STATUS EPILEPTICUS IN CHILDREN

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February 20th, 2019

Disclosure Statement

- I have no financial or personal relationships with commercial entities to disclose

Objectives

- Identify important information for evaluating a child presenting with status epilepticus
- Understand treatment principles for management of status epilepticus and differences in in-hospital versus home management
- Use various tools when providing education to patients and families regarding home seizure rescue therapy

Background Information

Pathophysiology

- Excessive synchronous abnormal electrical activity of neurons
- Excitatory neurotransmission exceeds inhibitory neurotransmission

Pediatrics In Review. 2013; 34(8): 333-342.
Image: http://ohio365.marshfieldclinic.org/wellness/recognize-and-respond-to-seizures/

Describing Seizures

- Focal
- Myoclonic
- Tonic
- Clonic
- Tonic-clonic
- Atonic
- Epileptic spasms
- Primary generalized
- Absence

Etiology of Seizures

- Infection
- CNS Infection
- Metabolic disturbance/disorder
- Sub-therapeutic AED concentrations
- Alcohol
- Idiopathic
- Toxin ingestion
- Anoxia/hypoxia
- CNS tumor
- CVA
- Trauma

Status Epilepticus

- Seizure > 5 minutes
- Recurrent seizures between which patient does not return to baseline
- Mechanisms to return brain to homeostasis fail
- Refractory Status Epilepticus
  - Persist after a benzodiazepine and a second anti-seizure medication
- Significant morbidity and mortality

Epilepsy Currents. 2016; 16(1): 48-61.

Initial Evaluation

- Laboratory parameters
  - Blood glucose
  - CBC
  - CMP, Magnesium
  - Seizure medication concentrations (if applicable)
  - Urine drug screen
- Imaging
- Lumbar Puncture
- EEG
- Other

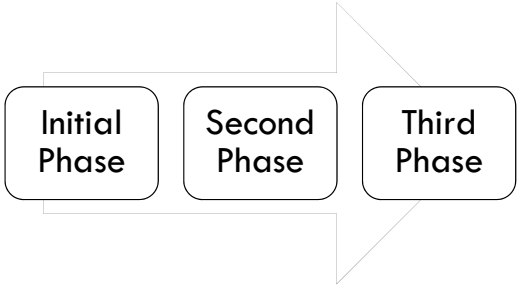
Curr Treat Options Neurol. 2014; 16: 301.; Epilepsy Currents. 2016; 16(1): 48-61.

MEDICATION MANAGEMENT

Goals of Therapy

- #1: Terminate seizure
- #2: Minimize adverse effects from treatment
- #3: Prevent recurrence of seizure activity

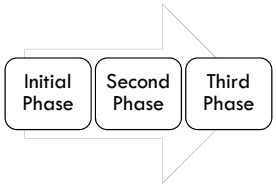
Medication Management



Curr Treat Options Neurol. 2014; 16: 301.

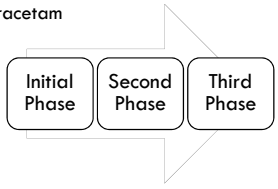
Initial Phase

- Benzodiazepines
  - Lorazepam (IV)
  - Midazolam (IM, IN, Buccal)
  - Diazepam (PR, IV)



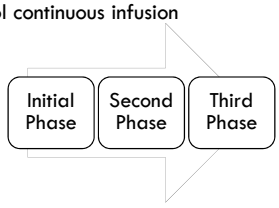
Second Phase

- Anti-epileptic medications
  - Phenytoin/Fosphenytoin
  - Phenobarbital
  - Valproic Acid
  - Levetiracetam



Third Phase

- Repeat urgent therapies or utilize another agent
- Midazolam continuous infusion
- Pentobarbital continuous infusion
- Propofol continuous infusion



First Phase

Benzodiazepines

Mechanism of Action	- Potentiates GABA receptors
General Dosing	- Lorazepam IV: 0.1 mg/kg (maximum 4 mg) - Midazolam IN: 0.2 mg/kg (maximum 10 mg) - Diazepam PR: varies based on age

PK/PD	- Onset of action
	  - Lorazepam IV: within 10 minutes
	  - Midazolam IN: ~5 minutes
	  - Diazepam PR: 2-10 minutes

Monitoring	- Hypotension - Respiratory Depression - Confusion/Somnolence
Other	- IV Lorazepam contains propylene glycol - IV Lorazepam is drug of choice if IV access - Diazepam may have a shorter duration of action

