Management of Status Epilepticus

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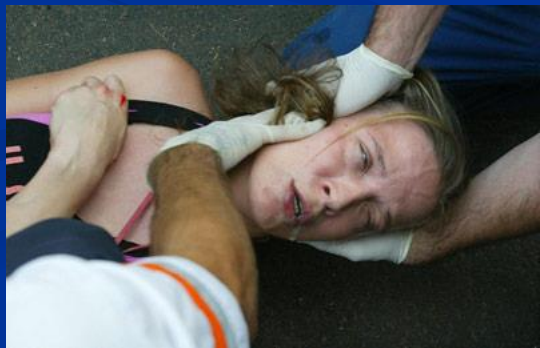


Objectives

- By the end of this lecture you should be able to know:
  - Definition of seizure and status epilepticus (SE).
  - Causes of SE
  - Approach to seizure disorders.
  - Bedside management of seizure and SE
  - Standard management protocol for SE

Notes taken by: Ashwaq Almajed

INTRODUCTION

- Seizures are dramatic and frightening for all who witness the event – and tend to induce panic, rather than rational thought, even on a neurology service.

- Clinical seizures are caused by an excessive, synchronous, abnormal discharge of cortical neurons that produces a sudden change in neurologic function.

Seizure will not happen if not excessive abnormal discharge that cause SUDDEN change in neurological function not only tonic clonic movement it could be tonic only, absences , drop attack or complex partial seizure...ect

- Seizures may be *focal*, involving a single brain region and causing limited dysfunction, or they may be *generalized*, involving the whole brain and producing loss of consciousness and convulsions.

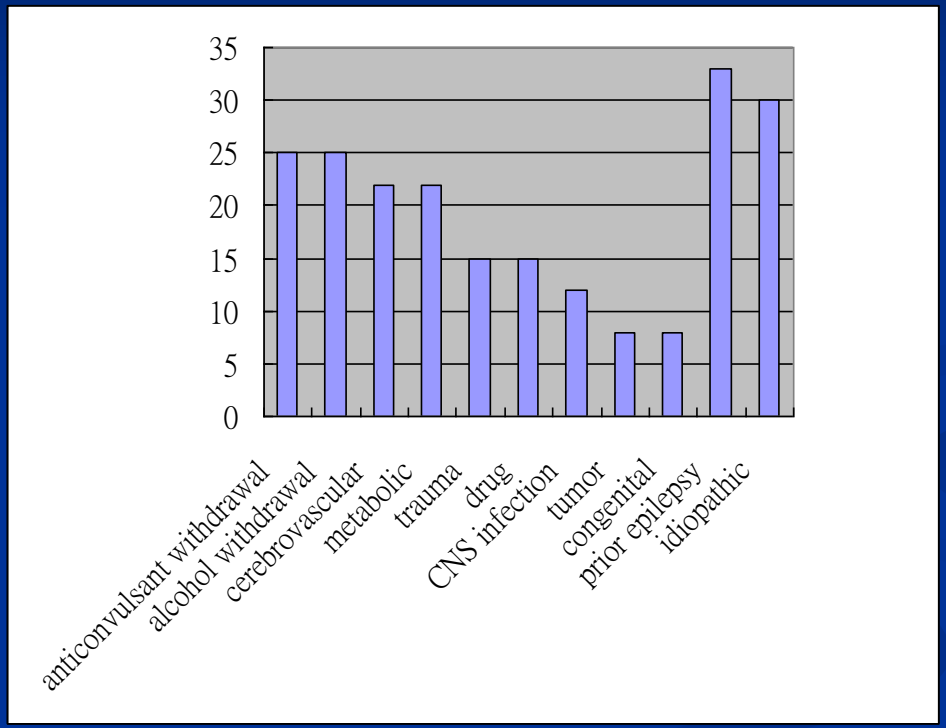
Definition of status epilepticus (SE)

	Strong Recommendations
High or Moderate Quality Evidence	•SE defined as 5 min or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures •Refractory SE should be defined as SE that does not respond to the standard treatment regimens, such as an initial benzodiazepine followed by another AED Anti epileptic drugs eg. Phenytoin •The etiology of SE should be diagnosed and treated as soon as possible Eg. واحد جته نوبه الساعة ٦ الصباح جلست دقيقة بعدين وقفت بعدين نام وجته نوبة ثانية الساعه ٨:٣٠ والحين الساعه ١١ وجته نوبة ثالثة، لازم تسأل هل صحى المريض بين النوبات وتكلم ورجع لوضعه الطبيعي? يقولك لا كلها كان نايم ومارجع لوضعه الطبيعي... this is status epileptics

