Review Article

Pediatric Epilepsy Care in Nigeria: A Management Approach for the Primary Care Physicians

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Abstract

Epilepsy is a neurologic disorder of the brain characterized by an enduring predisposition to recurrent unprovoked seizures. It is the most common childhood neurologic disorder world-wide. Poor management often impacts negatively on the child's neurodevelopmental, emotional, physical, and social well-being. In resource-poor countries, the majority of children with epilepsy are managed by primary care physicians who are not sufficiently trained to offer effective care in pediatric epilepsy. Many low income countries do not have nationally approved guideline on management of pediatric epilepsy. Access to specialist care is costly and may involve long distance travels from rural areas to the cities. This often leads to a huge treatment gap. Efforts aimed at increasing the management skills of primary-care physicians in diagnosing and giving appropriate treatment is necessary in ensuring reduction in treatment gap. This review article is based on the authors' clinical experience and a review of 20 published works from review articles, recommendations, and guidelines sourced from PubMed and Google using the search terms "Paediatric epilepsy, management, primary care." In the absence of any approved national guideline, a simplified approach to the clinical diagnosis, appropriate use of available diagnostic facilities, and cheap but cost-effective drugs will lead to better management of childhood epilepsy in resource-constrained settings.

Keywords: Management, pediatric epilepsy, resource-poor settings

Introduction

Epilepsy is a neurologic disorder of the brain characterized by an enduring predisposition to recurrent unprovoked seizures.[1] It is the most common and widespread neurologic disorder affecting over 50 million people worldwide.[2] Children constitute about 10.5 million of these patients. Epilepsy is a major public health burden in resource-poor settings where more than 80% of these people living with epilepsy are found.[3] Although it is a public health problem, Nigeria like many other countries in Africa does not have national programs or policies for epilepsy care. The majority of children with epilepsy living in these settings receive inadequate or no treatment. This often leads to huge treatment gap.

A proper diagnosis of epilepsy is one of the greatest challenges facing epilepsy care in resource-poor countries.[4] The first contact for patients with epilepsy usually involves all sectors of health care which often include the herbalists, spiritualist, and the orthodox medical practitioners in primary care settings.[5] Because pediatric neurologist are very few, primary care physicians have to provide care for children with epilepsy with insufficient knowledge and training on epilepsy care. Management of seizures in Nigeria as in other developing countries is also plagued by absence of national guidelines and lack of access to second line anti-epileptic drugs.[5,6] Hence, many patients in these settings thus do not receive appropriate treatment, a phenomenon known as the treatment gap. Nwani *et al*.[7] observed from a local epidemiologic study a treatment gap of 76% in south east Nigeria. This is compounded by resort to traditional and faith healing due to myths, local beliefs, and stigma associated with epilepsy. The morbidity and mortality associated with epilepsy are often high in those who receive little or inappropriate care.[3]

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Epilepsy is diagnosed clinically based mainly on a clear description of the event by the patient/firsthand eyewitness and the physician's clinical acumen. Not every jerk, stiffness or shaking is an epileptic seizure. The most important factor in misdiagnosis is the failure to obtain a thorough and good history from patients and the eyewitness of the event.[8] Some seizure types do not manifest with convulsions thus posing more challenges to diagnosis.

Having made a clinical diagnosis, an electroencephalography Electroencephalography (EEG) is usuallys needed to support the clinical diagnosis. Unfortunately, this important diagnostic tool may not always be reliable. A single interictal EEG may be normal in quite a number of people with epilepsy and may also show epileptiform abnormalities in people without epilepsy.[9] A repeat EEG is therefore necessary in management of epilepsy. The prevalence of epileptiform abnormalities in normal children is about 3.5%.[10] An EEG study alone therefore cannot be relied upon to make a diagnosis of epilepsy without regard to the clinical description of the paroxysmal event.

Other investigative tools such as neuro-imaging are useful but are not indicated in all patients with epilepsy. Many patients with epilepsy can be successfully managed in resource-poor settings without using EEG, computed tomography (CT) scan, and magnetic resonance imaging (MRI) because these are not readily available and when available are not affordable.

Successful management of epilepsy therefore begins with an accurate diagnosis, followed by initiation of appropriate dose of an effective antiepileptic drug (AED) for a sufficiently prolonged period of time. In order to guide epilepsy care in the primary care settings in the absence of approved national guidelines, there is a need to suggest a simplified practical approach that is adaptable and relevant to the needs of resource-poor settings. There is also the need for these primary care providers to update their knowledge on the diagnosis, treatment, and early referral of cases to specialty care when necessary.

