UNIVERSITY OF KWAZULU-NATAL ™

INYUVESI YAKWAZULU-NATALI

A Storm in the Brain….

Dr R Govender

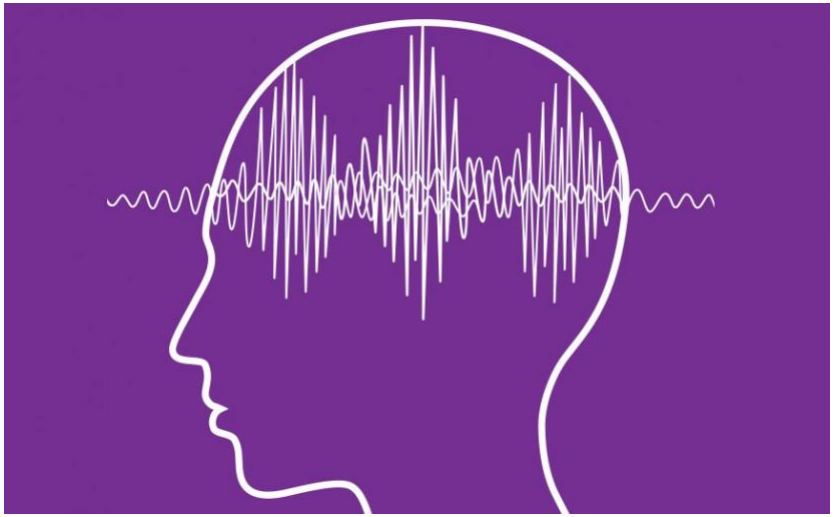
Paediatric Neurologist

Nelson R Mandela School of Medicine

UKZN

Outline

- Case Presentation
- Epidemiology
- Definitions
- Aetiology
- Management
- The Treatment Gap
- Outcome
- Take home message



Case Presentation

6yr old boy presented to GP with a history of a febrile illness, first time GTCS

Pre-morbid: well, going to school

No family history of note

Repeated doses of Lorazepam and Diazepam

Loading dose of Valproate

Ceftriaxone/ Acyclovir

CSF: Normal chemistry, 22 L, 0 Polys

Normal CTB

Progress

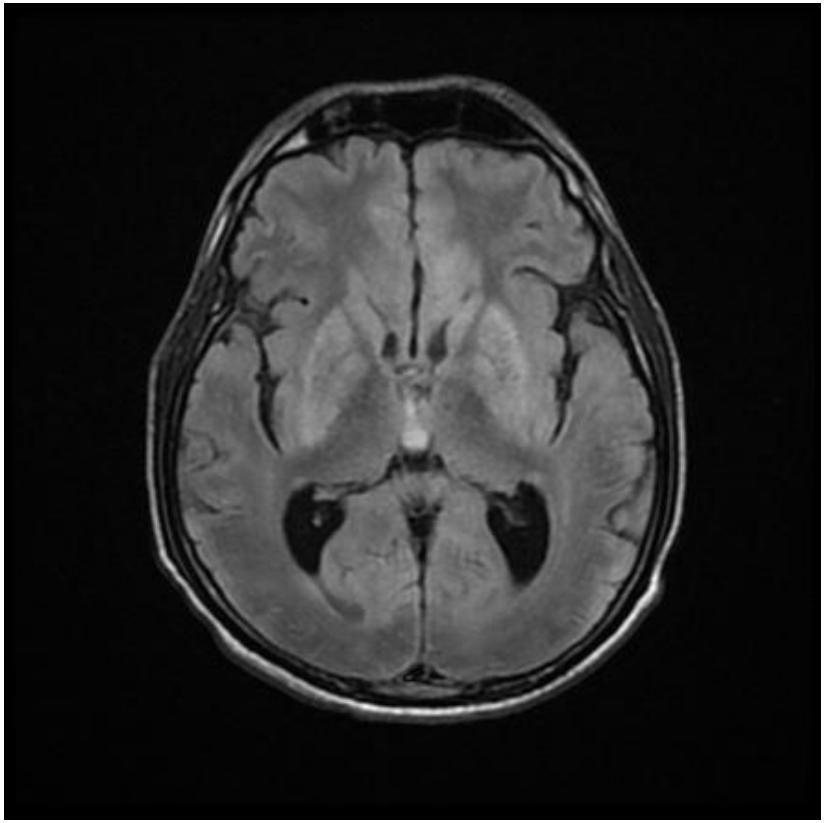
Continued fitting –transferred to high care

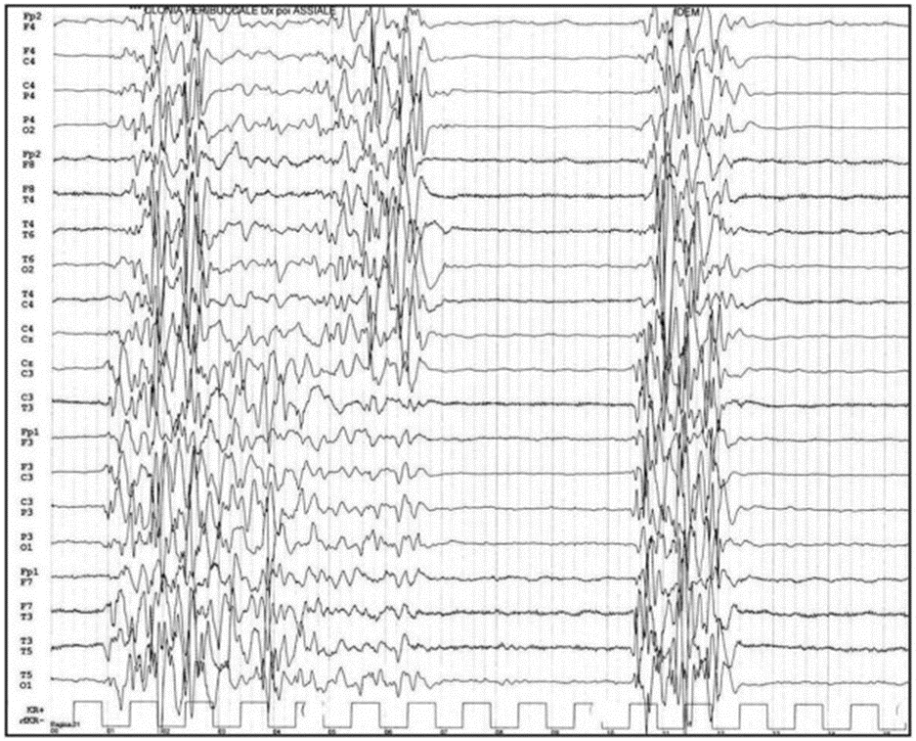
Encephalopathic

Received another dose of IV Lorazepam- respiratory arrest!

