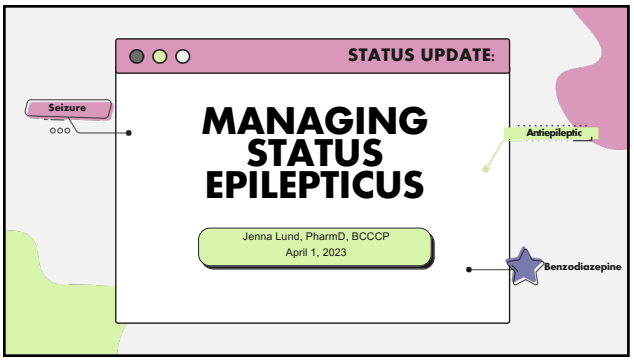


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DISCLOSURE STATEMENT

I have had no financial relationship over the past 24 months with any commercial sponsor with a vested interest in this presentation.

2

PHARMACIST LEARNING OBJECTIVES

Differentiate various traditional definitions including brief seizure, prolonged seizure, and status epilepticus	Summarize the 3 phases of status epilepticus treatment including which drugs are included in each phase	Evaluate the effectiveness of secondary therapy phase medications based on current literature

3

TECHNICIAN LEARNING OBJECTIVES

Describe status epilepticus	Recognize various anti-epileptic medication names	Identify the brand and generic names for benzodiazepines used to treat seizures

4

ABBREVIATIONS

- AED - anti-epileptic drug
- CNS - central nervous system
- FOS - fosphenytoin
- IM - intramuscular
- IV - intravenous
- kg - kilograms
- LEV - levetiracetam
- mg - milligrams
- SE - status epilepticus
- VPA - valproic acid

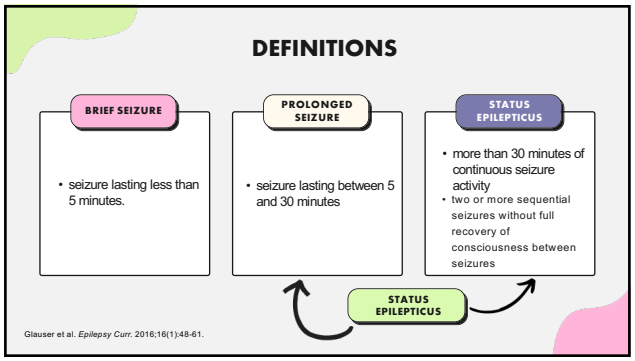
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DEFINITIONS

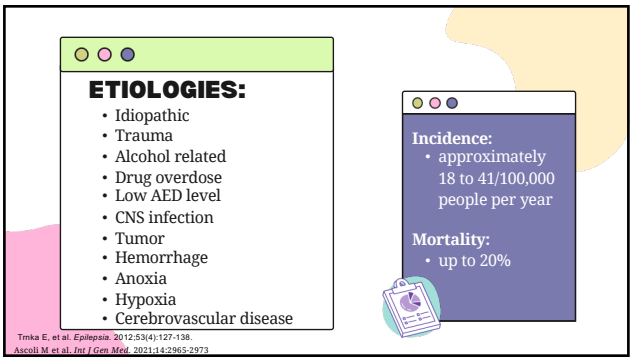
BRIEF SEIZURE	PROLONGED SEIZURE	STATUS EPILEPTICUS
• seizure lasting less than 5 minutes.	• seizure lasting between 5 and 30 minutes	• more than 30 minutes of continuous seizure activity • two or more sequential seizures without full recovery of consciousness between seizures

Glauser et al. *Epilepsy Curr.* 2016;16(1):48-61.

