity, severity of illness necessitating transport, thermoregulation, hemodynamic instability, maintaining optimal ventilation and oxygenation while on transport, and even the physical risks associated with transport itself. Given the possible increased risk of IVH and mortality associated with postnatal transport, in utero transport of high-risk pregnancies to a tertiary care center with a higher level NICU is preferable over the transport of critically ill neonates, especially in the first few days after birth. Current clinical trials on the effects of transportation on infants should shed light on the physiological effects of neonatal transport (PremiTranS NCT01851668, TRiPs NCT03754439).

DELIVERY MODE AND TIMING

Currently, the impact of infant delivery mode on IVH incidence is unclear. Previous studies have not demonstrated a significant difference in risk of severe IVH among VLBW infants delivered vaginally versus those delivered via cesarean section (CS). (16)(17) However, more recent published reports point to lower IVH rates associated with preterm infants delivered via CS compared with infants delivered vaginally. (16)(18)(19) Other studies suggest an association with increased IVH rates when a pregnant woman is in active labor. (20)(21)(22) It is therefore reasonable to conclude that preterm infants delivered via CS without labor may potentially further reduce the risk of IVH. However, this decision should be made carefully, balancing the risks and benefits to both the pregnant woman and fetus, given that CS poses significant later risks for the mother.

Another factor that may affect the risk of IVH is the time of day at which a preterm delivery occurs. A large retrospective chart analysis of over 47,600 VLBW infants has suggested that being delivered during "off-peak hours" may increase a VLBW infant's risk of severe IVH. (23) Off-peak delivery times were between 12:00 am and 7:00 am, with the highest risk associated with those infants born between midnight and 4:00 am. The authors propose that overnight staffing levels and decline in proficiency during night hours play a role. However, other inherent biologic factors may be possibly associated with overnight deliveries that are not accounted for, which contribute to these findings. For example, in this study, the authors controlled for many confounding maternal and infant factors, but they were unable to include antenatal steroid administration in the analysis.

A clearer understanding of this association between mode and timing of infant delivery is needed because this may affect overall neonatal morbidity and mortality and guide decision-making when determining delivery method. Until these matters are further settled through future study, the decision on method and timing of delivery to reduce the risk of IVH cannot be based upon these factors alone.

ADDITIONAL MATERNAL CONSIDERATIONS

The role of maternal health conditions, including inflammatory processes, placental abruption, preeclampsia, obesity, smoking, and administration of intrapartum medications (eg, tocolytics, nonsteroidal anti-inflammatory drugs, phenobarbital, vitamin K) on GMH-IVH have all been studied. The presence of chorioamnionitis appears to be an independent risk factor for the development of any grade IVH, (24)(25) whereas preeclampsia may provide some degree of protection against the development of severe IVH. (26)(27) In the EPIPAGE2 study, placental abruption was found to be an independent risk factor for severe IVH and, in the setting of a maternal inflammatory state, it also further increased IVH risk. (28) Although a host of maternal medications have been studied, only antenatal steroids, antibiotics in the settings of chorioamnionitis, and possibly maternal tocolytics during preterm labor, specifically nifedipine or atosiban, have been shown to reduce IVH. (29) More investigation is needed to further clarify and understand the impact of maternal health conditions and medications on GMH-IVH. Continued discovery of the maternal processes involved and their fetal effects may help reduce

and potentially even prevent GMH-IVH in the preterm population.

DELAYED CORD CLAMPING

Delayed cord clamping (DCC) has been recommended by ACOG and American Academy of Pediatrics for 30 to 60 seconds in vigorous term and preterm infants. (30) Placental transfusion during DCC can provide up to 80 mL of blood in a term infant in 1 minute and up to 40 to 50 mg/kg of iron, immunoglobulins, and stem cells. In multiple studies, DCC has been shown to decrease the incidence of all grades of IVH, but did not show any benefit in severe IVH. (31) However, because of the delay in resuscitation, DCC is not recommended when the infant is not vigorous, even though these neonates may benefit from placental transfusion. Umbilical cord milking (UCM), in which blood is stripped from an unclamped umbilical cord 2 to 3 times before clamping, can shorten the time to resuscitation. A meta-analysis of 7 randomized controlled trials of UCM versus control intervention of DCC or immediate cord clamping (ICC) in infants of less than 33 weeks' gestation showed reduced risk of all grades of IVH but not severe IVH. (32) Studies comparing UCM with ICC in preterm infants of less than 28 and 32 weeks of gestation, respectively, also showed a significant decreased incidence of all grades of IVH but not severe IVH. (33)(34)

