Epilepsy in children: Prescribing in special circumstances

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Scope

- Introduction
- Epilepsy and TB
- Epilepsy and HIV
- Infantile spasms / LGS
- Juvenile myoclonic epilepsy
- Epilepsy and ADHD / Epilepsy and Autism
- Epilepsy and mood disorders

Introduction

- Many LMICs are currently grappling with the double challenge of having to address both frequent infectious diseases – HIV, TB and Malaria as well as rising numbers on Non communicable diseases such as epilepsy, cardiovascular diseases and obesity. Tolu Oni; 2015

- Under these circumstance is it is highly likely that practitioners in this setting would encounter children with dual pathology and have to manage both conditions concurrently.

Epilepsy and Tuberculosis

- It is estimated that 49 million people worldwide live with epilepsy.

- It is also known that despite the fact that tuberculosis can be treated, prevented, and cured and hence an end put to the pandemic, 1.7 million people died of TB in 2017 Bloom BR, 2017,

- Contributing factors to this situation include:
  - Ant TB medication unavailability
  - Drug resistance
  - HIV pandemic
  - Diabetes
  - Poverty among others

Epilepsy and Tuberculosis

- This is a presentation that commonly evolves form TB Meningitis resulting in gliosis, abscess formation, acute hydrocephalus, tuberculoma formation or in severe cases infarcts and encephalomalacia.

- Seizures occurred in 22 of 93 (23.6%) of the patients with CNS tuberculomas. Both conditions remain largely treatable. Alsemari 2012

- Acute seizure at onset of illness would need to be managed appropriately to avoid evolution of status epilepticus.

Medication conundrum

- Medications utilized to manage TB are predominantly liver enzyme inducers eg Isoniazid
- Anti-seizure medications including carbamazepine, phenobarbitone and sodium valproate are also liver enzyme inducers
- Benzodiazepines may contribute to hepatopathy

Recommendation

- Use anti seizure medications less likely to cause hepatic injury
  - Levetiracetam
  - Topiramate
  - Lamotrigine

- Alternatively
  - Can use regular anticonvulsants but watch the dosing, liver function and seizure control very carefully

Epilepsy and HIV

- Convulsions in patients with human immunodeficiency virus type 1(HIV-1) may result from opportunistic infections, tumours, medications, metabolic and electrolyte derangements or as a result of HIV itself. 1. Power C. 2009; Kellinghaus C. 2008

- The prevalence of HIV associated convulsions is estimated between 2 and 20% in adult and paediatric studies. And is much higher than that in the general population.
  Samia P. 2013, Ssentongo 2019

- A Brazilian study found a 6% prevalence of seizures in children with HIV . A third of this cohort had HIV associated encephalopathy. Kellinghaus C. 2008

Epilepsy and HIV

- Garg et al postulate that the brain in HIV infected individuals has a lowered seizure threshold and impaired seizure terminating mechanisms that predispose these patients to recurrent and prolonged seizures.

- For about half of the children with epilepsy, no identifiable brain pathology is elicited.

- High baseline viral loads (116,000 copies per millilitre) were observed making it plausible that HIV infection itself predisposed these patients to convulsions.
- HIV is neurotropic and in itself is known to cause seizures especially around the time of seroconversion. Udgirkar VS, 2009