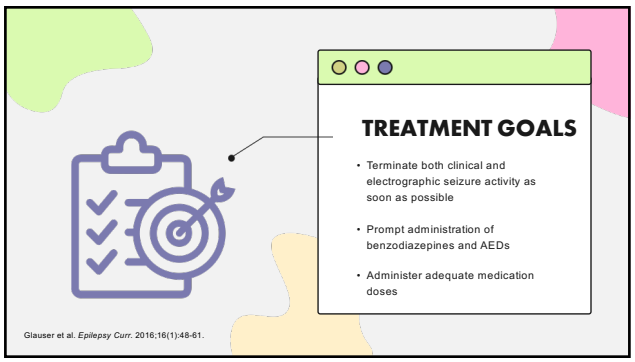
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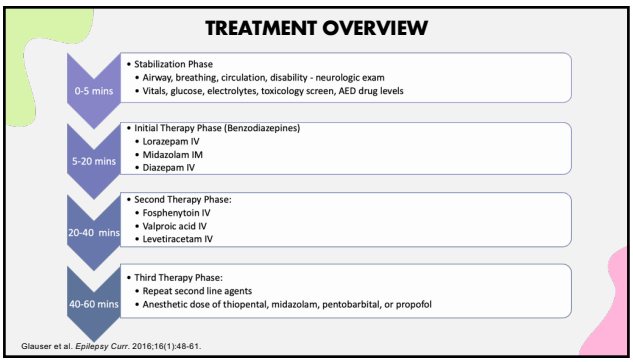
7


ETIOLOGIES:
• Idiopathic
• Trauma
• Alcohol related
• Drug overdose
• Low AED level
• CNS infection
• Tumor
• Hemorrhage
• Anoxia
• Hypoxia
• Cerebrovascular disease
Incidence:
• approximately 18 to 41/100,000 people per year
Mortality:
• up to 20%
Trnka E, et al. Epilepsia. 2012;53(4):127-138.
Ascoli M et al. Int J Gen Méd. 2021;14:2965-2973

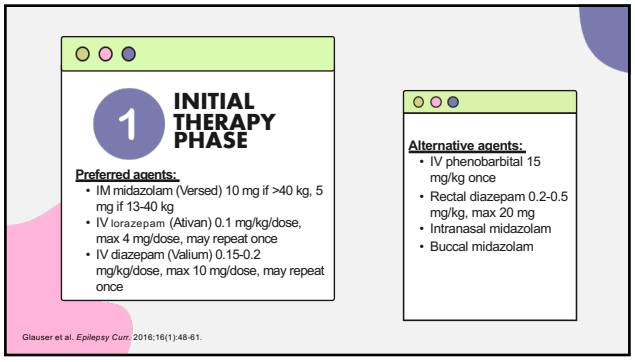
8


TREATMENT GOALS
• Terminate both clinical and electrographic seizure activity as soon as possible
• Prompt administration of benzodiazepines and AEDs
• Administer adequate medication doses
Glauser et al. Epilepsy Curr. 2016;16(1):48-61.

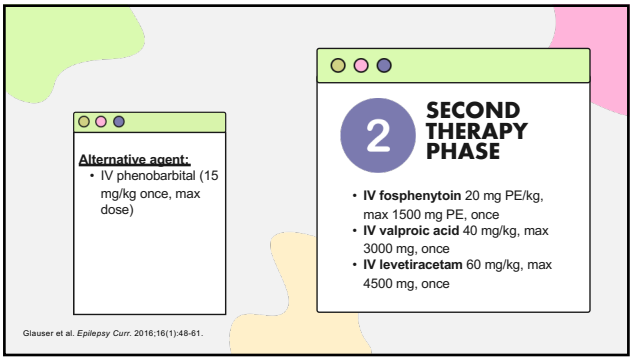
9


TREATMENT OVERVIEW
0-5 mins
• Stabilization Phase
• Airway, breathing, circulation, disability - neurologic exam
• Vitals, glucose, electrolytes, toxicology screen, AED drug levels
5-20 mins
• Initial Therapy Phase (Benzodiazepines)
• Lorazepam IV
• Midazolam IM
• Diazepam IV
20-40 mins
• Second Therapy Phase:
• Fosphenytoin IV
• Valproic acid IV
• Levetiracetam IV
40-60 mins
• Third Therapy Phase:
• Repeat second line agents
• Anesthetic dose of thiopental, midazolam, pentobarbital, or propofol
Glauser et al. Epilepsy Curr. 2016;16(1):48-61.

