

Pharma

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ملخصات

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Epilepsy

Single (once) :- Called Seizure, Sudden alteration of any ~~the~~ brain function, abnormal depolarization (abnormal neuronal discharge)

Frequent :- Called epilepsy

Convulsions :- Spasmodic skeletal muscles (muscles)

Pathology

GABA :- inhibitory ↓

Glutamate, Aspartate ↑↑

NMDA

Na⁺ influx
↓
epilepsy

Seizures = epilepsy

Causes :-

Genetics الأهم

- More than 200 genes
- most important related to GABA

Acquired

- Head Trauma
- Tumors
- strokes
- infections
- Birth defect, etc....

Symptoms :- Site and Size

Site :-

- Motor Cortex :- Convulsions
- Visual Cortex :- Visual abnormalities
- Temporal Cortex :- auditory hallucination

Size :- أص

Focal :- One hemisphere

Generalized :- Both hemisphere] الأغلب

Focal + 2ry generalization → نادر

focal — { with Preserved awareness (simple)
 impaired awareness (complex)
 2ry generalization

Generalized — { Absence
 Myoclonic
 Tonic-clonic

Other :- Tonic, clonic, Atonic

- ictal → epilepsy attack

Pre-ictal Phase (aura)

ictal Phase (< 2min)

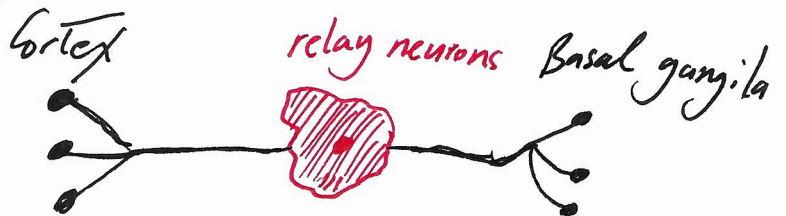
Post-ictal Phase (Drowsy)

} Generalized

(Petit mal) Absence seizure للأطفال فقط

- alternative type of epilepsy

- يغيب عن الوعي لمدة ثواني



- T-type Ca^{+2} channel :- Work before sleeping that delay for seconds also work with SA node to maintain heart rate

- any disease within these channel can lead to loss of awareness for (15-30s)

- و إذا ما قلص الطفل يحل ختمه ووجه

Tonic-clonic :- Tonic :- المرض يصير ختمه
Clonic :- يرتجف

Myoclonic :- $\leq 1s$ Contraction of Muscles (involuntary)

Status-epileptics :- More than 20 min (life-threatening)

Febrile Seizure :- only children less than 5 y.o

Anti-epileptics drugs

Classified by :- تصنيف اسي لان ملاكو علاج بيوي انفعلة :-
وهذه

- 1- increase GABA [Phenobarbital, Benzodiazepin, Vigabatrin, Tiagabine]
- 2- Block excitatory [Felbamate, Topiramate]
- 3- Block Na^+ channel [Phenytoin, Carbamazepine, Lamotrigine]
- 4- Block T-Type Ca^{+2} channel [Ethosuximide]
- 5- Mixed or unknown [Valproic acid, Levetiracetam, Gabapentin]

or by Therapeutic uses :- هم اسي :-

- 1- focal seizure [Carbamazepine, Lamotrigine]
- 2- Absence [Valproic acid, Ethosuximide, Clonazepam]
- 3- Tonic-clonic [Phenytoin, Valproic acid, Lamotrigine, Phenobarbital]
- 4- Myoclonic [Valproic acid, Lamotrigine]

By generations :-

الأدوية

1st gen :-

Phenytoin
Carbamazepine
Valproic acid
Ethosuximide
Phenobarbital
Benzodiazepine

Work on

GABA_A Na⁺ channel blocker + T-Type Ca²⁺ channel blocker

* all except excitatory

2nd gen :-

Vigabatrin
Lamotrigine
Topiramate
Levetiracetam
Gabapentin
Pregabalin
Tiagabine

* just excitatory

* في الغالب لا تسقم وجدها

Phenytoin (Diphenyl hydantoin)

Mechanism :- Block Na^+ channel (Brain and heart)

anti-arrhythmia
Class ~~1B~~ 1B

Uses :- 1- Tonic-clonic seizure
2- Class I_B anti-arrhythmia

Adverse effect - أضرار وآثار جانبية

1- CNS :- NAD (nystagmus, diplopia, ataxia)

2- Liver :- P₄₅₀ induction (activation)

3- Blood :- Megaloblastic anemia (folic acid metabolism)

4- Teratogenic :- Craniofacial anomalies (fetal hydantoin Syndrome)
↓
Neural tube defect (spina bifida)

5- Gingival hyperplasia

6- Lymphadenopathy → lymphoma-like

7- Hirsutism

8- Osteomalacia due to Vit D metabolism ↑

خاصات
بالعلاج

* important note : don't forget Zero Order elimination
Fosphenytoin : Can ~~Amuse~~ use Parentally (Water Soluble)