Evaluation of child with epilepsy

To evaluate the child with epilepsy, it is important to find the answers to these 5 important questions:[11]

1. Was this event an epileptic or nonepileptic seizure?
2. If it was epileptic, what type of seizure was it?
3. Is this seizure type, combined with such factors as age of onset, clinical features, electroencephalographic (EEG) findings, and if available, neuro-imaging findings, constitute an epilepsy syndrome?
4. What investigations are necessary in finding the underlying etiology?
5. What is the prognosis for neurological development in this child?

Clinical History and Examination

The clinical history should document the seizure (types) and frequencies from an eyewitness account. Other aspects of the history include medication, perinatal (gestational age, mode of delivery, birth weight, evidence of birth asphyxia, and neonatal seizures), developmental history prior to onset of seizures (normal or abnormal), previous history of head trauma, central nervous system infections, febrile seizures, and family history of epilepsy. The diagnosis of epilepsy requires that the patient should have had at least two unprovoked epileptic seizures that occurred more than 24 h apart.[1]

Paroxysmal nonepileptic events are very common in children and adolescents. To differentiate epileptic seizures from nonepileptic paroxysmal alterations in behavior or motor activity is a challenging task because many of these nonepileptic events can mimic epilepsy. Inability to distinguish these nonepileptic paroxysmal events can lead to misdiagnosis and initiation of inappropriate treatment. Some of the most common nonepileptic events that can mimic epilepsy in children include:[11]

1. Breath-holding spells
2. Syncope (fainting)
3. Psychogenic nonepileptic seizures (pseudo-seizures)
4. Parasomnias.

Having established that the witnessed event was an epileptic episode, it becomes necessary to classify the event into seizure types. A good history combined with an eyewitness account is most invaluable in the diagnosis of epilepsy. However, in our environment this information may not always be available, or when available it may lack informative description of the event, may seem vague, or may not correspond to any known seizure semiology. Moreover, children may not have developed the appropriate words to fully describe their feelings.

Physical examination including a neurologic examination is necessary in evaluation of the child with epilepsy. Examination will further help in finding features suggestive of syndromes such as skin stigmata of tuberous sclerosis, loss of speech in acquired epileptic aphasia, mental, and developmental retardation as in West and lennox–Gastaut syndromes.[6]

Addition of high quality outpatient smartphone video is an adjunct to routine history and physical exam.[12] This readily available tool is invaluable in supporting the eyewitness account and can aid in predicting the diagnosis with an accuracy of 89%.[13,14] Features of high quality smartphone video necessary for use in epilepsy management include:[13,14]

1. The entire episode must be recorded as much as possible under adequate lighting
2. The video must cover the whole body of the patient
3. Must demonstrate presence or absence of awareness by including interaction of a bystander with the patient.

Based on the eyewitness account supported by video recording, a clinician can classify the epileptic event simply into generalized seizures (tonic, clonic, atonic, tonic-clonic, absence, epileptic spasms, myoclonic) and focal-onset seizures. This simplified classification system can guide treatment decisions at the primary care level.

Investigations

The role of Electroencephalography (EEG) in the management of epilepsy.

An EEG study is recommended if a diagnosis of epilepsy is suspected from a good history, informative eyewitness account and/or a video recording. Even though it is an important test for the evaluation of patients with suspected epilepsy, its limitations must be recognized.

1. EEG may not detect epileptiform abnormalities in seizures arising from deeper brain areas, even during a seizure
2. Abnormalities can be seen even in normal children. An EEG may be normal initially and may need to be repeated because an initial normal inter-ictal EEG does not exclude epilepsy
3. EEG within 24–48 h after a seizure is more likely to be abnormal, but results must be correlated with clinical history
4. EEG test done by a qualified technician with facilities with proper interpretation is very reliable for diagnosis of some epilepsies as Absences, Juvenile Myoclonic, Benign Rolandic, Infantile spasms and other epileptic encephalopathies.

