Clinical Guidance

INFANTILE (EPILEPTIC) SPASMS AND WEST SYNDROME GUIDELINE

Introduction

Infantile epileptic spasms are part of an age related epileptic encephalopathy characterised by typical spasms and an abnormal EEG. The triad of epileptic spasms, with concordant EEG abnormality alongside developmental plateauing or regression is termed West Syndrome[1,2]. Aetiology is heterogeneous but includes underlying structural, genetic and metabolic disorders. Spasms may emerge on the background of a previously recognised brain abnormality e.g. following a perinatal hypoxic ischaemic encephalopathy or in context of tuberous sclerosis.

Clinical spasms can range from subtle, single spasms involving a flexion of the neck or bowing of the head, to full body flexor, extensor or mixed flexor-extensor spasms occurring in clusters many times throughout the day. Spasms typically cluster on waking from sleep, or sometimes going off to sleep, but rarely arise from sleep itself.

The EEG is always abnormal. The characteristic EEG pattern is termed hypsarrhythmia or modified hypsarrhythmia. However this may not be present throughout the EEG, and particularly in the early stages may only be demonstrated in sleep. In the presence of apparently typical spasms, but a normal EEG it is essential to capture spasms during the recording to confirm the diagnosis.

The incidence of West syndrome is estimated to be 1 in 2,500 – 3,000 children with 350-400 infants per year identified in the UK. Assuming a population of 3.5 million for SE London, Kent and East Sussex, this means approximately 20 – 25 infants per year identified with West syndrome.

Document Detail	
Document type	Clinical Guideline
Document name	INFANTILE (EPILEPTIC) SPASMS AND WEST SYNDROME GUIDELINE
Document location	GT*i* Clinical Guidance Database
Version	1
Effective from	
Review date	
Owner	Head of Paediatric Neurosciences
Author(s)	Dr Elaine Hughes, Dr Ruth Williams, Dr Nikil Sudarsan South East Thames Paediatric Epilepsy group (SETPEG)
Approved by, date	
Superseded documents	
Related documents	
Keywords	Guideline, Evelina, Paediatrics, Infantile spasms, Neonatal seizures, Hypsarrhythmia, West Syndrome, steroids.
Relevant external law, regulation, standards	

Change History		
Date	Change details, since approval	Approved by

Diagnosis:

Infants with possible epileptic spasms need to be seen urgently (within 48 hours) and discussed with a consultant paediatrician with epilepsy expertise as soon as possible.

Once diagnosis established all children with infantile epileptic spasms should be discussed with the Regional Epilepsy or Neurology service [3], but this should not delay treatment

Assessment to include:

- Detailed description of events including video footage where available
- Developmental history
- Background pregnancy, perinatal history and family history
- Physical examination including careful documentation of head circumference
- Wood's lamp examination unless underlying diagnosis already established.

Investigations [2, 4, 5]

EEG: urgent recording (within 72 hours) to include awake and sleep recording and seizure capture if possible – latter essential prior to commencing treatment if interictal EEG normal.
Imaging: MRI Brain with epilepsy protocol scan (unless previous diagnostic scan available e.g. in a child with pre-existing developmental delay or previous perinatal difficulties)
Referral for ophthalmology review (non-urgent)

Other possible first line investigations:
1. Blood – FBC, U&E's, LFT's, lactate, ammonia, blood gas, glucose, Ca, Mg, PO4, plasma amino acids, biotinidase
2. Urine – organic acids, AASA (for pyridoxine dependent seizures).
3. Genetic studies: CGH array and save blood for DNA analysis and further targeted gene testing (in discussion with tertiary service). In suggestive cases may proceed immediately to specific testing e.g. ARX or CDKL5 gene analysis.
4. Varicella serology for information regarding immune status pending possible steroid therapy
5. In selected cases: TORCH screen - urine for CMV, throat swab for viral culture, blood for toxoplasma, rubella and CMV IgG/ IgM.
6. In selected cases: trial of pyridoxine (in discussion with tertiary team)

