Epilepsy in South Sudan: practical guidelines for better control

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Abstract

Epilepsy is usually a chronic condition. In many regions of the world care is compromised by limited recognition, access to medication and stigma. Quality of life for people with epilepsy and their families can improve substantially when seizures are recognised and better control instituted with the appropriate medication. Recognition and classification of seizures, coupled with evidence-based and rational pharmacological management, can help resolve the many issues around this chronic neurological condition.

Keywords: Epilepsy, seizures, phenobarbital, antiepileptic drug, stigma

Introduction

Epilepsy is one of the commonest non-communicable neurological disorders, resulting from a variety of causes, a number of which are preventable or modifiable. It is an important cause of disability and mortality, and affects an estimated 70 million people worldwide.[1] However, epilepsy is more than a neurological dysfunction of the brain. Psychological, cognitive and socio-economic consequences impact severely on quality of life.[2] In South Sudan there are many potentially modifiable risk factors. Some are ubiquitous in low-income countries and directly associated with resource and infrastructure issues of the local healthcare system. Examples of these risk factors are birth asphyxia, head injuries, infections and stroke. Other causes are more specific for the region such as Onchocerciasis Associated Epilepsy.[3] This is an as yet unelucidated form of epilepsy occurring in areas with blackfly breeding sites, being fast flowing rivers, where settlers incur onchocerciasis infection and have a higher occurrence of seizures. The mechanism appears to be an interplay of inflammation and (epi) genetic factors.[3] Some aetiologies of epilepsy are structural and/or genetic with no demonstrable risk factor.

Epilepsy in sub-Sahara Africa

The prevalence of epilepsy in sub-Sahara Africa (SSA) seems greater than in high income countries, but studies of community-based prevalence are limited.

Uneven infrastructure in the health sector leads to a wide disparity in the provision of medicines between urban and rural areas. Health facilities for managing epilepsy in Juba are not replicated in rural areas with the consequence that many people with epilepsy remain undiagnosed and untreated. This epilepsy treatment gap [1] amounts to about 75% in most of SSA. The burden of neurological disease in Juba Teaching Hospital (JTH) was estimated from a sample of 124 patients in a thesis from 2014[4] to be 10%. This was a retrospective hospital-wide medical records study. The 10% (13/124 patients) prevalence might therefore be an under estimate compared with the estimated 20% reported in an Internal Medicine in-patient population study in Northern Tanzania.[2]

The obstacles to recognition of epilepsy as a chronic neurological condition

are many and include stigma, misconceptions about the condition, superstition and fear. These factors all limit access to first line healthcare facilities. Most semirural and urban dispensaries will have access to the easily available and cheap antiepileptic drug (AED), phenobarbital. So, once epilepsy has been recognised the first-line treatment with phenobarbital can be given and a high proportion of people have been shown to respond to this medication. However, follow up of people with epilepsy (PWE) has often not been possible due to poor record keeping and the long distances patients have to travel to see a healthcare professional. This means that young PWE might lapse into severe epilepsy having outgrown their dosage due to a higher body weight and run out of their initial course of medicines. It is often assumed that the prescribed course of the initial medication may be all that is required and prescriptions may not be renewed once the medicine runs out.

In those patients without a defined cause for their epilepsy, such as infection or tumour, knowledge about medication regimens, drug interactions and phasing out protocols can make all the difference to their quality of life. The prime purpose of this paper is to provide practical guidelines for recognition and prescription of first- and second-line drug treatment for seizure disorders. No patient related data were used for this practical review.

Inadequate perinatal care, malnutrition, endemic infections (ranging from malaria to locally occurring onchocerciasis.[2]), the hazards of road traffic accidents and violence all contribute to a high burden of epilepsy in SSA.[5] It is a region poorly equipped to deal with the diagnostic and therapeutic challenges due to inadequate healthcare infrastructure, social security and financial constraints. The stigma associated with epilepsy is a further obstacle to receipt of regular anti-epileptic medication with many people opting for traditional medicine or reliance on prayer only. It has been shown in SSA that the treatment gap can be reduced once the facilities are made available to healthcare workers and to PWE[6] coupled with health education.

The South Sudanese region within sub-Sahara Africa

The health system in South Sudan has three tiers: Primary Health Care Units, Primary Health Care Centres and Hospitals (which exist at state or county levels and as police or military health facilities).These are intended to deliver first- and second- line care for PWE. The Basic Package of Health Services covers preventive, curative, health promotion and managerial activities and is financed by the government with contributions from non-governmental organisations. These health facilities are meant to provide free healthcare to the majority of the population at the primary and secondary levels. Specialised care for PWE is available at JTH, South Sudan's tertiary care facility. Unfortunately, computed tomographic (CT) scanning is not available at the JTH, but may be accessed at a cost to the patients at the neighbouring Juba Medical Complex, a private hospital. Rehabilitation services and special needs schools are available in the private sector, but not provided as part of the services at JTH.

