Epilepsies of Childhood: An Over-view of Treatment
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Outline

1. General principles of treatment
2. When the first drugs don’t work
3. Non-drug treatments
4. Other considerations
1. Introduction to GOSH Epilepsy Team
1. General principles of treatment
1. General principles of treatment

i. Expectations of treatment
ii. Decision to treat
iii. Which first drugs
Decision to treat

• Frequency of seizure
  – Don’t always need to treat e.g. Childhood Epilepsy with Centro-Temporal Spikes (CECTS)

• Severity of seizures
  – Prolonged, injury sustained; more likely to treat

• Seizure syndrome
  – Infantile spasms (impact on development)
  – Juvenile myoclonic epilepsy (life-long)
Expectations of treatment and treatment response

Commonly

- Treatment aim is seizure freedom
- Achieved with:
  - first drug in 70%
  - second drug in a further 10-20%
Anti-epileptic drugs


phenobarbitone phenytoin carbamazepine sodium valproate tiagabine zonisamide stiripentol levetiracetam tiagabine topiramate gabapentin lamotrigine vigabatrin clobazam ketogenic diet cannabidiol brivaracetam perampanel lacosamide

Slide courtesy of Prof Helen Cross
Which drug to choose?

The ideal anticonvulsant!

- Effective on multiple seizure types
- No exacerbation of other seizure types
- No side affects
- Predictable pharmacokinetics
- No interaction with other AEDs

Which drug to choose?

- No ‘ideal AED’
- What have we got?
- What do we know?
- Trade-offs: efficacy, safety and tolerability
Epilepsies: diagnosis and management

Clinical guideline [CG137]  Published date: January 2012  Last updated: February 2016  Register as a stakeholder  Uptake of this guidance

Overview
- Introduction
- Person-centred care
- Key priorities for implementation
- 1. Guidance
- 2. Notes on the scope of the guidance
- 3. Implementation
- 4. Research recommendations
- 5. Other versions of this guideline
- 6. Related NICE guidance
- 7. Updating the guideline
- Appendix A: The Guideline

Guidance

The guideline covers diagnosing, treating and managing epilepsy and seizures in children, young people and adults in primary and secondary care. It offers best practice advice on managing epilepsy to improve health outcomes so that people with epilepsy can fully participate in daily life.

MHRA advice on valproate: In February 2016, we updated this guideline to link to the Medicines and Healthcare products Regulatory Agency’s (MHRA) toolkit to ensure female patients are better informed about the risks of taking valproate during pregnancy.

Recommendations

This guideline includes recommendations on:
- diagnosis of epilepsy and investigations to support a diagnosis
‘Older’ drugs

• Phenobarbitone
• Phenytoin
• Carbamazepine
• Sodium Valproate
• Ethosuximide

‘Newer’ AEDs

• Lamotrigine
• Topiramate
• Oxcarbazepine
• Tiagabine
• Levetiracetam
• Stiripentol
• Zonisamide
• Rufinamide
• Lacosamide
• Eslicarbazepine
• (Retigabine)
• Perampanel
2. When the first drugs don’t work
Drug Resistant Epilepsy

ILAE Consensus Proposal

Failure of:

- adequate trials of
- two tolerated
- appropriately chosen
- and used AED schedules (monotherapy or combination)
- to achieve seizure freedom

Kwan Epilepsia 2010
When the first drugs don’t work - What else should we think about other than the drugs?

- Review the diagnosis
- Is the right drug being used for the seizure type and syndrome
- Compliance
- Consider the underlying diagnosis
- Non-drug treatments
Different causes of epilepsy

Classification of the Epilepsies

Seizure types*
- Focal
- Generalized
- Unknown

Etiology
- Structural
- Genetic
- Infectious
- Metabolic
- Immune
- Unknown

Epilepsy types
- Focal
- Generalized
- Combined Generalized & Focal
- Unknown

Epilepsy Syndromes

Scheffer Epilepsia 2017
How many drugs should you try?

Quantifying the response to AEDs: Effect of past treatment history
Schiller, Y. et al. Neurology 2008;70:54-65
Non-drug treatments

Promptly consider:

- Ketogenic diet
- Pre-surgical evaluation
- Vagus Nerve Stimulation
- (Novel therapies)
3. Non-drug treatments
Ketogenic diet

- High fat, low carbohydrate diet
- Modified Atkin’s Diet for teenagers
Epilepsy surgery

Definition

- Removal of an area of the brain with the aim of alleviating seizures

Aims

- Primary: seizure freedom/reduction
- Secondary:
  - neuro-developmental gains
  - behavioural improvement
Types of surgery

Lesionectomy
Types of surgery

Lobectomy
Types of surgery

Hemispherotomy
Types of surgery

Corpus Callosotomy
Invasive monitoring

Co-registration CT & MRI

Slide Courtesy of Charlotte Wilkinson, Martin Tisdall
Why epilepsy surgery

- 70% chance overall for curing epilepsy
- No minimum age
- Consider the effect of epilepsy on early brain development
- Functional plasticity of the child’s brain
Epilepsy Service at GOSH

