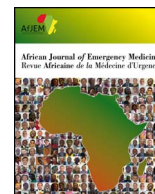


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REVIEW ARTICLE

Management of acute seizures in children: A review with special consideration of care in resource-limited settings

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ABSTRACT

Introduction: We sought to review recent evidence-based guidelines and where applicable, primary data to extrapolate insights into the appropriate management of acute seizures in children in resource-limited settings.**Methods:** PubMed and Google scholar searches were conducted with attention to publications from the last three to five years, including a focused search for acute seizure management guidelines relevant to resource limited settings. Since all guidelines to date, except the World Health Organization's, assume ready access to invasive ventilation and advanced diagnostic testing, guidelines and primary data were used to propose management appropriate for resource-limited settings where respiratory suppression from treatment presents a major challenge in management.**Results:** Acute seizures are among the commonest medical emergencies encountered in the African settings. Seizure management must occur simultaneously with the diagnostic assessment, which should include addressing life threatening causes (e.g. hypoglycaemia, malaria) and with attention given to the most likely aetiology in a particular region or setting. For ongoing seizures, initial treatment with benzodiazepines is indicated. There is evidence of efficacy for several agents and delivery modes. Longer-acting antiepileptic drugs (AEDs) should be on hand if acute seizures fail to respond to two doses of benzodiazepines. There is little direct evidence comparing the relative efficacy of different long-acting AEDs for acute seizure management in African children. Findings suggest that generalising data from Western settings, where different aetiologies and risk factors for seizures prevail, may be inappropriate.**Discussion:** Though treatment options and diagnostics may be dictated by available medications and capacity, it is possible for virtually any healthcare setting to develop a relevant and feasible local guideline for seizure management. Clear specifications on when to refer to a higher level of care should be part of the care plan.

African relevance

- Acute symptomatic seizures are a common paediatric medical emergency in the African setting.
- Poor epilepsy care contributes to the burden of seizures requiring emergency care.
- Status epilepticus is particularly challenging to manage in resource limited settings.
- More optimal management of acute seizures may decrease resulting brain injury.

Introduction

Acute seizures are a common manifestation of neurological disease in children worldwide. Most seizures are brief, meaning less than five minutes in duration. Seizures longer than five minutes are considered prolonged. Status epilepticus, a life threatening condition, occurs when a prolonged seizure lasts more than 30 min or when two or more seizures occur sequentially without return to consciousness between seizures [1].

Acute seizures have several aetiologies. Metabolic challenges including hypoglycaemia are common. Infections may precipitate seizures, either as febrile convulsions or acute symptomatic seizures that

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occur as a result of the infectious process itself [2]. Children with epilepsy may have seizures due to poor outpatient management, refractory epilepsy, medication non-adherence, lack of access to medication and/or inter-current illness lowering the seizure threshold. In immune competent children, seizures arising from infections have generally better outcomes [3,4]. The risk of seizures in children with human immunodeficiency virus (HIV) is particularly elevated with many potential contributing factors, including the primary effects of HIV on the developing brain and/or antiretroviral drug side effects [5–7]. Various studies have observed a higher risk of acute seizures in children living in developing countries compared to those in developed ones [8–10]. Reasons for the elevated burden include parasites and other infections, head trauma and poor perinatal care [11–13].

Optimal care of seizures has been linked to better outcomes [14]. Sub-optimal care arises from delays in care seeking and the relative lack of both trained personnel and pharmaceutical resources. Seizures and epilepsy have physical, social and cultural aspects which influence treatment and outcome [15,16]. The African setting is unique in many respects with regard to acute seizures and seizure management—the cause(s) of the underlying seizures differ from other settings, with malaria being a prominent example [2,17,18]. Timelines for care-seeking may also be quite delayed in the African setting, relative to environments with well-developed emergency services. Since seizure duration prior to care impacts response to medications, data from settings with well-developed emergency services may not be relevant in resource-limited settings. And finally, resources for supportive care, such as invasive ventilation are important delineators of what is possible for aggressive seizure management. This review is aimed at providing guidance on the management of acute seizure while addressing the various factors at play in a resource limited setting.

In the present study, we sought:

1. to review guidelines for the management of acute seizures in children,
2. to review additional literature on the management of acute seizures in children relevant to resource limited settings to provide support and guidance for management and diagnostic assessment in this setting.
3. and to propose a staged approach for care depending on the resources and suggestions for when referral to a higher level of care is appropriate.

