Sheffield Children's NHS
NHS Foundation Trust

Infantile Spasms (West Syndrome)

Reference:	1830v1
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Approved:	June 2018
Review Due:	June 2021

Purpose

To standardize initial investigation and management of patients suspected of having infantile spasms in the Sheffield region.

Intended Audience

This guideline is for paediatric health professionals in a secondary and tertiary care setting in the South Yorkshire region.

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1. Introduction

Infantile spasms, also known as West Syndrome, is a severe infantile epilepsy syndrome with a characteristic age of onset (2-14 months), pattern of seizures and electroencephalogram (EEG). There is high morbidity (intellectual impairment, ongoing epilepsy, etc.) associated with infantile spasms.

The spasms typically consist of a sudden truncal flexion with stiffening of arms and legs but can also be extension of the back, arms and legs. It may also be subtle, such as a head nod. The spasms can occur in clusters and multiple times a day. The child may have regressed or plateaued in their development.

Confirmation of the diagnosis requires an EEG. Hypsarrhythmia, disorganized activity with high voltage slow waves and multifocal spikes, is the characteristic EEG finding in infantile spasms (IS). If an EEG show supportive features of IS without showing the full features of hypsarrhythmia this is termed 'modified' or 'atypical' hypsarrhythmia. These EEG changes are identified more sensitively in sleep.

2. Intended Audience

This guideline is for paediatric health professionals in a secondary and tertiary care setting in the South Yorkshire region.

3. Guideline Content

A. DIAGNOSTIC EVALUATION FOR INFANTILE SPASMS

If a child is suspected to have IS a thorough history, physical examination and EEG, is necessary to establish if it is indeed IS. Many other conditions can mimic IS (benign sleep myoclonus, Moro reflex, etc).

Once the diagnosis is confirmed, efforts should be made to establish the underlying aetiology, as this significantly affects treatment decisions and prognosis. The differential diagnoses in IS is broad. Evaluation should follow a step-wise process to limit the number of low-yield or unnecessary tests being performed.

HISTORY & EXAMINATION

History should focus on:

- Semiology of the events (video recording from family often invaluable)
- Frequency & clusters (versus single spasms)
- Development prior and changes associated with onset of spasms
- Family history of similar events in infants
- Thorough birth and pregnancy history

Examination should include:

- Head circumference
- Neurocutaneous stigmata (using Wood's lamp)
- Blood pressure
- Identifying possible syndromes (e.g. Trisomy 21)

EEG

- EEG should ideally be performed urgently if IS is suspected. It should be done within 3 days.
- A routine video EEG, ideally capturing sleep, should be performed in the first instance. Sleep is an important part of the EEG evaluation for infantile spasms. Hypsarrhythmia may be present in non-REM sleep even if absent while awake.
- If initial EEG does not reveal hypsarrhythmia or a variant of hypsarrhythmia but did not capture sleep, a sleep EEG should be performed (e.g. at usual nap time or after feed).
- If the EEG has captured sleep and awake periods without revealing hypsarrhythmia, and IS is still suspected, a repeat sleep EEG should be performed in 7-10 days as clinical spasms may sometimes precede electrographic changes. If in doubt contact the paediatric neurology team.

REFERRAL TO PAEDIATRIC NEUROLOGY

All children with probable and confirmed IS should be discussed with the paediatric neurology team.

B. TREATMENT

Treatment should be initiated as soon as possible, once the diagnosis of infantile spasms is confirmed on EEG. The goals of therapy should be a complete cessation of the clinical events and resolution of hypsarrhythmia or modified hypsarrhythmia on video EEG.

Treatment is also directed by the aetiology of the spasms. Patients with tuberous sclerosis complex (TSC) are more likely to respond to treatment with vigabatrin. Hormonal therapy is associated with better developmental outcome in patients with IS without any proven aetiology for their spasms. Hormonal therapy with vigabatrin is significantly more effective at stopping infantile spasms than hormonal therapy alone in patients with IS, excluding patients with TSC. We have taken a pragmatic approach whilst further evidence emerge on the best treatment for IS due to different aetiologies.

FIRST LINE TREATMENT

- Treatment should be commenced as soon as possible, ideally on the same day as diagnosis confirmed on EEG.
- All patients should be offered combination therapy of vigabatrin and corticosteroids (O'Callaghan *et al.* 2017).
- Potential adverse reactions to medication should be discussed with the family.

CORTICOSTEROID TREATMENT

Corticosteroid treatment for IS is given in the form of oral prednisolone or intramuscular tetracosactide. Prednisolone is the preferred choice at Sheffield Children's Hospital.

PREDNISOLONE

Dose: 10 mg four times a day for 14 days.

If spasms continue on Day 7 or reappear between Day 8 and Day 14 the dose is to be increased to 20 mg three times a day for the remaining duration.

Adverse reactions to corticosteroids include:

- Irritability.
- Hypotonia and hypertonia
- Increased appetite and weight gain.
- Gastro-intestinal upset.
- Fluid and electrolyte disturbance, including systemic hypertension and its consequences.
- Endocrine and metabolic disturbance, including hyperglycaemia, hypernatraemia and hypokalaemia.
- Neuropsychiatric disturbance including sleep disturbance.
- Infections including varicella zoster infection (prophylaxis may be required in the event exposure to varicella zoster).
- Immunosuppression and its consequences (including vaccinations).

VIGABATRIN

Vigabatrin is given orally twice a day.

Dose:

25mg/kg for 2 doses (dose 1 &2) then;

50mg/kg for 6 doses (doses 3-8)

If no spasms in the previous 24 hours of dose 9 (at 96 hours after starting vigabatrin), maintain dose at 50 mg/kg twice daily.