Making a diagnosis or excluding epilepsy on the basis of the EEG findings alone is not therefore recommended. EEG is a useful tool to support diagnosis and classify epilepsy and epilepsy syndromes, but it should be done only in specialized centers where there is adequate expertise for recording and interpretation. To avoid misuse of EEG, the WHO recommends that EEG should not be used routinely for confirmation of diagnosis of epilepsy in non-specialty healthcare facilities in low- and middle-income countries. The recommendation further advises that if there is clinical evidence of epilepsy, treatment should be started without EEG.[15]

Neuroimaging in Epilepsy

Neuroimaging is most helpful in establishing the etiology of epilepsy and hence classifying them into syndromes. Cranial MRI is more sensitive and specific than CT scan in management of epilepsy. Besides their prohibitive costs and absence of well-trained pediatric neuro-radiologist in resource-constrained countries, not all patients will require neuroimaging. The indications[16] for neuroimaging in pediatric epilepsy include:

1. Onset of seizure in children before 2 years because seizures in these age group are more likely to be symptomatic
2. History, physical examination findings are suggestive of focal seizures such as focal fixed deficit on neurologic examination
3. Seizures have been refractory to treatment
4. Loss of control of seizures with drugs or a change in seizure pattern that may imply a progressive underlying lesion.

Is the Seizure an Epilepsy Syndrome?

An epilepsy syndrome is an epileptic disorder characterized by a cluster of signs and symptoms customarily occurring together.[17] In evaluating a patient with epilepsy, the diagnostic aim should always be to establish whether or not an epilepsy syndrome can be identified. If the history, clinical features, EEG, and the neuroimaging findings form a distinctive picture, an epilepsy syndrome will be recognized. Identification of an epilepsy syndrome is useful clinically because it has implications for management, treatment, and prognosis.

Treatment of Epilepsy in Children

AEDs are the mainstay of epilepsy treatment. AEDs suppress the seizures but have no effect on the underlying brain lesion that predisposed the patient to seizures. Other nonpharmacologic modalities of treatment which are indicated when drug therapy is ineffective but are not readily available include ketogenic diet, surgery, and vagus nerve stimulation. About 70% of patients on adequate and appropriate dosing are controlled with these medications. However, about 30% of cases remain refractory to drug therapy and these are the candidates for nonpharmacologic treatment.[10]

Rational Use of Antiepileptic Drug Therapy in Epilepsy

Factors influencing the choice of drugs are the individual circumstances of the patient, affordability, availability, accessibility, and side effect profile of the drug.

Table 1: Mechanism of action of commonly available drugs[20]

AED	Enhancement of GABA-mediated excitation	Blockade of sodium channels	Blockade of calcium channels	Inhibition of glutamate
Benzodiazepines	+	+		
Carbamazepin		+		
Phenobarbitone	+	+		+
Phenytoin		+		
Valproate	+	+		
Levetiracetam			+	+

AED: Antiepileptic drug, GABA: Gamma-Aminobutyric acid

Table 2: Available anti-epileptic drugs in many resource-poor countries

Drug	Formulations and strengths
Phenobarbitone	Tablets: 30 mg, 60 mg, injection: 200 mg/ml
Sodium valproate (EpilimR)	Tablets 200 mg, 500 mg, 500 mg CR, syrup 200 mg/5ml
Phenytoin (EpanutinR)	Capsule 100 mg, injection 250 mg/5 ml
Carbamazepine (TegretolR)	Tablets 200 mg, 400 mg, 200 mg CR, 400 mg CR, syrup 100 mg/5 ml
Diazepam (ValiumR)	Tablets 5 mg, 10 mg, injection 10 mg/2 ml
Clonazepam (RivotrilR)	Tablet 0.5 mg, 1 mg, 2 mg
Nitazepam (MogadonR)	Tablet 5 mg
Levetiracetam (KeppraR)	Tablets 250 mg, 500 mg, 750 mg, and 1000 mg, syrup 100 mg/5 ml

Table 3: A guide to dose recommendations of available drugs in Nigeria

Drug	Dose recommendations
Phenobarbitone	3-5 mg/kg/day in 2 divided doses, maximum 8 mg/kg
Carbamazepine	10-15 mg/kg/day in 2-3 divided doses, up to 30 mg/kg/day
Valproate	15-40 mg/kg/day in 2-3 divided doses, maximum 60 mg/kg
Phenytoin	5-10 mg/kg/day in single or 2 divided doses
Diazepam	0.3 mg/kg (IV), 0.3-0.5 mg/kg (rectal)
Clonazepam	0.01-0.1 mg/day in single or 2 divided doses
Nitrazepam	0.1-0.2 mg/kg in single or 2 divided doses
Levetiracetam	10-20 mg/kg/day in 2-3 divided doses, maximum 60 mg/kg

Table 4: Choice of antiepileptic drugs based on seizure type and available drugs in Nigeria