Lexicomp Online

Second Phase

Fosphenytoin/Phenytoin

Mechanism of Action	- Na channel stabilizer
General Dosing	- Initial: 20 mg/kg phenytoin equivalents IV - Maximum infusion rates differ
PK/PD	- Phenytoin interacts with tube feeds - Fosphenytoin is converted to phenytoin rapidly by plasma esterases - Many drug interactions
Monitoring	- Hypotension - Arrhythmias - Purple glove syndrome - Nystagmus, dizziness, ataxia - Therapeutic free phenytoin concentration: 1-2.5 mcg/mL
Other	- Phenytoin contains propylene glycol

Lexicomp Online

Phenobarbital

Mechanism of Action	- Potentiation of synaptic inhibition by GABA
General Dosing	- Initial: 20 mg/kg IV - Additional doses may be given after load if control not obtained
PK/PD	- Available PO and IV - Many drug interactions
Monitoring	- Hypotension - Respiratory depression - CNS depression or excitability - Thrombocytopenia - Ataxia - Therapeutic concentration 20-40 mcg/mL
Other	- Contains propylene glycol - C-IV

Lexicomp Online ; Curr Treat Options Neurol. 2014; 16: 301

Valproic Acid

Mechanism of Action	- Potentiates post-synaptic GABA receptors - Sodium and calcium channel stabilizer
General Dosing	- Initial: 20-40 mg/kg IV
PK/PD	- Available PO and IV
Monitoring	- Hepatotoxicity - Pancreatitis - Thrombocytopenia - Hyperammonemia - Alopecia - Therapeutic concentration: 50-100 mcg/mL
Other	- Platelet dysfunction

Lexicomp Online ; Curr Treat Options Neurol. 2014; 16: 301

Levetiracetam

Mechanism of Action	- Exact mechanism is unknown - Theories: inhibition of calcium channels, facilitation of GABA inhibitory transmission, reduction of potassium current, binding to synaptic proteins altering neurotransmitter release
General Dosing	- Initial: 20-60 mg/kg IV
PK/PD	- Available IV and PO - Not metabolized by the liver - Minimal drug interactions
Monitoring	- Sedation - Mood changes/alterations in behavior

Lexicomp Online, Curr Treat Options Neurol. 2014; 16: 301

Chronic Management

Long Term Medications

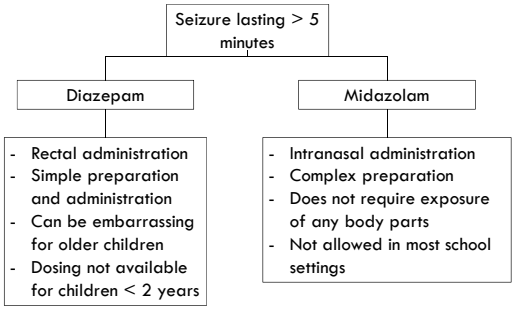
- Carbamazepine (Tegretol®)
- Clobazam (Onfi®)
- Ethosuximide (Zarontin ®)
- Ezogabine
- Felbamate (Felbatol ®)
- Gabapentin (Gralise ®)
- Lacosamide (Vimpat®)
- Lamotrigine (Lamictal®)
- Levetiracetam (Keppra®)

Long Term Medications

- Oxcarbazepine (Trileptal®)
- Perampanel (Fycompa ®)
- Phenobarbital
- Phenytoin (Dilantin®)
- Pregabalin (Lyrica ®)
- Rufinamide (Banzel ®)
- Tiagabine (Gabitril ®)
- Topiramiate (Topamax®)
- Valproic Acid (Depakote®)
- Vigabatrin (Sabril®)
- Zonisamide (Zonegran®)

HOME MANAGEMENT

Home Management



TIME TO PRACTICE…

Rectal Diazepam

Intranasal Midazolam

Available Resources

www.diastat.com

https://www.teleflex.com/usa/product-areas/ems/intranasal-drug-delivery/mad-nasal-atomization-device/AN_ATM_MAD-Nasal-Usage_Guide_AI_2012-1528.pdf

https://kidshealth.org/

QUESTIONS?

