Neonatal Seizures

Advances in Mechanisms and Management

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KEYWORDS

• Brain injury • Developmental disability • Infant, newborn • Electroencephalography • Epilepsy • Magnetic resonance imaging • Neurocritical care • Seizures

KEY POINTS

- Seizures occur in 1 to 5 per 1000 live births and are among the most common neurologic conditions managed by a neonatal neurocritical care service.
- The high rate of seizures in the neonatal period reflects age-specific developmental mechanisms that lead to relative excitability.
- Neonatal seizures are often caused by serious underlying brain injury such as hypoxia-ischemia, stroke, or hemorrhage.
- Clinical detection is unreliable; continuous video electroencephalogram is the gold standard for monitoring presence and burden of neonatal seizures.
- Seizures are refractory to first-line medications in approximately 50% of cases; expert opinion supports rapid treatment to abolish acute symptomatic seizures and early discontinuation of medication.

INTRODUCTION

Neonates are at especially high risk for seizures as compared to other age groups.[1] The high risk for seizures—and especially acute symptomatic seizures—is likely multifactorial and often caused due to the relative excitability of the developing neonatal brain as well as the high risk for brain injury due to global hypoxia-ischemia, stroke, and intracranial hemorrhage.[2] The estimated rate of seizures in term newborns is said to be approximately 1 to 5 per 1000 live births.[3–5] However, population-based studies do not take into account the low diagnostic accuracy of diagnosis by clinical

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observation alone,[6,7] and gold standard prolonged, continuous video electroencephalogram (cEEG) monitoring is not widely available enough to make population-based predictions; therefore the true incidence remains unknown.

The differential diagnosis for neonatal seizures is broad and includes structural, metabolic, and genetic causes (**Box 1**). Seizures that arise from an acute symptomatic cause, such as hypoxic-ischemic encephalopathy, transient metabolic disturbance, infection, stroke, or intracranial hemorrhage, are much more common than neonatal onset epilepsies, which may be due to malformation, prior injury, or genetic causes. Rare conditions such as inborn errors of metabolism, vitamin-responsive epilepsies, and neonatal epilepsy syndromes must be considered in the setting of refractory seizures.[8,9]

Neonatal seizures carry a high risk for early death. Among survivors, motor and cognitive disabilities, as well as epilepsy are common.[10] The outcome depends largely on the underlying disease process and severity of underlying brain injury. The impact of the seizures themselves is not known, although studies in animal models suggest that seizures can alter brain development, leading to deficits in learning, memory, and behavior.[11]

Box 1
Cause of neonatal seizures

Differential Diagnosis of Acute Symptomatic Seizures

Global hypoxia-ischemia (hypoxic-ischemic encephalopathy)

Focal hypoxia-ischemia

- Arterial stroke
- Venous stroke

Intracranial hemorrhage

- Intraventricular
- Parenchymal
- Subarachnoid
- Subdural

Transient metabolic deficit

- Hypoglycemia
- Hypocalcemia and hypomagnesemia
- Hyponatremia

Acute infection

Differential Diagnosis of Neonatal Onset Epilepsy

Brain malformation

Intrauterine injury or congenital infection

Inborn error of metabolism and vitamin-responsive epilepsies

Neonatal Onset Epilepsy Syndromes

- Benign familial neonatal seizures (eg., KCNQ2, KCNQ3)
- Neonatal epileptic encephalopathies
  - Early myoclonic epilepsy
  - Early infantile epileptic encephalopathy (Ohtahara syndrome)