Investigation and management of seizure disorders

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RCGP Clinical Champion for Epilepsy
Overview of today’s presentation

- Quick review of assessment of Transient Loss of Consciousness [TLOC]
- Features to make you suspect epilepsy
- Classification of epilepsy
- Management of epilepsy
  - Medication
  - Social
  - Psychosocial
Some hints for assessing Transient Loss of Consciousness

The management of TLOC

Key Factors
- Does the patient appear well?
- Are there any red flag symptoms?
- Is there risk of recurrence?

Pointers
- History, Examination and Investigation

Treatment
- Management Options
Does the Patient look unwell? – If so quick screen needed

If blackout was very recent and patient unwell a quick checklist;

- Recent M.I. [lowers threshold to admit]
- Pain – Head, Chest, Abdomen
- Secondary Injury
- Toxic, cyanosed, incoherent.
- FAST Test –
  - Facial weakness,
  - Arm or leg weakness
  - Speech Problems
  - Test these signs
History, Examination and Investigation

History

Events leading up to the attack
- Provoking factors?
- Supine or Erect?

What it felt like at onset – put yourself in their shoes

Sensation after the attack

N.B. Seek an eye witness account
Events leading up to the TLOC

Important features in the history

• Was the patient sitting or standing
• Physically or emotionally challenged
• Noxious stimuli – Pain, blood, emotion
• Enhancing factors – Hunger, sleep deprivation, infection, menses, flashing lights, hyperventilation
• Social factors – potential gain
• Patient’s assessment of what led to attack
What it felt like

If there was no warning an attack was coming

- Possible causes,

1. Cardiac e.g. Arrhythmia, heart block,
2. Neurological e.g. Primary Generalised Epilepsy, narcolepsy, cataplexy, neuromuscular disorders
3. Cerebro-Vascular event e.g. TIA / stroke, transient global amnesia
4. Psychiatric e.g. Confusing history
5. Diabetes?
6. Other e.g. Sleep apnoea, Sleep Paroxysms etc.
What it felt like

With Warning, i.e. Heralded Attack

Possible causes

1. Faintness – “Need to sit down”, vertical posture, sweaty, nausea, vision and auditory changes,

2. Epilepsy – “Odd feeling again” – Leading questions may be necessary


4. Endocrine - “Feeling hypo”

5. Cerebro vascular - Volley of unheralded attacks previously

6. Other - Migraine
Eye Witness Account

Events leading up to the attack
- Environmental
- Behavioural

Entry into the attack
- No warning
- Bizarre behaviour – purposeful or non purposeful
**Eye Witness Account**

**During the attack**

- Oxygen saturation - Patient’s colour
- Motor Signs - Version of head or arm
- Tone – floppy or else Tonic / Tonic- clonic movements, symmetrical?
- Symmetry - Neurologically congruence
- Actions – Purposeful or not ‘wrecked the room’

Eye witness can fill in amnesic events – clutched chest, saw flashing lights. Also duration of attack
Eye Witness Account

After the attack

• Speed to recovery
• Neurological sequelae – dysphasia, weakness
• Physical sequelae – pallor, sweating.
Examination

Especial attention to

CVS – Pulse, BP – sitting and standing, Heart sounds
CNS – Cognition, full GP-CNS examination. F.A.S.T. test

NB. The history is likely to yield more than the examination
TLOC Management Options

From the Clinic
• Emergency – Admit

Routine but soon
• 12 Lead ECG
• Baseline bloods +/- Blood Glucose testing
• MRI of head if focal or other intracranial concerns [CT if an MRI is contra indicated]

Referral
• Cardiology,
• Neurology for diagnosis of epilepsy, of if NEAD suspected for consideration of video telemetry.]
TLOC: Are there any red flag symptoms?

From History
- Recent discharge from hospital
- TLOC on Exertion
- Pain
- Volley of attacks
- FH of S.C.D. under 40yrs
- Evolving Neurological Symptoms

From Examination
- Dyspnoea
- Abnormal E.C.G.
- Structural Heart Disease
Features to suggest a diagnosis of epilepsy

- TLOC with features listed previously
- Similarity of attacks – patients recognise them as the same
- Neurologically it makes sense
- Spontaneous
- Eyewitness account to support the diagnosis

‘The key fits,’ – This requires an understanding of classification and basic neuro-anatomy
Revision: Traditional overview of Epileptic Syndromes

**Focal Seizures**
- 70% of Epilepsy
- Focal Cortical Disturbance
- Their origin usually determines the clinical picture
- Focal Spikes on eeg

**Generalised Seizures**
- Origin unclear either sleep spindles or hypersynchrony
- Commence bilaterally
- Spike and wave
- No aura
Previously: Focal and Generalised classification.

