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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

STIMULANTS IN EPILEPSY

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Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

GENERAL DISCLOSURES

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SPEAKER DISCLOSURES

- ✓ No conflicts of interest

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PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose:

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OBJECTIVES

1. Become familiar with the overlap between epilepsy and ADHD
2. Learn the risks and benefits associated with stimulant medications in individuals with ADHD and epilepsy

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UW PACC REGISTRATION

Please be sure that you have completed the full UW PACC series registration.

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CASE STUDY

- 10-year-old child with a 5-year history of severe hyperactivity and inattention.
- His medical history is significant for epilepsy since 8 years of age, with six tonic-clonic seizures in the past 2 years.
- The seizures are well controlled with carbamazepine, with only one seizure in the past 6 months.
- On assessment, he meets criteria for attention-deficit/hyperactivity disorder (ADHD), combined subtype, and oppositional defiant disorder.
- How would you address this case?

Gonzalez-Heydrich et al. 2006

HOW WOULD YOU APPROACH THIS CASE?

A) start methylphenidate, monitor for increased rate of seizures

B) start atomoxetine

C) refer for behavioral therapy to target ADHD

D) defer treatment to neurologist

E) discuss changing anti-epileptic medication with neurologist to rule out medication adverse effect

ADHD TREATMENT

- Children under 6 -> behavioral interventions are first line
- Children and adolescents over 6 meeting certain criteria* -> medications are first line, and stimulants are first line meds

Uptodate - Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis

Criteria for initiation of pharmacotherapy in children with ADHD

Diagnostic assessment is complete and confirms diagnosis of ADHD
Child is age six years or older*
Parents accept medication as a contribution to management
School will cooperate in administration and monitoring ¶
No previous sensitivity to the chosen medication
Child has normal heart rate and blood pressure
Child is seizure free Δ
Child does not have Tourette syndrome Δ
Child does not have pervasive developmental delay Δ
Child does not have significant anxiety
Substance abuse among household members is not a concern (for children who will be treated with immediate-release stimulants) ◇

ADHD: attention deficit hyperactivity disorder.

* Children younger than six years should be managed by or in consultation with a specialist since the effects of stimulants on preschool children are unpredictable.

¶ It is not safe to permit the child or adolescent to take his or her own medication to school.

Δ Children with these conditions should be managed by, or in consultation with, a specialist.

Uptodate - Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis

EPILEPSY AND ADHD OVERLAP - EPIDEMIOLOGY

- There is a **bidirectional association** between epilepsy and ADHD
  - ADHD is 2.54 times more common in children with epilepsy
  - Epilepsy is 3.94 times more common in children with ADHD
- ~1/3 of children/adolescents with epilepsy have ADHD
- Inattentive type ADHD is more prevalent in patients with epilepsy.

Auvin et al, 2013

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INCREASED CO-OCCURRENCE IS MULTIFACTORIAL

- Common brain pathology - genetic and environmental contributors
- Direct seizure effect
- Non-convulsive epileptiform discharges
- Medication effects

MORE ON ANTI-EPILEPTIC MEDICATION EFFECTS

- Many AEDs can have impact on attention: Any AED at toxic doses; Phenobarbital, Primidone, Benzodiazepines, Vigabatrine, Topiramate, Levetiracetam, Zonisamide
- Valproate worsens attention in children with absence seizures
- Polytherapy worse for behavior than monotherapy
- Drug-drug interactions

ADHD is often underdiagnosed and undertreated in individuals with epilepsy due to complexity of diagnosis and concerns about medication risks

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STIMULANTS AND SEIZURE RISK

- Well-documented increased risk of seizure with recreational stimulant use
- -> theoretical increased risk of seizures in individuals with epilepsy
- FDA package inserts for stimulants describing a risk of provoking seizures, although a literature review only yields support from an animal study, case reports, and a study of seizures after methylphenidate overdose.
- Mixed data about risk of seizure exacerbation in real life

105 PTS W/ EPILEPSY TREATED WITH METHYLPHENIDATE

- 21 (20%) subjects had aggravated seizures and 32 (32.3%) subjects had worsened EEG findings after treatment
- **Risk factors for aggravated seizures**: uncontrolled seizure or anxiety disorders at baseline
- **Risk factors for worsened EEG:** epileptiform discharges, anxiety disorders, not on AEDs
- Methylphenidate effective regardless of seizure aggravation

- **Limitations: NO CONTROL GROUP**

Park et al, 2018

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167 YOUTH WITH EPILEPSY AND ADHD

- 61 started methylphenidate, 106 started no ADHD meds
- Not randomized, not blinded
- Methylphenidate improved ADHD symptoms in 75% of patients (compared to 42% improved w/o meds)
- Methylphenidate not significantly associated with seizure relapse or worsening (12.5% of treatment group vs 3.4% of non-treatment group, not statistically significant)

Rheims et al 2016

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CONSENSUS GUIDELINES - ILAE

- International League Against Epilepsy 2018 guidelines
- Majority of data are on Methylphenidate: 7 studies suggest no seizure exacerbation; level B evidence supports tolerability and efficacy in this population
- One study of adults comparing response to methylphenidate versus amphetamines found greater efficacy in the methylphenidate group (not an RCT)
- “Methylphenidate is tolerated and effective in children with epilepsy and comorbid ADHD”

Auvin et al, 2018

CONSENSUS GUIDELINES - ILAE

- Amphetamines: insufficient data to support use in this population (safety, tolerability or efficacy)
- Atomoxetine: level C evidence for safety and tolerability in this population, insufficient evidence for effectiveness
- Clonidine: no studies in children with epilepsy

Auvin et al, 2018

BRIEF FORAY INTO THE ADULT WORLD

- Limited data about prevalence of ADHD in adults with epilepsy – one small study estimated ~20 percent
- Limited data about treatment in this population
- One small study showed effectiveness of methylphenidate for cognition in adults with epilepsy without increased risk of seizures; randomized initially then open label

Adams et al. 2017

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CONCLUSIONS

- High co-morbidity between ADHD and epilepsy
- Despite lack of high quality RCTs, consensus that methylphenidate is effective and safe in children (and likely adults) with epilepsy
- Very limited or missing evidence for other treatments
- Treatment seems to be effective even with poor seizure control

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ANY CHANGES IN HOW YOU APPROACH THIS CASE?

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