Epileptic Spasms; clinical guideline for diagnosis, investigation and management

NHS Birmingham Women's and Children's NHS Foundation Trust

Worcestershire NHS Acute Hospitals NHS Trust

1. Introduction and scope of guideline

- Epileptic spasms (ES) are a type of epileptic seizure presenting in infancy (typically from birth to 2 years of age) associated with early developmental impairment in the majority of children.
- There is evidence that early recognition, diagnosis and treatment of ES may lead to improved neurodevelopmental outcome.
- The treatment of ES differs significantly from that of other epilepsies.
- *ES* are of longer duration than myoclonus and shorter than tonic seizures.
- Semiology may be truncal flexion with stiffening of arms and legs (flexor spasms) or extension of the back, arms and legs (extensor spasms).
- Subtle events may be seizures such as a head nod. ES often occur in clusters and multiple times each day, often on waking. The child may be more irritable or may have regressed or plateaued in their development.
- West Syndrome is the triad of 1) epileptic spasms 2) developmental regression 3) hypsarrhythmia on EEG. ***Children do not need to have all of these features to benefit from treatment, with the focus based on the clinical semiology of events.***
- This guideline is for all health professionals in the West Midlands Regional Paediatric Neurology Network. It provides a framework for the diagnosis, investigation and treatment of ES. ***Nonetheless, we would strongly recommended discussion of all suspected cases of ES with the on-call Paediatric Neurology Team.***

2. Diagnosis of Epileptic Spasms

Clinical suspicion of Epileptic Spasms based on event semiology

Obtain urgent SLEEP EEG (NB all efforts must be made to capture a period of sleep) within 24 hours of presentation and ask parents to take videos of events

EEG reported as hypsarrhythmia/ modified hypsarrhythmia	EEG reported as showing epileptiform abnormalities but not hypsarrhythmia or modified hypsarrhythmia	Sleep EEG reported as normal but events still ongoing and clinically convincing of epileptic spasms
Start treatment (see section B) and obtain MRI brain and further investigations as appropriate (see section 3)	Discuss case with Paediatric Neurologist and email video of events if possible	Discuss case with Paediatric Neurologist and email video of events if possible

3. Management of Epileptic Spasms

Diagnosis of Tuberous Sclerosis

NO

- Start Prednisolone 40mg once a day depending on local availability
- Start vigabatrin
  D1- 25mg/kg BD
  D2- 50mg/kg BD-
  D5- If tolerated consider increasing to 75mg/kg BD if spasms still present
  Continue vigabatrin for 3 months
- Start oral gastroprotection- lansoprazole
- Discharge after 24-48 hours of inpatient monitoring of blood pressure/ blood sugars, then alternate day blood pressures and blood sugars. Aim for random blood sugar of less than 11mmol/L and blood pressure less than 99th centile systolic and diastolic (by days case unit or community nursing staff depending on local availability)
- In babies less than six months or less than 5 kilograms- check renal function weekly whilst on high dose steroids
- All families to go home with leaflet on precautions to take whilst on high dose steroids

YES

1. Start vigabatrin (no need for steroids)
   D1- 25mg/kg BD
   D2- 50mg/kg BD
   D5- if tolerated consider increasing dose to 75mg/kg BD if spasms still present on telephone review
2. Organize urgent echocardiogram (? Cardiac rhabdomyoma) and urgent renal ultrasound (? Angiomyolipomas) as well as Ophthalmology review
3. Send Genetics for TSC1/ TSC2 mutation
4. Referral to TS clinic at BCH (Paediatric Neurology and Nephrology)
5. Follow-up EEG in 2 weeks

If ongoing spasms/ hyspsarrythmia despite vigabatrin- discuss with Paediatric Neurology on-call team

Telephone review at 1 week

- If no spasms- continue prednisolone 40mg OD for 7 days

B. If clinical spasms still present- increase prednisolone to 60mg once a day

Repeat Sleep EEG at 2 weeks with clinical review

- ***If ongoing spasms or if EEG still shows (modified) hypsarrhythmia – discuss urgently with neurology***
- If no spasms and EEG shows improved background (i.e. not hypsarrhythmia/ modified hypsarrhythmia)- Wean off steroids;
- If on prednisolone 40mg OD- then give a weaning course of oral prednisolone- 30mg OD for 5 days, 20mg OD for 5 days, 10mg OD for 5 days and then stop
- If on prednisolone 60mg OD- then give a weaning course of oral prednisolone- 40mg for 5 days, 30mg for 5 days, 20mg for 5 days, 10mg for 5 days and then stop
- Continue Vigabatrin for 3 months. Review in clinic - if no seizures wean over 1 month

Further treatment options for ongoing clinical spasms or continued hypsarrhythmia (under expert Paediatric Neurology Guidance only)

- Consider a prolonged course of high dose steroids (upto six weeks) and switching from prednisolone to Depot ACTH*
- Consider a trial of pyridoxine-5-phosphate (particularly if MRI scan and other investigations all normal)
- Consider addition of Sodium Valproate (only if LFTs normal and mitochondrial disorder not suspected)
- Consider 'fast-track' epilepsy surgery referral if cortical dysplasia/ structural lesion is suspected on MRI
- Consider ketogenic diet if spasms still refractory to treatment on steroids
- Consider addition of nitrazepam particularly if significant irritability present

**NB Depot ACTH is contraindicated in neonates*

4. Pathway for investigation of Epileptic Spasms

Unnecessary and costly investigations for the cause of epileptic spasms can be limited by obtaining an MRI brain as the initial investigation with reporting by a Paediatric Neuroradiologist followed by targeted investigations

Obtain urgent (within 7 days of diagnosis) epilepsy protocol MRI brain (on a 3 tesla magnet if possible) ***Must be reported/ reviewed by a Paediatric Radiologist at BCH.*** If obvious clinical diagnosis i.e. Down's Syndrome then a MRI is only investigation needed

Clear abnormality- targeted investigations after discussion with Paediatric Neurology team i.e.