Second-line investigations: (depending on individual case and /or following discussion with tertiary neurology)
1. Blood - Copper, caeruloplasmin, acylcarnitine profile, VLCFA, transferrin electrophoresis for Congenital Disorders of Glycosylation (CDGs).
2. Urine - oligosaccharides, sulphocysteine.
3. CSF (ideally after 4 hour fast) - glucose, lactate, protein and cell count (with paired plasma samples, CSF amino acids (with paired serum samples) and CSF neurotransmitters.
4. ECG and Echo – if abnormal cardiac examination or suspecting Tuberous Sclerosis Complex (TSC).
5. Renal USS – if TSC suspected.
6. Epilepsy gene panel or other targeted gene analysis

Management

Information for families about infantile spasms:

Epilepsy Action	www.epilepsy.org.uk
UK Infantile Spasms Trust	https://ukinfantilespasmstrust.org [6]

First line Treatment

Treatment should be commenced as soon as possible after diagnosis, as the longer the lead time to starting treatment, the worse the outcome may be [7]. Inpatient treatment is ideal for the first few days for monitoring medication side effects and response, and discussing expectations with parents. Steroids and Vigabatrin are considered as the first line medications for infantile spasms[8] and ACTH injections are not considered superior to oral prednisolone in treatment of infantile spasms.[9, 10]

For TSC: Vigabatrin should be used as first line, without steroids

If **not** TSC: Combination therapy with steroids and vigabatrin has been shown to produce quicker spasm resolution.[11]

<table>
<tr><th colspan="4">COMBINATION THERAPY WITH PREDNISOLONE AND VIGABATRIN</th></tr>
<tr><th colspan="3">Prednisolone</th><th colspan="2">Vigabatrin</th></tr>
<tr><td rowspan="3">Day 1-6</td><td colspan="2" rowspan="3">10mg QDS for 1 week</td><td>Day 1</td><td>50 mg/kg per day in two divided doses</td></tr>
<tr><td>Day 2
Day 3</td><td>100 mg/kg per day in two divided doses</td></tr>
<tr><td>Day 4 (post 72 hrs)</td><td>If spasms ongoing: Increase to 150 mg/kg per day in two divided doses.</td></tr>
<tr><td>Day 7 review</td><td>Spasms on-going (last 24 hours) or spasm recurrence in the second week</td><td>Resolution of spasms (no spasm in the last 24 hours)</td><td colspan="2" rowspan="8">After Day 5:
Continue on 100 mg/kg/day or 150mg/kg/day for 3 months.
Then wean and stop over the next 4 weeks.</td></tr>
<tr><td></td><td>⬇</td><td>⬇</td></tr>
<tr><td>Day 8-14</td><td>20mg TDS</td><td>10mg QDS</td></tr>
<tr><td>Days 15-19</td><td>20mg BD</td><td>10mg TDS</td></tr>
<tr><td>Days 20-24</td><td>20mg daily</td><td>10mg BD</td></tr>
<tr><td>Days 25-29</td><td>10mg daily</td><td>10mg daily</td></tr>
<tr><td></td><td colspan="2">STOP</td></tr>
</table>

If monotherapy is chosen, by clinician or parent preference, follow same doses as above for steroid/vigabatrin.

Monitoring and counselling during treatment

STEROIDS

- Gastric protection (omeprazole/ranitidine) to be given during the entire steroid course
- Counsel regarding adverse effects – decreased immunity (particularly risk with chicken pox contact), irritability, increased appetite, weight gain, hypertension, rarely high blood sugars (usually not needing treatment)
- Monitoring – whilst inpatient, with daily blood pressure and urine sugar.
- Outpatient – alternate daily BP and urine sugar weeks 1 and 2, then twice weekly if stable thereafter. If BP>120/80 – obtain 3 serial readings; if consistently over 120/80 start antihypertensive treatment (amlodipine).
- If not immune to varicella, advice on steps to be taken if comes into contact with chickenpox (valid up to 3 months post steroid treatment; advice to be adapted as per local arrangements)
- Investigate for infection if becomes unwell/febrile

