Perinatal Brain Injury

Mechanisms, Prevention, and Outcomes

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KEYWORDS

• Perinatal brain injury • Encephalopathy • Intraventricular hemorrhage
• Periventricular leukomalacia • Perinatal arterial ischemic stroke • Cerebral palsy
• Hypothermia • Prevention

KEY POINTS

- Highlight the mechanism contributing to the development of common etiologies of perinatal brain injury in preterm and term neonates.
- Review the most up-to-date research and recommendations regarding preventive strategies aimed at improving outcomes for those neonates with or at risk for common etiologies of perinatal brain injury.
- Highlight the outcomes of neonates diagnosed with common etiologies of perinatal brain injury and the impact of preventive strategies currently used to improve outcomes.

INTRODUCTION

Perinatal brain injury may lead to significant long-term neurodevelopmental impairment, including cognitive, neurologic, motor, and sensory disability. Perinatal brain injury affects infants born at all gestational ages, but its incidence and morbidity increases with decreasing gestational age.[1]

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Improved perinatal care of the very preterm and low birth weight infant, and neuroprotective preventive strategies aimed at reducing the risk and severity of perinatal brain injury, have resulted in a greater number of affected infants surviving later in life with less severe neurodevelopmental disability.[2,3] Increased administration of antenatal corticosteroids is a possible explanation for the observed increases in survival, and decrease in cerebral palsy (CP) and neurodevelopmental impairment in extremely low birth weight infants from 1982 to 2002.[2] A single-center study of 536 very preterm infants born before 33 weeks of gestation with a 2-year follow-up, revealed a significant improvement in motor outcomes and decreased rate of CP from 12% in 2000 to 1% in 2010 that was, in part, attributed to the increased administration of magnesium sulfate to women at risk of preterm birth over the study periods.[3] More recently, improved outcomes are now being recognized for those neonates born at cusp of viability. Data from 4274 infants born between 22 and 24 weeks spanning 3 epochs (2000–2003, 2004–2007, and 2008–2011) at National Institute of Child Health and Human Development (NICHD) Neonatal Research Network centers showed an increase in overall survival from 30% to 36%, and survival without neurodevelopmental impairment from 16% to 20%, between epoch 1 and epoch 3, although the incidence of moderate to severe CP did not decrease significantly across epochs (15% in epoch 1 and 11% in epochs 2 and 3).[4]

In these sections, common etiologies of perinatal brain injury will be reviewed, including hypoxic–ischemic encephalopathy (HIE), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), perinatal stroke, and CP (**Table 1**). Although these causes of perinatal brain injury are separate clinical entities, they remain interrelated by their risk factors and pathogenesis. The underlying mechanism of injury involves an initial insult to the vulnerable, developing fetal brain that is usually either of hypoxic–ischemic, hemorrhagic, or infectious in nature, and sets off a cascade of events leading to further brain injury.[18]

COMMON MECHANISM OF INJURY

Perinatal brain injury can affect infants born at any gestational age; however, very preterm fetuses (born <32 weeks of gestation) are less equipped to adapt to perinatal insults as term infants, making them more prone to brain injury.[1] In most cases, a common pathway of injury is elicited by an initial hypoxic–ischemic or inflammatory insult that incites a cascade of events that potentiates perinatal brain injury.[18]

An excellent review by Giussani[19] highlights the adaptive physiologic mechanisms that are present in the term fetus that enables it to respond to a period of impaired oxygenation or systemic hypotension. When oxygenated blood supply is limited, the fetus meets its metabolic needs by binding a greater concentration of oxygen to hemoglobin, preferentially shunting oxygenated blood to tissues at greatest risk of hypoxic injury, and limiting oxygen consumption. In response to hypoxia, the fetal heart rate slows, permitting increased cardiac myocardial oxygen extraction, and increasing end-diastolic filling time and ventricular end-diastolic volume. This increases stroke volume, arterial blood pressure, and circulatory redistribution of blood flow secondary to peripheral vasoconstriction with vasodilation of the blood vessels that perfuse the brain, heart, and adrenal glands.

In contrast with the adaptive mechanisms of the term fetus, the preterm fetus has an immature cerebrovascular autoregulation system and exhibits a pressure-passive circulation. When faced with a period of hypoxia or systemic hypotension, preterm fetuses are unable to sustain increased cerebral perfusion, which makes them more prone to hypoxia–ischemia and neurologic injury. The initial hypoxic–ischemic insult is the primary