EVALUATION OF ANTIEPILEPTIC DRUGS

Submitted by:

Shaema M. Ali

Website: http://www.allimagetool.com

- A **seizure** is a clinical symptom or sign caused by abnormal electrical discharges within the cerebral cortex.

Website: http://www.allimagetool.com

- By contrast, **epilepsy** refers to the clinical syndrome of recurrent seizures, and implies a pathological state that predisposes to further future seizures.

Website: http://www.allimagetool.com

- Epilepsy affects 0.5-1% of the general population. This may remain localized (focal seizure) or may spread to cause a secondary generalized seizure, or affect all cortical neurones simultaneouusly (primary generlized seizure).

Practical guide to antiepileptic drugs

1-When to initiate

following a single seizure, anticonvulsants are not generally prescribed, whereas after two or more distinct seizure episodes (i.e. with more than a few weeks apart between episodes), they generally are prescribed.

2- Monotherapy

Initial therapy is confined to a single drug (i.e. monotherapy) that is usually effective in stopping seizures or at least significantly decreasing their frequency.

Website: http://www.allimagetool.com

The majority of epilepsy patients (70%) can remain on monotherapy for adequate control, although sometimes the choice of monotherapy may need to be switched to allow for tolerance or optimisation of seizure control.

3- What drug to initiate

Depending primary on seizure type, because in certain cases the spectrum of seizure efficacy is limited, and, moreover, certain seizure types can be worsened by ill-chosen drugs.

For example, carbamazepine is an effective first-line therapy for partial seizures but may worsen absence or myoclonic seizures.

similarly phenytoin can worsen absence and myoclonic seizures. Ethosuximide, by contrast, is only effective in primary generalised, and not partial, seizures.

4- Age and sex

This is particularly true of women, who avoid drugs associated with teratogenesis, ex. Valproate or that have adverse effects on their appearance, ex. Hirsutism from phenytoin.

4- Polytherapy

If a trial of three or so successive anticonvulsants (i.e. taken as monotherapy at adequate dosage for at least several months) does not control a patient's epilepsy, it may be worthwhile trying dual therapy.

5- **Abrupt withdrawal**

6- **Circumstantial seizures**

Pregnancy and epilepsy

One of the main concerns in this patient group is that all anticonvulsants increase the chance of teratogenicity, with valproate, and phenobarbital carrying most risk.

The toxicological hazard must be weighed against the risk of seizures which themselves can be harmful to mother and unborn baby, and are likely to worsen if anticonvulsants are discontinued.

Breast feeding

Antiepilepsy drugs pass into breast milk: phenobarbital, primidone and ethosuximide in significant quantities, phenytoin and sodium valproate less so.

Epilepsy and oral contraceptives

Many antiepileptic drugs induce steroid-metabolising enzymes and so can cause hormonal contraception to fail. This applies to: carbamazepine, oxcarbazepine, phenytoin, barbiturates, and topiramate

Note: Lamotrigine is not an enzyme inducer but can decrease levonorgestrel plasma concentration through other mechanisms

Epilepsy in children

Treatments are similar to those used in adults, but certain seizure types necessitate drugs that are rarely used in adults, e.g. ethosuximide for absence seizures, or vigabatrin for refractory partial seizures (partly because children may become irritable or more cognitively impaired with drugs such as valproate and phenobarbital).

Status epilepticus

Treatment of seizures is initially with the intravenous benzodiazepine lorazepam (0.5–4 mg). Lorazepam is preferred to diazepam because it has a longer effective t½ and is less lipophilic and so accumulates less in fat, causing less delayed toxicity (hypotension and respiratory depression)

- Phenytoin I.V. may be started simultaneously to suppress further seizures, given as a loading dose (15–20 mg/kg body-weight) over 1 h
- Phenobarbital may be given I.V. as a third-line drug when seizures continue.

Website: http://www.allimagetool.com

- If resuscitation facilities are not immediately available, diazepam by rectal solution is a useful option. In some cases, midazolam (nasally) may be preferred, e.g. in children or those with severe learning disabilit

Website: http://www.allimagetool.com

- Magnesium sulfate is the treatment of choise for seizure related to eclampsia.

Important note

-First line drugs are carbamazepine and sodium valproate

-Alternative monotherapy Lamotrigine, oxacarbazepine, topiramate… etc

-As part of combination therapy Gabapentine, , tiagabine, vigabatrin.

