How to Start and Stop Antiepileptic Drugs

When and how to start AED
Epilepsy management

- Indications for treatment
- Treatment of single seizure
- Principles of epilepsy management
  - Choice of antiepileptic drugs
- Maintenance therapy
- Monitoring strategies

Indications for treatment
Indications for treatment

- Two or more un-provoked seizures = epilepsy
- Hallmark = recurrence
- Recurrence may need prevention.
- However, not all patients with epilepsy need Rx!

Indications for treatment

- Some epilepsy are self-limited.
  - Overall 50% of epilepsy will remit spontaneously.
Indications for treatment

Severity of consequences of seizures vary widely on
- seizure type
- timing and frequency of attack
- age and condition of patients
- response of patient, family, society
- type of employment
- driving license
- consequence of treatment

Indications for treatment

- Based on assessing how seizures interfere with
  - ability to function
  - quality of life
  - health and well-being
- No single guideline applicable to all
- Individually interactive decision-making among patient, family and doctor
Treatment of single seizure

- Diagnosis problem
  - True seizure?
  - Un-provoked seizure?
  - Really first seizure?

- Probability of recurrence
  - High or low

- Consequence of recurrent seizure
  - Much or little

- Current antiepileptic drugs
  ≠ antiepileptogenesis
Risk of recurrence after first seizure

Recurrence risk factors

(++) strong, (+) weak

- Known etiology ++
- Epileptiform EEG ++
- History of epilepsy in sibling +
- Sleep state: sleeping +
- Prior provoked seizures +
- Time elapsed from seizure +
- Todd’s paresis +
- Absence or myoclonic seizure types †

Conflicting data

- Seizure type: partial seizure
- Status epilepticus

Not recurrence risk factors

- Age
- Sex
- Abnormal neurological examination †
When to treat single seizure

- Definitely to treat
- Possibly to treat
- Probably not to treat

Definitely to treat single seizure

- With structural lesion
  - Brain tumour, AVM, Infection
- Without structural lesion
  - History epilepsy in sibling
  - EEG with definite epileptic pattern
  - Previous brain injury
  - Previous symptomatic seizure
  - Status epilepticus at onset
Possibly to treat single seizure

- Unprovoked seizure without any risk factor of recurrent seizure
  - Associated with high risk medical or neurologic conditions
  - Risky occupation or environment
  - Driving license

Probably not to treat single seizure

- Specific benign epilepsy syndrome
- Alcohol withdrawal, alcohol related
- Drug abuse
- Seizure in context of acute illness
  - Acute symptomatic seizure
  - Provoked seizure
- Postimpact seizure
  - Post cerebral concussion
Principles of epilepsy management

Epilepsy management

- Epileptic seizures = manifestation of many brain disorders
- To control epileptic seizures = symptomatic Rx
- Identify etiology
- Provide treatment for etiology
- Set goal:
  - To improve quality of life
  - Not only to control seizures
Seizure control

- Medical Rx
  - Non-pharmacological Rx
  - Pharmacological Rx
- Surgical Rx

Non-pharmacological seizure control

1. Avoiding seizure precipitating factors
   - Sleep deprivation
   - Fever
   - Prolonged fasting state
   - Major physical and mental stress
   - Lowering seizure threshold drugs
   - Lowering efficacy of antiepileptic drugs
   - Flashing light in photosensitive epilepsy

2. First AID management
Choices of antiepileptic drug

Principles

- Mono-therapy first
- Rational poly-therapy after
- Minimum effective dose
- Maximum tolerated dose
- Efficacy
- Adverse effects
- Cost
- Availability, local treatment guideline

Choices of antiepileptic drug

Principles

- Drug to drug interaction
- Concurrent medical illnesses
- Special groups
  - Infant and toddler age group
  - Child-bearing women
  - Pregnancy
  - The elderly
Choice of antiepileptic drug

- Consider
  - Etiology
  - Epilepsy syndrome
  - Epilepsy type
  - Types of seizure

AEDs induce seizure

- AEDS induce absence:
  - phenytoin, carbamazepine, phenobarbital
- AEDS induces myoclonic seizure:
  - phenytoin, carbamazepine ✫
Rational poly-therapy AEDs

- Polytherapy
  - Efficacy: less than additive
  - Side effects: supra-additive
- Not more than three AEDs!
- Consider
  - Modes of action
  - Drug to drug interaction (metabolism induction, protein binding, etc.)
  - Adverse effect profiles

Maintenance AED therapy
**Maintenance AED therapy**

- Start with small dose
  - to minimize risk of initial side effects and allergic reaction
- Gradually increase to minimum effective dose
- Allow sufficient time between dose or drug changes for efficacy evaluation (5 times of half life)

**Maintenance AED therapy**

- Dose frequency: depend on
  - half life
  - preparation i.e. slow release form
  - metabolism: age, co-medication, liver or renal function
- The more frequent dosing the poorer compliance!
- The more complicated AED regimen the poorer compliance! ♦
Maintenance AED therapy

Principles of adding a second drug

- After reaching un-tolerable level of first AED
- Adjust un-tolerable level of 1<sup>st</sup> AED
- Sufficient drug titration time
- If seizures not under control, switch to another combination

If becoming seizure-free, stay on poly-therapy or only add-on AED

If seizures return during or after first AED withdrawal
  - Titrate the 2<sup>nd</sup> AED
  - Back to previous effective dose of poly-therapy
Monitoring strategies

- Inform patient about adverse effects
- Pre-treatment screening
  - Complete blood count
  - Liver function test
  - Renal function test
- Intermittent adverse effect monitoring may not cost-effective in healthy patients
- However, monitoring may benefit in high risk patients
- Notify physician as soon as possible when side effects or allergic reaction develop
Monitoring strategies

**Indication for drug level monitoring**

- **Optimal therapeutic dose**
  - No good relationship between dose and efficacy
  - Good relationship between *active* drug level, efficacy and side effect
- **To ensure drug compliance**
- **To guide dose adjustment**
- **To guide poly-therapy**
- **To document toxic level**

**WHEN AND HOW TO STOP AED**
Discontinuing antiepileptic drugs

- Patient and family decision with provided information
- Weighing between risk of:
  - Drug discontinuation recurrent seizure
  - Continuing AED
- Gradually discontinue AED in 2-3 months

Discontinuing antiepileptic drugs

- After seizure-free for 2-5 years in adults, 1 year in children
- Not having high risk of seizure-recurrence brain pathology
- Not having high risk of seizure-recurrence epilepsy syndrome
- Easy to control epilepsy
- Well control with mono-therapy
- EEG is not strong predicting factor!
Risk factors of relapse

- Short duration of seizure freedom prior to drug withdrawal
- Age above 16
- Epilepsy with onset in adolescence or adulthood
- Juvenile myoclonic epilepsy
- Remote symptomatic epilepsy
- History of myoclonic epilepsy

Risk factors of relapse

- History of atypical febrile seizure
- Prolonged period before achieving seizure control
- Seizures while on treatment
- Seizure control requiring multiple drug therapy
- Abnormal EEG
- Learning disability