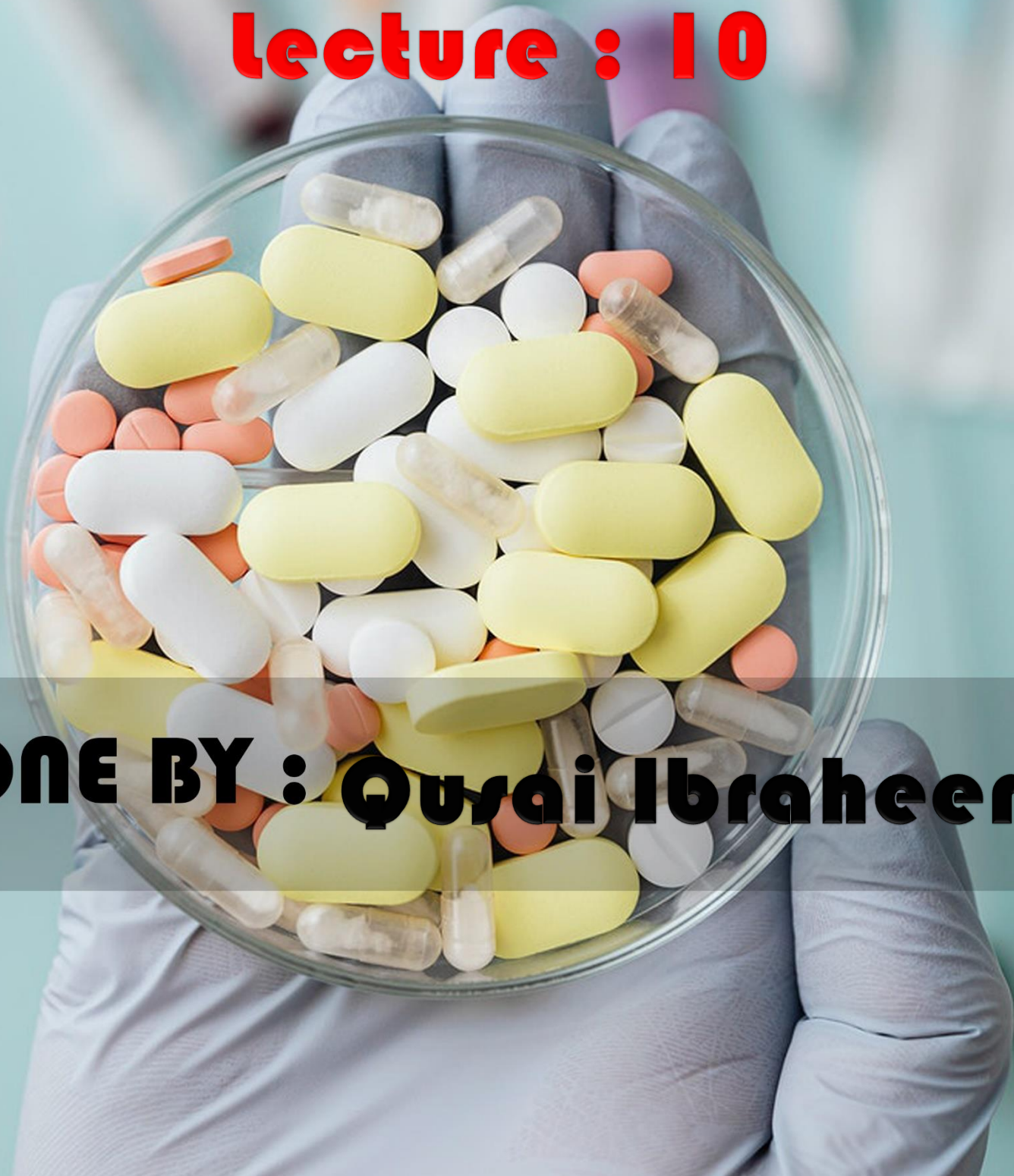




PHARMACOLOGY

Lecture : 10



DONE BY : Qusai Ibraheem

Antiepileptics

هسا هون بدنا نعرف بدنا نعرف 3 مصطلحات ونفرق بينهم

- Seizures
- Abnormal excessive neuroactivity in the brain

هسا ال seizures هو generalize term non specific بعبر عن any abnormal (increase neural firing) excessive neuroactivity

