

PSYCHOPHARMACOLOGICAL TREATMENT OF CHILDREN WITH EPILEPSY AND COMORBID PSYCHIATRIC DISORDERS

S, Mohammadzadeh, MD
Child and Adolescent Psychiatrist
Kurdistan University of Medical Sciences



دانشگاه علوم پزشکی
و خدمات بهداشتی درمانی کردستان



انجمن روانپزشکی کودک و نوجوان ایران
Iranian Academy of
Child & Adolescent Psychiatry

the 11th

یازدهمین همایش سراسری روانپزشکی کودک و نوجوان
National Congress of Child and Adolescent Psychiatry
27,28-Jan & 3,4-Feb 2022

۱۴۰۰ بهمن ۱۵ و ۱۴ و ۸ و ۷

دارای امتیاز باز آموزشی

www.iacap.ir

انجمن روانپزشکی کودک و نوجوان ایران

وبینار
WEBINAR

- Incidence of neurobehavioral disorders is higher in patients with epilepsy than in the general population.
 - temporal lobe
 - complex partial epilepsy



PSYCHIATRIC DISORDERS IN CHILDREN WITH EPILEPSY

PSYCHIATRIC DISORDERS	CHILDREN WITH EPILEPSY	Controls
ADHD	23%	6%
Conduct Problems	16%	3%
Anxiety	17%	3%
Depression	8%	2%
Developmental Delays	51%	3%
Intellectual Disability	20-40%	1%
Autistic Spectrum Disorder	5-46%	0.5-1%



Attention-Deficit/Hyperactivity Disorder

- The prevalence of ADHD in children in the general population is 5%–7%, whereas in children with epilepsy it is 20%–40%.
- Inattention is more common than hyperactivity and impulsivity as a form of ADHD symptom in children with epilepsy.

- Dunn DW, Kronenberger WG. Childhood epilepsy, attention problems, and ADHD: Review and practical considerations. *Semin Pediatr Neurol* 2005;12:222-8. 8.
- Kaufmann R, Goldberg-Stern H, Shuper A. Attention-deficit disorders and epilepsy in childhood: Incidence, causative relations and treatment possibilities. *J Child Neurol* 2009;24:727-33. 9.
- Hesdorffer DC, Ludvigsson P, Olafsson E, Gudmundsson G, Kjartansson O, Hauser WA. ADHD as a risk factor for incident unprovoked seizures and epilepsy in children. *Arch Gen Psychiatry* 2004;61:731-6.



TREATMENT

- Some studies have shown that **methylphenidate and atomoxetine** use in children with ADHD without a history of epileptic seizure is safe.

- Kerdar MS, Scheuerpflug P, Srdinko P, Wewetzer C, Warnke A, Romanos M. [Quantitative effect of treatment with methylphenidate on EEG: A pilot study] [German]. Z Kinder Jugendpsychiatr Psychother 2007;35:247-55.
- Wernicke JF, Holdridge KC, Jin L, Edison T, Zhang S, Bangs ME, et al. Seizure risk in patients with attention-deficit-hyperactivity disorder treated with atomoxetine. Dev Med Child Neurol 2007;49:498-502.



- **Methylphenidate** can cause aggravate seizures in patients with ADHD, although generally it is considered safe in those who are seizure free.

- Stimulants for youth with epilepsy should be closely watched by a child psychiatrist.
- If the number of seizures increases in **the three months** after the medication is started, other treatments should be considered for ADHD in these children.
- **Atomoxetine** seizure risk unclear. Use judiciously



- In cases where epilepsy and ADHD are comorbid, **carbamazepine** and **lamotrigine** may be more beneficial compared with other antiepileptics in that apart from the control of epileptic seizure they have better effects on attention and behavior.



Autistic Spectrum Disorder

- According to the literature data, epilepsy is more common among individuals **with autistic spectrum disorder (ASD) (5–46%)** compared to the general population (0.5–1%) .

- Spence, S.J.; Schneider, M.T. The role of epilepsy and epileptiform EEGs in autism spectrum disorders. *Pediatr. Res.* 2009, 65, 599–606. [CrossRef] [PubMed] 3. Tuchman, R.; Rapin, I. Epilepsy in autism. *Lancet Neurol.* 2002, 1, 352–358. [CrossRef] 4. Amiet, C.; Gourfinkel-An, I.; Bouzamondo, A.; Tordjman, S.; Baulac, M.; Lechat, P.; Mottron, L.; Cohen, D. Epilepsy in autism is associated with intellectual disability and gender: Evidence from a meta-analysis. *Biol. Psychiatry* 2008, 64, 577–582. [CrossRef] [PubMed]



Table 1. Type of seizures in patients with ASD and epilepsy.

