Antiepileptics

Drugs

- Carbamazepine
- phenytoin
- Barbiturates
- Ethosuximide
- Benzodiazepines
- Divalproex
- Febamate
- Gabapentin
- Lamotrigine
- Levetiracetam
- oxcarbazepine
- pregabalin
- primidone
- Tiagabine
- Topiramate
- Zonisamide.

Epilepsy عرجال

- Not one intity, = different seizure types.

- definition = sudden, excessive and synchronous discharge of cerebral neurones.
  ie = Neurological disease, very common.
  abnormal electrical activity.

- incidence = 3% of population

- syndrome = . Loss of consciousness
  . abnormal movements
  - atypical behaviour
  - distorted perception
  - recurrent seizures
  - limited duration.

- site of origin = - motor cortex → abnormal movement
  - local.
  - generalised.
  - parietal lobe → ~~convulsions~~ auditory olfactory
  - occipital lobe → visual

- tt → . Medicine → . monotherapy 80%.
  . electrical . . failure - add another drugs, but with documentation of blood level
  . monitor blood picture CBC, B12, folate

- Mechanism - idiopathic
  - secondary - tumour - trauma etc.

Drug treatment: Drug choice

- ~~weight~~ proppper diagnosis:
- proppper drug depend on many factors:
  - a- Type of epilepsy.
    - e.g. absence syndrom.
      - simple epilepsy
      - complex epilepsy.
      - generalized
      - febrile epilepsy
      - status epilepticus
      - etc -
  - b- patient's factors :- a- age- young, old =
    - b- medical conditions. e.g. associated diseases
    - c- life- style
    - d- etc.
  - c- drugs : specific pharmacokinetic & pharmacodynamic properties.
    - drug- drug interactions;
    - cost.
    - - etc -

therapeutic strategies

Step I :-

I Monotherapy : single drug : best choice تجربي empirical

is the best. because more than one drug may cause :- a- More side effect ;

b- Not necessarly synergestic effect may add antagonistic effect.

c- less compliance.

d. drug - drug interactions.

For optimization of therapy :-

. optimal seizure control :-

. pharmacokinetics :- optimal blood level (TDM)

- patient compliace (TDM)

. pharcodynamics : - efficacy seizure control after documentation of blood level.

- toxicity :- particularly monitor blood picture CBC, B_{12} & folate

Results → . controlled epilipy → continue therapy.

. kinetic
. dynamic ← . failed (seizure) persist → second steps → replacement therapy another drug.

II - Second step:

- second drug choice:
  - a - if drug failed to control seizure inspite of therapeutic blood level documentation
  - b - if the first drug is associated with significant side effects.

Don't stop the first drug upruptly. → epilepsy

Sudden withdrawal → epilepsy
- phenytoin + الصرع

- add the second drug → titrate to the therapeutic level - clinical titration
  - TDM

} control seizures before withdrawal of first drug.

gradually discontinue the first drug.

possibilities: 1- Seizure controlled → continue therapy with continuous monitoring.

2 - Seizures persist, add another drug

III Rational drug combination (two or three drugs) (poly therapy)

continuous monitor drugs:
- toxicity
- kinetics (TDM)

IV failure of therapy → consider vagal nerve stimulation

phenytoin & fosphenytoin

- Mechanism of action:
  - Block Na^+ channels
- indications:
  - partial seizures
  - generalized seizures
  - status epileptics
- pharmacokinetics
  - dosage form: - tab.
    - susp.
    - injection.
  - distribution = . Zero-order
    - well distributed
    - 90% plasma ptn bound
    - pass BBB.
  - Elimination : . liver metabolism
    - Cyt p450
    - Enzyme induction
      - autoinduction
      - heteroinduction
    - metabolism - Zero-order kinetics
      "saturable enzymes"
      dosage adjustment - TDM
      - clinical:

side effects : - Gingival hyperplasia.
- confusion
- slurred speech
- double vision
- ataxia
- sedation
- dizziness
- hirsutism
- severe - Johnson system
- drug - drug interaction.

Carbamazepine :

Mechanism of action : . blocks Na^+ channels

tt :- . partial seizures
. secondary generalized tonic - clonic seizures.
. trigeminal neuralgia.
. bipolar disease

Kinetics : absorption : - gradual
- erratic عشوائي

distribution : cross BBB.

Metab. : Cyt p450 syst
. enzyme inducer
. glucuronidation

Side effects : . Stevens-Johnson syndrome
· Blood dyserasias · Neutropenia
·leukopenia
·thrombocytopenia
·pancytopenia
·anaemia
· B_{12} deficiency
. hyponatremia — elderly
·drowsiness
- fatigue
-dizziness
- blurred vision.
- Drug - interaction - Cyt p450 syst.
_ hypersensitivity

not : should not be used for patient with abscence seizures → ↑ seizures

Ethosuximide:

use : only abscence seizures.

Mech: Blocks Ca^{++} channels.

side effects : - Drowsiness, hyperactivity
- Nausea - vomiting
- weight gain
- lethargy
- hypersensitivity - rash
- Blood dyscrasia

Benzodiazepines:

- Mech. of action = . GABA

- . Diazepam, lorazepam,
- +++ : . partial epilepsy
  . Generalized epilepsy

phenobarbital: - GABA

+++ : . status epilepticus
. febrile epilepsy in children.