وهون بناء على وين المكان الي صار فيه abnormal activity بكون عنا symptom مثلا في

seizures in motor cortex so the clinical presentation is motor symptom and if temporal lobe so the symptom is result from affect auditory or olfactory center and if the occipital lobe affect so affect visual center so may lead to visual hallucination

so the clinical presentation depend on the site of abnormal activity and other factor

- Convulsions:
- Rapid, repeated muscle contraction and relaxation resulting from excessive neuroactivity in the brain.

هسا ال convulsion هو rapid, repeated muscle contraction followed by relaxation يعني هو involuntary result from contraction-relaxation cycle وهاي اسمها jerky movement وهاي بتكون seizure ولكن مش كل seizure هو convulsion وبالتالي ال abnormal neuroactivity in brain لانو حكينا ممكن بال seizure ياتر على ال visual او ال auditory مش شرط دايمما يؤدي ل convulsion هسا ال convulsion هي نوبة الصرع وتسمى tonic-clonic seizure

- Epilepsy:
- A neurological disorder of multiple, different seizures resulting from excessive discharge of cerebral neurons.

هسا ال convulsion وال seizure هم مش disease هم disorder of disease يعني هم بيجيو incidental مثلا واحد انضرب على راسه او نتيجة دوا معين زي او barbiturate withdrawal هذول هم امثلة على ال seizure اما ال epilepsy هو disease بتميز انو multiple, different seizures resulting from excessive discharge of cerebral neurons

So epilepsy is constant seizure from idiopathic abnormal brain function lead to multiple seizure all the time

Seizures: Etiology

- Trauma

نتيجة truma ادى الي loss of consciousness وصار معو seizure

- viral infection lead to Encephalitis or meningitis
- Drugs may result from adverse effect from drug lead to seizure
- Withdrawal from depressants like barbiturate or alcohol
- Tumor
- High fever and these type called febrile seizure result in children when have infection and increase temperature
- Hypoglycemia
- Extreme acidosis
- Extreme alkalosis
- Hyponatremia
- Hypocalcemia
- Idiopathic

Most cases of epilepsy are idiopathic

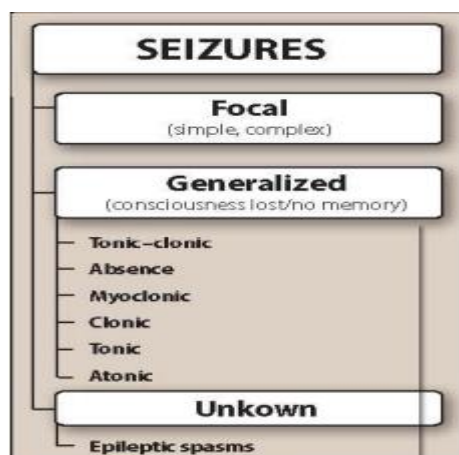
حكيانا انو ال epilepsy هو سببها unknown بصير by EEG and by MRI and see there is abnormal activity but do not know the cause

And epilepsy is repeated seizure not incidental as result from fever or trauma but it is unknown cause

Classification of Seizures

We classified seizure because not all drug best for every seizuer

And seizure have two type: focal and generalized



A-Focal (partial) seizures:

- Involves one portion of the brain i.e. one lobe.
- Symptoms depend on the site of discharge “primary focus”.
- Possibility of progressing into a generalized tonic-clonic seizure.