*Any pt reach ER seizing should be treated with SE protocol

Brophy, et al NCC 2012

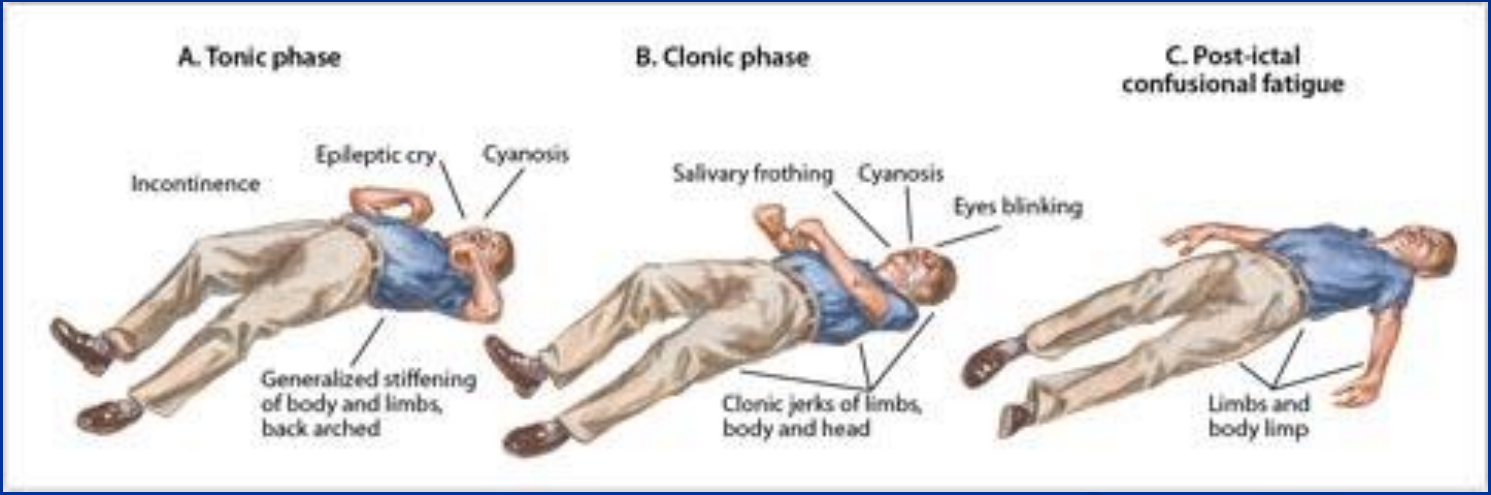
Cause



Most common cause in SA is drugs withdrawal

The comprehensive evaluation and treatment of epilepsy,Steven C.Schachter,Donald L,Schomer

Your patient have seizure !!!!!



Flaccid , weak and postictal confusion

Patient with seizure in your ward

At night you receive a call that your patient have seizure: What you have to do ???

- **At night you receive a call that your patient have seizure: What you have to do ???**
- **Questions** If the pt is still seizing that means i have to go Immediately

1. Is the patient still seizing? If yes, how long has it been going on?
2. What is the patient's level of consciousness? To know the type of seizure
3. Is this the first known seizure for this patient? It means acute cause eg. Stroke, metabolic changes...etc
4. Is the patient on anticonvulsant medication?
5. Is the patient diabetic? Hypoglycemia could cause seizure

Orders

- **If the patient is still seizing:**
  1. Have two intravenous (IV) setups ready at the bedside.
  2. Have oral airway and Ambu bag available at the bedside.
  3. Have lorazepam 8 mg ready at the bedside. Diazepam 10 mg is an alternative.
  4. Clear any sharp or hard objects from the bed, put the side rails up, and pad the side rails.
  5. Perform a finger stick glucose test.

On the Way

- **What is the differential diagnosis of seizures?** VITAMINS

V (vascular): Intracranial hemorrhage, acute or chronic ischemic infarction, subarachnoid hemorrhage, arteriovenous malformation, venous sinus thrombosis.

I (infectious): meningitis or abscess .

T (traumatic): new head injury old head injury with subdural hematoma

A (autoimmune): systemic lupus erythematosus, (CNS) vasculitis.

M (metabolic/toxic): hypo- or hypernatremia, hypo- or hypercalcemia, hypomagnesemia, hyper-thyroidism, uremia, hyperammonemia, ethanol (EtOH) toxicity or EtOH withdrawal, drugs cocaine, phenycyclidine, and amphetamines

I (idiopathic/iatrogenic): idiopathic epilepsy or medications

N (neoplastic)

S (structural) Eg, Mesotemporal Sclerosis, developmental changes...ect

Management on Bedside

- ***Treatment of an Ongoing Seizure***

1. **Keep calm.** It is likely that others in the room are reacting with fear or panic. Ask family members to leave the room. Tell them you will speak with them as soon as the situation is evaluated and under control.
2. **Ensure that all measures have been taken to protect the patient from physical injury and aspiration of gastric contents.** Have one or two people maintain the patient in a lateral decubitus position.
3. **Administer oxygen by nasal cannula or face mask.**
4. **Watch and wait for 2 minutes.** A majority of seizures will stop spontaneously within a short time.