Methods

To identify guidelines published in the last two decades, we conducted a PubMed and Google Scholar search on “seizure” and “guideline”. Only guidelines or formal recommendations were reviewed. Studies detailing chronic management or care in adults only were discarded. See Table 1 for a summary of these guidelines.

All of the available guidelines except the World Health Organisation’s (WHO) Paediatric Emergency Triage, Assessment and Treatment (ETAT) were developed for use in highly developed medical setting with ready availability of invasive ventilation and advanced diagnostic testing. The WHO ETAT recommendations were developed for use in resource-limited settings, but only addressed oxygen monitoring, oxygen use, and the choice and delivery mode of first and second line agents. Furthermore, in evidence-based guidelines, especially those grading of evidence quality, no data or limited quality data was often all that was available.

To identify the most relevant recent literature, we initially conducted a PubMed search on “seizures” AND “children” AND “Africa” from 2011 to present. This was complemented by a Google Scholar search on “guidelines for acute seizure management in children”, with a focused review looking for guidelines relevant to resource limited settings and more recent guidelines. Where guidelines differed (for example, choice and route of benzodiazepine) a focused search for the

most recent literature was made. Unless otherwise cited, general recommendations for acute clinical management are congruent with recommendations from the WHO guidelines [19,20].

Discussion

Acute clinical care

Acute seizures represent a medical emergency. Although most seizures are brief, the longer an acute seizure continues, the more difficult it is to terminate, and the greater the risk of developing convulsive status epilepticus with its associated neurological sequelae. Therefore, the approach to clinical management of a child who presents with a seizure lasting more than five minutes should be the same as that to a child in “established” status epilepticus [1,21]. Given the urgency of terminating seizures, the initial diagnostic assessment and medical treatment should occur simultaneously [20]. A brief history and rapid clinical examination should be conducted to ascertain the possible underlying aetiology (for example, head trauma, neuro-infection, poisoning, established epilepsy) and to confirm that the event of concern is indeed a seizure.

General measures – stabilisation phase (0–5 min)

The child presenting with an active convulsion should be stabilized. Airway, breathing and circulation (ABCs) should be assessed to ensure that the child has nothing in his/her mouth, is ventilating well and has a stable pulse. The child should be turned on his/her side to avoid aspiration in case of vomiting or excessive oral secretions [19]. Any object or clothing around the neck or face should be removed to facilitate respiration and prevent injuries. Respiratory rate, blood pressure, temperature and if possible, oxygen saturation, should be measured and recorded. Where available, oxygen should be administered by nasal cannula or mask even if the oxygen saturation is normal to optimize oxygenation since acute seizures place an extreme metabolic demand upon the brain and cardiovascular system. If blood oxygen saturation is low, suction may be needed to clear the airway of secretions and/or vomitus. Aside from the suction device, nothing should be inserted in the mouth to avoid the risk of oral injuries. Administration of oxygen whether by face mask or nasal cannula will have limited efficacy during ongoing tonic-clonic activity and/or apnoea, so focusing upon seizure cessation while suctioning with passive oxygen delivery is critical.

An intravenous (IV) line should be inserted to facilitate medication administration and blood should be drawn for diagnostic investigations. Hypoglycaemia requires immediate treatment both to stop seizures provoked by low glucose and to prevent hippocampal injury that might result in memory impairment, behavioural problems and/or possibly long term epilepsy. If IV access cannot be obtained, acute treatment with benzodiazepines through other routes is possible, but treatment for hypoglycaemia is best when given IV so efforts at IV access are warranted. Ideally, a rapid blood glucose level measured via bedside glucometer should be assessed prior to glucose administration, but if this is not readily available, treatment for possible hypoglycaemia should be undertaken presumptively. Hypoglycaemia is present if the measured blood glucose level is < 2.5 mmol per litre (mmol/l) (45 milligrams per decilitre [mg/dl]) in a well-nourished child, or < 3 mmol/l (55 mg/dl) in a malnourished child. Actual or presumed hypoglycaemia should be treated by giving 5 millilitre per kilogram (ml/kg) of 10% glucose solution rapidly by IV injection; another bolus of 5 ml/kg of 10% glucose solution can be repeated after 30 min if the glucose level remains low, or hypoglycaemia is suspected but glucose cannot be measured and the clinical condition remains poor. In healthcare facilities lacking the necessary equipment and expertise for intravenous administration of medications and fluids, nasogastric access for enteral treatments should be obtained. Unconscious children should be kept on maintenance IV fluids that include glucose or be

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