Management	• Resuscitated/Ventilated • LD Phenytoin • Midazolam infusion • Thiopentone infusion
ICU Care	• Started on maintenance phenytoin/valproate • Once seizure free for 24 hours –weaned off thiopentone

Investigations





Outcome

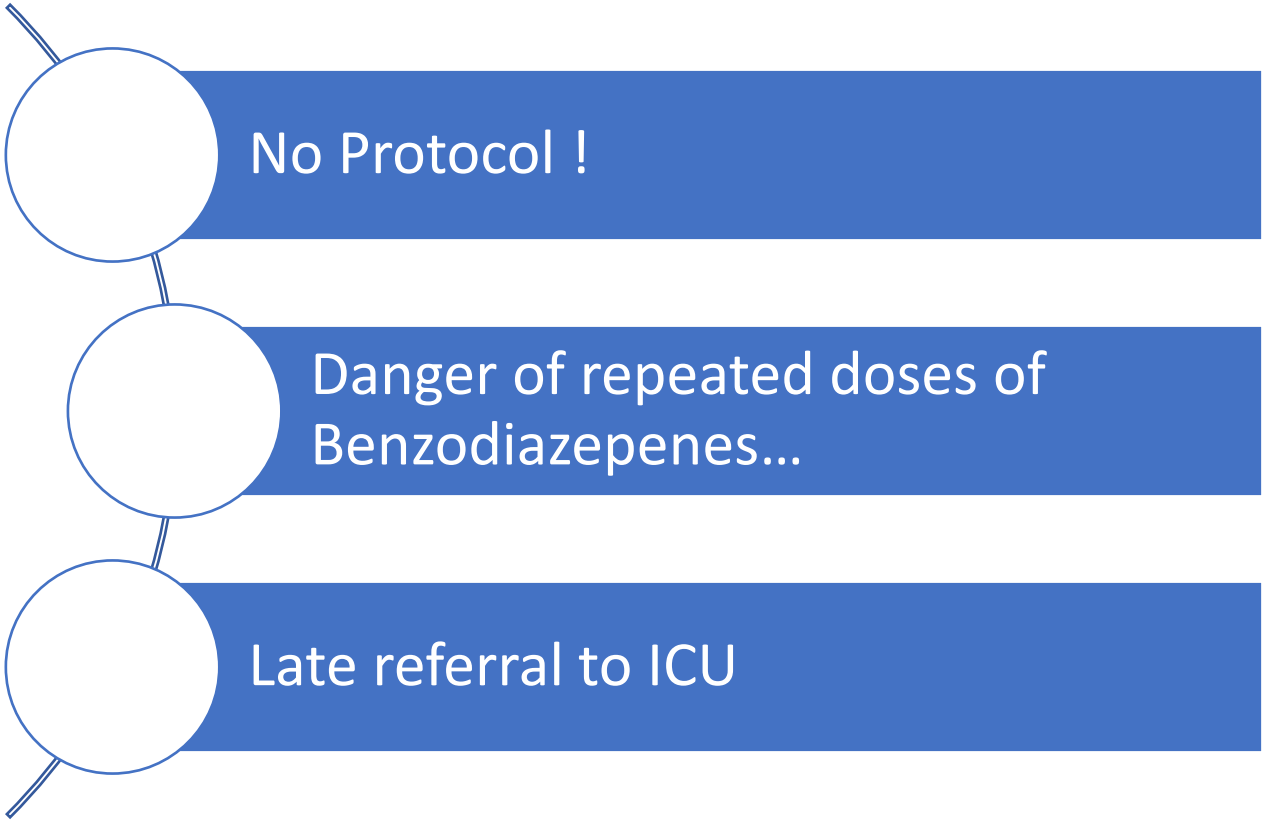
Assessment:

- Encephalitis with Status Epilepticus
- Hypoxic brain injury
- Sub-optimal management

Sequelae:

- Global neuro-regression
- Cortical blindness/hearing impairment
- Dyskinetic
- Pseudobulbar palsy need PEG

Things that went wrong!



Introduction

- Acute, potentially life-threatening neurological emergency.
- Requires prompt therapy.
- Modern era: protocol- driven approach.
- This alone has improved outcomes.
- **Large randomised trials do not exist**
- ***TIME IS BRAIN….***

Epidemiology

- Incidence of SE:
  - 17–23 episodes per 100,000 children
  - 10% - 40% develop RSE
  - 10 -25% of children will have 1 episode of SE
  - 12-30% of newly diagnosed epileptics will present in SE
- *Chin RF et al Lancet 2006*
- Kenyan study: 28-46 per 100000 per year.
- South Africa: Agincourt: 1.9/1000 people.
- Bimodal incidence: peaks < 1yr and >65yrs.
- Convulsive Status is most common form.

Seizure: European Journal of Epilepsy 68 (2019) 3–8

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Review

The burden of pediatric status epilepticus: Epidemiology, morbidity, mortality, and costs

Kevin Gurcharran[a,b], Zachary M. Grinspan[a,b,c,*]

[a] Department of Pediatrics, Weill Cornell Medicine, New York, NY, United States
[b] New-York Presbyterian Hospital, New York, NY, United States
[c] Department of Healthcare Policy & Research, Weill Cornell Medicine, New York, NY, United States

Table 1
Population Based Studies of Status Epilepticus in Children.