DCC after cesarean delivery has been shown to have a lack of adequate placental transfusion with nonsignificant increases in blood volumes after DCC compared with early cord clamping. (35) Most studies on DCC do not stratify based on mode of delivery. A randomized controlled trial comparing UCM with DCC in preterm infants of less than 32 weeks' gestation delivered via CS showed higher hemoglobin and blood pressure over the first 15 hours after birth but was not powered to assess difference in IVH. (36)

Although UCM is not routinely recommended, studies demonstrate that UCM is better than ICC when DCC cannot be performed and may be more beneficial than DCC in CS deliveries. Larger clinical trials on DCC, DCC with ventilation, and UCM (NCT02996799, VentFirst NCT02742452, PREMOD2 NCT03019367, NCT03200301) are ongoing and will hopefully further clarify this matter.

HYPOTHERMIA

The ideal neonatal body temperature lies between 97.7°F (36.5°C) and 99.5°F (37.5°C), with mild hypothermia defined as 96.8°F (36.0°C) to 97.5°F (36.4°C), moderate hypothermia ranging between 91.2°F (32.9°C) and 96.6°F (35.9°C), and severe hypothermia at less than 89.6°F (32°C). (37) In the delivery room, newborns experience evaporative, radiant, convective, and conductive heat loss. Preterm infants are at higher risk for neonatal hypothermia, with birthweight being the most significant determining predictor of admission hypothermia in VLBW infants. (38) A cohort study of VLBW infants showed no increased risk for severe IVH with mild hypothermia, but higher odds of severe IVH with moderate hypothermia. (39) Given the need to maintain normothermia, the Neonatal Resuscitation Program recommends that for preterm newborns, the delivery room temperature should be set to 73.4°F (23°C) to 77°F (25°C), and for newborns of less than 32 weeks' gestation, a plastic wrap/bag, thermal mattress, and hat should be used to reduce heat loss. (40)

OXYGENATION

Preductal oxygen saturation (SpO_2) monitoring is standard in delivery room resuscitation and oxygen is titrated to goal SpO_2 levels based on full-term infants. According to current recommendations, preterm resuscitation should be initiated with low fraction of inspired oxygen (Fio_2), beginning with Fio_2 of 0.21 to 0.3. (40) Meta-analysis of 8 randomized controlled trials comparing resuscitation with low (Fio_2 <0.3) versus high (Fio_2 >0.6) oxygen in preterm infants of less than 28 weeks' gestation found no difference in overall risk of death or other preterm morbidities including IVH greater than or equal to grade 2. (41) However, infants requiring resuscitation initiated with low oxygen were less likely to reach a goal 5-minute SpO_2 of 80% to 85%. Failing to meet this 5-minute SpO_2 goal was associated with an increased risk of grade 3 or higher IVH. (42) The To2rpido Study, an international, multicenter, randomized, unmasked study in preterm infants of less than 32 weeks' gestation was designed to determine the effect of using room air or 100% oxygen in delivery room resuscitation. The study showed a statistically significant increase in hospital mortality for infants of less than 28 weeks' gestation who received room air resuscitation. (43) These studies suggest that for preterm infants with a birth gestational age of less than 28 weeks, resuscitation should be initiated with higher oxygen than Fio_2 0.21 and close attention should be paid to goal saturations for age. However, more studies are needed in preterm infants to determine optimal goal SpO_2 targets because current targets are based on data from full-term infants. Current clinical trials to assess oxygen parameters in delivery room resuscitation of preterm infants (HiLo NCT03825835, MONITOR NCT03256578,

STARTPreterm NCT03115463) may help guide optimal saturation goals in the delivery room.

