Review Article

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Perspective on Neonatal Seizures in Low- and Middle-Income Countries

Abstract

The most frequent neurological emergency is neonatal seizures, which have a negative impact on neurodevelopment. Although they are typically challenging to identify and cure, doctors in low and Middle Income Countries (LMIC) face a substantial clinical problem. The majority of them are triggered seizures brought on by an abrupt brain injury, such as Hypoxic-Ischemic Encephalopathy (HIE), an ischemic stroke, an intracranial hemorrhage, a central nervous system infection, or an abrupt change in metabolism. Less frequently occur early-onset epilepsy disorders. Since clinical signs of seizures in the neonatal period are often difficult to separate from nonseizure behaviour, clinical diagnoses of seizures are usually erroneous. Additionally, a significant portion of seizures have only electrical activity and no other clinical symptoms, necessitating an EEG or aEEG for diagnosis. Clinically, only focal clonic and focal tonic seizures can be identified with sufficient diagnostic assurance. Evidence suggests that early therapy enhances the response to anti-seizure medication, making prompt diagnosis and treatment crucial. Because so many published researches come from high-income nations and cannot be extrapolated to LMIC, it is critical to understand the etiologies, comorbidities, and medication trials assessing safety and efficacy in LMIC. The authors of this review study provide the most recent information on neonatal etiology, diagnosis, categorization, and management guidelines, with a focus on low-resource environments.

Keywords: Neurological emergency • Neonatal seizures • Neurodevelopment • hypoxic-ischemic encephalopathy • Intracranial hemorrhage, Anti-seizure medication

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Introduction

The most frequent neurological emergency in the neonatal era is neonatal seizures, which frequently provide diagnostic and treatment issues for doctors worldwide. Numerous researches that have recently been published aim to enhance neonatal seizure diagnosis, care, and results. The majority of these studies, however, are from High Income Nations (HIC). There is evidence that newborn seizures occur more frequently and have different etiologies in High-Income Countries (HIC) compared to low- and Middle-Income Countries (LMIC), which may have significant therapeutic consequences. Furthermore, due to the limited accessibility of Electroencephalography (EEG) and Amplitude-Integrated EEG (an EEG), the majority of studies from LMIC primarily depend on clinical diagnosis for seizure identification. In this review, we discuss the many neonatal seizure presentations, occurrence, and etiology, diagnostic value of an EEG/EEG, assessment, and therapy in low resource environments. Because there is a dearth of high-quality evidence from LMIC, the authors' recommendations heavily rely on the data from HIC [1].

Neonatal seizure

Seizures are temporary occurrences of signs and/or symptoms brought on by abnormally excessive or synchronized neuronal activity in the brain, according to the International League Against Epilepsy (ILAE). The electrographic-only seizures, which account for 40%-60% of all seizures in critically sick neonates, are not included in our classification. Seizures can be classified as clinical-only, electro-clinical, or electrographic-only seizures by the American Clinical Neurophysiology Society. A paroxysmal aberrant, continuous alteration in the EEG that has a repeating and

evolving pattern, a minimum voltage of 2 volts (peak to peak), and lasts at least 10 seconds is referred to as an electrographic seizure [2].

Cause of neonatal seizure

The majority of neonatal seizures are acutely induced seizures, which means that they are a result of a recent systemic trauma or severe brain injury. Only 10% to 15% of seizures during the neonatal period constitute the initial symptom of an epilepsy syndrome (unprovoked seizures), usually caused by a structural or genetic etiology. The most frequent reason for neonatal seizures is still hypoxic-ischemic encephalopathy (HIE). Other causes include inborn metabolic or genetic epilepsy syndromes, cerebral hemorrhage, metabolic and electrolyte disturbances, systemic and central nervous system infections, and neonatal stroke. In HIC and LMIC, newborn seizures have different etiologies. Infections have been identified as the second most prevalent cause of seizures in LMIC, even though HIE is the primary cause in both HIC and LMIC. Although cerebral hemorrhage and prenatal stroke have been said to occur less frequently than infections in LMIC, it is likely that under diagnosis occurs because neuroimaging is not widely available. In general, newborns with encephalopathy in HIC and LMIC have similar infection rates [3].

Diagnosis of neonatal seizure

The gold standard for determining whether a newborn has seizures is an EEG. However, due to its time-intensive nature, high cost, and need for professional interpretation, EEG is rarely provided 24/7 in neonatal hospitals, even in HIC. Most LMIC have limited access to EEG or even aEEG, and as a result, there is insufficient knowledge of how to interpret neonatal data. Due to the possibility of both an underdiagnosis and an overdiagnosis of seizures, clinical diagnosis is inaccurate. Over 50% of seizures are electrographic-only, which results in underdiagnosis, and overdiagnosis results from misdiagnosing aberrant nonepileptic movements as seizures [4].

