Epilepsy - a practical guide

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Aims

• To improve understanding of current treatments of epilepsy in primary care

• To improve communication between primary and secondary care

• To facilitate inquisitive and collaborative environment for epilepsy care
Objectives

• Idiot’s guide to epilepsy

• Use of new drugs in epilepsy

• How to use anti-epileptic drugs in primary care
  • do’s and don’ts

• Women and epilepsy

• Alcohol and drugs
Seizure

• Clinical manifestation of a set of cortical neurones

• Generalised or focal

• Generalised - affects the whole brain

• Focal (partial) - affects part of the brain
Epilepsy

- What people have when they have recurrent, unprovoked seizures

- Depression

- Anxiety

- Short term memory loss

- Behavioural and personality changes

- Reduced fertility

- Increased risk of death (inc suicide)

- Sociobiological consequences
Not just the patient
Acute symptomatic seizures

- Caused by external noxious stimulus
  - alcohol
  - drugs
  - Alcohol and drug withdrawal
  - trauma/haemorrhage/infection
  - fever in children
- Don’t usually require AEDs
Common seizure types

• Focal epilepsies
  • Simple partial seizure
  • Complex partial seizure
  • Secondary generalised tonic clonic seizure

• Generalised epilepsies
  • Absence seizure
  • Myoclonic seizure
  • Primary generalised tonic clonic seizure
What’s the difference between an absence and a complex partial seizure?
Why does it matter?

- Absence seizures
  - Childhood epilepsy syndrome
  - Usually easy to treat
  - Respond well to valproate, ethosuximide, clonazepam
  - “mild” seizure type
  - Normal MRI brain
  - Complex partial seizures
    - Childhood or adult syndrome
Anti epileptic drug development

Number of licensed AEDs

Year of licence

Old AEDs

- Phenytoin
- Carbamazepine
- Sodium Valproate
- Lamotrigine
- (Phenobarbitone)
- Clonazepam
- Clobazam
Newer AEDs

- Pregabalin
- Levetiracetam
- Zonisamide
- Topiramate
- Gabapentin
- Oxcarbazepine
Newest AEDs

- Lacosamide
- Eslicarbazepine
- Retigabine
- Perampanel
What’s the difference between older and newer drugs?

- Old drugs
  - More drug interactions
  - More side effects
  - Often difficult to use properly
  - Broad therapeutic efficacy
  - Multiple preparations
  - Cheap

- New drugs
How do you choose between AEDs?

• Efficacy

• Side effect profile

• Mechanism of action (side effect profile)

• Titration regime

• Interactions

• Dose regime

• Half life
Generic Substitution

- Raises risk of breakthrough seizures in seizure free patients
- Less important for those with incomplete seizure control
- Massive anxiety in some patients
- Variability in side effects
Epilepsy management

• Increasingly specialised

• NICE

• SANAD

• UK Epilepsy and Pregnancy Registry
General rules for AED titration

• Start low, go slow

• Ask for help
  • Epilepsy nurses - 020 359 40701
Self-help guide

- Refer to BNF

- Identify starting dose

- Divide by 2

- Increase by starting dose **NO FASTER** than every 2 weeks
How high?

- BNF states initial target dose for all AEDs
- Only increase beyond this if ongoing seizures
- Increase by the longer of:
  - Every time the patient has a seizure, OR
  - Every 2 weeks
How high??!!!!?!?

• Until the first of 3 things happen:
  • Seizures stop
  • Side effects limit further dose increases
  • Maximum licensed dose is reached
Side effects

• Drowsiness

• Cognitive slowing

• Nausea

• Headache

• Diplopia

• Ataxia
What to watch out for

- Rash
  - Usually mild
  - Occasional Stevens Johnson syndrome
  - Up to 5% on carbamazepine/lamotrigine/phenytoin
- Behavioural changes (Levetiracetam)
- Kidney stones (Topiramate or Zonisamide)
- Combination of lamotrigine and sodium valproate
<table>
<thead>
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<th>Week Range</th>
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<td>Wk 3-4</td>
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<td>Wk 5-6</td>
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<td>Wk 7-8</td>
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<td>Wk 9-10</td>
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</table>
• You will need to see them every 2 weeks or so