Medication conundrum

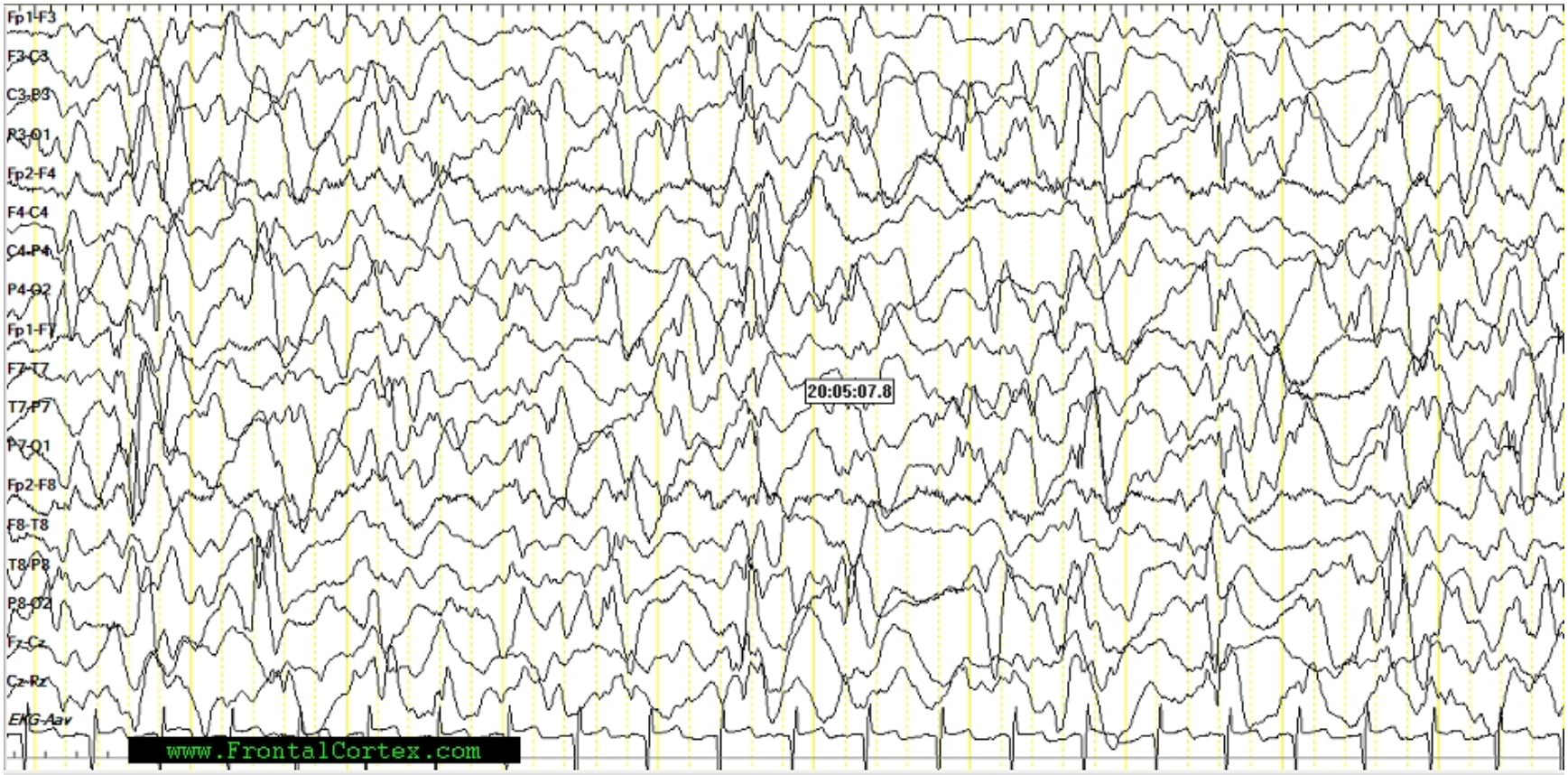
- Many interactions Liedtke MD 2004, Robertson 2005
- Avoid Carbamazepine, phenobarbitone and phenytoin for patients on HAART : lower HAART levels Samia P. 2013, Ssentongo 2019
- Efavirenz (NNRTI) lowers Sodium valproate: choose other AED
- Regular dug level monitor
- Lamotrigine, Tiagabine, levetiracetam, valproate preferable

Infantile Spasms

- Previously known as West Syndrome
- Age of onset 3-6 months
- Presents with clusters of usually flexor spasms associated with a cry.
- A medical emergency – delayed treatment is associated with worse outcomes

- Typical EEG pattern - Hypsarrhythmia

Hypsarrhythmia EEG



Infantile spasms

- Uniformly poor outcome
- Causes neuronal death and permanent changes in neuronal function
- Early appropriate intervention could ameliorate effects
- Management
  - ACTH
  - Vigabatrin 100 – 150mg/kg/day
  - Prednisone 4 – 8 mg/kg/day
  - Sodium Valproate
    - Family support