10


1
INITIAL THERAPY PHASE
Preferred agents:
• IM midazolam (Versed) 10 mg if >40 kg, 5 mg if 13-40 kg
• IV lorazepam (Ativan) 0.1 mg/kg/dose, max 4 mg/dose, may repeat once
• IV diazepam (Valium) 0.15-0.2 mg/kg/dose, max 10 mg/dose, may repeat once
Alternative agents:
• IV phenobarbital 15 mg/kg once
• Rectal diazepam 0.2-0.5 mg/kg, max 20 mg
• Intranasal midazolam
• Buccal midazolam
Glauser et al. Epilepsy Curr. 2016;16(1):48-61.

11


Alternative agent:
• IV phenobarbital (15 mg/kg once, max dose)
2
SECOND THERAPY PHASE
• IV fosphenytoin 20 mg PE/kg, max 1500 mg PE, once
• IV valproic acid 40 mg/kg, max 3000 mg, once
• IV levetiracetam 60 mg/kg, max 4500 mg, once
Glauser et al. Epilepsy Curr. 2016;16(1):48-61.

12

RANDOMIZED TRIAL OF THREE ANTICONVULSANT MEDICATIONS FOR STATUS EPILEPTICUS

Kapur J, Elm J, Chamberlain J, et al. *N Engl J Med*. 2019; 381(22): 2103-2013.

13

ESETT TRIAL

- Multicenter, randomized, blinded, comparative-effectiveness study of both children and adults with benzodiazepine resistant SE.
- Randomized 1:1:1
  - levetiracetam (60 mg/kg IV, max 4500 mg)
  - fosphenytoin (20 mg/kg IV, max 1500 mg)
  - valproic acid (40 mg/kg IV, max 3000 mg)
- 384 unique patients (intention-to-treat)
  - 16 patients enrolled twice (per protocol)

Kapur J et al. *N Engl J Med*. 2019;381(22):2103-13.

14

ESETT TRIAL

- **Primary outcome:** absence of clinically evident seizures and improvement in consciousness level by 60 minutes after AED initiation.
- **Safety outcomes:** life-threatening hypotension, cardiac arrhythmia, intubation, seizure recurrence, death
- **Inclusion:** ≥ 2 years old, treated with appropriate benzodiazepine dose and seizures persisted for at least 5 mins, no more than 30 mins had lapsed after last benzodiazepine dose
- **Exclusion:** seizure caused from trauma, hypoglycemia, hyperglycemia, cardiac arrest or post anoxia.

Kapur J et al. *N Engl J Med*. 2019;381(22):2103-13.

15

OUTCOMES

Outcome	LEV (n=145)	FOS (n=118)	VPA (n=121)
Primary efficacy # (%)	68 (47)	53 (45)	56 (46)
Median time (min) to seizure termination	10.5	11.7	7.0
Seizure recurrence (1-12 hrs post infusion) # (%)	16 (10.7)	14 (11.2)	14 (11.2)
Life-threatening hypotension # (%)	1 (0.7)	4 (3.2)	2 (1.6)
Intubation # (%)	30 (20)	33 (26.4)	21 (16.8)
Arrhythmia # (%)	1 (0.7)	0	0
Death # (%)	7 (4.7)	3 (2.4)	2 (1.6)

Kapur J et al. *N Engl J Med*. 2019;381(22):2103-13.

16

ESETT TRIAL SUMMARY

- No difference in efficacy for second therapy agents seen between levetiracetam, fosphenytoin and valproic acid
- Similar safety profiles between the three agents

Kapur J et al. *N Engl J Med*. 2019;381(22):2103-13.

17

3 THIRD THERAPY PHASE

- Repeat second line therapy
- Anesthetic doses of:
  - Midazolam
  - Propofol
  - Pentobarbital
  - Thiopental



Glauser et al. *Epilepsy Curr*. 2016;16(1):48-61.