**Focal Epilepsy**
- Aura
- Simple Sz.’s
- Complex Partial Sz’s
- Secondary Generalised Sz.’s

**Generalised Epilepsy**
- Myoclonic Jerks
- Absence
- Atonic Sz’s
- Tonic Sz’s
- Tonic-clonic Sz.’s
1. Classification Changes

COMMISSION ON CLASSIFICATION AND TERMINOLOGY

- Previously rested largely upon astute observations and expert opinions.
- The original authors foresaw that changes to the classification would be needed
- Predates modern neuroimaging, genomic technologies and concepts in molecular biology.

Now classification includes input from experts in genetics, neuroimaging, therapeutics, paediatric and adult epileptology, as well as statistics and research design.
Latest Classification of Seizures

1) Generalised
   - Tonic-Clonic
   - Absence
   - Clonic
   - Tonic
   - Atonic

   - Typical
     - Absence with special features
       - Myoclonic absence
       - Eyelid Myoclonia
   - Atypical

2) Focal
   - Focal seizures
     - Originating within networks limited to one hemisphere
     - Characterized according to one or more features:
       - Aura
       - Motor
       - Autonomic
       - Awareness/Responsiveness: altered (dyscognititve) or retained

     - May evolve to
     - Bilateral convulsive seizure

3) Unknown
   - Insufficient evidence to characterize as focal, generalized or both
     - Epileptic Spasms
     - Other

Epilepsia, 51(4) 676-685, 2010
Classification of Seizures; 1) Generalised Sz

Generalised Seizures
Arising within and rapidly engaging bilaterally distributed networks

Tonic Clonic  
Absence  
Clonic  
Tonic  
Atonic  
Myoclonic
- Myoclonic-atonic
- Myoclonic-tonic
Generalised Seizures; Absence

Absence

- Absence with Special Features
  - Myoclonic Absence
  - Eyelid Myoclonia

- Typical

- Atypical
Classification of Seizures; 2) Focal Sz

Focal Seizures

Originating within networks limited to one hemisphere

Characterised to one or more features
Aura, Motor, Motor Autonomic
Awareness / Responsiveness; Altered [dyscognitive] or retained

May Evolve to bilateral convulsive seizure
Classification of Seizures; 3) Unknown

Unknown

Insufficient evidence to characterise as focal, generalised or both

Epileptic Spasms

Other
Changes in Terminology and Concepts

<table>
<thead>
<tr>
<th>Old Term;</th>
<th>New Term;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td>Genetic</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>Structural-metabolic</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>Unknown</td>
</tr>
<tr>
<td>Benign</td>
<td>Self-limiting</td>
</tr>
<tr>
<td>Catastrophic</td>
<td>Pharmaco-unresponsive</td>
</tr>
<tr>
<td>Complex Partial</td>
<td>Focal Seizures</td>
</tr>
<tr>
<td>Simple Partial</td>
<td>Focal Seizures</td>
</tr>
<tr>
<td>Secondarily generalised</td>
<td>Evolving to a bilateral convulsive seizure</td>
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</tbody>
</table>
Cerebral cortex regions
- Functional Areas of the Brain

The location of the epileptogenic focus will determine seizure

e.g. occipital lobe focus likely to have visual changes
Q. Who makes the diagnosis?
   \[ A = \text{Epilepsy Specialist [NICE]} \]

Q. When do you commence treatment?
   \[ A = \text{On-going liability to seizures} \]

Q. Has a diagnosis been reached?
   \[ A = \text{No ‘trial of anticonvulsants’} \]

Q. Which anti-epileptic medication?
   \[ A = \text{Discussion between patient and doctor, treatment is personalised e.g. female issues} \]

Involve the person with epilepsy in the decision making
Treatment of Epilepsy

- Overview of established AEDs
- Newer AEDs
- Buccal Midazolam
Overview of established Anti Epileptic Drugs

Carbamazepine

- Partial Epilepsy – Not for Absence or Myoclonic Jerks
- Start at 100-200mg a day increase slowly
- S/E- diplopia, nausea, headache, dizziness
- Idiosyncratic reactions possible [up to 10%]
- Monitoring needed- increase ‘MR’ dose
- Beware of interactions
Overview of established Anti Epileptic Drugs

Clobazam

- Used intermittently
- Extra cover for catamenial seizures, stressful events, clusters of attacks
- Dose - 10mg [SLS] once or twice a day for 3 days
Overview of established Anti Epileptic Drugs

Clonazepam

- Limited role due to tolerance, sedation and withdrawal seizures
- Usually reserved for refractory seizures especially Myoclonic jerks
Overview of established Anti Epileptic Drugs

**Gabapentin**
- Add on therapy for **partial** seizures only
- Dose starts at 300mg a day and increases to 1800-2400 mg a day with t.d.s dosing
- No interactions [not metabolised]
- Side effects – well tolerated occas. drowsiness, dizziness, diploplia, ataxia and headaches
- ? Efficacy
Overview of established Anti Epileptic Drugs