	Richmond, Virginia [1]	Minnesota [2]	Japan [3]	Switzerland [4]	California [5]	London [6]
Status Subtype	All	All	All	All	Convulsive only	Convulsive only
Age Categories	Adults and Children	Adults and Children	Children only	Children only	Adults and Children	Children Only
Study Design	Prospective	Retrospective	Retrospective	Prospective	Retrospective	Prospective
Overall Incidence (episodes per 100,000 residents per year)	41	18.3 (48% convulsive)	–	9.9 (44% convulsive)	6.18	–
Pediatric Incidence	38 (71% convulsive)	19.8	42 (86% convulsive)	0–4: 38.7 5–14: 10.9	3.86	18–20
Peak Age of Incidence (years)	< 1 and > 60	< 1 and > 60	< 2	0–4	< 5 and > 60	< 1
Male:Female	1.2:1	2:1	1.4:1	1.6:1	1:1	1.2:1
Pediatric Mortality	3%	< 1yo: 17% 1–19: 5%	< 1%	6.2%	Under 5: 1.4%	3%
Years of Study	1989–91	1965–84	2003–5	1998	1991–98	2002–2004

Incidence difficult to calculate (1/50/year)
Peak below 1-2 years
Mostly convulsive
Mortality lower than in adults

Status epilepticus is a heterogeneous electro-clinical syndrome with diverse causes, inconsistent and dynamic clinical manifestations, and variable clinical course…..

Definitions

- Xth Marseilles Colloquium (1962)
  - Development of modern conceptual basis of SE
  - First meeting devoted to SE

- Intuitive Approach- any seizure causing neuronal damage.

- Initial ILAE definition (1981):

"a seizure that persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur" –lacked a specific time duration

Definitions

- Point in time when a prolonged seizure becomes SE has changed over the last 20yrs!
- *"a seizure lasting longer than 30 minutes or a series of seizures without a return to baseline level of alertness between the seizures"*
- Resource poor settings: duration is rarely documented – most patients arrive convulsing at health facility without documentation of duration.
- Increasing recognition that medication administration delay results in refractoriness of seizures.
- Operational definition

SPECIAL REPORT

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

*†‡Eugen Trinka, §Hannah Cock, ¶Dale Hesdorffer, #Andrea O. Rossetti, **Ingrid E. Scheffer, ††Shlomo Shinnar, ‡‡Simon Shorvon, and §§Daniel H. Lowenstein

Epilepsia, 56(10):1515–1523, 2015
doi: 10.1111/epi.13121

Eugen Trinka is professor and chairman of Department of Neurology, Paracelsus Medical University Salzburg Austria.

Summary

The Commission on Classification and Terminology and the Commission on Epidemiology of the International League Against Epilepsy (ILAE) have charged a Task Force to revise concepts, definition, and classification of status epilepticus (SE). The proposed new definition of SE is as follows: *Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t_1). It is a condition, which can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.* This definition is conceptual, with two operational dimensions: the first is the length of the seizure and the time point (t_1) beyond which the seizure should be regarded as "continuous seizure activity." The second time point (t_2) is the time of ongoing seizure activity after which there is a risk of long-term consequences. In the case of convulsive (tonic–clonic) SE, both time points (t_1 at 5 min and t_2 at 30 min) are based on animal experiments and clinical research. This evidence is incomplete, and there is furthermore considerable variation, so these time points should be considered as the best estimates currently available. Data are not yet available for other forms of SE, but as knowledge and understanding increase, time points can be defined for specific forms of SE based on scientific evidence and incorporated into the definition, without changing the underlying concepts. A *new diagnostic classification system* of SE is proposed, which will provide a framework for clinical diagnosis, investigation, and therapeutic approaches for each patient. There are four axes: (1) semiology; (2) etiology; (3) electroencephalography (EEG) correlates; and (4) age. Axis 1 (semiology) lists different forms of SE divided into those with prominent motor systems, those without prominent motor systems, and currently indeterminate conditions (such as acute confusional states with epileptiform EEG patterns). Axis 2 (etiology) is divided into subcategories of known and unknown causes. Axis 3 (EEG correlates) adopts the latest recommendations by consensus panels to use the following descriptors for the EEG: name of pattern, morphology, location, time-related features, modulation, and effect of intervention. Finally, axis 4 divides age groups into neonatal, infancy, childhood, adolescent and adulthood, and elderly.

KEY WORDS: Status epilepticus, Seizure, Definition, Classification, Seizure duration.

A new conceptual definition of status epilepticus with two operational dimensions (t1 and t2) proposed
-Time point **t1** indicates when treatment should be initiated
-Time point **t2** indicates when long-term consequences may appear

Definition

Status Epilepticus	• Is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t1) and which can have long-term consequences (after time point t2)
Refractory status epilepticus	• Seizure activity that persists for >60mins despite the use of an initial benzodiazepine and a second appropriate antiseizure medication
Super Refractory SE	• SE that has continued or recurred despite 24 h of general anesthesia (*Shorvon & Ferlisi, 2011).*

Type of SE	Time (t1), when a seizure is likely to be prolonged leading to continuous seizure activity	Time (t2), beyond which long term consequences are increasingly likely (including neunonal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic clonic SE	5 minutes	<30 minutes
Focal NCSE with impaired consciousness	10 minutes*	30-60 minutes*
Absence status epilepticus	2 minutes**	unknown*