Practical guidelines for recognising and treating seizure disorders

Diagnosis

The International League Against Epilepsy (ILAE) classification is used worldwide.[6] It is based on history and physical examination. Seizure observation is important with reports from eye witnesses. The detection of underlying causes of a seizure, such as focal brain abnormalities or infection, is crucial and usually

Table 1. Features of a typical seizure

- Duration attack itself: usually less than five minutes
- Can be stereotypical: recuring in a same recognisable sequence of signs and symptoms.
- Short aura: possible
- Generalised Tonic Clonic Seizures (GTCS): starting with cry, tonic phase with apnoea, clonic phase with involvement of all limbs, postictal sedation
- Eyes are usually open in GTCS due to contraction of the facial musculature, and not closed until the postictal phase
- Tongue bite (lateral>anterior)
- Injuries (cuts, bruises, broken teeth, broken bones)
- Incontinence (in case of full bladder/bowel)
- Amnesia for attack when generalised
- Postictal coma, sleepiness, confusion, myalgia, fatigue, malaise (up to 24 hours)
- Complex partial, frontal seizures can present with automatisms and dystonic arm posturing
- Go to great lengths for eyewitness account

Table 2. Features of an atypical attack

- Ever-changing presentations
- Motionless/eyes closed from onset of attack
- Duration >10 minutes
- Can be interrupted (e.g., in infantile self-gratification behaviour)
- Never incontinence/tongue bite/injury
- Pale, sweating, nauseous, dizzy (vasovagal/hypoglycaemia/cardiac)
- Premonitory symptoms 'long enough to seek a comfortable position
- Quick postictal recovery (BUT: often in frontal lobe epilepsy/absence seizures)
- Emotional, thrashing; pelvic thrusting; crying; whining; shouting
- Never eye-witnessed; solely patient's own account
- Consistently in one setting (school, work or certain situations)
- 'Patient benefit' (teenagers, boarders, soldiers etc.)
- No response on adequately doses of AEDs
- 'Fits' happening right in front of the doctor

requires neuroimaging and laboratory tests. However, while awaiting these investigations, seizures should be treated with AEDs. Therefore, clinical classification is essential. Classification has been described elsewhere.[7] Mimics of epileptic seizures such as convulsive syncope or psychogenic attacks can cause diagnostic confusion.[8] Features of typical seizures versus features of conditions which may not be epileptic are summarised in Tables 1 and 2 respectively.

The ILAE classification comprises three steps of increasing complexity dependent on available resources. The first step is the most important one for the low resource setting where clinical assessment and history taking largely determine management. seizure type at onset: focal, generalised or unknown. Generalised convulsive seizures may be generalised from the onset (generalised tonic-clonic seizures) or focal at onset but generalised later (focal to bilateral tonic clonic). A focal onset may not be clinically evident. Non-convulsive seizures can be focal or generalised but they are different and often clinically subtle, such as myoclonic and absences. The second and third steps are more detailed and not relevant outside the area of epilepsy neurology, and epilepsy research.

Electro-encephalography (EEG) can be helpful in supporting a clinical suspicion of epilepsy and especially in suspected non-convulsive status epilepticus. Adequate treatment choices, however, can largely be made without the support of EEG which has a significant false negative rate. In any case availability and affordability are limited in the region.

The AEDs which are available in South Sudan are phenobarbital, phenytoin, carbamazepine, and diazepam. More expensive and difficult to acquire AEDs are sodium valproate, lamotrigine, levetiracetam, pregabaline and might have to be ordered from Sudan, Uganda or Kenya.

A clinician's overview of the most commonly used AEDs is given in Table 3.

Phenobarbital is by far the best available and affordable AED in most of the world. More modern AEDs with better side effect profiles are alternative but seizure control can be effective with phenobarbital. Phenobarbital is an AED for daily and long-term preventative use. This an important message to convey to the patient as part of their health education. A clear explanation to the patient concerning compliance and benefits of medication is vital. A layperson cannot be assumed to understand treatment principles and should not be blamed for non-compliance. Treatment of epilepsy is not simply a short-term course.

For PWE, there are everyday hazards. Operating motorised instruments (e.g., a car, a wood saw), open cooking fires, handling small children, herding animals, fetching water at the riverside, swimming, climbing heights, crossing roads. Such risks affect everyday living and limit employment opportunities. It is the responsibility of the doctor to explore and explain these risks to PWE and how to avoid them.