Image: http://fit50.files.wordpress.com/2010/08/question-mark-image-7-1-102.jpg

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ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD)

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Objectives

- Identify symptoms required for the diagnosis of ADHD
- Recognize medications used for the treatment of ADHD and common adverse effects
- Identify those at increased risk for cardiovascular events when prescribing stimulants
- Use various tools when providing education to patients and families regarding ADHD

Background Information

Through the years

- **DSM-I**
  - No information
- **DSM-II**
  - Hyperkinetic Reaction of Childhood
- **DSM-III**
  - Attention Deficit Disorder, with or without hyperactivity
  - DSM-III-R eliminated ADD without hyperactivity
- **DSM-IV**
  - Attention Deficit/Hyperactivity Disorder (ADHD)
  - 3 subtypes: predominately inattentive, predominately hyperactive-impulsive, combined
- **DSM-V**
  - Slight changes in diagnosis and wording

Neuropsychiatry. 2012; 2(5): 455-458

Epidemiology

- Most common neurobehavioral disorder in childhood
- ~7-10% of children
- Many will remain symptomatic into adulthood
- Often have comorbid conditions
  - Oppositional defiant disorder
  - Conduct disorders
  - Smoking/substance abuse disorders
  - Learning/language problems
  - Mood disorders

J Am Acad Child Adolesc Psychiatry. 2007; 46(7): 894-921.
Image: https://sciencebasedmedicine.org/another-adhd-denier/

Diagnostic Criteria: Symptoms

Inattention

- Lack attention to detail/make careless mistakes
- Difficulty staying focused in tasks or play
- Seems to not listen when spoken to
- Does not follow through on instructions and may fail to finish tasks
- Difficulty organizing tasks and activities
- Avoids or does not enjoy tasks that require continuous attention
- Loses things
- Easily distracted
- Forgetful in day to day activities

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.).

Diagnostic Criteria: Symptoms

Hyperactivity and Impulsivity

- Fidgets, taps hands, squirms
- Stands up when expected to remain seated
- Runs or climbs when it is not appropriate
- Unable to play quietly
- "on the go"
- Talks excessively
- Interrupts or states answer before question is asked
- Cannot wait turn
- Interrupts others or infringes on others

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.).

Diagnostic Criteria

- 6 or more symptoms PLUS
- Symptoms prior to age 12
- Symptoms in more than one setting
- Symptoms effect social, academic, or occupational functioning
- Symptoms are not a result of another illness

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.).
Image: https://www.pediatricsoffranklin.com/tag/adhd-franklin/

Treatment

Treatment of ADHD

Nonpharmacologic

- Psychoeducation
- Parent administered behavioral therapy
- Teacher administered behavioral therapy
- Cognitive behavioral therapy

Pharmacologic

- Stimulants
  - Methylphenidate
  - Amphetamine
- Non-stimulants
  - Atomoxetine
  - Guanfacine
  - Clonidine
  - Bupropion
  - Tricyclic antidepressant

J Am Acad Child Adolesc Psychiatry. 2007; 46(7): 894-921.
Pediatrics. 2011; 128 (5): 1007-1022

Available Guidelines

	AACAP (2007)	AAP (2011)
Step 1	Stimulant Atomoxetine in certain circumstances	Age 4-5 years: parent and/or teacher administered behavioral therapy
		Age 6-11 years: stimulant and/or parent and/or teacher administered behavioral therapy
		Age 12-18 years: Medication, may prescribe behavioral therapy
Step 2	Atomoxetine	Age 4-5 years: methylphenidate
		Age 6-18 years: atomoxetine, guanfacine, clonidine
Step 3	Review Diagnosis	
Step 4	Bupropion, TCAs, clonidine	

J Am Acad Child Adolesc Psychiatry. 2007; 46(7): 894-921.
Pediatrics. 2011; 128 (5): 1007-1022

Stimulant Medications

Methylphenidate: Short Acting

Brand Name	Dosage forms	Onset of Action	Duration of Action
Focalin	Tablet: 2.5 mg, 5 mg, 10 mg	Rapid, within 1-2 hours	3-5 hours
Ritalin	Tablet: 5 mg, 10 mg, 20 mg	20-60 minutes	3-5 hours
Methylin	Solution: 5 mg/5 mL; 10 mg/5 mL; Tablets: 2.5 mg, 5 mg, 10 mg	20-60 minutes	3-5 hours

Lexicomp Online
Pediatrics. 2015; 136(2): 351-359

Methylphenidate: Long Acting

Brand Name	Dosage forms	Onset of Action	Duration of Action	Notes
Focalin XR	Capsules: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg	Within 1-2 hours	9-12 hours	Capsule can be opened
Concerta	Tablets; 18 mg, 27 mg, 36 mg, 54 mg	20-60 minutes	8-12 hours	Must be swallowed whole
Ritalin LA	Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 60 mg	20-60 minutes	6-8 hours	Capsule can be opened
Metadate CD	Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg	20-60 minutes	6-8 hours	Capsule can be opened