Type of Seizures	N = 26	%
Focal with or without secondary generalization	14	53.4
Generalized tonic-clonic	5	19.2
Absences	2	7.7
Polymorphic seizures	4	15.4
Preceding infantile spasms	3	11.5

Treatment

- **Risperidone**
- **Aripiprazole**
 - drugs approved by the FDA for children with autism spectrum disorder.
 - It can be prescribed for children between 5 and 16 years old to help with irritability.
- **First generation antipsychotic:**
 - chlorpromazine NO
 - Use judiciously
 - Haloperidol low risk

Psychotic Disorders

- There are no epidemiologic studies examining the comorbidity of psychosis and epilepsy in children.
- **Vuilleumier and Jallon found that 2-9% of patients with epilepsy have psychotic disorders.**



Factors in the development of psychosis

- **Family history of psychosis** - Patients who had a positive family history of psychosis were extremely susceptible to psychosis, so a genetic factor appears to be involved
- **Age at onset of epilepsy** - Patients with interictal psychosis showed a significantly earlier onset of epilepsy.
- **Type of seizure** - The existence of complex partial seizure (mostly temporal lobe epilepsy) may be strongly associated with interictal psychoses.
- **Intelligence** - Patients with **borderline intellectual functioning** tend to develop psychotic symptoms relatively frequently.



Treatment

- Status epilepticus and ictal abnormalities are treated in the same way as nonpsychiatric epileptic events.
- **Interictal psychosis** is treated with antipsychotic drugs.
- Medications that lower the seizure threshold should be avoided.



- Some studies indicate that risperidone, molindone, and fluphenazine may have better profiles than older antipsychotic medications;
- clozapine has been reported to confer a particularly high risk of seizures.



Bipolar Affective Disorders

- Bipolar symptoms were 1.6-2.2 times more common in subjects with epilepsy than with migraine, asthma, or diabetes mellitus
- depression (8% vs. 2% in children never diagnosed with epilepsy),



Treatment

- **Lithium:**

- Use judiciously. Considered proconvulsant

- **Benzodiazepines:**

- Anticonvulsant
- but proconvulsant if suddenly discontinued.

Risk factors for the development of depression in patients with epilepsy include :

Temporal lobe (but not frontal lobe) seizures

partial complex seizures

Family history of psychiatric illness, particularly depression



Depression in epilepsy may also result from iatrogenic causes (pharmacologic and surgical).

Phenobarbital

Primidone

Vigabatrin

Levetiracetam

Felbamate

Topiramate



Depressive disorder can also occur following the discontinuation of AEDs

Carbamazepine

Oxcarbazepine

Valproic acid

lamotrigine



Treatment (Mood disorders in patients with epilepsy)

reevaluation of the anticonvulsant regimen

use of antidepressants,

psychotherapy

- **First and foremost**, treatment involves seizure control with appropriate anticonvulsant therapies.
- There is evidence that some anticonvulsant therapies, including **vagus nerve stimulation, valproate, gabapentin, carbamazepine, and lamotrigine**, also have antidepressant effects and may prove effective in treating depression in patients with epilepsy.



Antidepressants

- When an antidepressant is prescribed, the **epileptogenic potential, adverse effects, and drug interactions** must be evaluated.
- Selective serotonin reuptake inhibitors (SSRIs) such as citalopram (owing to its lack of drug interactions)
- multireceptor-active compounds such as nefazodone or venlafaxine
 - are suggested as first-line treatments.
 - doxepin, trazodone, and fluvoxamine appear to have the lowest risk



MAOI

Bupropion

Amoxapine

Maprotiline

Clomipramine



Electroconvulsive therapy

- Is not contraindicated
- May prove effective for epilepsy patients with MDD:
 - severe
 - treatment-resistant
 - psychotic depression



Suicidal Behaviors

- **Suicidality** (completed suicide, suicide attempt, and suicidal ideation) is significantly more frequent among people with epilepsy than in the general population.
- The risk of suicide in the **general population** averages **about 1.4%**.
- The risk of suicide in **depressed patients** is believed to be **around 15%**.
- On average, the risk of suicide in **patients with epilepsy** is **about 13%** (prevalence rate ranges from **5-10 times** that of the general population).
- Risk of suicide in patients with **temporal lobe epilepsy** is increased to much as **25-fold** that of the general population.

- In the study, suicidality occurred in **4.3 of 1,000 patients treated with AEDs** in the active arm, compared **with 2.2 of 1,000 patients** in the comparison arm.
- **The FDA** has decided to insert **suicide warnings** in the package inserts of all AEDs; thus, physicians need to identify patients with increased risk of suicide.



Anxiety Disorders

- Anxiety is common in patients with epilepsy;
- Anxiety in patients with epilepsy can be ictal, postictal, or interictal.