But if you arrive and the attack was running for the last 3 min or more don't wait, just goahead and start your treatment

- Check the **finger stick glucose** level. For hypoglycemia
- Make sure there are **two IV setups available**, at least one with 0.9% normal saline (NS). If the patient has no IV access, start an IV line. One for medication and one for IV fluids
- Draw Diazepam 5mg IV slowly. Slowly over 3-5 min
  To prevent cardiopulmonary arrests (imp!!)
- **Elicit any further history** not obtained initially.
- Is this a first-ever seizure? Is the patient on anticonvulsants? What is the patient's admitting diagnosis? Is the patient diabetic? Has the patient been febrile in the last 24 hours? Ask for the chart to be brought to the bedside.
- **Observe the seizure type.**

Important to know if is it partial or generalized to decide the management plan

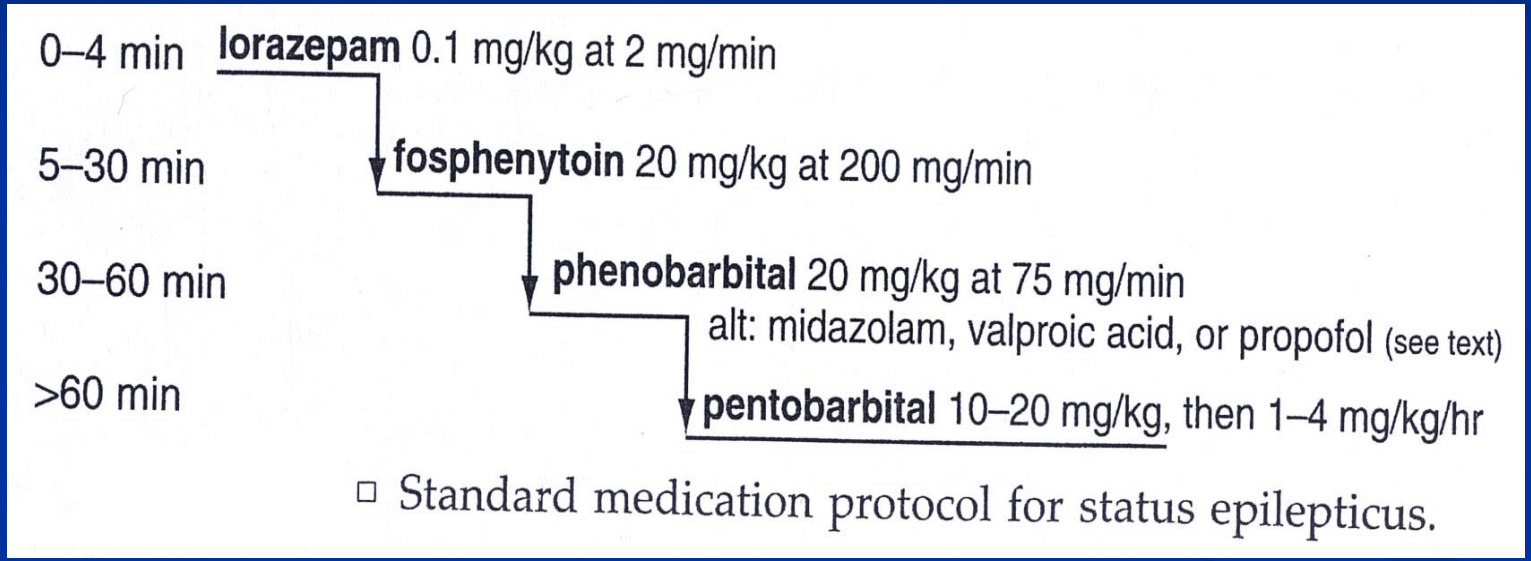
- **If the seizure has not remitted in 2 minutes,** ensure that an IV line is available.
- Avoid the antecubital area because convulsions may cause flexion of the arm and block off the IV site. It should be on the Dorsum of the hand or arm
- Order the following **blood tests:** (CBC), electrolytes, glucose, magnesium (Mg), calcium (Ca), ammonia, EtOH level, toxicology screen, and anticonvulsant level (if applicable). To know the etiology
- If the patient is hypoglycemic, give **glucose (50 ml of D50W).** Additional to diazepam
- If there is any history or suspicion of alcoholism, administer **thiamine 100 mg by slow, direct injection over 3 to 5 minutes.**

- **An Ambu bag with face mask should be at the bedside because benzodiazepines can cause respiratory depression.**

Treatment of Status Epileptics

الدوز مهم تكون مناسبة لوزن المريض عشان يستفيد منها

- If the seizure has not stopped with a full dose of a benzodiazepine, administer **phenytoin 15 to 20 mg/kg as a slow IV infusion.** (This loading dose corresponds to approximately 1500 mg in a 70-kg patient.)
- The rate of administration should not exceed 50 mg/min because phenytoin can cause cardiac arrhythmias, prolongation of the QT interval, and hypotension.
- **(ECG)** should be monitored continuously, and the blood pressure should be checked during the infusion.
- Approximately 70% of prolonged seizures will be brought under control.
- **If the seizure lasts longer than 30 minutes, transfer the patient to an intensive care unit (ICU)** for probable intubation. Why? Bc. Pt not responding to phenytoin dose and loading dose, phenobarbital should not be given except in ICU settings bc. risk of respiratory depression is very high.



□ Standard medication protocol for status epilepticus.

