Epilepsy Currents
2020, Vol. 20(4) 189-190
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DOI: 10.1177/1535759720923292
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Continuous EEG Monitoring in Neonates: One Size Does Not Fit All

The Probability of Seizures During Continuous EEG Monitoring in High-Risk Neonates

Worden LT, Chinappen DM, Stoyell SM, et al. *Epilepsia*. 2019;60(12):2508-2518. doi: 10.1111/epi.16387

Objective: We evaluated the impact of monitoring indication, early electroencephalography (EEG), and clinical features on seizure risk in all neonates undergoing continuous EEG (cEEG) monitoring following a standardized monitoring protocol. Methods: All cEEGs from unique neonates 34 to 48 weeks postmenstrual age monitored from January 2011 to October 2017 (n = 291) were included. We evaluated the impact of cEEG monitoring indication (acute neonatal encephalopathy [ANE], suspicious clinical events [SCEs], or other high-risk conditions [OHRs]), age, medication status, and early EEG abnormalities (including the presence of epileptiform discharges and abnormal background continuity, amplitude, asymmetry, asynchrony, excessive sharp transients, and burst suppression) on time to first seizure and overall seizure risk using Kaplan-Meier survival curves and multivariable Cox proportional hazards models. Results: Seizures occurred in 28% of high-risk neonates. Discontinuation of monitoring after 24 hours of seizure freedom would have missed 8.5% of neonates with seizures. Overall seizure risk was lower in neonates monitored for ANE compared to OHR ($P = .004$) and trended lower compared to SCE ($P = .097$). The time course of seizure presentation varied by group, where the probability of future seizure was less than 1% after 17 hours of seizure-free monitoring in the SCE group, but required 42 hours in the OHR group, and 73 hours in the ANE group. The presence of early epileptiform discharges increased seizure risk in each group (ANE: adjusted hazard ratio [aHR] 4.32, 95% CI: 1.23-15.13, $P = .022$; SCE: aHR 10.95, 95% CI: 4.77-25.14, $P < 1e\text{-}07$; OHR: aHR 56.90, 95% CI: 10.32-313.72, $P < 1e\text{-}05$). Significance: Neonates who undergo cEEG are at high risk for seizures, and risk varies by monitoring indication and early EEG findings. Seizures are captured in nearly all neonates undergoing monitoring for SCE within 24 hours of cEEG monitoring. Neonates monitored for OHR and ANE can present with delayed seizures and require longer durations of monitoring. Early epileptiform discharges are the best early EEG feature to predict seizure risk.

Commentary

Nonconvulsive seizures and nonconvulsive status epilepticus are not uncommonly seen in comatose patients. Children and neonates in particular appear to be at higher risk. The diagnosis of seizures in sick newborns based on clinical signs alone is inaccurate. In a study of term newborns monitored with continuous electroencephalography (cEEG) for 72 hours, only one-third displayed clinical signs; overdiagnosis was equally common—only 27% showed electrographic seizures when suspected clinically.[1]

In a 2006 study, Jette et al[2] observed seizures in 51 (44%) of 117 of critically ill children. Although half were detected in the first hour of recording, it is noteworthy that 20% occurred beyond the 24-hour mark and 13% after 48 hours. In a prospective study of 100 children with acute encephalopathy, Abend et al found electrographic seizures in 46% and electrographic status in 19%; seizures were exclusively nonconvulsive in 32%. Only half were detected within the first hour, 87% by 24 hours, and 97% by 48 hours. Young age was a strong risk factor for nonconvulsive seizures.[3] Among children, neonates are at even greater risk for nonconvulsive seizures.

Wietstock et al published a large series of 595 newborn infants at 3 US centers; cEEG monitoring captured electrographic seizures in 105 (26%) of 400 of newborns; one-fourth had only electrographic seizures. Median duration of monitoring was 49 hours (interquartile range: 22-87 hours); median duration was longer (85 hours) in those on hypothermia for hypoxic–ischemic encephalopathy (HIE). Electroencephalography findings affected clinical management in 39% of patients (26% had subclinical seizures and 13% has paroxysmal events without EEG correlate).[4]

Therapeutic hypothermia reduces the seizure burden of neonates with moderately severe HIE[5,6]; nevertheless electrographic seizures still occur in a sizable proportion. Glass et al found electrographic seizures in 48% and electrographic status in 10% in their series of 90 neonates treated with therapeutic

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hypothermia treated at 3 institutions. Abnormalities of EEG background (excessive discontinuity, depressed and undifferentiated, background suppression, extremely low voltage, or burst suppression) were strongly associated with seizures. However, clinical variables such as Apgar scores, pH <6.8, or base excess ≤ -20 were not associated with seizures.[7]

The 2011 American Clinical Neurophysiology Society Guidelines on Continuous Electroencephalography Monitoring recommended tailoring the duration of monitoring based on the clinical scenario.[8] The following points in the Guidelines are noteworthy:

a. Assessment of the EEG background requires a minimum of 1 hour in order to assess the effects of the sleep–wake cycle.
b. Neonates with high risk for seizures should be monitored for a minimum of 24 hours to screen for seizures. Infants undergoing therapeutic hypothermia for HIE and those undergoing congenital heart surgery have an elevated risk for seizures. Furthermore, seizures may occur even in the presence of a normal or mildly abnormal EEG background. In certain low-risk infants, EEG monitoring could be discontinued sooner after consulting with the child neurologist.
c. If seizures are detected, EEG monitoring should continue until the patient has been seizure-free for at least 24 hours (unless decided otherwise by the child neurologist).
d. EEG monitoring to evaluate suspicious clinical events (SCEs) should be long enough to capture multiple typical events.

Worden et al examined seizure occurrence in high-risk neonates and reported seizures in 28%.[9] The probability of seizures was $<1\%$ after 17 hours of EEG recording in those with SCEs but 42 hours in infants with other high-risk conditions (central nervous system [CNS] infection, CNS trauma, perinatal stroke, inborn errors of metabolism, genetic/syndromic conditions, cardiopulmonary risk factors, sinovenous thrombosis, prematurity with additional risk factors such as intraventricular hemorrhage or weaning antiseizure medication in a high-risk infant). By contrast, those with acute neonatal encephalopathy (ANE) had a longer period of seizure risk ($<1\%$ after 73 hours); the median duration of monitoring for this group of infants was 84 hours. Epileptiform discharges increased the likelihood of seizures in each of the groups; when detected on early EEG recordings, they were predictive of seizures occurring within 24 hours in those with SCE. The finding of burst suppression on early EEGs increased seizure risk only in patients with ANE.

A conservative approach would be to monitor at-risk neonates with cEEG monitoring for at least 48 hours when the EEG background is severely abnormal and/or epileptiform discharges are present. In the presence of a normal EEG background, after recording typical paroxysmal events that are determined to be nonepileptic, EEG recording may be terminated by 24 hours. Infants with HIE requiring therapeutic hypothermia have an extended period of vulnerability to seizures including the rewarming phase and thus require longer duration of recording. Finally, conventional EEG monitoring is preferable to amplitude-integrated EEG, which may miss many neonatal seizures if they are brief, of low amplitude or infrequent.[10] Timely review of the cEEG (twice a day or more frequently as indicated) for providing feedback to the clinical team is essential.

Prakash Kotagal

ORCID iD

Prakash Kotagal https://orcid.org/0000-0002-8978-2680

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