ال focal seizure او بسموها ال partial seizure هذول غالبا involve one hemisphere غالبا one lobe وهو
characterize by site of abnormal electrical discharge at certain locaolity like frontal
,temporal,... so called primary focus

limiting clinical presentation to affect lobe but may spread from hemisphere to ال هسا ممكن ال
other and these called progressing of focal seizure into a generalized tonic-clonic seizure

Focal seizure have two type:

1-Simple partial

- Confined to a single locus in the brain rare progress to become generalize seizure
- NO loss of consciousness usually happened without loss of consciousness
- Single muscle group or a limb like abnormal focused in temporal lobe near to auditory center so the patient will have auditory hallucination with no loss of consciousness or in center motor cortex lead to abnormal movement in one limb without loss of consciousness

2-Complex partial

- Consciousness is altered but not completely loss of consciousness
- Motor dysfunction/hallucination /distortion

ال الفرق بينه وبين ال simple partial seizure هو ال level of consciousness

B-Generalized seizures:

بال generalize seizure بصير complete loss of consciousness even people loss of consciousness
after the seizer(postictal)

- Starts at a focal point and spreads to involve both hemispheres.so generalize seizure result from abnormal activity involve two hemisphere
- Could be convulsive or nonconvulsive.
مش شرط تكون tonic clonic(convulsive)jerky movement or motor abnormality تكون other
different form(non convulsive)
- Associated with immediate loss of consciousness.

The generalize seizure type:

1-Tonic -clonic

- Loss of consciousness
- Tonic (continuous contractions) and clonic (rapid contraction and relaxation)
- Followed by confusion/exhaustion

so start as tonic phase constant contraction very rigid (lead pipe rigidity) followed by clonic phase which is rapid contraction followed by rapid relaxation which called jerkey movment and after the seizure (postictal) patient become confusion/exhaustion

there are other symptom like loss voiding control and tongue biting

2-Absence

Opposite tonic colnic seizure there is no convulsion

- **Brief, abrupt, self-limiting** very short for second
- Pediatric: **3-5 until puberty**

مثلا ولد بتلاقيه بلعب فجأ صفن وبطل يتحرك وبحرك عينه بسرعة وبهدين رجع لعب عادي هون ما في convulsion بهاية اللحظة وهو non consciousness

- very short movment of Starring/rapid –eye blinking and with loss of consciousness
- Characteristic EEG profile

3-Myoclonic

- Short episodes of muscle contractions i.e., jerks of the limbs

مثلا رجله بصير فيها jerky movment

4-Clonic

- Also brief episodes of muscle contraction **similar to myoclonic** but with Consciousness is more impaired with clonic

5-Tonic

- Increased muscle tone • < 60 seconds

Just increase muscle tone less min without clonic movement

6-Atonic

- Sudden loss of muscle tone “drop attacks ” drop foot

لما تكون ماشي في muscle tone بال muscle حولين ال ankle joint عشان هيك بتقدر ترفع اجرک وتنزلها وانت بتمشي

Epilepsy: Therapeutic Strategy

- “No cure” there is no drug eliminate disease and stop seizure completely after discontinuous drug
- but the aim of therapy is to Complete suppression of seizures in mild to moderate cases, or
- Decrease the number of episodes with minimal side effects in some sever epilepsy so try to at least decrease convulsion seizure happened to patient

How?

- Pharmacological
- Ketogenic diet
- Surgery/Vagal Nerve Stimulation
- Correct the underlying cause

Epilepsy: How to select which drug?

Choice of drug treatment is based on:

1-type of seizure so should carefully diagnosis and classified seizure (absence,,tonic clonic,.....)

many drug have wide rang coverage different type of seizure and every drug have the same efficacy but some drug useful in some type than other and some drug worse some other type like phenytoin useful in tonic clonic but worse in absence seizure

2- patient-specific variables (age(pediatric ,old,..), comorbidities(liver disease, kidney disease,..), lifestyle(what is the job,..)....)

3- characteristics of the drug (cost, adverse effects, interactions...)