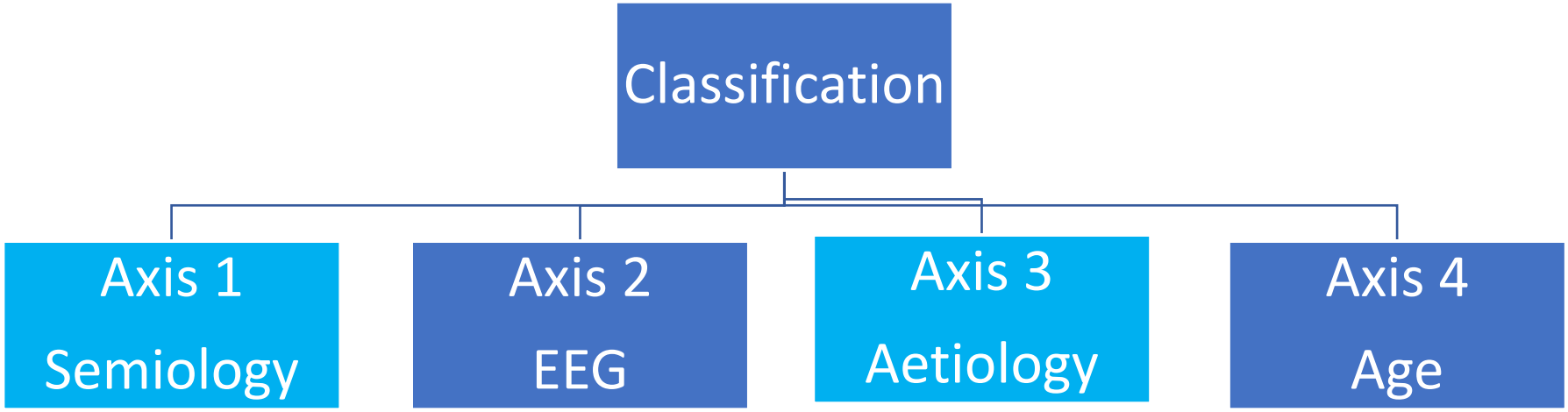
mplications o treatment

Time point 1 determines the earliest time when treatment should be considered or started

Time point 2 determines the time at which status should be controlled to prevent long term consequences

* Best available evidence, but insufficient data to give a definite timepoint

Classification of Status Epilepticus



Commission on Classification ILAE, Epilepsia 1981; 2 Drislane et al. Epilepsy Behav. 2000;1(5):301-14; 3 Trinka Lowenstein et al. Epilepsia 2015

Axis 1- Semiology

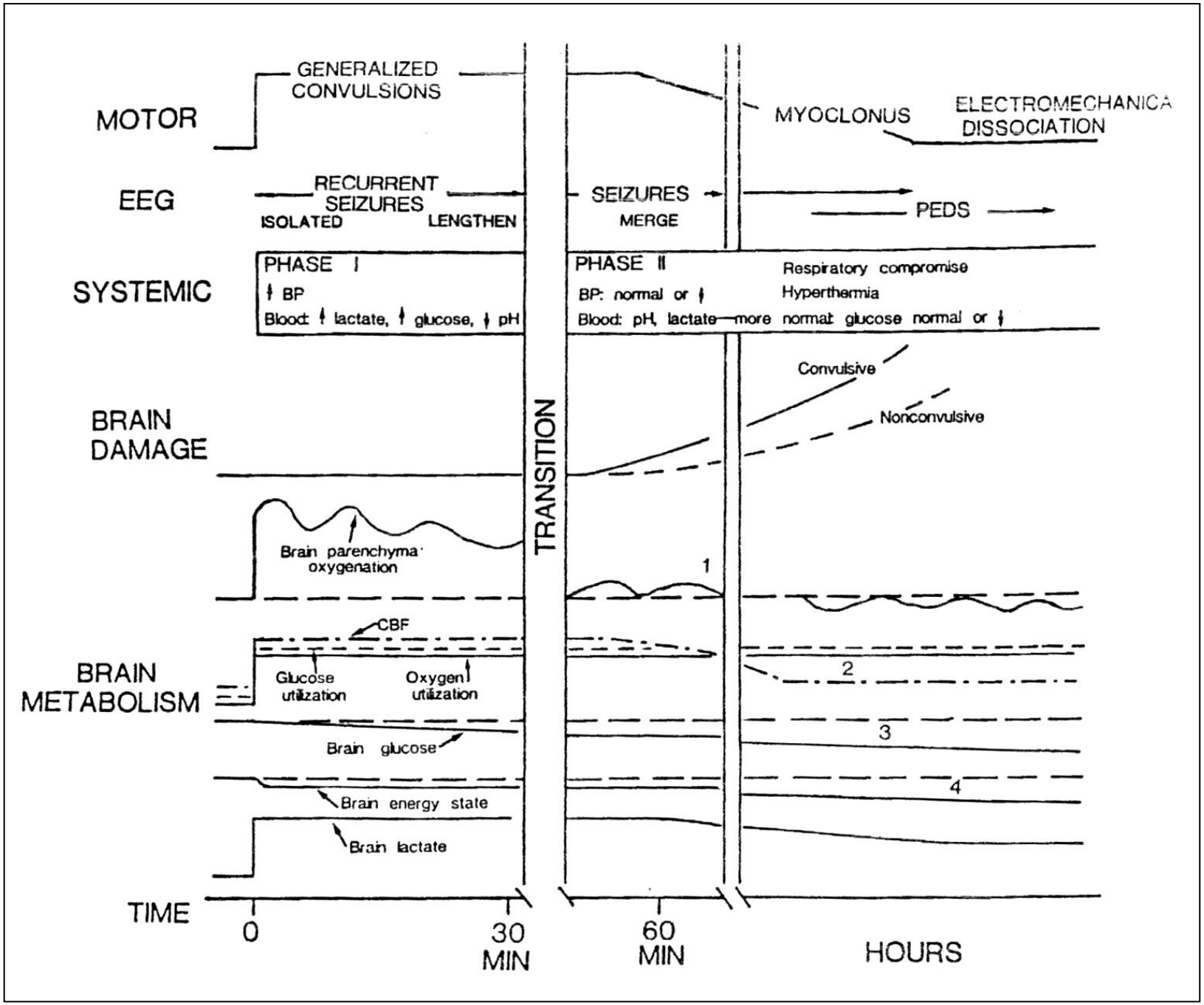
With prominent motor symptoms:

- ❖ Convulsive SE (Tonic-clonic)
- ❖ Myoclonic SE (prominent epileptic myoclonic jerks)
- ❖ Focal motor (including EPC)
- ❖ Tonic SE
- ❖ Hyperkinetic SE

Without prominent motor symptoms (Non-Convulsive: under-recognised!)