CEREBRAL BLOOD FLOW

Cerebral perfusion relies on cardiac output and regional vascular resistance, which is affected by autoregulatory capacities. Premature infants have diminished autoregulatory mechanisms. Changes in arterial blood pressure cause changes in cerebral blood flow. (44) Fluctuations in cerebral blood flow or obstruction of the venous system have been postulated to lead to vessel rupture in the cerebral capillary bed. (45) When possible, the factors that affect cerebral blood flow, as discussed later in this article, should be monitored in the delivery room.

Hypotension has not been consistently associated with IVH, but that may be because of differences in definitions of hypotension across studies. (46)(47) In a beagle pup model, it was shown that low blood pressure followed by a period of reperfusion or isolated hypertension alone can increase IVH. (48) However, in preterm infants, in the first 48 hours after birth, there is no positive association with blood pressure and systemic blood flow. (49) A retrospective cohort study of ELBW infants showed permissive hypotension, as defined by mean blood pressure less than gestational age but good perfusion (ie, capillary refill, heart rate, urine output, and no acidosis), had no significant increased mortality compared with normotensive patients. (50) However, the study showed a significant decrease in survival without severe neonatal complications in the hypotension group with signs of poor perfusion compared with both the normotensive and permissive hypotensive groups. This suggests that rather than blood pressure, signs of perfusion should guide treatment. (50) Therefore, delivery room goals should be to assess signs of systemic blood flow and perfusion along with blood pressure and to avoid fluctuations in blood pressure. Current clinical trials are investigating hypotension in preterm infants and effects of various treatments (HIP NCT01482559, NCT02016599, ELGANBP NCT00874393), which may help determine the best treatment goals in the delivery room.

A neonate's respiratory status also affects his/her cerebral blood flow. Regional carbon dioxide (CO_2) levels affect cerebral perfusion, such that hypercapnia results in vasodilation and increased cerebral blood flow. (44) Hypercapnia in the first 72 hours after birth is associated with severe IVH in a dose-dependent manner. (51) Bicarbonate infusions can lead to a rapid rise in CO_2 levels and increase the risk of IVH. (52) Hypoxemia contributes to cerebral vasodilation and increased cerebral blood flow to maintain oxygen delivery while hyperoxemia decreases cerebral blood flow. (44) As discussed earlier, the normal SpO_2 targets for preterm infants are not well defined so hypoxemia and hyperoxemia in the delivery room are difficult to assess. The goal in the delivery room is to avoid extremes in SpO_2 and CO_2 levels and maintain "normal" SpO_2 and CO_2 levels.

It has been shown that cerebral blood flow is lower in infants who develop IVH, (18)(53) raising the possibility that monitoring cerebral blood flow may be a marker of developing IVH. Cerebral blood flow can be indirectly monitored by cerebral oximetry using near-infrared spectroscopy (NIRS) which measures the regional tissue oxygenation saturation of hemoglobin. (54)(55) Suggested goal NIRS saturation is 55% to 85% in infants and persistent values outside the range should prompt clinical assessment (Fig 2). (56) The recent Neu-Prem trial showed that it is feasible to perform NIRS in the delivery room for a preterm infant. The trial also showed that infants with severe IVH or death had lower cerebral oxygenation from 8 to 10 minutes after birth. (55) Given that cerebral blood flow plays an important role in IVH and is not well correlated with blood pressure or other standard delivery room monitoring, use of NIRS may add value. Clinical trials are under way to determine normal values, safety of NIRS, and association with IVH for neonates (NCT02147769, NCT02601339, NCT01620203, SafeBoosC NCT03770741). However, currently NIRS is not part of routine monitoring in the delivery room or the NICU.