The wider perspective

Epilepsy can be a disabling condition, limiting PWE from taking part in a normal working life or building up normal relations. Many goals with regards to primary prevention of epilepsy include risk management in perinatal care, rendering road traffic safer, controlling of infectious diseases and reducing the effects of trauma to the head. However, even in the best controlled circumstances, PWE remain vulnerable due to the chronic nature of the

Table 3. Commonly used AEDs

Antiepileptic drug	Phenobarbital	Phenytoin	Carbamazepine	Sodium valproate	Lamotrigine	Clonazepam
Primary indication	A first line treatment for all epilepsies and status epileptics, most affordable and best available drug worldwide	All epilepsies, well affordable and available. Can be used in oral and intravenous form for status epilepticus. Less effective in absence seizures.	Globally first choice in focal onset epilepsies. Less effective in complex partial epilepsy. Can worsen myoclonic seizures. Can be useful in case of psychiatric co-morbidity.	Primary generalised epilepsies, less effective in focal onset epilepsy. Can be effective in myoclonic seizures. Preferably not for epilepsy below age 18 months. Can be useful in case of psychiatric co-morbidity.	Can be used in all epilepsies, especially recommended for women of childbearing age. Can potentially worsen myoclonic seizures. Can be useful in case of psychiatric co-morbidity.	Myoclonic or generalised seizure disorder. Used as an add-on antiepileptic drug in severe epilepsies. Is, just as lorazepam, a very long-acting variant of diazepam which is a drug of choice in status epilepticus in Sub Sahara Africa.
Dosage principles	Children: 15-90 mg/day in 1 or 2 dosages *Adults: 90-180mg/day in 1 or 2 dosages **Status epilepticus in adults: infusion iv 10 mg/kg/@100 mg/ min/ over 7-10 minutes (adult total dose is 700 mg). In children dependent on age and body weight under monitoring vitals.	Children: 25-150 mg/ day in 1 or 2 dosages *Adults: 250-450 mg/ day in 1 or 2 dosages Status epilepticus: 15-20 mg/kg stat slow infusion under monitoring vitals	Children 100-1000mg/day, always in 2 dosages Adults: 800-1600mg/day, always in 2 dosages Not in 1 daily dosage because half-life is too short	Children 100-1000mg/day, always in 2 dosages Adults: 800-1600mg/day, always in 2 dosages Status epilepticus: 15-20 mg/kg infusion under monitoring vitals Not in 1 daily dosage because half-life is too short 0.4-1.4 gm/bd	Children 5-100mg/ day, in 1 or 2 dosages Adults: 100-250mg/ day, in 1 or 2 dosages See below, gradual and slow introduction reduces risk of skin rash	Children 0.125-0.5 mg/ day *Adults: 0.25-1 mg/day In 1 daily dosage before bedtime. Half-life is long.
Common side effects	Sedation, sleeplessness, cognitive changes, drug-drug interaction.	Sedation, ataxia. Facial coarsening, gum hypertrophy and skin changes in longer term use. First line pharmacokinetics cause rapid increase in plasma levels with dehydration.	Sedation, ataxia, rash, haematological changes (rare), drug-drug interaction	Teratogenicity, contraindicated in women of childbearing age. Sedation, weight gain, hair loss. Polycystic ovary syndrome. Due to its pharmacological properties a recommended antiepileptic drug in concomitant use of antiretroviral drugs.	Skin rash, which can be dependent on speed of medication introduction (increase very slowly over several weeks to months), sedation. Can work in synergy with sodium valproate.	Sedation, drug-drug interaction. Decreased effect over time due to hepatic enzyme induction.

This table serves as a guideline only. For detailed instructions regarding use please refer to the pharmaceutical information leaflet provided with the specific medication. All antiepileptic drugs have potential adverse effects on neurodevelopmental outcome during pregnancy. Lamotrigine (shown here) and levetiracetam have a notably better risk profile and are recommended during childbearing age, to be started prior to conception and to be continued throughout pregnancy.

condition, associated neuropsychological impairments and stigma. Nevertheless, with proper management, even when the most modern AEDs and other facilities are unavailable, quality of life can be improved with adequate information about what the disorder is.

Lack of AED for PWE and poor long term drug adherence is a concern. Shortage of medication may lead PWE to change the initially prescribed drugs which may result in the destabilisation of the control of epilepsy. Education about epilepsy, training of medical and nursing professionals to manage epilepsy in South Sudan is the cornerstone for appropriate medical treatment and, ultimately, the acceptance of epilepsy as a condition compatible with normal life. The stigmatisation of epilepsy will be reduced or eliminated with appropriate education and adequate control of symptoms. Reduction in complications of epilepsy such as injuries or death may motivate PWE and their caregivers to adhere to treatment and seek gainful employment.

With rational prescribing of the top three available medications: phenobarbital, phenytoin and carbamazepine for the majority of PWE in South Sudan, epilepsy can be better controlled as well as more acceptable in society.

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