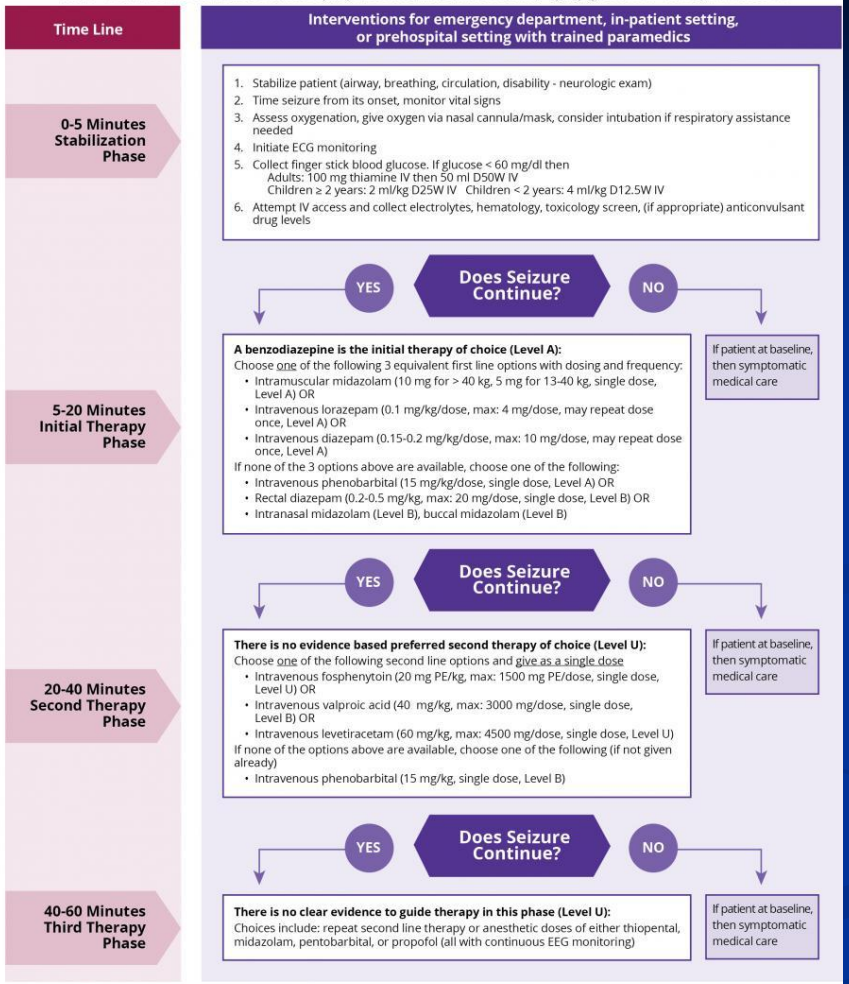
- **Once the patient is in the ICU,** if the patient is continuing to seize despite a full phenytoin load, the next step is to administer barbiturates. **Phenobarbital should be infused loading dose of 15 to 20 mg/kg.**
- Twenty to 30% of patients will continue to have electrographic seizure activity that is not clinically apparent.
- Alternatives to phenobarbital include **midazolam (Versed) 0.2 mg/kg bolus, followed by IV infusion of 0.1 to 2 mg/kg/hour, propofol 3 to 5 mg/kg loading dose.**

Don't memorize the doses

- General anesthesia with halothane and neuromuscular blockade has been used in some cases to avoid rhabdomyolysis, but this eliminates the ability to follow the neurologic examination.

Proposed Algorithm for Convulsive Status Epilepticus

From "Treatment of Convulsive Status Epilepticus in Children and Adults," *Epilepsy Currents* 16.1 - Jan/Feb 2016



American Epilepsy Society

Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytic framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate.

