PREHOSPITAL MANAGEMENT OF STATUS EPILEPTICUS

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December 3, 2019

DISCLOSURES

- Consulting: Marinus Pharmaceuticals, Inc
- Funding: American Academy of Neurology, NIH/National Institute on Aging
- I am not a paramedic or emergency medicine physician
- I enjoy email: Elan.Guterman@gmail.com

Case study:
55 year old man found down on the street and EMS called. On arrival, he has continuous involuntary jerking of both arms and legs. **What is the best initial treatment?**

A) Wait until he has been seizing for 5 minutes and then give ativan 4mg IV

B) Give midazolam 2mg IM and repeat q2 minutes to max 6mg

C) Give midazolam 10mg IM

D) Check glucose while obtaining an IV and then give ativan 2mg IV

E) Give diazepam 10mg IV after IV obtained

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When does seizure become status epilepticus?

+

5 minutes

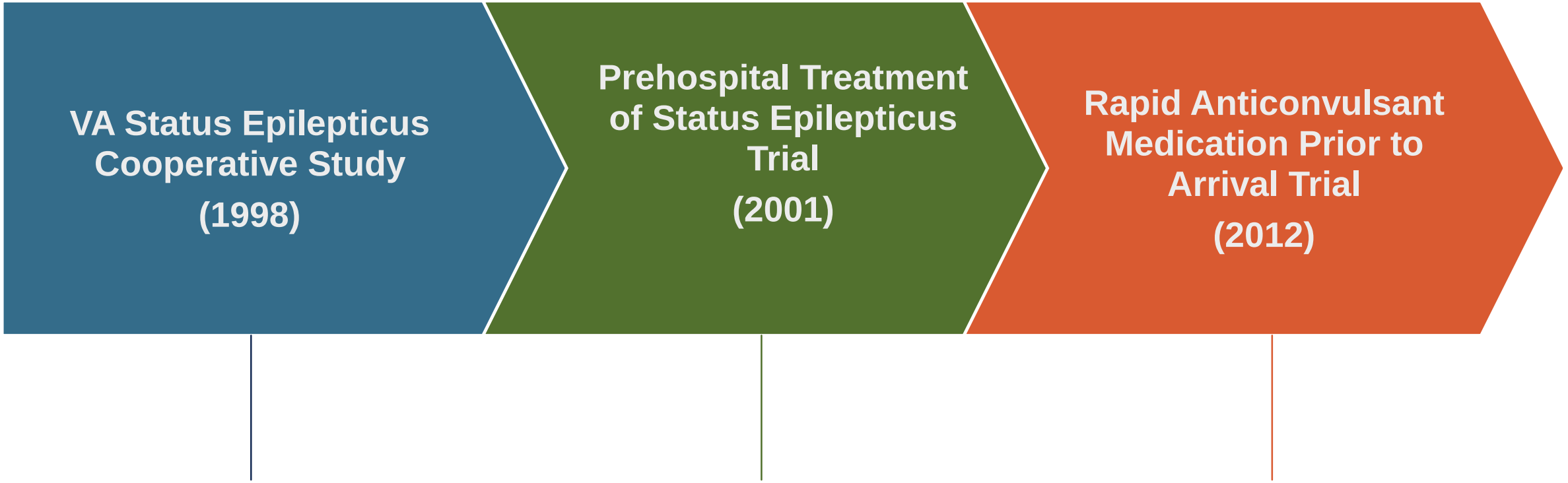
"Continuous seizure activity or recurrent seizures without recovery between seizures"

Incorporated **time** to delineate the point when continuous seizures lead to pharmacoresistance and neuronal injury

We understand and define status epilepticus on a scientific, clinical, and practical level

Clinical Definition	Practical EMS Definition
≥ 5 minutes of (a) continuous seizures or (b) 2 or more discrete seizures between which there is incomplete recovery of consciousness.	Seizure activity **upon arrival of prehospital personnel** or new/recurrent seizure activity lasting ≥ 5 minutes