- ❖ NCSE with coma
- ❖ NCSE without coma
- ❖ Following CSE – electromechanical dissociation(16% of comatose children in ICU) *Sharma et al. Epilepsia 2006:47*

(Trinka, Lowenstein et al. ILAE Task Force on Classification of SE, Epilepsia 2015 (R))

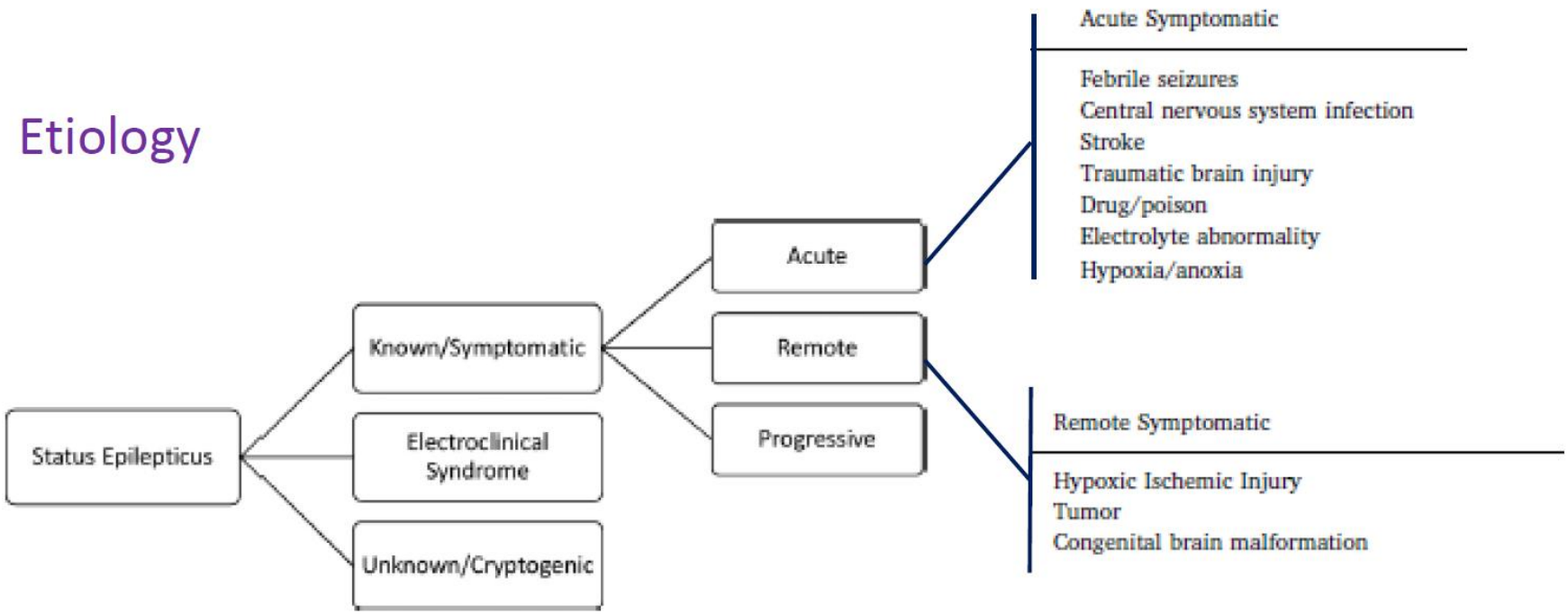

MOTOR
GENERALIZED CONVULSIONS
MYOCLONUS
ELECTROMECHANICA DISSOCIATION
EEG
RECURRENT SEIZURES
ISOLATED
LENGTHEN
SEIZURES
MERGE
PEDS
SYSTEMIC
PHASE I
↑ BP
Blood: ↑ lactate, ↑ glucose, ↓ pH
PHASE II
BP: normal or ↓
Blood: pH, lactate—more normal glucose normal or ↓
Respiratory compromise
Hyperthermia
BRAIN DAMAGE
Convulsive
Nonconvulsive
TRANSITION
Brain parenchyma oxygenation
1
CBF
BRAIN METABOLISM
Glucose utilization
Oxygen utilization
2
3
Brain glucose
4
Brain energy state
Brain lactate
TIME
0
30 MIN
60 MIN
HOURS

Aetiology

- Differs significantly between 1st and 3rd world countries.
- Important to establish underlying cause- impacts management and considered most important factor determining outcome.
- Third world countries- infectious aetiologies commonest.
- Anoxic SE associated with worse outcome.

Classification of Causes

Etiology



Gurcharran and Grinspan,Seizure 2019

SUPPLEMENT ARTICLE

Epilepsia

Etiologies and characteristics of refractory status epilepticus cases in different areas of the world: Results from a global audit

Monica Ferlisi[1] | Sara Hocker[2] | Eugen Trinka[3] | Simon Shorvon[4] | on behalf of the International Steering Committee of the StEp Audit*

	Asia n %	Europe n %	Americas n %
Unknown/cryptogenic	50 (25.5)	98 (21.6)	34 (22.8)
Vascular	11 (5.6)	75 (16.6)	17 (11.4)
Anoxic	13 (11)	51 (16.6)	17 (17.4)
Trauma	1 (0.5)	28 (6.2)	7 (4.7)
Infection (all)	59 (30.6)	56 (12.3)	23 (15.4)
Encephalitis	41 (20.9)	26 (5.7)	7 (4.7)
Meningitis	6 (3.1)	9 (2)	3 (2)
Alcohol	0	28 (6.2)	6 (4)
Other toxins	4 (2)	3 (0.7)	3 (2)
Metabolic	11 (5.6)	17 (3.8)	7 (4.7)
Tumor	5 (2.6)	33 (7.3)	6 (4)
ASM withdrawal	16 (2.8)	20 (4.4)	14 (9.4)
Genetic	6 (3.1)	8 (1.8)	2 (1.3)
Immunological	7 (3.5)	9 (1.9)	6 (4)
Mitochondrial	4 (2)	4 (0.9)	3 (2)
Miscellaneous	9 (4.6)	23 (5.1)	4 (2.7)