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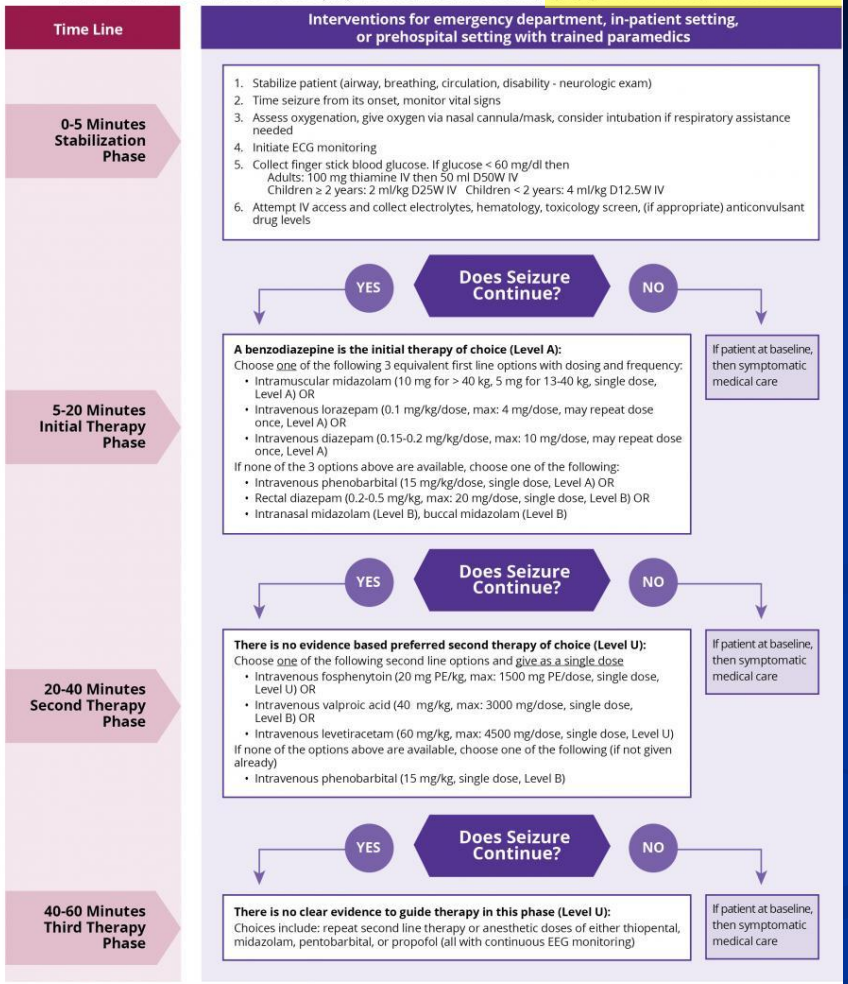

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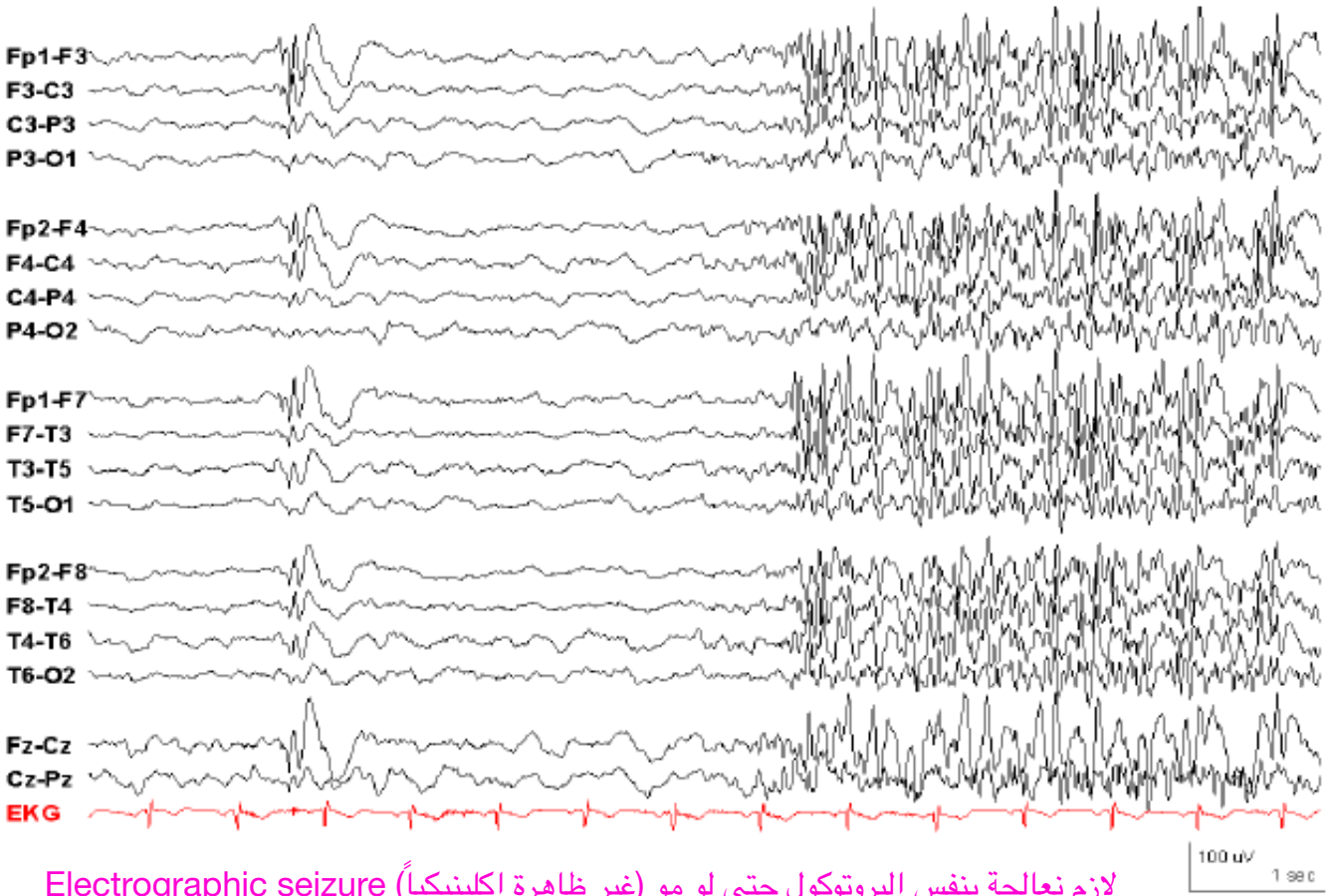
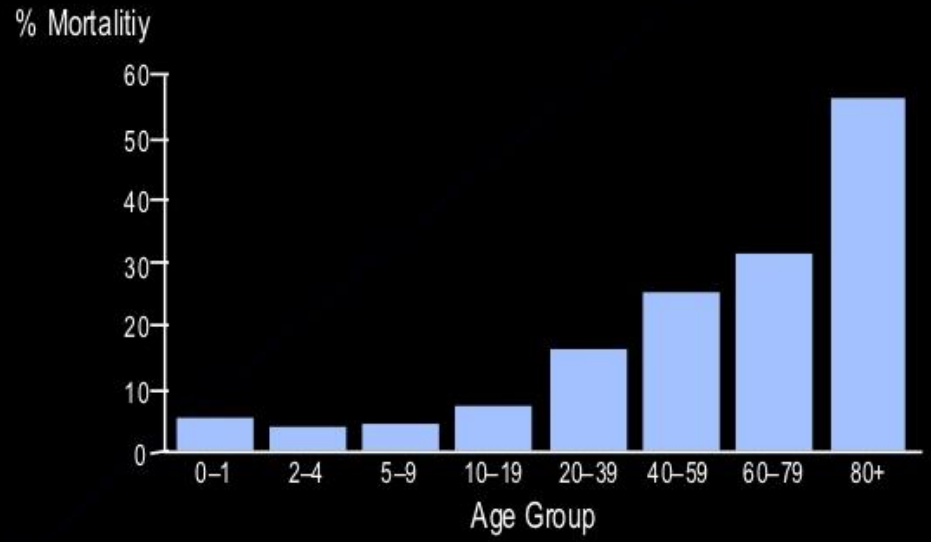