Treatment

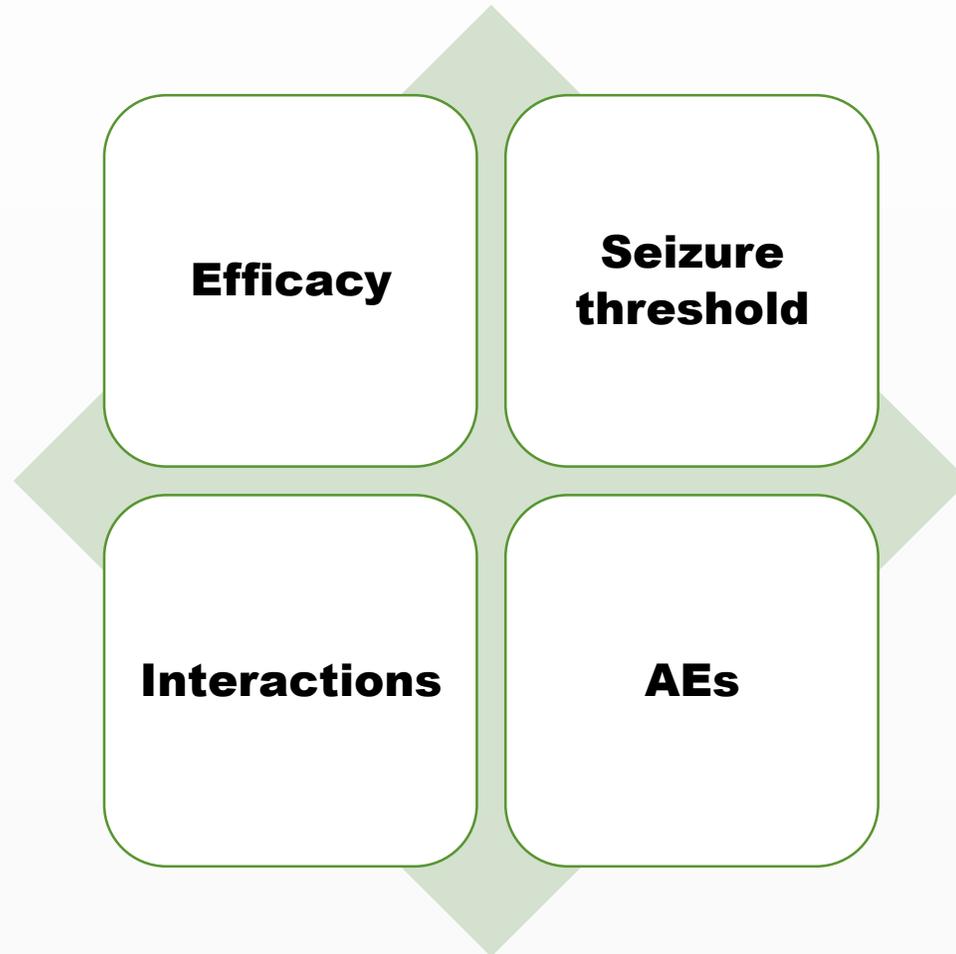
- Several studies have shown that **pregabalin**, used as an adjunct for partial seizures, has been an effective, rapidly active, and safe treatment for **generalized anxiety disorder**.
- **SSRIS/SNRIS:**
 - Seizure low risk
 - Fluoxetine and Fluvoxamine may Increase Carbamazepine level

OCD

**Clomipramine
Avoid**



When the time comes to choose a psychopharmacological agent, four considerations should be borne in mind:



RECOMMENDATIONS FOR COMMONLY USED PSYCHOTROPICS IN THE CHILD WITH A SEIZURE DISORDER

Medication or Class	Recommendations (Low Seizure Risk ≠ Absent Risk)	Key Drug–Drug Interactions with AEDs
First-generation antipsychotics	Use not advised for chlorpromazine and loxapine Use others judiciously Haloperidol has lowest risk	Carbamazepine, phenobarbital, phenytoin, and perhaps oxcarbazepine may reduce levels through cytochrome P450 3A4 induction
Second-generation antipsychotics	Use not advised for clozapine Seizure risk low for others	Risperidone, quetiapine, aripiprazole, and ziprasidone may be reduced by above AEDs through 3A4
SSRIs/SNRIs	Seizure risk low Venlafaxine may have increased risk over others	Fluoxetine and fluvoxamine may increase carbamazepine levels through 3A4 inhibition
Trazodone	Seizure risk low	Substrate of 3A4; above AEDs may reduce
Alpha agonists	Seizure risk low	No known drug interactions with AEDs
Bupropion	Use not advised	Phenytoin and phenobarbital may reduce levels through 2B6 induction
Atomoxetine	Seizure risk unclear. Use judiciously	No known drug interactions with AEDs
Lithium	Use judiciously. Considered proconvulsant	Neurotoxicity with carbamazepine and phenytoin
Stimulants	FDA contraindicates when comorbid seizures are present, but data suggest they can be used judiciously	No known drug interactions with AEDs
TCAs/tetracyclic antidepressants	Use not advised for clomipramine, amoxapine, and loxapine Use others judiciously	Valproate may increase and carbamazepine may decrease TCA levels
Benzodiazepines	Anticonvulsant, but proconvulsant if suddenly discontinued	Alprazolam, diazepam, midazolam, and triazolam are substrates of 3A4



Thank you for your attention