Lennox Gastaut Syndrome

- Identified in the Marseille School 1966
- Typical onset between 1-8yrs
- Etiologies: cortical malformations, Neuro-cutaneous syndromes, Trauma (Symptomatic)
- 10% of childhood epilepsy
- Majority of the children have intellectual disability

Lennox Gastaut Syndrome

- Seizure types;
  - Tonic / vibratory axial
  - Atypical absence of long duration
  - Non Convulsive status epilepticus
  - Myoclonic seizures
- 20% of cases of LGS evolve from infantile spasms

- Sodium Valproate, Lamotrigine, Topiramate, Phenobarbitone, Rufinamide (Inovelon), ketogenic, Vagal nerve stimulator

Rational Polyphamacy

- As far as possible use one single effective agent at the outset

- Ensure adequate dosing and compliance with one agent before adding another.
  - History
  - Serum drug levels
  - Avoid medication combinations that have significant interactions or additive side effects. (Benzodiazepines and phenobarbitone in high doses)

- Use the fewest possible and only the most efficacious anticonvulsant drugs.

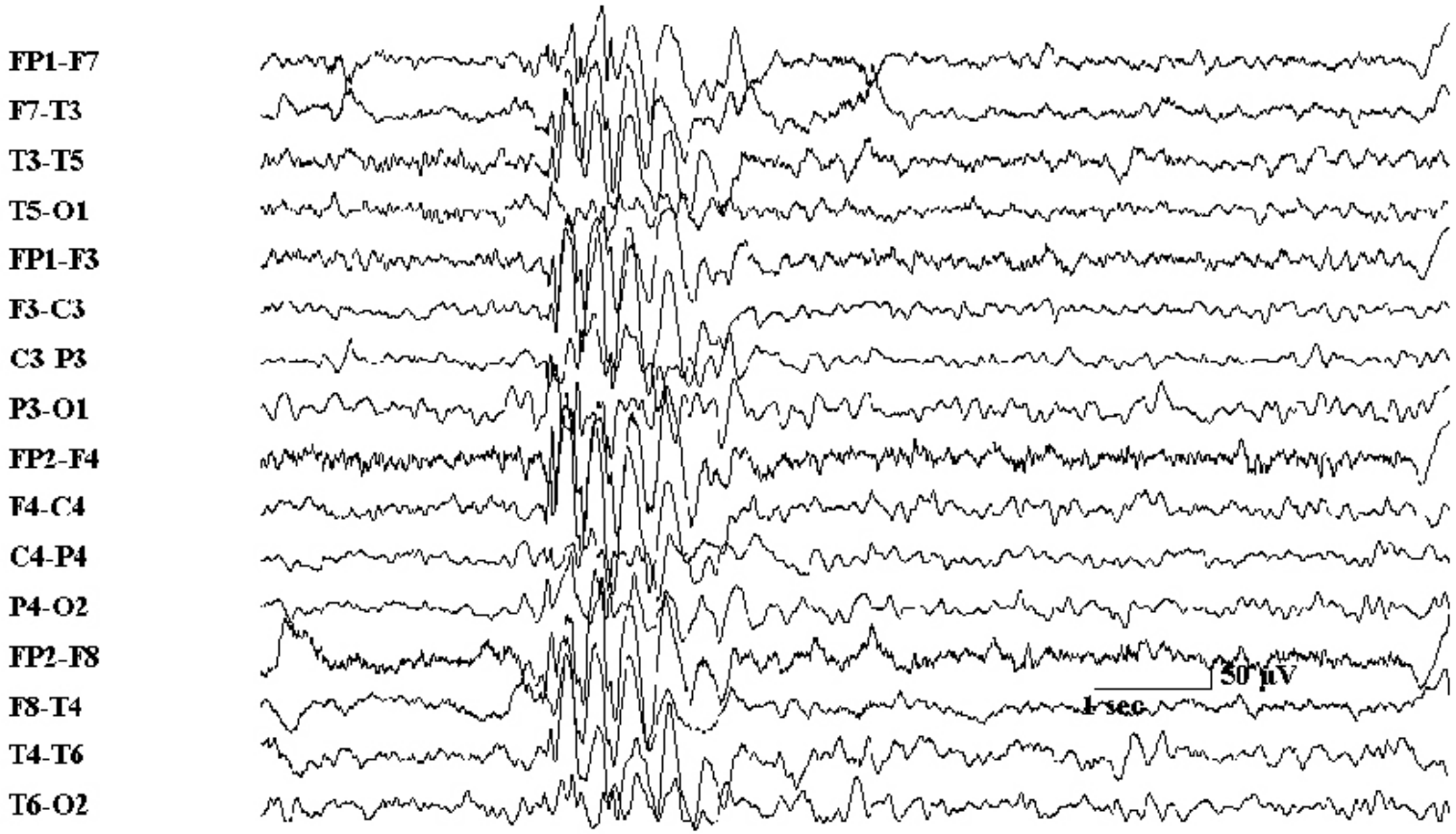
Juvenile Myoclonic Epilepsy

- Most common IGE in adolescence
- Onset 8-14 years

- GTC's preceded by subtle myoclonic jerks
  - Primarily on waking
  - Absence seizures may occur
- Photosensitivity common (20-30%),
- Abnormal sleep EEG pre-requisite for dx

- Lifelong therapy with Sodium Valproate /Lamotrigine /levetiracetam is expected Bakayan, 2011, 2013

JME polyspike and wave discharges



Psychiatric comorbidities

- Overall they occur in 25% of children with epilepsy

- Occur independently of quality of seizure control
- Mood disorders
    - Depression associated with a 33% risk of suicide, significant problem in adolescents with epilepsy
        - Seizures themselves
        - Abnormal electrical activity
        - Medications
        - Psychosocial stressors associated with a chronic illness

Psychiatric comorbidities

- Anxiety
  - 15-50% of children with epilepsy
  - Associated with fear of physical harm,
  - Unpredictability of the seizures