Epilepsy: therapeutic strategy

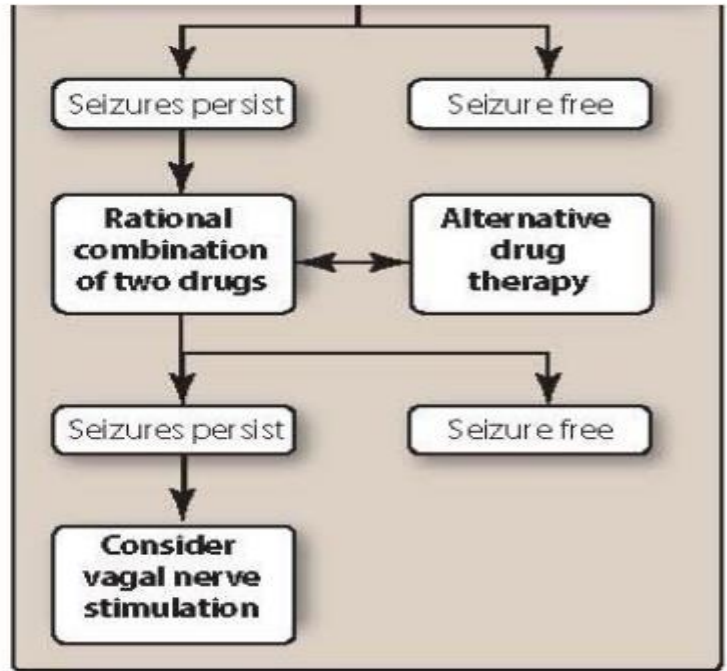
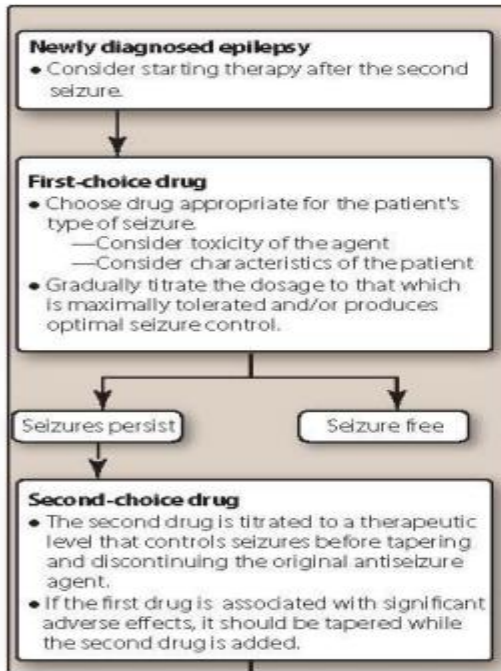
هسا احنا ما بنبدأ العلاج من single episode seizure حتى لو كان idiopathic بس بنيلش بال pharmacology therapy بعد ال second episode seizure واكيد بعد ما established diagnosis of epilepsy ودايما بالعلاج بنفضل يكون (single drug(monotherapy) هسا غالبا المريض بتحسن بس احيانا ال seizure persist فهون لازم نغير ال drug بس لما بدنا نغير الدوا بدنا نعمل اول اشئ tittering لانو ما لنوصل لل therapeutic dose مباشرة لازم بالتدريج لما نوصل لل therapeutic dose بنوقف الدوا الاول ليش هيك to maintain seizure control

اذا ما تحسن وصار persist to seizure هون بنستعمل combination وهاض خيار ثالث لانو ال combination بعمل لل seizure بس association with toxic and adverse effect

هسا اذا اخذنا two or more drug ولسا ما استجاب هون لازم surgery/vagal nerve stimulation

بالصورة الي تحت بتلخص الموضوع:

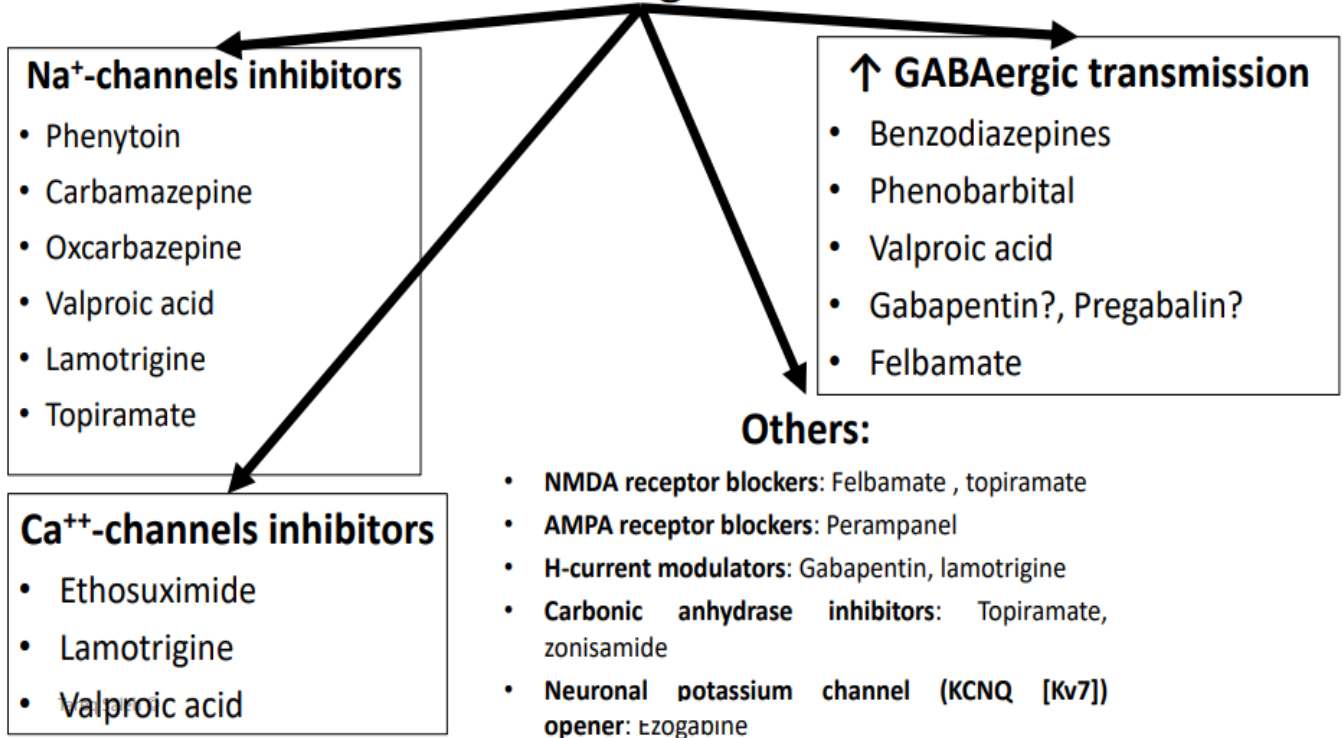
Epilepsy: Therapeutic Strategy



How do **antiepilepsy medications** work?

- 1-Blocking voltage-gated channels (Na⁺ or Ca⁺⁺)
- 2-Interfering with excitatory glutamate transmission
- 3-Enhancing inhibitory GABAergic impulses

Antiepileptic drugs

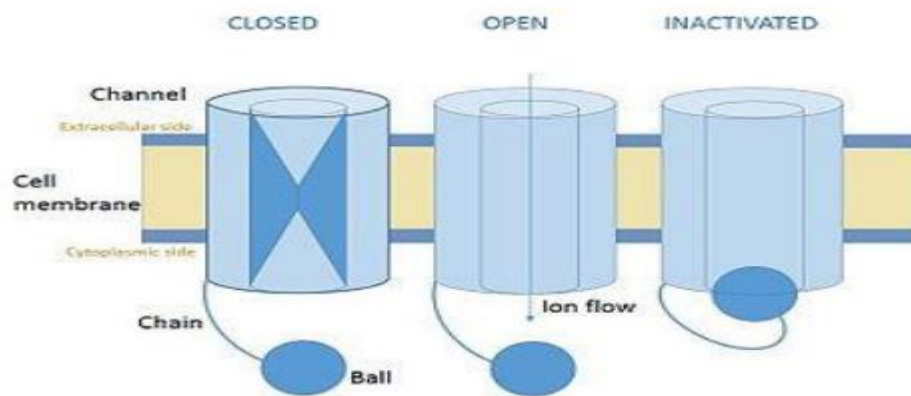


1-Phenytoin

Mechanism of action:

Blocks voltage-gated Na⁺ channels by binding to inactive state → slow recovery

بال resting membrane potential ال voltage gated Na channel بتفتح لما توصل لل threshold level ولما تخلص مرحلة ال depolarization ال intracellular Na gate ال اسمها inactive Na gate بتسكر فال channel بتكون مفتوحة بس ال inactive Na gate بتكون مسكرة وبتضل مسكرة لحد ما يرجع لل resting membrane potential وهاي المرحلة بتكون ال channel not respond to another stimulus قال phenytoin بعمل bloke to Na channel by binding to inactive state



Indications:

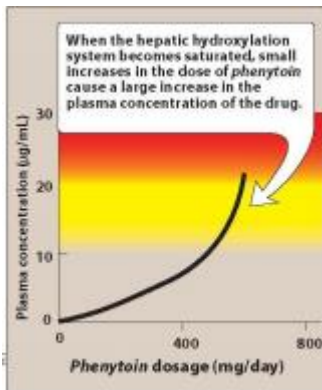
- Focal seizures
- generalize Tonic-clonic
- NOT good for absence seizures . it is wore seizure if give to absence
- Status epilepticus (after Benzodiazepine or alternative to benzodiazepine)
- Antiarrhythmic/digoxin toxicity

Pharmacokinetics:

- Induces hepatic microsomal enzyme CYP2C, CYP3A, UGT so these lead to many drug-drug interaction
- “saturable enzyme metabolism”
- Non-linear kinetics
- Toxicity

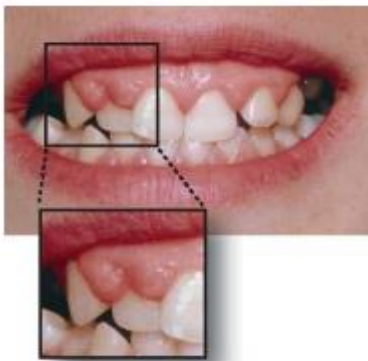
هسا هاض بصيرلو metabolism in liver بس بعمل quick saturation ل enzyme وبيطلو يعملو further metabolism وبالتالي

When increase phenytoin dose the curve of plasma concentration not curve but it is linear because when increase dose not increase metabolism so more increase in plasma concentration



Adverse effects

- Nystagmus, ataxia
- Diplopia, sedation
- Gingival hyperplasia



- Peripheral neuropathy/osteoporosis
- Teratogenic so avoid use in treatment epilepsy in woman
- Blood: ↓ folate → Megaloblastic anemia
- Drug-drug interactions: e.g., warfarin because warfarin metabolize in liver by CYP2C9 and CYP2C19 so when use with phenytoin these lead to decrease anticoagulant activity

Fosphenytoin for IM administration these is pro drug of phenytoin and it is rapid convert to active form in plasma and use as IM and phenytoin not give IM just oral because cause tissue damage



2-Carbamazepine

Mechanism of action:

Blocks Na⁺ channels

Indications:

- Focal seizures
- Tonic-clonic
- NOT good for absence seizures it is worse these type of seizure
- treatment neuropathic pain caused by Trigeminal neuralgia
- Bipolar disorder

Pharmacokinetics:

- Absorbed slowly from gut
- Long half-life (~ 30 hours)
- Induces CYP2C, CYP3A, UGT

Adverse effects

- Hyponatremia
- Aplastic anemia
- Teratogenic: Spina Bifida so contraindicated in pregnancy
- Drowsiness; headache; dizziness; nausea

-Oxcarbazepine

- carbamazepine Prodrug
- Less side effects

نهاية التلخيص سامحونا على اي اخطاء