Electrographic seizure لازم نعالجة بنفس البروتوكول حتى لو مو (غير ظاهرة اكلينيكياً
واضحة عنده اعراض النوبة


FP1-F3
F3-C3
C3-P3
P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
Fz-Cz
Cz-Pz
EKG
75 uV
1 sec

Mortality in Status Epilepticus by Age Group

Among 546 patients with status epilepticus in Richmond, Virginia, from 1982 to 1989.



DeLorenzo RJ, et al. Epilepsia. 1992; 33(suppl 4):515-525.

*Mortality rate increases with age

Complication

Cardiac: HTN,tachycardia,arrhythmia

Pulmonary: apnea,hypoxia,respiratory failure

Hyperthermia

Metabolic derangement

Cerebral:neuronal damage

Death 1-2% Bc. of suffocation

MAJOR THREAT TO LIFE

- Aspiration of gastric contents if the airway is not protected
- Head injury
- Lactic acidosis, hypoxia, hyperthermia, rhabdomyolysis, cerebral edema, or hypotension from a prolonged seizure. These conditions may produce permanent brain injury.
- The patient should be positioned in the *lateral decubitus* position to prevent aspiration of gastric contents. All hard or sharp objects should be removed from the bed.

Table 3. Mortality of SE with Different Etiologies

High Mortality:	Anoxia Multiple medical problems; sepsis
Intermediate Mortality:	[depends on setting, patient population, and follow up] Stroke Tumor Infection (CNS or systemic) Trauma
Low Mortality:	Earlier epilepsy and some precipitant (e.g. reduced AEDs) Medication, drug toxicity Alcohol withdrawal

Summary

Treatment
Step 1

- ABCDE
  - Maintain Airway- patient at risk for aspiration
  - Breathing- place O_2, be ready for intubation
  - Circulation- obtain IV access
  - Dextrose: check glucose levels
  - Electrolytes: check electrolytes (Na, Ca, Mg), and anticonvulsent levels

Treatment Medications

- Ideal drug for treating SE
  - Rapid entry into CNS
  - Rapid onset of action
  - Long duration of action
  - Safety
  - Absence of sedation
  - Useful as maintenance AED

Treatment
Step 2

- Benzodiazepine Therapy
  - Diazepam
  - Lorazepam

Diazepam

- Highly lipid soluble
  - Rapid CNS entry- stops seizures in 1-3 minutes
- Rapid redistribution in fatty tissues
  - Brain concentrations fall quickly
  - Duration of action is 15-30 minutes
  - T1/2= 30 hr

احفظوها بالشكل هذا:

5 mg if no response give another 5 mg (Slowly over 3-5 min)

- Dose: <3yrs, 0.5mg/kg, >3yrs, 0.3mg/kg
- Side Effects: sedation, decreased respiration and blood pressure

Lorazepam

- Less lipid soluble than diazepam
  - Slower CNS, stops seizures in 6-10 min
- Not as rapidly redistributed to fat stores
  - Longer duration of action 12-24 hr
  - $T_{1/2}$ =14 hr
- Dose: 0.05—0.1mg/kg
- Side Effects: decreased LOC, respiration and BP

