

Disclosure/s

All the planners and presenters for today's CE activity declare they do not have a financial interest/arrangement <u>or</u> affiliation with one or <u>more</u> organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this activity.

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Thank you



James Chamberlain, MD

PI, PECARN Pediatric Seizure Study Pediatric PI, ESETT Study

LEARNING OBJECTIVES

- Define SE
- Understand why early, aggressive treatment is important
- Develop a stepwise approach to SE
- Understand differences between benzodiazepines



SCOPE

Convulsive (generalized)

NOT

- Focal motor
- Absence
- Temporal lobe, etc.



DEFINITION

- > 5 minutes continuous
- Recurrence without recovery between
- Series of convulsions (e.g. 3 in one hour)

Newer concept of T1 and T2

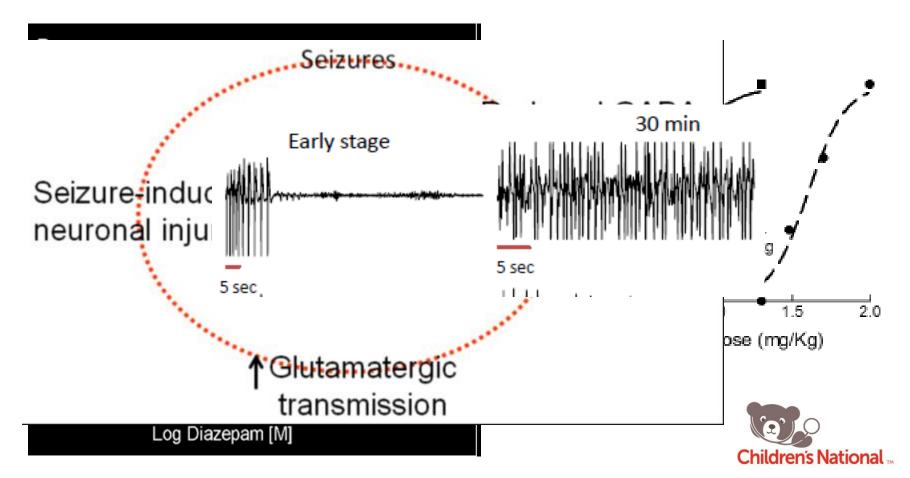


WHY IS SE BAD FOR US?

- Increased metabolic demands
- Ischemia
 - Ca⁺⁺ influx
 - Inflammatory mediators
- Irreversible damage at >30 mins.
 - Lactic acidosis
 - Loss of autoregulation
 - Autonomic dysfunction
 - Increased ICP



THE MORE YOU SEIZE...



HUMAN EVIDENCE FOR 30 MINUTES

- Time = neurons
- 10% of children with febrile SE had hippocampal changes on MRI versus o% not status
- Half of those had permanent changes with either hippocampal sclerosis or volume loss a year later

FEBSTAT (Lewis DV et al. Ann Neurology 2014)



HUMAN EVIDENCE FOR EARLY TREATMENT

April 2018

Association of Time to Treatment With Short-term Outcomes for Pediatric Patients With Refractory Convulsive Status Epilepticus

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JAMA Neurol. 2018;75(4):410-418. doi:10.1001/jamaneurol.2017.4382

- 218 patients
- Timely (< 10 mins.) in only 34%
- Untimely:
 - Longer duration of SE
 - More likely to require continuous infusion
 - More like to have hypotension
 - More likely to die

STEPWISE APPROACH

- Benzodiazepines*
- Second-line agent
- Another second-line agent OR aggressive induction of coma



BENZODIAZEPINES FOR SE

- Midazolam (Versed)
- Diazepam (Valium)
- Lorazepam (Ativan)
- Clonazepam (Europe)



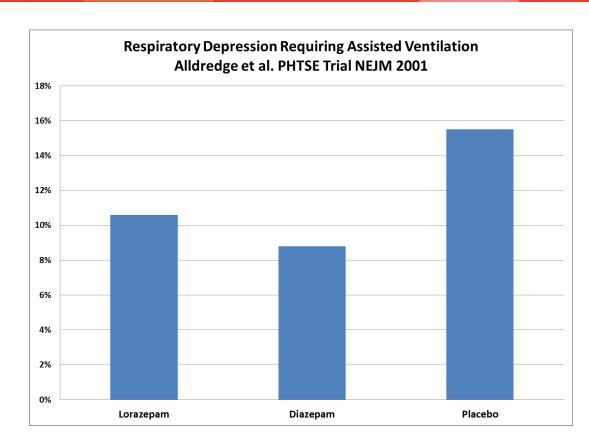
THREE IMPORTANT STUDIES

- PHTSE
- RAMPART
- PECARN



PHTSE

- 205 adult patients
- Prehospital
- LOR vs. DIA vs. placebo
- 2nd dose allowed
- Outcome: SE on ED arrival





RAMPART

- 893 adults and children
- Prehospital
- IM MID vs. IV LOR
- IM route faster

- $\begin{array}{c} H_3C \\ N \\ N \\ CI \\ PH > 4.0 \end{array}$
- IM route more effective (73% vs. 63%)
- Pediatric subgroup analysis (n = 120): (68% vs. 72%)

Silbergleit R et al. NEJM 2014 Welch RD et al. Epilpesia 2015



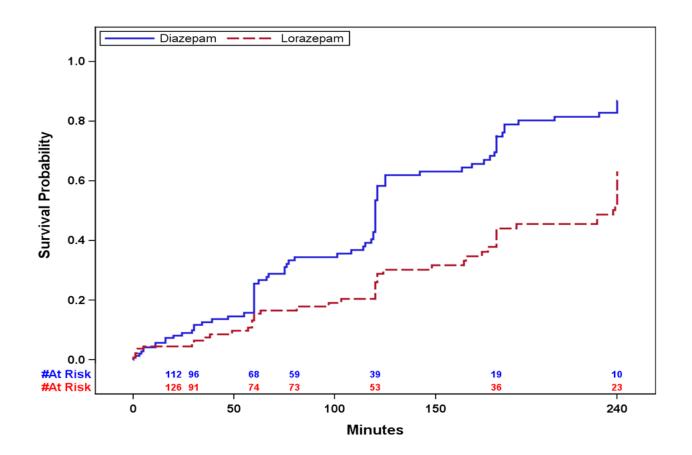
PECARN SEIZURE STUDY

- 273 children
- IV DIA vs. IV LOR

- Success equal (72%)
- Need for assisted ventilation 15% versus 16%)
- LOR more likely to be deeply sedated
- LOR had longer sedation



PECARN SEIZURE STUDY: RETURN TO BASELINE





BENZODIAZEPINES FOR SE

- Effectiveness ~70% in children
- Assisted ventilation in ~15%

- MID can be given IM, IN, buccal
- LOR causes 4-6 hours of sedation



ONGOING RESEARCH

ESETT: Established Status Epilepticus Treatment Trial

- Established = has failed benzos
- Adults and children
- Treatment
 - fos-Phenytoin
 - Leviteracetam
 - Valproate



2018 Advances in Pediatric Emergency Medicine Event ID # 35029

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