Lexicomp Online
Pediatrics. 2015; 136(2): 351-359

Methylphenidate: Long Acting

Brand Name	Dosage forms	Onset of Action	Duration of Action	Notes
Cotempla XR-ODT	ODT: 8.6 mg, 17.3 mg, 25.9 mg	-	-	
Daytrana	Patch: 10 mg/9hr; 15 mg/9hr, 20 mg/9hr, 30 mg/9hr	60 minutes	11-12 hours	
Quillivant XR	Suspension: 25 mg/5mL	-	-	
Aptensio XR	Capsule: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg	-	</= 16 hours	Capsule can be opened

Lexicomp Online
Pediatrics. 2015; 136(2): 351-359

Amphetamines: Short Acting

Brand Name	Dosage forms	Time to Peak	Duration of Action
Adderall	Tablet: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 30 mg	3 hours	4-6 hours
Zenzedi	Tablet: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg	~3 hours	4-6 hours
Procentra	Solution: 5 mg/5 mL	~3 hours	4-6 hours

Lexicomp Online
Pediatrics. 2015; 136(2): 351-359

Amphetamines: Long Acting

Brand Name	Dosage forms	Time to Peak	Duration of Action	Notes
Vyvanse	Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg Tablet (chewable): 10 mg, 20 mg , 30 mg, 40 mg, 50 mg, 60 mg	1 hour	8-14 hours	Prodrug; capsule may be opened and dissolved
Adderall XR	Capsules: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg	7 hours	8-12 hours	Capsule may be opened
Dexedrine	Capsules: 5 mg, 10 mg, 15 mg	3.5 hours	8 hours	

Lexicomp Online
Pediatrics. 2015; 136(2): 351-359

Non-stimulant Medications

Non-Stimulant Medications

Generic Name	Brand name	Dosage forms	Notes
Guanfacine	Intuniv	Tablet (IR): 1 mg, 2 mg Tablet (ER): 1 mg, 2 mg, 3 mg, 4 mg	May be taken at bedtime to reduce somnolence
Clonidine	Kapvay	Tablet: 0.1 mg	
Atomoxetine	Straterra	Capsules: 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg	Must swallow whole BBW: suicidal ideation in children and adolescents

Lexicomp Online
Pediatrics. 2015; 136(2): 351-359

Monitoring

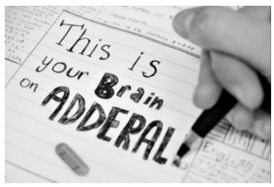
Common Adverse Effects: Non stimulants

- GI upset
- Somnolence
- Decreased appetite
- Headaches
- Blood pressure/heart rate changes
- Liver toxicity (atomoxetine)
- Suicidal Ideation (atomoxetine)
- Priapism (atomoxetine)

J Am Acad Child Adolesc Psychiatry. 2007; 46(7): 894-921.
Pediatrics. 2011; 128(5): 1007-1022

Common Adverse Effects: Stimulants

- Appetite decrease
- Abdominal pain
- Weight loss
- Sleep issues
- Headaches
- Emotional lability
- Psychotic symptoms
- Priapism
- Cardiovascular issues



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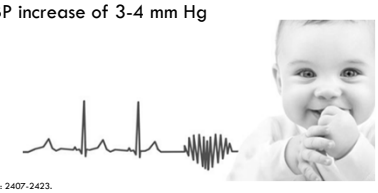
Pediatrics. 2011; 128 (5): 1007-1022.
Image: https://www.mentalfitton.com/why-adderall-might-be-the-most-dangerous-drug-on-earth/

Cardiovascular Monitoring

- ADHD may be more prevalent in those with existing heart disease
- Stimulants typically result in:
  - HR increase of 1-2 bpm
  - BP increase of 3-4 mm Hg



Circulation. 2008; 117: 2407-2423.
Image: http://commonwealthmedicalcurriculum.com/courses/approach-to-a-pediatric-heart-disease/

Before beginning therapy

- Prior to initiation of a stimulant:
  - Thorough evaluation of history to identify risk factors
    - Patient history
    - Family history
    - Physical examination
    - ECG at baseline is reasonable
- If risk factors identified, referral to cardiologist is warranted

Circulation. 2008; 117: 2407-2423.

After starting therapy

- Carful monitoring is warranted for the following:
  - Any patient with a heart condition associated with sudden cardiac death (SCD)
  - History of arrhythmia requiring resuscitation, cardioversion, defibrillation, or pacing
  - History of arrhythmia associated with SCD
  - Previously aborted SCD
  - Other clinically significant arrhythmia not controlled
  - QTc > 460
  - HR or BP > 2 SD above mean for age

Circulation. 2008; 117: 2407-2423

Available Resources

https://www.cdc.gov/

https://kidshealth.org/

American Academy of Pediatrics

American Heart Association

American Academy of Child and Adolescent Psychiatry

QUESTIONS?

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