Treatment
Step 3

Phenytoin/Fosphenytoin

Fosphenytoin مو موجود في السعودية
ميزته ممكن تعطيه IM ومايسبب arrhythmia

Phenytoin

- IV dosing 20 mg/kg load
- Stops seizures in 10-30 minutes
- Duration of action 24 hrs, T ½=24hr
- Max infusion rate of 1mg/kg/min, max- 50 mg/min
- Side Effects: arrhythmias, hypotension, wide QT interval, phelibitis
- pH=11-12, may only give IV or po

Treatment
Step 3

Fosphenytoin- phenytoin prodrug

- IV dosing: 20 mg/kg load
- Safer than phenytoin
- pH=8-9
- May give IV or IM
- May give faster than phenytoin(100-150mg/min)
- Much more expensive

Treatment
Step 4

- Phenobarbital
  - Lipid solubility < phenytoin
  - Duration of action>48 hrs, $T_{1/2}$= 100 hours
  - Dose 20 mg/kg
  - Side Effects: sedation, decreased respiration and BP
  - Be ready to intubate!!

Treatment
Step 5

- If you haven't called Neurology, please call !!!
- Consider IV Valproic Acid (Depacon)
  - FDA approved only for replacement or oral dosing
  - Rapid loading dose appears safe
  - 25-30mg/kg rapidly infused
  - Side Effects: dizziness, HA, nausea

- Consider levetiracetam IV Load

بعض المرضى عندهم allergy of phenytoin فلازم نختار
Valproic acid or levetiracetam as IV infusion

Treatment: Emergent initial therapy

	Strong Recommendations
High or Moderate Quality Evidence	•Benzodiazepines should be given as emergent initial therapy •Lorazepam is the drug of choice for IV administration •Midazolam is the drug of choice for IM administration •Rectal diazepam can be given when there is no IV access and IM administration of midazolam is contraindicated

Treatment: Urgent control therapy

	Strong Recommendations
High or Moderate Quality Evidence	•Urgent control AED therapy recommendations include use of IV fosphenytoin/phenytoin, valproate sodium, or levetiracetam

Brophy, et al NCC 2012

Skip

Treatment	Class/Level of evidence
Emergent treatment	
Lorazepam	Class I, level A
Midazolam	Class I, level A
Diazepam	Class IIa, level A
Phenytoin/fosphenytoin	Class IIb, level A
Phenobarbital	Class IIb, level A
Valproate sodium	Class IIb, level A
Levetiracetam	Class IIb, level C
Urgent treatment	
Valproate sodium	Class IIa, level A
Phenytoin/fosphenytoin	Class IIa, level B
Midazolam (continuous infusion)	Class IIb, level B
Phenobarbital	Class IIb, level C
Levetiracetam	Class IIb, level C

Brophy, et al NCC 2012

Refractory Status Epilepticus

Didn't respond to initial 2 lines of protocol (benzodiazepines and phenytoin)

- Intubation, IV access
- Continuous EEG monitoring
- Medication Coma
  - Pentobarbital
  - Midazolam
  - Propofol

Refractory Status Epilepticus

	Strong Recommendations
Low or Poor Quality Evidence	•Refractory SE therapy recommendations should consist of continuous infusion AEDs, but vary by the patient's underlying condition •Dosing of continuous infusion AEDs for RSE should be titrated to cessation of electrographic seizures or burst suppression •During the transition from continuous infusion AEDs in RSE, it is suggested to use maintenance AEDs and monitor for recurrent seizures by cEEG during the titration period. If the patient is being treated for RSE at a facility without cEEG capabilities, consider transfer to a facility that can offer cEEG monitoring Stop seizure as fast as possible Continues EEG monitoring

Brophy, et al NCC 2012

Treatment	Class/Level of evidence
Refractory treatment	
Midazolam	Class IIa, level B
Propofol	Class IIb, level B
Pentobarbital/thiopental	Class IIb, level B
Valproate sodium	Class IIa, level B
Levetiracetam	Class IIb, level C
Phenytoin/fosphenytoin	Class IIb, level C
Lacosamide	Class IIb, level C
Topiramate	Class IIb, level C
Phenobarbital	Class IIb, level C