Current guidelines driven by high quality data supporting rapid prehospital benzodiazepines for treatment of status epilepticus



The Prehospital Treatment of Status Epilepticus Trial (PHTSE) demonstrated superiority of benzodiazepines as compared to placebo

	Placebo N = 71	**IV Diazepam** N = 68	**IV Lorazepam** N = 66
Status epilepticus termination	15 (21.1%)	29 (42.6%)	39 (59.1%)
		vs placebo: OR 2.3 (95% CI 1-5.9)	vs placebo: OR 4.8 (95% CI 1.9-13)
BVM or Intubation	11 (15.5%)	6 (8.8%)	7 (10.6%)
	P = 0.08		

Highest rates of seizure termination among patients that received lorazepam (Ativan)

Lowest rates of respiratory complications among patients that received lorazepam (Ativan) but this did not reach statistical significance

Which benzodiazepine is best suited for the ambulance?

IV Lorazepam

- Rapid acting
- High quality evidence supporting use
- Requires IV placement
- More rapid degradation in high temperature and after 120 days

IM Midazolam

- Rapid administration
- Slower acting than IV
- Less sensitive to longer storage
- Less sensitive to higher temperatures

The Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) demonstrated IM midazolam as least as effective as IV lorazepam

		IV Lorazepam N = 445	IM Midazolam N = 448
Status epilepticus termination		282 (63.4%)	329 (73.4%)
		Risk difference 10% (95% CI 4-16) p < 0.001 for noninferiority; p < 0.001 for superiority	
Intubation		64 (14.4)	63 (14.1)
		RR 0.98 (0.70–1.34)	
Time	**Time to treatment**	4.8 minutes	1.2 minutes
	Time from treatment to seizure termination	1.6 minutes	3.3 minutes
	Total time	6.4 minutes	4.5 minutes

10% higher rates of seizure termination with midazolam (Versed) with no difference in intubation need

IM administration has quicker ***treatment***

IV administration has quicker ***effect***

Prehospital benzodiazepine administration is the current standard of care for status epilepticus

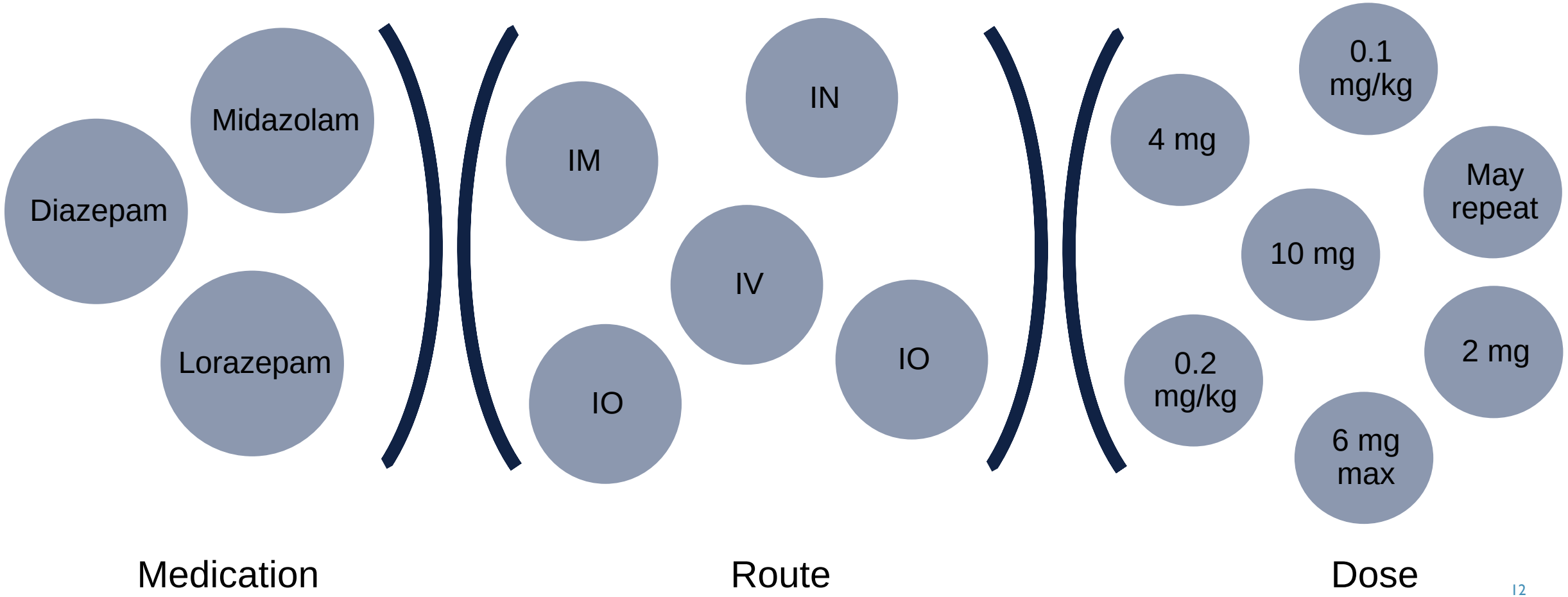
- Current guidelines endorse benzodiazepines as first-line initial treatment for adults with status epilepticus.
- For out-of-hospital status epilepticus, this involves immediate benzodiazepine administration by EMS providers.