Lamotrigine

- Broad spectrum and first line [less teratogenic than VPA]
- Dosing – slow to minimise side effects usually 25mg a day increasing every 2 weeks, b.d. dosing. Max dose around 400mg a day.
- Interactions – VPA, CBZ and PHT
- Idiosyncratic reactions in up to 5%
Overview of established Anti Epileptic Drugs

Phenytoin

- Was considered first line for partial seizures
- Poor side effect profile: rash, liver toxicity, blood dyscrasias, cosmetic changes, neurotoxicity etc.
- Dosing difficulties – saturation kinetics
- Many interactions
Overview of established Anti Epileptic Drugs

Phenobarbitone [and Mysoline]
- World-wide best seller for partial seizures
- Side –effects largely unacceptable- effects on cognition, mood and behaviour. Also arthritic changes, dupytren’s contracture, frozen shoulder
- Interactions- accelerates metabolism of many lipid soluble drugs
Overview of established Anti Epileptic Drugs

Sodium Valproate

- Broad Spectrum and Powerful [no-longer first line in women]
- Dose – 300- 500mg a day, usually bd dosage
- Side effects- tremor, wt. gain, POS, possible hepatotoxicity, blood dyscrasias and pancreatitis
- Interactions- can inhibit liver enzymes
Overview of the Newer Anti Epileptic Drugs

**Topiramate**
- Second line – Broad Spectrum [5 mechanisms of action]
- Dose starts at 25mg a day - 2 in 3 tolerate it slowly increased to 200-400mg a day
- Side effects - Irritability, drowsiness, headaches, dizziness, cognitive slowing, speech impairment, weight loss and paraesthesia.
- Beware of kidney stones [occurs in 4 %]
Overview of the Newer Anti Epileptic Drugs

Zonisamide

• Treatment of partial seizures, with or without secondary generalisation

• Sulphonamide derivative with related potential for allergy/rash including Stevens-Johnson
Overview of the Newer Anti Epileptic Drugs

Oxcarbazepine- analogue of CBZ

- Indications – same as CBZ, may worsen absence and myoclonic epilepsy.
- Dose – start at 300mg a day and increase to 900 – 2400mg a day as needed
- Side effects – hyponatraemia, headaches, occas. rashes and teratogenicity
Overview of the Newer Anti Epileptic Drugs

Levetiracetam

- Licensed now generic, ‘if the drop in price is over 50% can be offered first/second line as second line both for generalised and partial epilepsy,’ NICE 2012
- Dose- start at 250mg a day and build up to max of 3,000mg if needed
- Side effects – no known idiosyncratic reactions may cause somnolence, irritability [initially]
- Interactions – Nil definite ?? CBZ and PHT
New AEDS

Lacosamide ‘Vimpat’

- Add on treatment for focal epilepsy
- Novel action – enhances sodium channel slow inactivation
- Twice daily dosing
- No clinically relevant interactions with P450
- Gaining popularity,
- Cost – 60 x 750mg = £84.02

N.B. Increase in PR time on ECG reported – recommendation for ECG prior to initiation and use with caution in pre-existing cardiac disease especially known heart block or medication that causes this
New AEDS

Eslicarbazepine [Zebinix]-

‘*adjunctive therapy for people who are experiencing tolerability issues with carbamazepine*’

- Adjunctive therapy for partial onset seizures
- Once daily dosing
- Additional mode of action compared to carbamazepine
- Does not affect sodium levels as much as carbamazepine
- Cost – pack of 30 x 800mg = £154
New AEDs

Buccal Midazolam – different products

1. ‘Epistatus’ – all ages, Special Products limited and UL Medicines Limited also produce a similar preparation –
   • Strength is 10 mg per ml

2. ‘Buccolam’ – licensed for 3 months to <18yrs
   • Strength is 5mg per ml
New AEDs

Retigabine [Trobalt]
• adjunctive treatment for partial onset seizures for adults 18yrs and above

NB Adverse Event Warning – blue pigmentation skin, sclera and retina.
Perampanel [Fycompa®]

- is indicated for the adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients with epilepsy aged 12 years and older
- selective, non-competitive AMPA receptor antagonist
- Once daily
Management of epilepsy; some important considerations

Overview;

- Contraception and pregnancy
- Driving
- Social
- Psychosocial
Management of Epilepsy in women and girls of childbearing age,

- **QOF: Epilepsy 9**

| EPILEPSY 9. The percentage of women under the age of 55 years who are taking antiepileptic drugs who have a record of information and counselling about contraception, conception and pregnancy in the preceding 15 months | 3 | 40–90% |

**NICE menu ID: NM03**

QOF 2012 = second highest area for exception reporting
A woman's guide to epilepsy

Useful resources available e.g.