INTUBATION

Intubation is often accompanied by physiological responses including desaturation, bradycardia, hypotension or

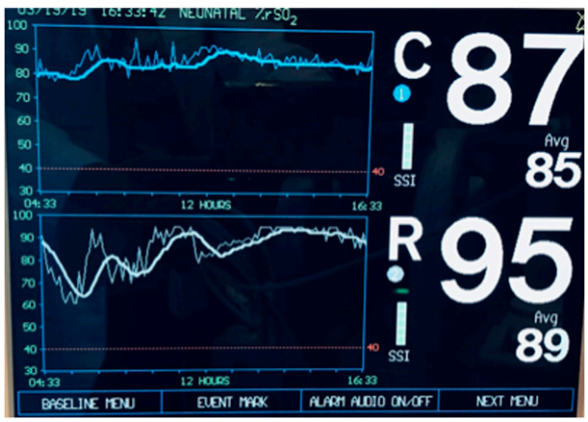

Figure 2. Example of a near-infrared spectroscopy (NIRS) monitor screen. NIRS measures regional tissue oxygenation and is a proposed hemodynamic monitoring tool with potential use in the delivery room. NIRS probes are commonly placed on the forehead to measure cerebral saturation (C) and on the posterior flank to measure renal saturation (R). The average cerebral tissue oxygenation saturation in the figures is 85%, which is within the suggested normal range for infants.

hypertension, and increased intracranial pressures. (57) A retrospective cohort analysis of 188 VLBW infants who underwent intubation in the delivery room showed that those with no or mild IVH (grade 1 or 2) required significantly fewer intubation attempts than those with severe IVH. (57) Neonates with birthweights less than 750 g and who experienced more than 3 intubation attempts in the first 4 days after birth were 28 times more likely to develop severe IVH. (58) More studies are needed but results suggest that in the delivery room, VLBW infants should undergo intubation by an experienced caregiver.

HEAD POSITIONING

Head positioning and effects on cerebral hemodynamics have been implicated in the development of IVH in preterm infants. Turning the head toward 1 side may functionally occlude jugular venous drainage on the ipsilateral side, causing poor venous drainage and increased intracranial pressure and blood flow. Recommendations for midline positioning with elevation of the head of the incubator has been identified as a potential practice for preventing IVH. (59) However, to date, 2 systematic reviews have showed insufficient evidence for neutral head positioning and tilt. (59)(60) No definitive recommendation on infant head positioning can be made at this time. Currently, there is a clinical trial investigating 72 hours of optimal midline positioning (NCT03543046), which may aid in clarifying recommendations for premature head positioning.

CONCLUSION

Obstetric and pediatric specialists have made great efforts to understand the pathogenesis of GMH-IVH in preterm infants, mainly because of the associated outcomes and prognosis. Short-term IVH complications include the development of posthemorrhagic ventricular dilation. Long-term complications and prognosis are dependent on the infant's degree of prematurity, extent of hemorrhage, and presence of parenchymal involvement. A recent meta-analysis found that preterm infants with mild IVH, when compared with those without IVH, were associated with higher odds of death or moderate to severe neurodevelopmental impairment without an increase in cerebral palsy or cognitive delay at 18 to 24 months. Infants with severe IVH were at even higher odds of developing moderate to severe neurodevelopmental impairment, cerebral palsy and cognitive delay compared with those with mild IVH. (61)

The reduction in rates of severe IVH over the last few decades is likely because of advances in perinatal and postnatal medical care and research. As we continue to define GMH-IVH risk factors and adapt our practice guidelines, we hope to see an even further reduction in the incidence of all grades of IVH and its associated short- and long-term complications.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the pulmonary and non-pulmonary effects on the fetus and/or newborn infant of maternally administered steroids (including betamethasone, dexamethasone, and prednisone).
- Know the complications and effects of chorioamnionitis in the mother and the fetus.
- Know the risk factors for development, proposed mechanisms, clinical and laboratory features, and diagnosis of pediatric intraventricular hemorrhage (IVH).
- Know the proposed prevention strategies, evolution, early complications, management, and long-term consequences of pediatric IVH.
- Know the appropriate monitoring of acute and subacute pediatric IVH during the neonatal period.