Carbamazepine (Tegretol) سر

Mechanism : Block Na^+ (Brain only)

Uses :- 1- 1st line in focal Seizure ممكن
2- 2nd line Tonic-clonic Seizure ممكن
3- Trigeminal neuralgia

Adverse effect : نقص الأوكسجين (cleft Palate)

5 - increase ADH Secretion → hyponatremia and edema

important notes :- induce its metabolism (autoinduction)

Valproic acid (Depakin) (البازا)

أعظم علاج بالصيغة
علا البنائين ☺

Mechanism :- 1- GABA ↑ (By inhibit GABA-T which is responsible for GABA breakdown)
2- Block Na^+ channel
3- Block Ca^{+2} channel

Uses :- all types

adverse effect :-
2- liver :- P_{450} inhibition
3- Blood :- neutropenia (WBC ↓)

5- Alopecia (Phenytoin عكس)

6- Pancreatitis

7- ~~fulminant~~ fulminant hepatic] Rare but fatal

important note :- More teratogenic

(خطر جنين)

Ethosuximide (Zarontin) :- least toxic drug

mechanism :- Block T-Type Ca^{+2} channel

Uses :- 1st line for absence seizures

Adverse effect :- لا يوجد أربع نقاط

1- GIT upset

2- Headache and dizziness

Phenobarbital :- *limited uses*

mechanism :- GABA ↑

Uses :- 1- Tonic - clonic seizures
2- Status epilepticus

Adverse effect :- *فقدان الشهية*

5- Tolerance, physical dependence
6- Respiratory depression

Diazepam :- *limited*
mechanism :- GABA ↑

Uses :-

1- 1st line for status epilepticus
2- 1st febrile convulsions
(rectal)

adverse effect :-

1- Tolerance, physical dependence
2- Memory disturbance

2nd gen

Vigabatrin :- *فانجول*

mechanism :- inhibit GABA-T $\Rightarrow$ GABA ↑

Uses :- 1- focal only

2- Infantile Spasm (West Syndrome)
Very rare and fetal

Adverse effect :- irreversible visual loss (40% patient)
Vi = Vision

important notes :- should check eye every 6 ~~months~~ months
- Used for refractory to other drugs

Lamotrigine :-

Mechanism :-

- 1- Na^+ channel blockers
- 2- glutamate release ↓

Uses :- all types of seizures even absence by unknown mechanism

Adverse effect :-

- 1- Steven-Johnson Syndrome (Rare) increase with Valproic acid Combination
- 2- insomnia ??

important notes :- - may replace Carbamazepine in focal seizures
- low teratogenic potential

Topiramate + Mechanism :- Block Na^+ channel + GABA ↑ +
Block AMPA / Kinate receptor

Uses :- 1- all types
2- Migraine Prophylaxis

Adverse effect :- 1- IOP ↑ (glaucoma)
2- Renal stones
3- Teratogenic → cleft Palate
4- Weight loss → fat metabolism ↑ → fat mass ↓

Levetiracetam (Keppra) لڤٻ

Mechanism :- inhibit SV_2A that responsible for open of Glutamate Vesicles

Uses :- all types

adverse effect :- very low

Important notes :-

- Broad spectrum
- low Toxicity
- favorable PK Profile
- No drug interaction

Gabapentin گابان

Mechanism :- inhibit of Presynaptic P/Q-Type Ca^{+2} channel
Via action on the $\alpha_2\delta$ subunit $\rightarrow Ca^{+2}$ influx $\downarrow$

Uses :-

- 1- adjuvant drugs and focal seizures $\rightarrow$ glutamate $\downarrow$
- 2- Neuropathic Pain $\rightarrow$ 99% use

<u>Seizures</u>	<u>1st line</u>	<u>2nd line</u>	<u>3rd line</u>
Focal	Carbamazepine	Lamotrigine Valproic acid	Levetiracetam
Tonic-clonic	Valproic acid	Lamotrigine Carbamazepine	Levetiracetam
Absence	Ethosuximide	Valproic acid Lamotrigine	Clonazepam
Myoclonic	Valproic acid	Lamotrigine	Levetiracetam
Pregnancy Seizure	(Levetiracetam or Lamotrigine)		

Status epilepticus :- 1st line :- (I.V Diazepam) or rectal for children

2nd line :- Fosphenytoin and Levetiracetam

الوقاية الأولية

1- AED after second attack

2- Start with one drug if fail replace it if all fail use combinations

3- Lamotrigine + Valproic acid = don't

4- > 2 y.o without attack stop drugs within 2-3 months

Pregnancy : 1-2% without drugs
3-4% with AED

- all Pregnancy Women should continue their AED "in part"
- Take folic acid with AED 5mg/day
- Best drugs :- Lamotrigine, levetiracetam
Worst :- Valproic acid
- Breast feeding acceptable with all AED