- Tubers- gene for TSC1/ TSC2 as well as echocardiogram and renal ultrasound
- Perinatal Stroke- targeted investigations for cause of stroke i.e. echocardiogram
- Imaging suggestive of hypoxic ischemic injury no further investigations if history consistent
- Lissencephaly/ polymicrogyria/ pachygyria- consider targeted genetic investigations
- Features suggestive of mitochondrial/ metabolic disorder- liaise with IMD/ neurology teams for targeted metabolic investigations. Investigations such as white cell enzymes will need special arrangement with the lab.

2nd line investigations- MRI brain reported as normal or non-specific abnormalities

Suggest the following 2nd line investigations

- Urgent Microarray and save DNA
- Metabolic 'screen' – urine organic acids, plasma amino acids including sulphocysteine and homocysteine, carnitine and free acylcarnitine profile, biotinidase, uric acid, urine 5-AASA, urine oligosaccharides, urine glycosaminoglycans, urine creatinine and guadinoacetate ratio, copper & ceruloplasmin (in boys), transferrin glycoforms , very long chain fatty acids
- Lumbar puncture for paired CSF and serum glucose, paired CSF and serum lactate, CSF neurotransmitters (if possible), paired CSF and serum amino acids

3rd line investigations- Send for Urgent GOSH epilepsy gene panel or Whole Genome Sequencing (from 2021)

- Consider repeat 3T MRI brain scan after completion of myelination after 2 years of age especially if ongoing seizures

5. Management of hypertension/ hyperglycaemia

- Monitor blood pressure with an appropriate size cuff on the upper extremity only whilst on steroids
- Hypertension is a commonly encountered side effect of steroids while resolves when steroids are weaned
- Treat hypertension only if systolic blood pressure is above 99th centile for child's sex/length
- Treat with amlodipine 100micrograms/kg once a day- aiming for a blood pressure below the 99th centile systolic
- Amlodipine can be increased to 400micrograms/kg once daily but if blood pressure is still not below 99th centile systolic- please liaise with Paediatric Nephrology urgently
- Significant hyperglycemia is rare in children with ES on steroids, if blood sugars are above 11mmol/L please check ketones and liaise with Paediatric Endocrinology on an urgent basis

6. Important information on risks of treatment

- Vigabatrin may be associated with increased sedation/ drowsiness initially but this will often subside after the first week of treatment
- Vigabatrin may cause peripheral visual field loss with prolonged use. Parents should be aware of this as a possibility.
- Vigabatrin therapy may cause a hyperkinetic movement disorder. Liaise with Paediatric Neurology regarding reducing/ stopping vigabatrin if this occurs.
- Vigabatrin is also known to cause reversible changes on MRI scans which may be mistaken for a neu rometabolic disorder
- Steroids may be associated with significant weight gain, irritability and susceptibility to infection particularly s evere chicken pox / shingles
- If there is ***no*** previous clinical history of chicken pox in a child on/within 3 months of stopping steroids for ES and there is a significant exposure to an individual with chicken pox or shingles then give oral acyclovir on days 7-14 after exposure
- If a child currently on steroids/ has previously been on steroids for ES in the last 3 month develops clini cal features of chicken pox/ shingles they should be treated with IV aciclovir until vesicles have crusted over followed by oral aciclovir for 5 days in total
- All **live** vaccines should (i.e flu ,MMR and BCG) should be postponed until 3 months after stopping steroids. Attenuated vaccines can still be safely given.
- All children on/within three months of stopping steroids for ES should have an urgent medical assessment if if they develop a fever with a low threshold for starting antibiotics if appropriate

7. Suggested follow-up

- Outpatient follow-up with local Paediatrician with expertise in Epilepsy until at least 2 years of age
- In accordance with NICE guidelines outpatient clinical review by a Consultant Paediatric Neurologist at least once even in cases where spasms have responded to treatment
- Neurodevelopmental follow-up for all children with ES involving Community Paediatrics and therapy services where appropriate

8. Criteria for ongoing Paediatric Neurology follow-up

- Ongoing or recurrent Epileptic Spasms despite treatment with steroids/ vigabatrin
- Diagnosis of neurometabolic disorder, tuberous sclerosis or no cause of ES identified

9. Suggested standards

- All children with suspected ES. Should have a sleep EEG within 24 hours of presentations during normal working days.
- All children with ES should have treatment initiated after EEG where appropriate on the same day
- All children with ES should have an MRI brain scan within 7 days of diagnosis with the MRI reviewed by a Paediatric Radiologist.
- All children with ES should be discussed with a Paediatric Neurologist with further investigations and treatment recommended on a case by case basis where appropriate

10. References

O'Callaghan, Finbar JK, et al. "Vigabatrin with hormonal treatment versus hormonal treatment alone (ICISS) for infantile spasms: 18-month outcomes of an open-label, randomised controlled trial." *The Lancet Child & Adolescent Health* 2.10 (2018): 715-725