

When and How To Start and To Stop Antiepileptic Drugs

ศส.นพ.รังสรรค์ ชัยเสวีกุล
คณะแพทยศาสตร์ศิริราชพยาบาล

When and how to start AEDs

Epilepsy management

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

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3

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! 🚗

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5

Indications for treatment

- ◆ Not all paroxysmal events are seizures
- ◆ Not all seizures are manifestations of epilepsy!
 - Provoked seizures
- ◆ Some seizures are self-limited.
 - Occurring in acute medical or neurological illness 🚗

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6

Indications for treatment

- ◆ Some epilepsy are self-limited.
 - Overall 50% of epilepsy will remit spontaneously.

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7

Indications for treatment

Nature and 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 ☺

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8

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 ■

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9

Treatment of single seizure

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 ■

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11

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 ■

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12

Risk of recurrence after first seizure

- ◆ Conflicting data
 - Seizure type: partial seizure
 - Status epilepticus
- ◆ Not recurrence risk factors
 - Age
 - Sex
 - Abnormal neurological examination ■

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13

When to treat single seizure

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

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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

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15

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

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16

Probably not to treat single seizure

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

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17

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 .

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19

Seizure control

- ◆ Medical Rx
 - Non-pharmacological Rx
 - Pharmacological Rx
- ◆ Surgical Rx ☺

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20

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 Treat medical and neurological illness .

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21

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 ☺

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22

Choices of antiepileptic drug

Principles

- ◆ Drug to drug interaction
- ◆ Concurrent medical illnesses
- ◆ Special groups
 - Infant and toddling age group
 - Child-bearing women
 - Pregnancy
 - The elderly .

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Choice of antiepileptic drug

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

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Choice of antiepileptic drug

- ◆ Etiology of epilepsy
 - Infantile spasm
 - ◆ Tuberos sclerosis
 - Vigabatrin
 - ◆ Other causes
 - ACTH

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25

Choice of antiepileptic drug

Epilepsy syndrome

- ◆ Infantile spasm
 - Vigabatrin, ACTH, nitrazepam, valproate, B₆, surgery
- ◆ Juvenile myoclonic epilepsy
 - Valproate, lamotrigine, topiramate, levetiracetam

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26

Choice of antiepileptic drug

Epilepsy type

- ◆ Localization-related epilepsy (partial epilepsy)
 - Many antiepileptic drugs (AEDs)
- ◆ Generalized epilepsy
 - Many AEDs
 - However, some AEDs induce seizures
 - Idiopathic generalized epilepsy: prefer valproate, lamotrigine, topiramate, levetiracetam, (phenobarbital)

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27

AEDs induce seizure

- ◆ AEDs induce absence:
 - phenytoin, carbamazepine, phenobarbital
- ◆ AEDs induces myoclonic seizure:
 - phenytoin, carbamazepine

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28

Choice of antiepileptic drug

Types of seizure

- ◆ Generalized tonic-clonic, partial seizure:
 - Any AEDs
- ◆ Absence:
 - Valproate, lamotrigine, topiramate, levetiracetam
- ◆ Myoclonic seizure:
 - Phenobarbital, valproate, lamotrigine, topiramate, levetiracetam

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29

Rational poly-therapy AEDs

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

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30

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)

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32

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! ■

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33

Maintenance AED therapy

Principles of adding a second drug

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

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34

Maintenance AED therapy

Principles of adding a second drug

- ◆ If becoming seizure-free, stay on poly-therapy or only add-on AED
- ◆ If seizures return during or after first AED withdrawal
 - Titrate the 2nd AED
 - Back to previous effective dose of poly-therapy ■

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35

Monitoring strategies

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

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37

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

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38

WHEN AND HOW TO STOP AEDS

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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

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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!

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41

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

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42

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