Midazolam (Versed) 10mg IM

Lorazepam (Ativan) 4mg IV, may repeat

Diazepam (Valium) 6-10mg IV, may repeat

Multiple treatment options contribute to variable and confusing treatment protocols

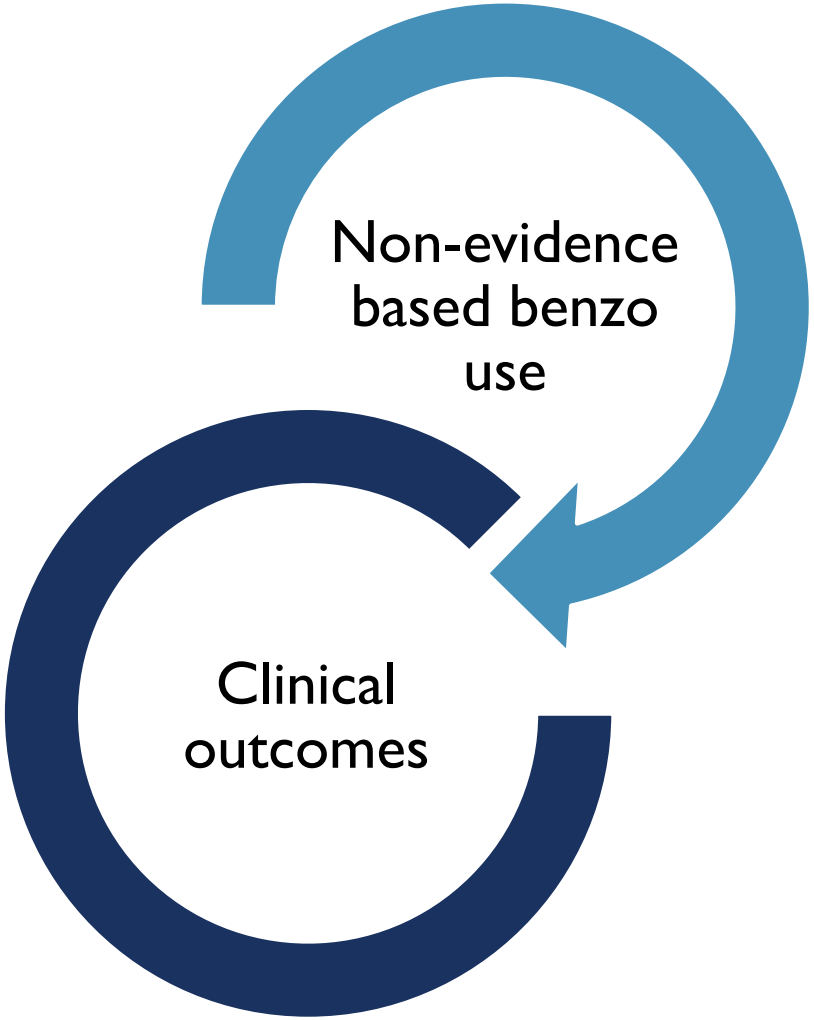


Variable and confusing treatment protocols contribute to variable treatment

Midazolam dose	Intramuscular	Intranasal	Intraosseous	Intravenous	Total
0-5 mg	76 (37.1%)	70 (10.0%)	9 (64.3%)	395 (69.1%)	**550**
5 mg	129 (62.9%)	629 (89.6%)	5 (35.7%)	175 (30.6%)	**938**
5-10 mg	0 (0.0%)	2 (0.3%)	0 (0.0%)	2 (0.3%)	**4**
10 mg	0 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	**1**
	205	**702**	**14**	**572**	**1493**

- The most common forms of midazolam used:
  - 5mg intranasal
  - < 5mg intravenous
- 40% patients received < 5mg midazolam
- Only 5 patients (1%) received > 5mg midazolam

Local experience with prehospital status epilepticus care



- Midazolam was administered to 62% of patients with status epilepticus
- There were **no** patients who received midazolam at a dose and route consistent with national guidelines
- Higher midazolam starting dose was associated with decreased need for rescue therapy
- Higher midazolam starting dose was **not** associated with more respiratory complications

Model EMS Guidelines

What are the best ways to improve current status epilepticus treatment protocols?

5. Assess neurologic status
6. Routes for treatment
   a. IN/IM routes are preferred over rectal (PR), IV, or IO routes, if within the provider's scope of practice
      i. If none of these routes (IN/IM/IV/IO) of medication administration are in provider's scope of practice, diazepam 0.2 mg/kg PR (maximum dose 10 mg) is an acceptable route of administration
   b. IV placement is not necessary for treatment of seizures, but could be obtained if needed for other reasons