If spasms have occurred in the previous 24 hours of dose 9 (at 96 hours after starting viagabatrin), or if spasms reappear after dose 9 but before day 14, increase dose to 75 mg/kg twice daily.

Administration:

Available as 500mg sachets. Dissolve the contents of each 500mg sachet in 10ml water to produce a mixture containing 50mg/ml. Round doses to the nearest 25mg (0.5ml). The child's weight at diagnosis is used during the first 14 days of treatment.

Adverse reactions to vigabatrin include:

- Drowsiness.
- Hypotonia.
- Increased appetite and weight gain.
- Gastro-intestinal upset.
- Visual field constriction.
- Neuropsychiatric disturbance including sleep disturbance.
- Movement disorders.

MONITORING AND PROPHYLAXIS WHILST ON TREATMENT

For corticosteroids:

- Concomitant gastric protection (H2-receptor antagonist or proton pump inhibitor) for the duration the child is on steroids.
- Blood pressure before treatment and on days 2 and 7 of treatment.
- Urine for glycosuria daily if in-patient, and days 2 and 7 if outpatient.
- Urea and electrolytes pre-treatment and on day 7.
- Varicella serology status pre-treatment.

For vigabatrin:

For vigabatrin no specific monitoring is required. If duration of treatment is shorter than 6 months, the occurrence of visual field defects is low (about 5%). This seems to increase with length of treatment but in reality, visual field testing in very young children is impractical.

WEANING STEROIDS

This should start on day 15, regardless whether spasms continue or abnormal EEG persists.

If receiving prednisolone at 10 mg four times a day wean as follows:

10 mg three times a day for 5 days

10 mg twice a day for 5 days

10 mg once daily for 5 days then stop.

If receiving prednisolone at 20 mg three times a day wean as follows:

10 mg four times a day for 5 days

10 mg twice a day for 5 days

10 mg once daily for 5 days then stop.

WEANING VIGABATRIN

This should occur only after 3 months from initiation of treatment (day 0) if the child has responded to the initial treatment by day 14. The vigabatrin dose will continue at the same dose on body weight basis (but to the nearest 25 mg per dose) for 3 months.

At 3 months wean vigabatrin as follows (all done to the nearest 25mg or 0.5ml):

- Four fifths of maximum total daily dose prior to weaning for 1 week
- Three fifths of maximum total daily dose prior to weaning for 1 week
- Two fifths of maximum total daily dose prior to weaning for 1 week
- One fifth of maximum total daily dose prior to weaning for 1 week
- Then stop.

If child has not responded by day 14 please discuss with the paediatric neurology team regarding weaning vigabatrin.

SECOND LINE TREATMENT.

- If first line treatment has not stopped spasms on or after day 14 second line treatment should be discussed with the paediatric neurology team.
- If relapse of spasms occur after 3 months from initial treatment of spasms clinicians are recommended to discuss this with the paediatric neurology team.
- Potential second line treatment are pyridoxal phosphate, pyridoxine, sodium valproate, nitrazepam, topiramate, zonisamide, the ketogenic diet and epilepsy surgery.

C. MONITORING ELECTROGRAPHICALLY

- All patients should have an EEG at 2 weeks (day 12-15) after commencing treatment regardless of whether the spasms have stopped.
- Children with normal EEG or an acceptable improved EEG should have their steroids weaned as above.
- Those with persistent EEG abnormalities supporting IS should be discussed with the paediatric neurology team for consideration of second line treatment.

D. OTHER INVESTIGATIONS (DIAGNOSTIC)

- Every effort should be made to determine the aetiology of the IS as this can help determine the likelihood of response to treatment, guide therapeutic decisions and help provide a more definitive prognosis for the child.

- The most common aetiologies were: hypoxic-ischemic encephalopathy (10%), chromosomal (8%), malformations (8%), stroke (8%), TSC (7%), and periventricular leukomalacia or haemorrhage (5%).
- An MRI brain scan is the first diagnostic investigation recommended if an aetiology is not already obvious from clinical evaluation. Clinical evaluation and MRI provided a specific diagnosis in 55% of children presenting IS.
- If no obvious cause is found after performing an MRI brain a CGH array genetic test is recommended.
- Perform also serum lactate, serum amino acids, urine organic acids.
- If the CGH array and other tests have not provided a definitive aetiology, discuss performing an epilepsy gene panel and further investigations with the paediatric neurology team. Ophthalmology assessment may be helpful in identifying a diagnosis.
- Other investigations may be required once a cause has been found (e.g. echocardiogram and renal ultrasound scan for TSC).

E. References

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Appendix 1
Infantile spasms management algorithm
(Refer to full guideline for specific details)

Initial assessment & diagnosis

- History & examination (including OFC, Wood's light, BP, developmental status)
- Urgent EEG (within 3 days) capturing sleep and awake periods confirming 'hysparrhythmia' or 'modified hysparrhythmia'
- Referral to paediatric neurology

First line treatment

- Treatment to be commenced as soon as possible after confirmatory EEG
- Discuss potential adverse reactions of treatment with family
- Start combined treatment of
  - Prednisolone 10 mg four times daily
  - Vigabatrin 25 mg/kg twice daily

  (Refer to guideline for further information)
- Monitor BP, urine glycosuria, UE
- Take varicella serology pre-treatment
- Gastric protection with steroid treatment

Further investigations

- Repeat EEG at 2 weeks
- Diagnostic investigations if cause of IS unknown performed in the following order until cause identified:
  - MRI brain
  - CGH array, serum lactate, serum amino acids and urine organic acids. Ophthalmology assessment (may be helpful in identifying a diagnosis)
  - Discuss further investigations with paediatric neurology team and this may include an Early Epilepsy Gene Panel