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journal homepage: www.elsevier.com/locate/yseiz

Convulsive status epilepticus in a quaternary hospital paediatric intensive care unit (PICU) in South Africa: An 8 year review

Yavini Reddy[a,*], Yusentha Balakrishna[b], Lawrence Mubaiwa[a]

[a] Department of Paediatric Neurology, University of KwaZulu-Natal, Durban, South Africa
[b] Biostatistics Unit, South African Medical Research Council, Durban, South Africa

Table 2
Aetiology (n = 76).

Aetiology (n = 76)	n[%]
Acute Symptomatic	**65 (86)**
Infections	*40 (61)*
Gastroenteritis with metabolic derangements	*19 (29)*
Trauma related	*3 (5)*
Tumours	*2 (3)*
Intracerebral haematoma	*1 (2)*
Remote Symptomatic	**6 (8)**
Idiopathic Epilepsy Related	**1 (1)**
Prolonged Febrile	**3 (4)**
Unclassified	**1 (1)**

Table 3
Infectious Aetiology Subgroup (n = 40).

Infectious Aetiology Subgroup (n = 40)	n [%]
Presumed viral encephalitis	18 (45)
Bacterial/Viral meningitis	10 (25)
Tuberculosis meningitis	5 (13)
Malaria	2 (5)
Sepsis	4 (10)
HIV Vasculitis	1 (2)

CRITICAL REVIEW AND INVITED COMMENTARY

Epilepsia

Proposed consensus definitions for new-onset refractory status epilepticus (NORSE), febrile infection-related epilepsy syndrome (FIRES), and related conditions

Lawrence J. Hirsch[1] | Nicolas Gaspard[2] | Andreas van Baalen[3] | Rima Nabbout[4] | Sophie Demeret[5] | Tobias Loddenkemper[6] | Vincent Navarro[7] | Nicola Specchio[8] | Lieven Lagae[9] | Andrea O. Rossetti[10] | Sara Hocker[11] | Teneille E. Gofton[12] | Nicholas S. Abend[13] | Emily J. Gilmore[1] | Cecil Hahn[14] | Houman Khosravani[15,16] | Felix Rosenow[17] | Eugen Trinka[18,19]

Is a clinical presentation, not a specific diagnosis, in a patient with no pre-existing epilepsy or neurological disorder with new onset SE without a clear acute or active structural, toxic or metabolic cause on initial investigations.

FIRES is a subcategory that requires a prior febrile infection, with fever starting between 2 weeks and 24 hours prior, with or without fever at onset of SE

Aetiology remains unclear –neuro-inflammatory/infectious

Hypothesis: Genetic predisposition with auto-immune mechanisms

Refractory to anti-seizure medication, sometimes responds to immuno-modulation and the ketogenic diet

New onset refractory status epilepticus (NORSE) Claudine Sculier etal. Seizure 2019