  - Social ramifications of seizures – significant issue in Africa due to associated stigma
  - May occur in younger children

- Initiate psychologist review early to address anxiety and mood problems

- Interactions between anti- anxiety medication and ASM, (adolescents for short periods) watch for drowsiness, drooling, ataxia

Attention deficit Hyperactivity Disorder

- The most common co morbidity having been identified in 20 to 60% of children with epilepsy

- Predominantly **inattentive type** of ADHD is the most prevalent.
- ADHD is associated with academic underachievement and a lowered quality of life.
- AED's do not fully address ADHD

- ADHD in children with epilepsy is amenable to safe treatment with **methylphenidate** and behavior therapy and hence should be actively sought and managed.

Epilepsy and Autism

- Currently there are several established genetic linkages between epilepsy and Autism spectrum disorder (ASD)– Tuberous sclerosis is a good example.
- Many other genetic mutations that cause epilepsy have also been linked to autism
- ASD is associated with a higher occurrence of EEG abnormalities identified in 4 – 86% Roberto K, 2017

Epilepsy and Autism

- One third of children with ASD have epilepsy with a documented increase in proportion with age.
  Francis A, 2013

- Where a genetic cause for dual presentation is known eg TSC – epilepsy is Vigabatribn at the onset with consideration for Clobazam and everolimus afterwards

- A multidisciplinary approach to management is very important – Occupational therapist, speech therapists, psychiatrists – may add mood and behaviour modulating medications eg Risperdal

Summary

- Prescribing for children is not a one size fits all, this process is modified and individualized

- Consideration for
  - Concurrent diseases eg HIV & TB
  - Epilepsy syndrome; IS, LGS & JME
  - Epilepsy co-morbidities: ADHD, Autism, anxiety and depression
  - Individual patient factors such as obesity, response to specific anticonvulsants as well as past adverse reactions.

Thank you!!