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1. A male neonate born at 24 weeks' gestational age is 12 hours old and receiving mechanical ventilation. He has cardiovascular instability and has received packed red blood cell transfusion for anemia. The team is considering ultrasonography to check for intraventricular hemorrhage. With regard to the timing of ultrasonographic detection of intraventricular hemorrhage in preterm infants, what is the earliest time point at which approximately 90% of lesions are detectable?
    A. 6 hours.
    B. 24 hours.
    C. 48 hours.
    D. Day 4 after birth.
    E. Day 14 after birth.
2. A pregnant woman who is at the 25th week of gestation presents with rupture of membranes and is in preterm labor. The health care team is considering the administration of antenatal glucocorticoids. Which of the following statements regarding this therapy is correct?
    A. Although dexamethasone has been shown to reduce incidence of respiratory distress syndrome, it has not shown any benefit for reduction of intraventricular hemorrhage.
    B. Although glucocorticoids do not cross the placenta, they induce maternal hormones that engage the hypothalamic-pituitary axis in the fetus, and thereby induce fetal maturity for various organ systems.
    C. Betamethasone reduces the likelihood of intraventricular hemorrhage, but has not shown benefit in reducing respiratory distress syndrome or mortality.
    D. Extremely low-birthweight infants exposed to antenatal dexamethasone are more likely to have neurodevelopmental and hearing impairment than infants exposed to antenatal betamethasone.
    E. Although there are benefits of antenatal glucocorticoids, the team should wait for 1 week while tocolytic medications are administered.
3. Your team is preparing for a delivery of a neonate at 25 weeks' gestational age. Because of breech position, preeclampsia, and signs of fetal distress, a probable cesarean delivery is discussed. With regard to delivery management, which of the following strategies is appropriate?
    A. Because of maternal health considerations, cesarean delivery is not an appropriate option before 26 weeks' gestational age.
    B. Because of the risk of brain injury, including intraventricular hemorrhage, the latest research shows that it is appropriate to attempt passive hypothermia in the first 24 hours after birth.
    C. Recommended treatment protocols include immediate cord clamping regardless of the patient's clinical status.
    D. The delivery room or operating room temperature should be set to 73.4°F (23°C) to 77°F (25°C).
    E. The preterm newborn's temperature will reflect the maternal temperature, and interventions to influence the neonatal temperature during the first hour after birth have been ineffective.

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4. A female preterm neonate born at 25 weeks' gestational age is 12 hours old. An umbilical arterial catheter provides a continuous measure of blood pressure. The blood pressure has decreased since birth and the mean arterial pressure is now 24 mm Hg. Which of the following is most concerning with regard to risk of mortality?
    A. A mean arterial blood pressure that is consistently below the gestational age at birth.
    B. Blood pressure that is close to the median for population norms in the context of a patent ductus arteriosus.
    C. Low blood pressure in combination with signs of poor perfusion, such as decreased capillary refill, tachycardia, and acidosis.
    D. Systolic blood pressure that is lower than the 10th percentile for gestational age.
    E. Urine output that is greater than 2 mL/kg per hour.
5. A male neonate born at 25 weeks' gestational age received continuous positive airway pressure since resuscitation in the delivery room and is now in the NICU. He is experiencing increased respiratory distress, repeated apnea, and increasing oxygen requirement. The team is considering intubation and giving surfactant, with subsequent plans for mechanical ventilation. Which of the following statements is correct regarding prevention of intraventricular hemorrhage for this patient?
    A. After intubation and stabilization on the ventilator, the optimal position for the neonate's head will be tilted 30 degrees to one side, with switching to the alternate side every 6 to 12 hours.
    B. Both hypoxemia and hyperoxemia lead to cerebral vasodilation and increased cerebral blood flow.
    C. Hypercapnia in the first 72 hours after birth is associated with severe intraventricular hemorrhage in a dose-dependent manner.
    D. Prophylactic infusion of sodium bicarbonate over the first 24 hours to prevent acidosis has been associated with decreased incidence of both any and severe intraventricular hemorrhage.
    E. The number of intubation attempts has not been shown to correlate with intraventricular hemorrhage risk.