If vascular access absent: IM midazolam 0.2 mg/kg, max 10mg

If vascular access present:

IV midazolam 0.1 mg/kg, max 4 mg/dose OR

IV lorazepam 0.1 mg/kg/dose, max 4 mg/dose OR

IV diazepam 0.1 mg/kg/dose, max 4 mg/dose

following interventions provide symptomatic relief for fevers but do not stop the seizure:
   a. Acetaminophen 15 mg/kg, maximum dose 650 mg, PR/IV/IO (if unable to swallow) or PO (if able to swallow)
      and/or
   b. Ketorolac 1 mg/kg, maximum dose 15 mg, IV (if unable to swallow) OR Ibuprofen 10 mg/kg, maximum dose 600 mg, PO (if able to swallow)
      and/or
   c. Removing excessive layers of clothing
      and/or
   d. Applying cool compresses to the body
10. Consider acquiring a 12-lead EKG following cessation of seizure in patients without a history of seizure to determine possible cardiac cause

- ❑ Fewer benzodiazepine options
- ❑ Simplify dosing
- ❑ Fewer route options

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For adults: IM midazolam 10mg

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Summary and research conclusions

- ***Prehospital*** benzodiazepines remain first-line treatment for status epilepticus
- Benzodiazepines should be administered as a single first dose of midazolam 10mg IM, lorazepam 4mg IV, or diazepam 6-10mg IV according to national guidelines and Alameda EMS treatment protocol
- Midazolam 10mg IM has advantages in the prehospital setting
- Failure to administer benzodiazepines at all or at a low dose is associated with increased need for subsequent doses presumably because of breakthrough seizures
- Starting with a higher dose of midazolam is not associated with more respiratory complications and may even lower the need for intubation

THANKS

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