• Use treatment plans

• Some patients need a lot of support

• Use secondary care
  • Epilepsy nurses
  • Epilepsy Pharmacist
  • Me
Example - lamotrigine

- 25mg OD
- Increase by 25mg OD every 2 weeks
- Stop at 75mg BD
- Increase further if more seizures
  - Every time they have a seizure, or
  - Every 2 weeks
- Stop when
  - Seizures controlled
  - Side effects limit further increases
  - 250mg BD reached
## Do’s and don’ts

<table>
<thead>
<tr>
<th>Do</th>
<th>Don’t</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ask for help</td>
<td>• make big changes</td>
</tr>
<tr>
<td>• follow gut feeling</td>
<td>• do anything quickly</td>
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<tr>
<td>• listen to the patient</td>
<td>• work in isolation</td>
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<tr>
<td>• read the BNF</td>
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<tr>
<td>• optimise the dose if necessary</td>
<td></td>
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<tr>
<td>• make small changes</td>
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</table>
Epilepsy in pregnancy

• Epilepsy prevalence ~ 0.5% in women of childbearing age

• Epilepsy most common serious neurological disorder in pregnancy - 0.3-0.6% gestations

• Pregnancy prevalence in women of childbearing potential - 16.9 - 47.1 per 1000 patient years at risk

• Fertility in WWE 1.455-1.94 live births per 1000

• 18190 to 24254 pregnancies in WWE in UK per year


uk Epilepsy and pregnancy register

<table>
<thead>
<tr>
<th>Table 2</th>
<th>United Kingdom pregnancy registry outcome data</th>
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<td>All AEDs monotherapy</td>
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<tr>
<td>No AED</td>
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<tr>
<td>Carbamazepine monotherapy</td>
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<tr>
<td>Lamotrigine monotherapy</td>
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</tbody>
</table>

AED = antiepileptic drug; MM = major malformations.

Uk epilepsy and pregnancy register

- High dose lamotrigine (>200mg/day) - 5.4% MCM rate

- Folic acid may not prevent NTDs in WWE

- Topiramate
  - 9% MCM (all pregnancies)
  - 4.8% MCM (monotherapy)
  - 11.2% MCM (polytherapy)


Cognitive effects

- Valproate - associated with low verbal IQ compared with CBZ, PHT, and other monotherapies

- Analysis included maternal IQ, epilepsy syndrome, socioeconomic status, alcohol and smoking, family history

- Levetiracetam may be associated with a lower risk than VPA

  - LEV 8% cw VPA 40%


cognitive effects - dose

Figure 1 Scatter plots of verbal index and non-verbal index versus standardized dose for each antiepileptic drug during pregnancy.

SIGN

- Information on risks of uncontrolled seizures
- Pre-pregnancy review
- Consider drug withdrawal if in remission and low risk of recurrence
- Discuss relative risks of AEDs and seizures in pregnancy
- Aim for lowest possible dose of monotherapy
- Folic acid
- IM (and oral, for high risk pregnancies) vit K

Scottish Intercollegiate Guidelines Network. (n.d.). *Diagnosis and Management of Epilepsy in Adults*. (Royal College of Physicians of Edinburgh, Ed.) sign.ac.uk.
• Obstetric clinic with specialised physician

• Monitor seizure frequency and adjust AEDs to minimise seizures

• 18 week USS

• Increase AEDs on clinical grounds only

• Routine monitoring of blood levels not indicated

Scottish Intercollegiate Guidelines Network. (n.d.). Diagnosis and Management of Epilepsy in Adults. (Royal College of Physicians of Edinburgh, Ed.) sign.ac.uk.
what we don’t know

• Treat or not
  • partial seizures or absence seizures only?

• Drug dosages

• Changes throughout pregnancy

• How to monitor

• What to do if you observe a change
Drugs and Alcohol

- Both can cause acute symptomatic seizures
- Chronic use can cause epilepsy
- Can be very hard to tell the difference
  - Might not be practically useful distinction
- Chaotic lifestyle
- Compliance issues
My practice

• Examine
  • Consider brain imaging

• Encourage abstinence

• If abstinence impractical, treat
  • Levetiracetam 500mg BD
  • avoid/replace benzodiazepines
  • do nothing else
Any questions?