One- or two-channel amplitude integrated EEG (aEEG) can be useful for long-term monitoring in NICU when and if EEG is unavailable. According to a study from Brazil, only a small percentage of neonatal units (5%) have access to continuous video EEG, indicating that Electroencephalography (EEG) is the most widely used type of neuromonitoring. The same group provided evidence demonstrating the value of aEEG in an LMIC environment. Additionally, there is a chance that artifacts will be incorrectly interpreted as seizures, so the recording needs to be properly labelled. Many modern aEEG devices include the option of adding one or two raw channels for interpretation, which improves the rate of seizure detection and artifact identification. According to a recent study, aEEG has a median sensitivity of 78% and specificity of 78% for detecting individual seizures, but without raw traces, the sensitivity drops to 54%. Therefore, it is advised to use a full-montage video EEG whenever possible or, in the absence of an EEG, an EEG with raw channels [5].

Neonatal seizure management

Management of the airway, breathing, and circulation is crucial in any neurologic emergency. For neonatal seizures to be effectively controlled, the underlying etiology must be identified and treated, especially when they are brought on by metabolic disturbances. Every suspected seizure should start with a bedside blood glucose and electrolyte assessment. Any hypoglycemia needs to be immediately treated. If seizures stop once the underlying metabolic disturbances (hypocalcemia, hypoglycemia, hypomagnesemia, or hyponatremia) are corrected, anticonvulsant medication may not be necessary [6].

Anti-seizure therapy

Experts concur that anti-seizure medication should not be used unless absolutely essential in the treatment of seizures. When the overall seizure burden on an EEG or aEEG is greater than 1-2 minutes, it is advised to start anti-seizure drugs absent of supporting data. The degree of diagnostic certainty must be taken into consideration if an EEG is not available. The most easily recognized epileptic types are focal tonic and focal clonic seizures, and treatment must start right once.

It is crucial to treat subclinical seizures as well because it is thought that clinical and subclinical seizures differ principally in their anatomical origin. The likelihood of clinical symptoms increases when the motor cortex is implicated. Additionally, due to uncoupling, seizures are more likely to be electrographic-only with anti-seizure medication. When clinical symptoms of seizures disappear while electrographic seizures continue, a condition known as uncoupling occurs [7].

Ceasing anti-seizure drugs

The risk of a seizure recurrence should govern the choice to quit anti-seizure medication. Since acute symptomatic seizures typically recover within two to three days and the risk of recurrence is low, anti-seizure medication should be abruptly stopped before or soon after discharge in these cases. It is recommended to use one or two anti-seizure medications during the newborn period if seizures were difficult to control, and phenobarbital should be the last medication to be stopped using. Anti-seizure medications should be kept up to date in babies with early-onset epilepsy or newborns whose seizures were uncontrollable, and the infant should be referred to a physician or child neurologist for advice on whether and when to wean from the medication [8, 9].

The Future of EEG monitoring systems in LMICs

Telemedicine may play a fascinating role in delivering distant specialized support in an environment with limited resources. A huge number of centres may be reached in real-time by centralized systems, which also provide educational resources, consulting, and monitoring to improve the standard of treatment. Protecting Brains and Saving Futures (PBSF) has successfully established such a system in over 30 hospitals throughout all of Brazil after demonstrating the value of aEEG monitoring in an LMIC. EEG or aEEG is used to monitor babies, and a team at a remote monitoring centre helps. Encrypted EEG data is sent to a secure cloud-based server [10].

Conclusion

In conclusion, newborn seizures present a variety of diagnostic and treatment difficulties in LMIC:

- The social, economic, and environmental circumstances of LMICs specifically affect the etiology and comorbidity of newborn seizures.
- Access to EEG and/or aEEG.
- The accessibility of ventilators and monitors in settings with constrained resources (which may affect the use of therapeutic doses of various anti-seizure medications, such as phenobarbital, phenytoin, or midazolam).
- The accessibility of infusion pumps and the resulting risk of medication mistakes.
- The availability of folinic acid, pyridoxal-5 phosphate, and pyridoxine (both IV and oral dosages).
- The accessibility and price of genetic and metabolic testing.

Some of these issues are also relevant to newborn facilities in high-resource environments, as is widely acknowledged. All of these require immediate attention in order to enhance diagnosis, treatment, and ultimately.

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