Welcome to the Children's Epilepsy Surgery Service

Information for families

Great Ormond Street Hospital for Children
NHS Foundation Trust

Great Ormond Street Hospital for Children
International and Private Patients Service
Identification of suitable candidates for Presurgical Evaluation (All)

Phase 1 investigations (All)

Phase 1 investigations—extended (selected children)

Phase 2 investigations (selected children)

Outcome of PSE (All)

Drug-resistant epilepsy and/or lesion on MRI

Detailed clinical history and examination for localising or lateralising features

To localise/lateralise the epileptogenic zone

MRI—high resolution
Video-EEG—scalp, including sleep, usually long-term monitoring but in high seizure burden a prolonged recording may be adequate

MRI –3T
Interictal source localisation
- MEG
- EEG-fMRI
Ictal source localisation
- High density EEG
Interictal hypoperfusion
- PET
Ictal hyperperfusion
- SPECT

To assess the risk of post-operative deficit

Neuro-psychology
Neuro-psychiatry
Neuro-ophthalmology

Functional imaging
- fMRI language, motor, visual
Tractography
- Motor
- Optic
Wada test (largely replaced by language fMRI)
Physiotherapy, occupational therapy, dysphagia assessments

Discussion at the multi-disciplinary team Epilepsy Surgery Meeting

Intracranial recording— ictal localisation or mapping of eloquent cortex

Declined—not suitable for epilepsy surgery.
Offer—ongoing medical management, stimulation therapies, ketogenic diet

Offer epilepsy surgery

Varadkar, and Tisdall. OUP in print
VNS Therapy
VNS Therapy

- Non-pharmacological therapy for epilepsy
- Repeated electrical stimulation of the left vagus nerve by a programmable pulse generator device
- Ramped up stepwise over months
- Magnet swipe may shorten the stop seizures
VNS is recommended in the UK
VNS effectiveness in different paediatric epilepsies?

VNS efficacy by etiology

<table>
<thead>
<tr>
<th>Condition</th>
<th>VNS Efficacy</th>
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<tbody>
<tr>
<td>Infection</td>
<td>45%</td>
</tr>
<tr>
<td>Neuronal migration disorder</td>
<td>50%</td>
</tr>
<tr>
<td>Lennox Gastaut</td>
<td>51%</td>
</tr>
<tr>
<td>Unknown</td>
<td>65%</td>
</tr>
<tr>
<td>Genetic/metabolic syndrome</td>
<td>67%</td>
</tr>
<tr>
<td>Cerebral palsy/static encephalopathy</td>
<td>69%</td>
</tr>
<tr>
<td>Tuberous Sclerosis</td>
<td>75%</td>
</tr>
</tbody>
</table>

VNS efficacy by epilepsy classification

<table>
<thead>
<tr>
<th>Type</th>
<th>VNS Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-focal partial</td>
<td>50%</td>
</tr>
<tr>
<td>Symptomatic generalised</td>
<td>63%</td>
</tr>
<tr>
<td>Idiopathic generalised</td>
<td>67%</td>
</tr>
<tr>
<td>Multi-focal partial/ symptomatic generalised</td>
<td>72%</td>
</tr>
<tr>
<td>Focal</td>
<td>86%</td>
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</tbody>
</table>

Median seizure reduction at 12 months (N=141)^

Elliott J Neurosurg Pediatrics 2011
VNS Effectiveness Over Time

% of patients with >50% seizure reduction vs. baseline

Last Visit Carried Forward (N=440)

- 3 Months: 23%
- 1 Year: 37%
- 2 Years: 43%
- 3 Years: 43%

New Generation VNS Therapy

AspireSR

What’s new? Cardiac-based seizure detection

- (Standard VNS Therapy stimulation with on-demand magnet stimulation)
- Seizure detection algorithm based on ictal tachycardia
- Automatic stimulation upon seizure detection
Even Newer Generation VNS Therapy

SenTiva

**Personalised features**

- Guided programming
- Scheduled programming
- Day and night programming
New treatments

Drug
• Revisiting old drugs
• New drugs
• Drugs that have new targets
• Drugs that target new pathways

Non-drug
• Immune therapies
• New surgical approaches
• Neuro-modulation
4. Other considerations
4. Other considerations in treatment
Be a normal child/young person

**Aim**
- Develop and play
- Go to school and learn
- Interact and enjoy life with family and friends
- Grow in independence

**Consider**
- Sensible weighing up of risks
Be a normal child/young person

Encourage

• Assessment of development
• Assessment of education needs
• Activities including swimming

Think about

• Triggers
• Compliance with medication
• Medic-alert bracelets
• Keeping safe when out and about
• Plan for prolonged seizures
Co-morbidities of epilepsy in childhood

**Commonly**
- Motor disorder
- Learning difficulties
- Attention Deficit Hyperactivity Disorder (ADHD)
- Autism
- Mood disorder

**Good news**
- These do respond to appropriate treatment
Summary

• There are many types of epilepsy in childhood
• The first AED will work for 70% of patients
• If it doesn’t, consider the seizure type, syndrome, cause and compliance
• In children with drug-resistant epilepsy, non-drug options should be considered early and include ketogenic diet, epilepsy surgery and Vagus Nerve Stimulation therapy
• Lead a full life with epilepsy
Thank You