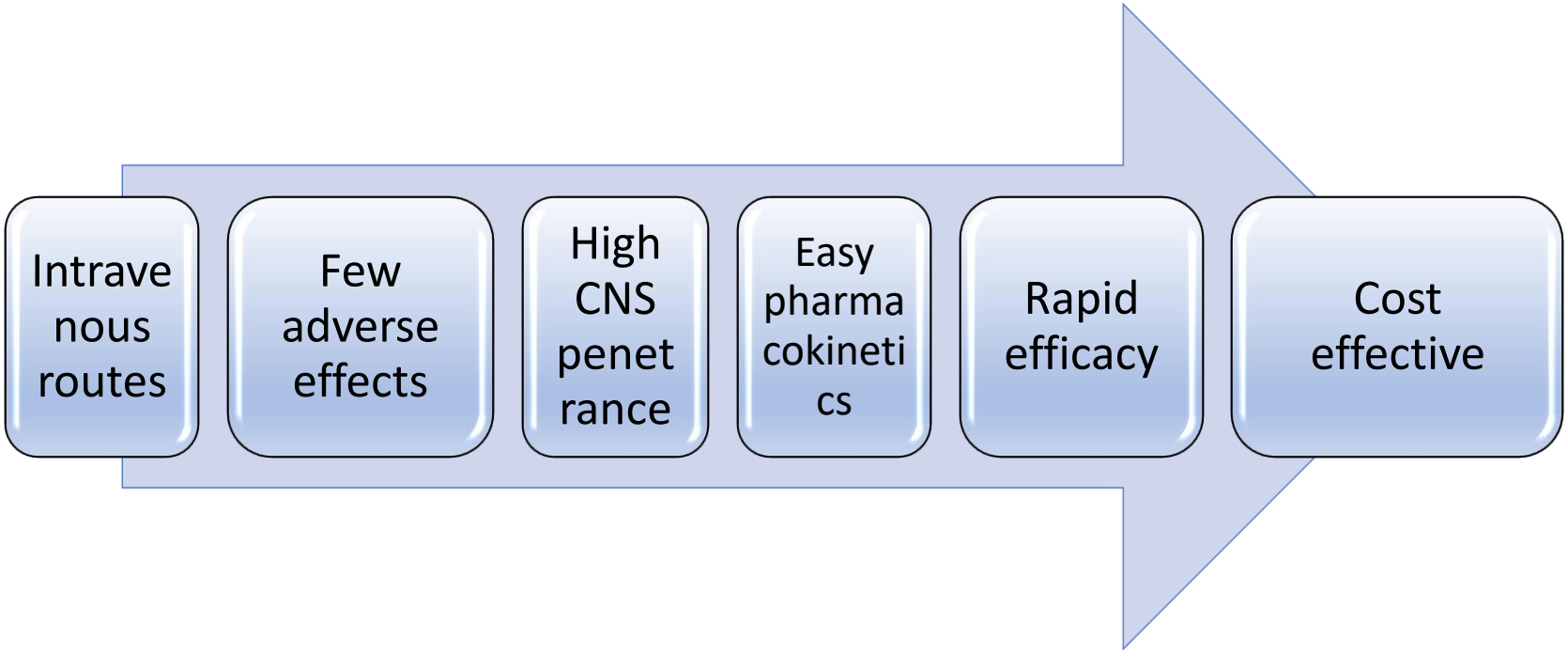
Approach

- Recognise the patient in SE!
- In patients with prolonged seizure activity- movements may become gradually more subtle.
- ICU setting may be difficult- paralysed patient.
- Non-motor manifestation- obtundation/ altered mental status.
- Clinical assessment alone –insufficient.
- Compelling evidence-role of EEG monitoring in ICU setting.

Approach

- Initial assessment
  - A, B, Cs, check GM
  - Brief history/rapid neurological exam
  - Give high flow oxygen
- Call for help.
- Establish IVI access.
- Empower families/ communities to start treatment outside of hospital.
- START Anti-seizure medication ASAP!

Ideal Anti-seizure Medication



EPILEPSY CURRENTS

American Epilepsy Society Guideline

Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society

Tracy Glauser, MD,[1] Shlomo Shinnar, MD, PhD,[2] David Gloss, MD,[3] Brian Alldredge, PharmD,[4] Ravindra Arya, MD, DM,[1] Jacquelyn Bainbridge, PharmD,[5] Mary Bare, MSPH, RN[1], Thomas Bleck, MD,[6] W. Edwin Dodson, MD,[7] Lisa Garrity, PharmD,[8] Andy Jagoda, MD,[9] Daniel Lowenstein, MD,[10] John Pellock, MD,[11] James Riviello, MD,[12] Edward Sloan, MD, MPH,[13] David M. Treiman, MD[14]

Epilepsy Currents, Vol. 16, No. 1 (January/February) 2016 pp. 48–61

Phase 1 (0-10 minutes)

- Benzodiazepene- initial agent of choice (Level A evidence- 3 Class 1 trials)
- Options (if no IV access available)
  - Rectal Diazepam (0.2-0.5mg/kg)- Level B
  - Buccal/Intranasal Midazolam- Level B
  - IM Midazolam (5-10mg)- Level A
- IV Access available:
  - IV Lorazepam- 0.1mg/kg (max- 4mg)- Level A
  - IV Diazepam- 0.1-0.2mg/kg (max -10mg)- Level A

**Above can be repeated x1*

Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children (Review)

McTague A, Martland T, Appleton R

1. Intravenous lorazepam and diazepam : similar rates of seizure cessation and respiratory depression
2. Low risk of adverse events, specifically respiratory depression
3. Consider time needed to get intravenous access
4. In the absence of IV access : buccal midazolam and rectal diazepam first-line anti-convulsants for convulsive seizures lasting > 5 minutes
5. No evidence to support the use of intranasal midazolam or lorazepam

Cochrane Database of Systematic reviews, 2018

Phase 2 (10- 30 minutes)

- Emerging evidence.
- Options:
- IV Phenytoin/ Fosphenytoin -20mg/kg(Level U)
- IV Valproate- 20mg/kg (Level B)
- IV Levetiracetam- 60mg/kg (Level U)
- IV Phenobarbitone -20mg/kg- Level B-(availability an issue!)
- Oral Phenobarbitone LD- is there a role?

Levetiracetam versus phenytoin for second-line treatment of paediatric convulsive status epilepticus (EcLiPSE): a multicentre, open-label, randomised trial

*Mark D Lyttle, Naomi E A Rainford, Carrol Gamble, Shrouk Messahel, Amy Humphreys, Helen Hickey, Kerry Woolfall, Louise Roper, Joanne Noblet, Elizabeth D Lee, Sarah Potter, Paul Tate, Anand Iyer, Vicki Evans, Richard E Appleton, with support of Paediatric Emergency Research in the United Kingdom & Ireland (PERUKI) collaborative**

Convulsive status, second line treatment after benzodiazepines

Randomisation :

levetiracetam 40 mg/kg (max 2500mg) over 5 minutes

phenytoin 20 mg/kg (max 2000mg) over 20 minutes

End point : time from randomisation to cessation of all clinical convulsive activity

Lancet 2019; 393: 2125–34

Levetiracetam not significantly superior to phenytoin as second line agent.
Safety profile of Levetiracetam better than phenytoin.

Phase 3-(>30 minutes)

- No evidence from RCTs.
- Intensive care setting, EEG monitoring important.
- Consider IV Pyridoxine < 18 months of age.
- Established Protocols:

	Loading dose	Maintenance dose	Comments
Midazolam	0·2 mg/kg	0·2–0·6 mg/kg per h	Increasing doses needed with time
Propofol	2 mg/kg	2–5 mg/kg per h, in some cases can be raised to 10 mg/kg per h	Attention to PRIS, especially in young children; combine with benzodiazepines
Barbiturates	Thiopental: 1–2 mg/kg Pentobarbital: 5 mg/kg	Thiopental: 1–5 mg/kg per h Pentobarbital: 1–5 mg/kg per h	Both need loading with repetitive boluses and have long wash-out times

PRIS=propofol infusion syndrome.