Seizure type	First choice	Alternative drugs
Partial	CBZ, PHT	PHB, valproate, levetiracetam, clonazepam
Absence	Valproate	Clonazepam
GTC	CBZ, PHT, valproate, PHB	Levetiracetam, clonazepam
Myoclonic	Valproate	Clonazepam, levetiracetam
Clonic	Valproate	PHB
Tonic	Valproate	CBZ, PHT, PHB
Atonic	Valproate	PHB, clonazepam
Infantile spasms	Prednisolone	PHB, clonazepam

CBZ: Carbamazepine, PHB: Phenobarbitone, GTC: Generalized tonic-clonic, PHT: Phenytoin

1. Chose the appropriate AED for the seizure type/syndrome because some AED may worsen some seizures. Begin with small doses and increase gradually in weekly or 2 weekly increments to minimize side effects
2. Stick to one brand and formulation if possible. The bioavailability of generic formulations is erratic. Know the side effects of the chosen AED and counsel caregivers accordingly
3. Drug treatment will continue for at least 2–3 years of seizure freedom in most pediatric epilepsy. Some syndromes will remit with age
4. Ascertain the costs, availability, and the family's ability to provide the chosen drugs and put these factors into consideration in prescribing medications
5. Dosing schedule must be convenient for easy compliance with prescribed medication-once or twice daily dosing is the most convenient and easy to comply with
6. Consider substituting with another AED if the maximum dose of the first AED is reached and it is still not effective or unacceptable side effects are noticed. Gradually wean the patient off the first AED. If two drugs are to be used, choose those with different mechanism of action to minimize side effects [Table 1]. The physician must be notified before any dose modification by patient/care-giver
7. Avoid sudden drug withdrawal except in cases of severe hypersensitivity reactions. Note that sudden drug withdrawals may likely precipitate seizures/status
8. Counsel patients/care-givers appropriately in order to dispel stigma, cultural myths, and misconceptions about epilepsy. Adolescents should also be counseled on personal safety measures. The need for good compliance to medication and routine clinic attendance must be stressed to adolescents.

The risk of recurrence after the first episode of unprovoked seizures in children is about 50%.[14] Drug treatments are commenced after the second seizure. In many resource-poor countries, the drug management of epilepsy relies mostly on the use of first line drugs such as phenobarbitone, carbamazepine, benzodiazepines, valproic acid, and phenytoin [Tables 2 and 3]. Majority of cases of epilepsy can be successfully managed with these drugs if chosen appropriately and given in adequate doses [Table 4]. Some newer drugs which are currently available in some places are lamotrigine, levetiracetam, gabapentin and topimarate; however, these are very expensive and thus not readily available nor affordable for the majority of the patients with epilepsy in these settings.

Dose Recommendations

Selecting antiepileptic drug

The choice of an AED depends mainly on the type of seizure/syndrome, drug formulation; availability and sustenance.[18,19] Also note the presence of comorbidities, mechanism of action of drug, and possible drug-drug interactions and adverse drug reaction profile of the patient. Other considerations include:[20]

1. Carbamazepine, phenytoin, and phenobarbitone are enzyme-inducers with significant drug-drug interactions
2. If seizure type is not clearly known choose a broad spectrum drug like Valproate
3. Avoid levetiracetam in those with co-morbid psychiatric symptoms.
4. Levetiracetam: As an add-on therapy for partial seizures in children less than 16 years and as a mono-therapy for primary Generalized,tonic-clonic seizures and Juvenile myoclonic seizures in those above 16 years of age.

Prednisolone: For treatment of epileptic spasms at a high dose of 8 mg/kg/day for 2 weeks followed by a 2-week tapering of the dose.

Discontinuing Antiepileptic Drugs

Children who have been seizure-free for more than 2 years can be weaned-off their medications.[21] Majority of children who are seizure-free on medications for at least 2 years remain seizures-free when medications are withdrawn.[18] Some may however have recurrences shortly after drug withdrawal especially within 6 months of drug withdrawal. The important considerations in deciding whether to withdraw drugs include type and etiology of seizure/syndromes, age of onset, duration of the epilepsy before commencing appropriate treatment, frequency of seizures and EEG features.[19]

Conclusions

The greatest challenge in epilepsy care in resource-poor countries is in the area of diagnosis and the choice of appropriate available first line antiepileptic medications.

Policies to develop epilepsy care should be tailored to meet the needs of the local settings based on available resources. Furthermore, primary care should be integrated with specialist care to train primary care physicians for diagnosis, treatment and prompt referral of difficult cases for specialist care. By training primary care physicians to diagnose and treat epilepsy, it becomes feasible to reduce the epilepsy treatment gap in resource-poor settings.

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Conflicts of interest

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