Treatment of partial seizures (simple, complex, with or without secondary generalization)

Preferred monotherapy carbamazepine

Alternative: valproic acid, lamotrigine and levetiracetam

Treatment of generalized seizures

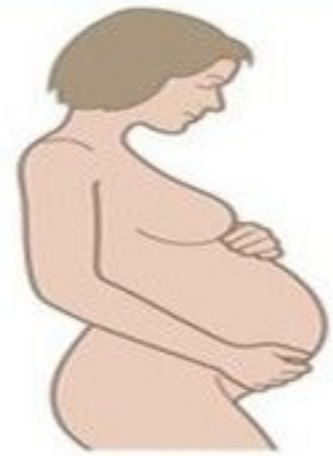
- Preferred monotherapy Sodium valproate and lamotrigine are effective against all the generalized seizures.

Alternative monotherapies Depend on seizure type.

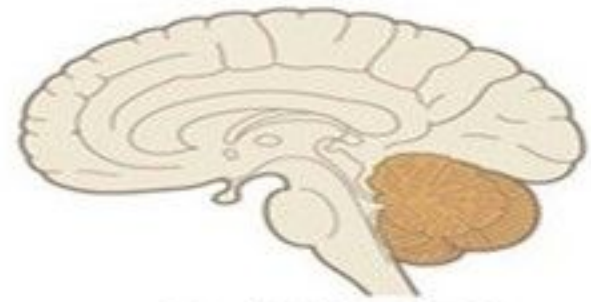
Tonic-clonic	levetiracetam.
Absence	Ethosuximide.
Myoclonic	Clonazepam.

Side effects of AEDs

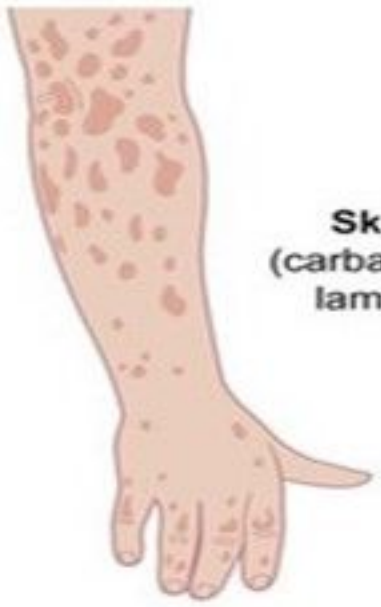
Drowsiness or sedation
(most agents)



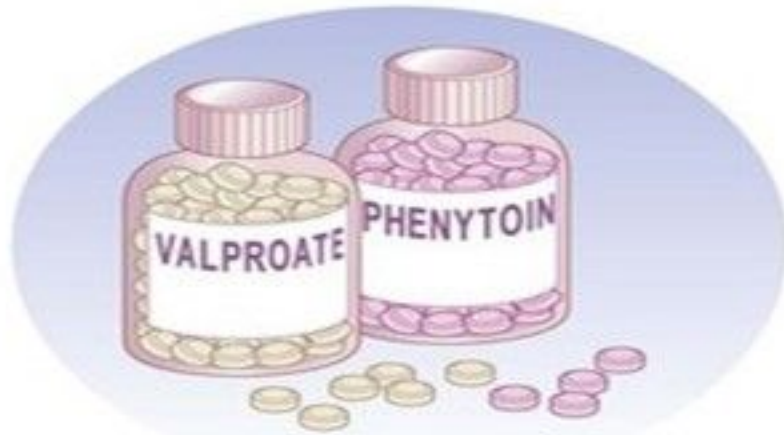
Risk of birth defects
(sodium valproate)

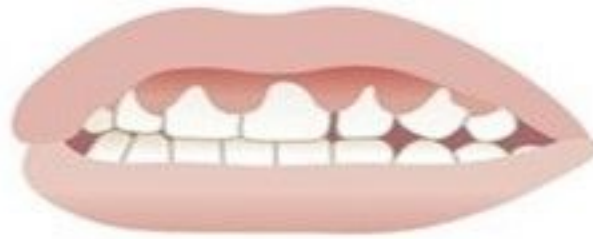


Cerebellar ataxia
(most agents)



Skin rash
(carbamazepine, lamotrigine)





Gingival hypertrophy
(phenytoin)

Bone marrow suppression
(carbamazepine)