Vasquez et al, Seizure 2019

Management of SE (EDL)

Early SE
0-5mins
Emergent Treatment

- IV Access: IV Lorazepam- 0.1mg/kg
- If no IV access: Lorazepam IM- 0.1mg/kg
- OR
- Diazepam: Rectal 0.5mg/kg
- OR
- Midazolam: Buccal 0.5mg/kg

Established SE
5-30 mins

- Repeat Lorazepam IV 0.1mg/kg
- Load Phenytoin 18mg/kg
- OR
- Phenobarb IV 20mg/kg
- Continues fitting:
- Alternative option not used – Refer ICU

Refractory SE
30-60 mins

- ICU setting
- Intubation
- Midazolam Infusion (LD: 0.2mg/kg, infusion: max 2mg/kg/h)
- Thiopental infusion (LD: 2-7mg/kg, infusion: max:5mg/kg/h)

Remember:-
cardiorespiratory support
-systemic complications
-treatment-emergent adverse events

Complications

- Respiratory: respiratory depression/aspiration/secretions
- Cardiac: hypotension/arrythmias
- Raised Intra-cranial pressure:
  - Cerebral Oedema:
    - Mannitol IV: 250mg/kg over 30-60 minutes
    - Sodium Chloride 5% - IVI- 2ml/kg- over 30 minutes
  - If associated SOL: Dexamethasone: IV 0.5mg/kg 12hrly
- Electrolytes: hyponatraemia/central DI/ glucose
- Hyperthermia
- Musculoskeletal: rhabdomyolysis/joint dislocation

The Treatment Gap

- Epidemiological burden of CSE in resource limited settings not known.
- Factors contributing:
  - Lack of second-line ASMs at primary care hospitals.
  - Significant delay in patient transportation to the hospital.
  - Shortages of intensive care unit facilities.
  - Absence of trained physicians.

Other Modalities

- Isoflurane: fast acting GABA' ergic, inhalational
- Primary/ Secondary effects on inflammation:
  - Steroids/ IVIG/Plamapharesis
  - Ketogenic Diet
  - IL1 Receptor antagonist - Anakinra
- Vagal nerve stimulator
- Transmagnetic stimulation
- Electroconvulsive therapy

Diagnostic assessment

- Clinical scenario determines the approach: history/ clinical examination.
- Monitoring must not be overlooked while searching for an aetiology.
- Only once patient stable.
- First time fitter distinctly different from those with known epilepsy presenting in CSE.

Investigations

Table 1
Recommended diagnostic workup for pediatric RSE/SRSE.

Always recommended
- Finger stick blood glucose
- Monitor vital signs
- CT/MRI (almost always appropriate except in epileptic patients with a prior normal neuroimaging or with a generalized seizure syndrome and generalized seizures)
- Serum electrolytes including calcium and magnesium
- cEEG monitoring

Specific circumstances

Known epilepsy patient
- ASD levels
- Consider CT/MRI
- Consider Electrolytes
- *Decision making largely dependent on the patient's seizure history and associated comorbidities.

Febrile patient

SE with fever (presumed Febrile SE) in a patient ≤5 years, improved clinical state and SE resolving (no concerns for CNS infection)
- Identification of primary source of fever

SE with fever in a patient>5 years, improved clinical state and SE resolving
- Identification of primary source of fever
- CT/MRI consider giving IV contrast if possible

SE with fever of unknown etiology and no improvement of clinical state
- CBC
- Lumbar puncture with CSF investigation of infectious etiologies
- CT/MRI consider giving IV contrast if possible

Suspected non-infectious encephalitis (immune/inflammatory)
- CRP
- ESR
- Auto-antibodies including ANA, anti-dsDNA, ANCA, APS & ENA panel
- Serum anti-neuronal antibodies including anti-NMDAR, –AMPA & –VGKC, –GABA
- Lumbar puncture with oligoclonal bands, and CSF anti-neuronal antibodies (as above)
- Paraneoplastic evaluation if appropriate

Suspected genetic syndrome
- Genetic consultation
- Tiered genetic testing per age, clinical exam and seizure phenotype

Additional considerations
- Toxicology screen
- Consider medication side effect (chemotherapeutics, immune-modulators, etc.)
- In rheumatologic disease consider: CRP, ESR, CMP, ANA, ANCA, APS panel, ENA panel

Pediatric refractory and super-refractory status epilepticus
Alejandra Vasqueza, Raquel Farias-Moeller, William Tatum, Seizure 2019

Epileptic in SE

- Children with newly diagnosed epilepsy have 10% risk of SE (first 2.5 years).
- Highest risk: young age, symptomatic cause, previous SE
- Systemic febrile illness often a trigger for CSE.
- FBC; U,E; drug levels
- LP/ Cultures- individualise
- Imaging: less urgent
- EEG: if prolonged obtundation

Then what?

- Start maintenance ASMs.
- 24-48 hours seizure free on infusion.
- Confirm no NCSE on EEG.
- Burst suppression on thiopentone.
- Optimize maintenance ASMs.
- Wean infusion- 4ug/kg/min every 6-8 hours.
- If weaning failure: rebolus 0.1mg/kg and increase infusion by 4ug/kg/min while adding other maintenance ASMs.

Outcomes

Determinants of outcome

- Aetiology- acute symptomatic cause.
- Time to treatment. *(Gainza-Lein M, Fernandez IS, Ulate-Campos A, Loddenkemper T, Ostendorf AP. Timing in the treatment of status epilepticus: from basics to the clinic. Seizure 2018)*
- Age < 5yrs.
- Duration of seizure: > 2hours.

- Lower mortality than in adults: 2.7-8%.

Morbidity:

- Neurological deficits (10-20%)
- Long-term epilepsy (5-36%)
- Cognitive Impairment (28-34%)
- Recurrent SE (20% in RSE)

Conclusion

- SE is a life-threatening emergency!
- Protocol driven /time sensitive approach critical!
- Delay in treatment results in increasing refractoriness to therapy.
- Current clinical practice is challenged by the heterogeneous etiologies and multiple factors involved in the progression from SE to RSE and SRSE.
- No large RCT supporting specific algorithms- imperative to have protocol driven approach which impacts on morbidity and mortality.
- *Time is brain…*

- Side effects of therapy and systemic complications!

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ANY QUESTIONS??