18

KEY TAKEAWAYS

1. **TREAT AS A MEDICAL EMERGENCY**
   Rapid, treatment initiation is essential
2. **BENZODIAZEPINES ARE FIRST**
   IV or IM benzodiazepine is first line
3. **LEVETIRACETAM, FOSPHENYTOIN, OR VALPROIC ACID SECOND**
   Utilize one of these three agents at appropriate recommended doses as the next step

19

REFERENCES

- Ascoli M, Ferlazzo E, Gasparini S, et al. Epidemiology and outcomes of status epilepticus. *Int J Gen Med*. 2021; 14: 2965-2973.
- Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the guideline committee of the American Epilepsy Society. *Epilepsy Curr*. 2016; 16:48-61.
- Kapur J, Elm J, Chamberlain J, et al. Randomized trial of three anticonvulsant medications for status epilepticus. *N Engl J Med*. 2019; 381(22):2103-13.
- Trinka E, Hofler J, Zerbs A. Causes of status epilepticus. *Epilepsia*. 2012; 53(4):127-138.

20

Pharmacist Assessment Question 1

Which of the following terms and definitions are matched correctly?

A. Brief seizure - seizure lasting less than 5 minutes
B. Prolonged seizure - seizure lasting 5 to 15 minutes
C. Status epilepticus - more than 30 minutes of continuous seizure activity or two or more sequential seizures without full recovery between
D. A and C are correct

21

Pharmacist Assessment Question 2

Which of the following medications are included in the second therapy phase of status epilepticus management?

A. IM midazolam
B. IV lorazepam
C. IV propofol
D. IV levetiracetam

22

Pharmacist Assessment Question 3

True or false: based on the findings from the ESETT trial, fosphenytoin, valproate, and levetiracetam all had similar efficacy and side effects in treating benzodiazepine-refractory status epilepticus?

A. True
B. False

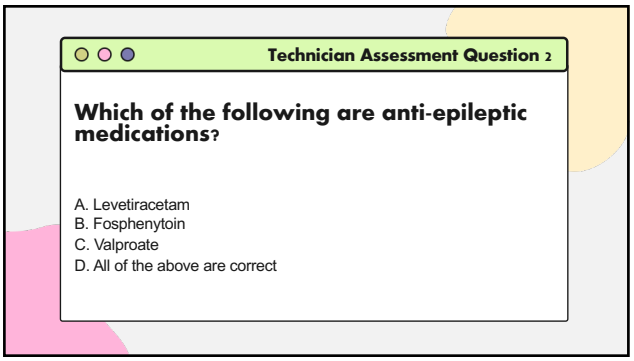
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Technician Assessment Question 1

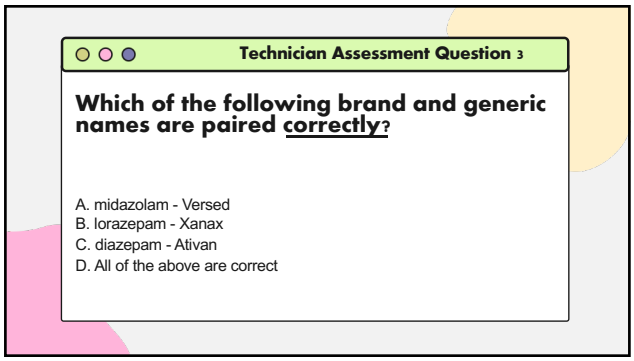
True or false: status epilepticus is defined as more than 3 minutes of continuous seizure activity?

A. True
B. False

24


Technician Assessment Question 2
Which of the following are anti-epileptic medications?
A. Levetiracetam
B. Fosphenytoin
C. Valproate
D. All of the above are correct

25


Technician Assessment Question 3
Which of the following brand and generic names are paired correctly?
A. midazolam - Versed
B. lorazepam - Xanax
C. diazepam - Ativan
D. All of the above are correct

26


QUESTIONS?

27