Epilepsy and breastfeeding
Mothers with epilepsy taking AEDs should be encouraged to breastfeed their babies. They should also be told that a few of the AEDs will be present in their breast milk. There is a risk that their baby may develop hypersensitivity to the AEDs present in the breast milk. Mothers taking AEDs should report any symptoms of hypersensitivity in their baby to their epilepsy specialist or GP. Symptoms of hypersensitivity include rash, sluggishness or excessive drowsiness and poor sucking.

On a positive note, available evidence shows that babies who have been exposed to their mother’s AEDs in the womb, and are then breast fed, can be weaned off their mother’s AEDs more easily. A recent study concluded that babies exposed to AEDs in their mother’s breast milk did not develop any intellectual impairment.

Further information from the British National Formulary: www.medicines.org.uk/bnf

Epilepsy and postnatal depression
Depression is a common experience for many people, but it is known to occur more often in people with epilepsy. Parents who may be depressed need thorough investigation. The underlying cause for any depression may be related to their epilepsy or their AEDs, or may be linked to their pregnancy.

There is little research available relating to postnatal depression in women with epilepsy. However a 2006 study found that over twice as many mothers with epilepsy experienced post-partum depression than mothers without epilepsy.

Children exposed to seizures and anti-epileptic drugs in the womb
Health visitors should be aware that there is a small but increased risk of malformation or neuro-developmental problems in children born to mothers with epilepsy. It is important that any child with a suspected undiagnosed malformation or neuro-developmental problem is referred to a paediatrician for early and appropriate interventions.

- **Major congenital malformations** include malformation of the spinal cord, heart, and bladder. Approximately four per cent of mothers with epilepsy who take AEDs will have a baby with a major congenital malformation (about twice the background rate).
- **Minor malformations** may not be immediately noticeable or permanent. They are variations in appearance from the norm, for example: flat nasal bridge, wide set eyes, absent or small ears. The prevalence of a number of these features may be an indication of foetal anti-convulsant syndrome and a precursor of neuro-developmental problems. (The risk of minor malformations in children born to mothers using AEDs is about twice the background rate).
- **Neuro-developmental impairment** including delayed development, delayed speech, low verbal IQ and behavioural difficulties, have been observed in children born to women with epilepsy. However, this is an area that needs more research. As current evidence suggests that AEDs play only a minor role in any neuro-developmental impairment.

For further information about AEDs and foetal malformations: www.epilepsy.org.uk/node/1177

Information resource pack for health visitors and community practitioners.
Changes to DVLA regulations for epilepsy, March 15th 2013

- Drivers who have only ever had seizures whilst asleep can set a pattern of asleep seizures after one year. There is no change for drivers who have a history of awake and asleep seizures.

- Drivers who have only ever had seizures which do not affect their consciousness or their ability to act (subject to expert medical opinion) can for the first time be licensed to drive after a 1 year pattern of such seizures has been set.
Factors which can impact on people with epilepsy

- Unemployment – occasionally exacerbated by poor job-seeking skills, non competitive, unskilled manual employment as a result of disadvantaged education, pressure of keeping current job
- Social – Social isolation as a result of no driving licence, unable to drink alcohol, stigma
- Tiredness
- Over protective parents
Marriage / Partnership

The potential impact of epilepsy on marriage / partnerships

• Less likely to marry if seizures started before 10yrs in women and before 20yrs in men
• However if seizures well controlled by 12yrs marriage rate the same as general pop.
• Men with poorly controlled seizures since childhood have high rates of separation or divorce [? linked to deception and hiding of sz. And infidelity relating to sexual problems]
• Sexuality – often lowered by AED and hypo sexuality reported in 50% of PWE involving the temporal lobe
Sexual dysfunction in epilepsy

Hypo sexuality – surveys suggest 22-67% reduction in sexual interest

Erectile Dysfunction – occurs in 57%[ Toone et al 1989], up to 83% in TLE

Sexual Functioning in Males [1989]

- Previous SI 56% [compared to 98% controls]
- S.I. in the previous month 43% [compared to 91% in controls]
- Previous erectile dysfunction 57% [compared to 18% controls]
Psychosocial aspects of epilepsy care

Psychiatric

- Depression – Up to 2/3 of PWE are depressed, with 2’ reduced libido and effects of antidepressants
- Anxiety – self medicate with alcohol

Psychosocial

In one study [1988] of 92 patients with poorly controlled epilepsy

- 68% Had no friends
- 34% Never had a “true” friendship
- 57% Never had a steady relationship
Conclusion

- Epilepsy lends itself to a logical history, investigation and diagnosis
- Diagnosis best left in the hands of an epilepsy specialist
- A diagnosis of epilepsy can change the course of someone’s life
- On-going support of epilepsy benefits from a multi-faceted approach