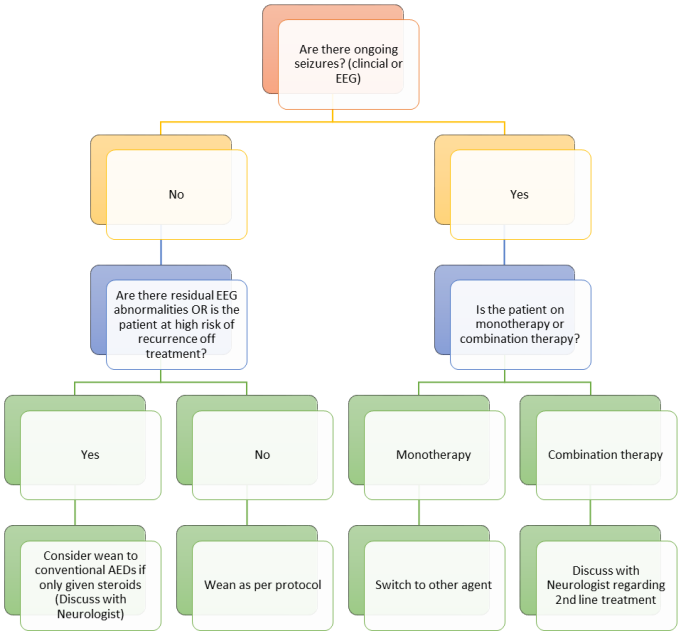
VIGABATRIN

- Counsel regarding drowsiness, irritability and rarely a movement disorder as side effects.
- Discuss regarding the potential side effect of peripheral visual field constriction if used for longer than 6 months.

Further review:

After 2 weeks on high dose steroids and/or vigabatrin, reassess for any clinical spasms or other seizures as well as EEG (between 14-21 days) response.
If seizure free but on-going residual EEG abnormalities or considered high risk for seizure recurrence off treatment – consider weaning to conventional AEDs if only given steroids - discuss with tertiary neurology team. Otherwise wean off treatment as per protocol
If continuing seizures, then switch to other agent if previously had monotherapy with either vigabatrin or steroids. If continuing seizures in spite of trials of vigabatrin and steroids or one of these agents contraindicated for any reason, will need to discuss second line treatment again in consultation with Regional Epilepsy or Neurology service.

Assess ment



Second line treatment

May include (in no recommended order as this will depend on the infant's presentation and possible underlying aetiology):

1. Trial of pyridoxine – see separate protocol

2. Topiramate or zonisamide
3. Sodium valproate
4. Nitrazepam
5. Ketogenic diet
6. Evaluation for epilepsy surgery
7. Where prednisolone has been used but ineffective or partially effective, there are occasional children who appear to respond to depot tetracosactide (Synacthen).

Follow up

Close follow up required for developmental monitoring by a Community Paediatrician, following referral and ongoing treatment of seizures.

Table of abbreviations used:

Abbreviation	Meaning
AASA	Alpha-amino adipic semialdehyde
ACTH	Adrenocortiotropic Hormone
AEDs	Anti-Epileptic Drugs
ARX gene	Aristaless related homeobox gene
CDKL5 gene	Cyclin dependent kinase like 5 gene
CGH Array	Comparative genomic hybridisation array
CSF	Cerebrospinal Fluid
EEG	Electroencephalogram
TORCH screen	Toxoplasma, Other (Syphilis), Rubella, Cytomegalovirus, Herpes Simplex Virus
TSC	Tuberosclerosis Complex
VLCFA	Very Long Chain Fatty Acid

References: 1. Pavone P, Striano P, Falsaperla R, Pavone L, Ruggieri M. Infantile spasms syndrome, West syndrome and related phenotypes: What we know in 2013. Brain Development. 2014;36(9):739-51.
2. Pellock J et al Infantile spasms: a US consensus report Epilepsia 2010 (51) 2175 –