In Brief

Neonatal Seizures

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Author Disclosure

Drs Mosley and Serwint have disclosed no financial relationships relevant to this In Brief. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

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Neonatal seizures (NS) result from rapid depolarization of brain cells that leads to excessive synchronous electrical activity. The brain cells of a newborn are immature and vulnerable to insults. Therefore, NS often indicate an underlying neurologic disturbance. They require immediate assessment to determine the underlying cause and necessary interventions. Recurrent seizures have been found, in some studies, to be more likely to increase the risk of later epilepsy and long-term cognitive disability and to have more deleterious effects on the brain cells compared with prolonged seizures.

The incidence of NS varies widely, depending on the gestational age, infant weight, and cause. In preterm infants who weigh less than 1,500 g, the incidence ranges from 19 to 57.5 per 1,000 live births, but in infants who weigh more than 2,500 g, the incidence is as low as 2.8 per 1,000 live births.

Hypoxic-ischemic encephalopathy is the most common cause of NS, accounting for 50% to 60% of cases. Seizures usually occur within the first 24 hours after birth, and their severity can increase with time.

Intracranial infections, accounting for 5% to 10% of seizures, are the most common cause in developing countries. Viral infections include those caused by herpes simplex virus, cytomegalovirus, and rubella; bacterial causes include infections with group B *Streptococcus, Listeria*, and *Escherichia coli*. Toxoplasmosis also can cause NS. Prompt recognition and initiation of appropriate treatment is essential for the best outcome.

Intracranial hemorrhage accounts for about 10% of cases. In preterm infants, small amounts of germinal matrix and intraventricular hemorrhage usually do not cause seizures unless surrounding parenchyma is involved. In these cases (grade III or IV intraventricular hemorrhage), seizures often can be focal and persistent. For neonates who have been discharged from the hospital, it always is important to consider nonaccidental trauma (abuse).

Subarachnoid hemorrhage may cause seizures in otherwise healthy newborns but is not associated with long-term neurologic sequelae. However, subdural hemorrhages often are caused by trauma, and 50% of affected patients develop seizures.

Additional causes of NS include cortical (structural) brain malformations, hypoglycemia, hypocalcemia, hypomagnesemia, and hypo- and hypernatremia as well as inborn errors of metabolism such as aminoacidopathies, urea cycle defects, mitochondrial disorders, beta-oxidation defects, and pyridoxine dependency.

Genetic epileptic syndromes include benign familial neonatal convulsions, which occur 15 to 20 times per day and are outgrown by 1 year of age. "Fifth day fits" are observed in term infants during the first postnatal week and resolve within 24 hours. Ohtahara syndrome, also known as early infantile epileptic encephalopathy, may be due to malformations of cortical development and often is manifested by brief, repetitive tonic spasms similar to infantile spasms. Electroencephalography (EEG) shows a burst-suppression pattern. Treatment often is ineffective and the prognosis poor.

Due to the immature myelination of the neuronal network, some behavioral or motor manifestations of NS may not be detected by surface EEG, particularly seizures originating in the subcortical regions of the brain. Conversely, surface EEG findings may be present when there is no observable clinical manifestation. Such electrographic and clinical seizures, respectively, are seen periodically in the newborn, yet are relatively uncommon in older children who usually have "electroclinical" (typical) seizures.

Subtle-type seizures, found more commonly in preterm infants, often originate in the subcortical region and

have no EEG correlate. In both preterm and term infants, ocular manifestations are the most common clinical finding. Roving eyes, sustained eye opening or fixation, bicycling, lip smacking, and unresponsiveness often are observed in preterm infants. For term infants, sustained tonic horizontal eye deviation with or without jerking or apnea may be the presenting finding. Apnea alone in preterm infants often is due to causes other than NS.

Clonic-type seizures, seen commonly in term infants, consist of rhythmic, slow jerks. Focal-type clonic seizures include well-localized events of the face, upper or lower extremities, neck, or trunk involving one side of the body. Multifocal type clonic seizures consist of jerking movement occurring in several parts of the body.

Tonic seizures involve sustained extension or posturing. Focal-type tonic seizures involve sustained posturing of a limb or asymmetric posturing of the trunk. Generalized-type tonic seizures involve extension of upper and lower limbs in decerebrate posturing or tonic flexion of upper limb and extension of lower limb mimicking decorticate posturing.

Myoclonic seizures are faster jerks, often of flexor muscles. They may be focal, multifocal, or generalized single or multiple jerks of limbs.

Sometimes jittery infants can be misdiagnosed as having seizures, but jittery infants have normal gaze, nonsustained wandering eyes, and tremors but not jerks, and they experience no autonomic changes. Movements are stimulus-sensitive and cease with passive flexion of the limbs. Jitteriness may be due to a sustained or exaggerated Moro reflex, medication effect, or withdrawal from drugs of abuse by the mother.

Cause is the most important factor that determines the outcome of NS. Patients who have self-resolving conditions such as "fifth day fits" do well; those who have underlying brain disorders are most likely to have long-term sequelae. Birthweight and concomitant gestational age also are important prognostic factors. Sixty percent of term infants who have NS and weigh more than 2,500 g have been found to be developmentally normal. In contrast, only 20% of preterm infants who weighed less than 1500 g were found to be normal. Other factors that affect prognosis include Apgar scores, need for mechanical ventilation, neurologic findings, and findings on EEG and ultrasonography, reinforcing the concept that specific causes and the need for interventions affect outcomes.

Comment: NS cause much anxiety for parents and practitioners. Expeditious evaluation is needed to discern the cause from the wide array of possibilities and to initiate treatment for those seizures caused by metabolic disturbances, infections, or brain trauma. Animal studies have shown that seizures: 1) affect energy metabolism, 2) may quickly outstrip the brain's ability to compensate for the heightened metabolic rate, 3) result in a decrease in energy reserve, and 4) lead to subsequent brain cell injury. More research is needed to establish practice-based guidelines for anticonvulsant administration, to select the best anticonvulsants for treating neonates, and to determine the long-term outcomes from NS, including language and developmental status at school age.

Janet Serwint, MD
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Pediatrics in Review 2010;31;127
DOI: 10.1542/pir.31-3-127

Pediatrics in Review®
AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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