Brophy, et al NCC 2012

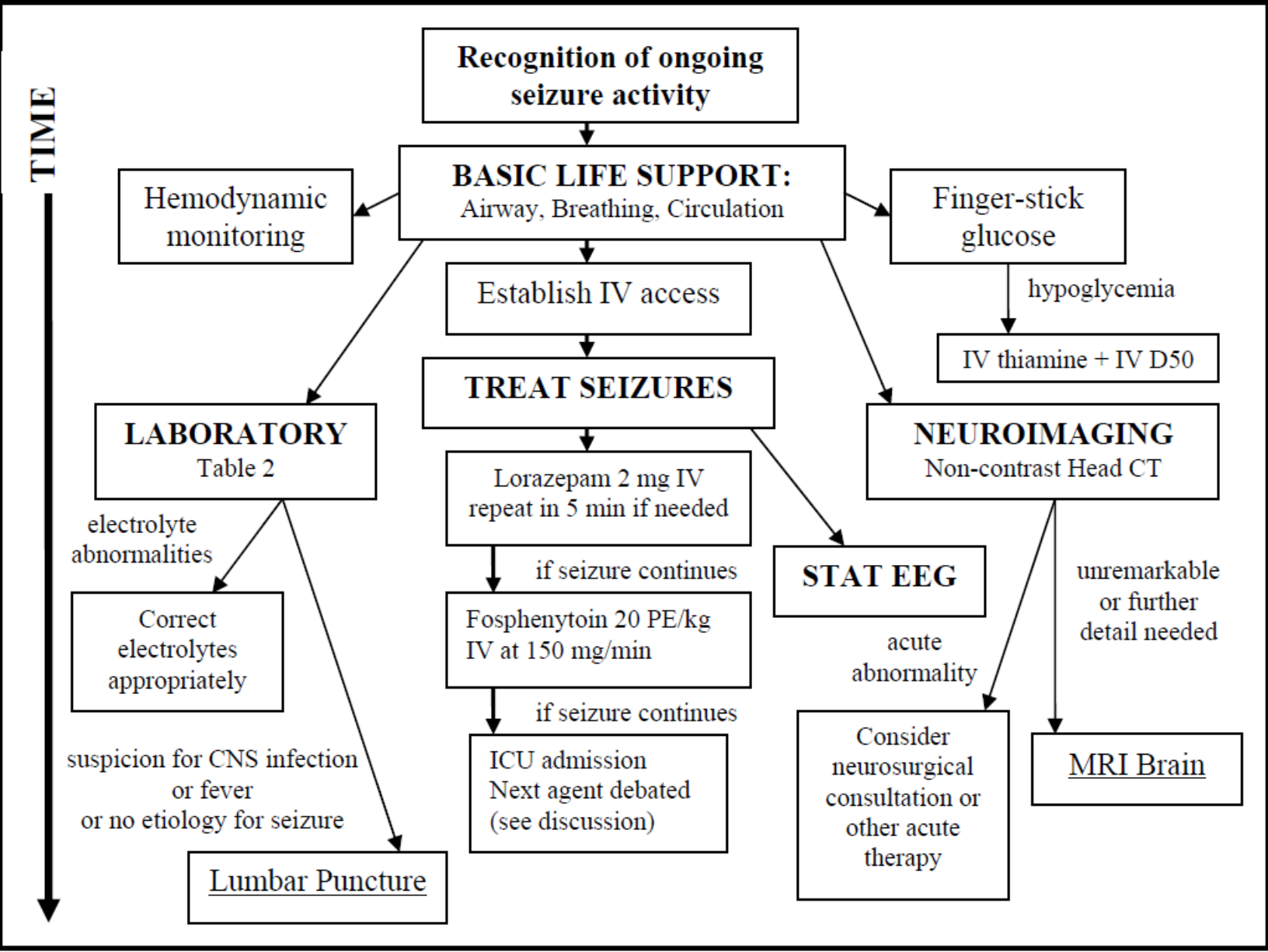
Seizure Under control , What next?

You have to investigate the cause of seizure:
-check glucose level
-do head CT to r/o stroke, brain lesions..ect
-labs
-vitals

Approach: Diagnostic workup

All patients
• FS glucose
• Monitor vital signs.
• Head CT (appropriate for most cases)
• Labs: blood glucose, CBC, BMP, Ca, Mg
• cEEG monitoring
Consider based on clinical presentation
• Brain MRI
• Lumbar puncture
• Toxicology panel (i.e. isoniazid, TCAs, theophylline, cocaine, sympathomimetics, ETOH, organophosphates, cyclosporine)
• Other Labs: LFT, troponin, T&H, coags, ABG, AED levels, tox screen (urine/blood), inborn errors of metabolism

Brophy, et al NCC 2012


TIME
Recognition of ongoing seizure activity
BASIC LIFE SUPPORT:
Airway, Breathing, Circulation
Hemodynamic monitoring
Finger-stick glucose
hypoglycemia
IV thiamine + IV D50
Establish IV access
TREAT SEIZURES
LABORATORY
Table 2
NEUROIMAGING
Non-contrast Head CT
Lorazepam 2 mg IV
repeat in 5 min if needed
if seizure continues
Fosphenytoin 20 PE/kg
IV at 150 mg/min
if seizure continues
ICU admission
Next agent debated
(see discussion)
STAT EEG
electrolyte abnormalities
Correct electrolytes appropriately
suspicion for CNS infection
or fever
or no etiology for seizure
Lumbar Puncture
acute abnormality
Consider neurosurgical consultation or other acute therapy
unremarkable or further detail needed
MRI Brain

Home Messages:

Seizure is a medical emergency.

Don't panic and always keep the protocol in your mind.

Don't hesitate to call the neurology team immediately after you stabilized the patient OR prolonged seizure.

Keep in your mind that seizure is a symptom not a diagnosis .

Thank You