Clinical Guideline

IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH): INVESTIGATION AND MANAGEMENT IN CHILDREN

SETTING	Bristol Royal Hospital for Children
FOR STAFF	Medical staff looking after children with suspected IIH
PATIENTS	Paediatric patients with suspected IIH

GUIDANCE

Introduction:

Idiopathic intracranial hypertension (IIH) has been defined as a condition in which there is increased intracranial pressure (ICP) without a space-occupying lesion or hydrocephalus and with a normal cerebrospinal fluid (CSF) composition.

The term IIH has replaced the previously used Benign Intracranial Hypertension (BIH). This condition can cause severe debilitating headaches, visual loss and the treatment procedures can be distressing, hence the term benign is no longer used.

Alternative term used is ‘Pseudotumour cerebri’ as the presentation can mimic a ‘brain tumour’

This review of IIH also includes secondary cases, and IIH associated with predisposing medical conditions and pharmacotherapy which are listed below. Most secondary causes have specific management strategies and have to be worked up as part of the diagnostic investigations.

Scope of document:

1. To provide a comprehensive overview of IIH including diagnostic criteria, secondary causes, investigations and management strategies.
2. To provide clarity on the process of Lumbar puncture as an important diagnostic and management tool.
3. To list the medical management with doses and side effects.
4. To provide an algorithmic approach to aid in diagnosis and management of IIH.

Diagnostic criteria:

1. **IIH with papilloedema (Definite Diagnosis**)

A. Papilloedema
B. Normal neurologic examination
C. Neuroimaging with MRI and MR Venogram (MRV): Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion. MRV to exclude cerebral venous thrombosis; or venous stenosis
D. Normal cerebrospinal fluid (CSF) composition (including cells, protein, glucose and MC&S)
E. Elevated lumbar puncture opening pressure >28 cm of H_2O in a properly performed lumbar puncture.(Avery et al 2011)

2. **Additional features in IIH without papilloedema: (Probable Diagnosis)**
   - Presence of cranial nerve abnormalities such as 6th nerve.
   - Imaging abnormalities such as:
     i. Empty sella
     ii. Flattening of the posterior aspect of the globe
     iii. Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
     iv. Transverse venous sinus stenosis (this may be primary to secondary to high venous flow from raised pressure)

Ophthalmology assessment:

Formal Paediatric ophthalmological assessment is recommended, to ensure that true papilledema is diagnosed and differentiated from optic disc crowding and optic nerve head drusen. Examination and investigations would include

- Visual fields and visual acuity
- Fundal photo
- B scan
- Optical coherence tomography (The average nerve fibre thickness to detect nerve oedema is a measurement that can be tracked over time to follow patients)

History, examination and investigations are aimed towards excluding secondary causes of raised intra-cranial pressure.

History:
In addition to bearing in mind the above differential diagnosis, the following points should be noted:

a) Headache:
- Exacerbation with Valsalva manoeuvre, lying flat or bending down are useful clues
- Pulsatile tinnitus that is described as a 'whooshing sound' in the ears is commonly reported

b) Vision:
- Asymptomatic visual field impairment is usually an early sign.
- The blind spot is commonly affected first followed by the peripheral fields.
- Visual disturbance is an alarming symptom and warrants immediate treatment (Malignant IIH)

c) History suggestive of analgesic overuse headache should be sought
d) Sleep difficulties or snoring or features of nocturnal hypoventilation

Secondary causes of raised intracranial pressure (i.e Risk factors)

Cerebral venous abnormalities:
- Cerebral venous sinus thrombosis
- Middle ear or mastoid infection
- Hypercoagulable states
- Increased right heart pressure
- Superior Vena Cava syndrome
- Arteriovenous fistulas
- Decreased CSF absorption from previous intracranial infection or subarachnoid haemorrhage

Medications and exposures:
- Antibiotics: Tetracyclines, Nalidixic acid, sulphonamides, nitrofurantoin, penicillin
- Hormones: Human growth hormone, levothyroxine, levonorgestrel, anabolic steroids
- Vitamin A
- Lithium
- Withdrawal from chronic steroids
- Ciclosporin
- Amiodarone
- Phenytoin

Endocrine disorders:
- Addison Disease (random cortisol)
- Hypoparathyroidism/ Hyperparathyroidism (Bone profile, Alkaline phosphate)
- Hypothyroidism/ Hyperthyroidism

Sleep apnoea
Refeeding of malnourished children
Behcet syndrome
Lyme disease
Anaemia
Renal failure
Vitamin D deficiency
Turner syndrome, Down syndrome

Clinical Examination:

By definition, the neurological examination should be normal apart from the following exceptions:
- papilloedema
- reduced visual acuity
- visual fields defects
- unilateral or bilateral sixth nerve palsy

General examination should include:
- Blood pressure
- Weight/height measurements with calculation of the BodyMass Index (BMI) (kg/m2), and BMI centile or BMI standard deviation score (SDS). (For plotting BMI see: http://www.rcpch.ac.uk/improving-child-health/public-health/uk-who-growth-charts/school-age-2-18-years/school-age-charts-an#bmi
- Ear, nose and throat examination for signs of otitis media, mastoiditis, or sinusitis
- A search for clinical signs of medical conditions causing secondary intracranial hypertension is recommended.

Investigations:

First line: • MRI and discuss about MRV with neuro-radiologist • LP (Opening and closing pressure, microscopy, culture, virology, glucose, lactate, protein, save sample) • Bloods: FBC, U&E, LFT, Bone profile, TFT, CRP, ESR, Vitamin D and lactate and glucose paired with CSF.
Other Investigation to consider: • Clotting, lyme serology, early morning blood gas (if sleep difficulties or snoring) , early morning cortisol, PTH

Treatment:

- The primary goals of treatment are preservation of vision and improvement of headaches. Indicators of successful treatment are improvement in headaches, and resolution of visual symptoms and signs.
- Generally, the severity of the visual symptoms and signs dictates the suitability of treatment (ie, medical, surgical, or combined). The risks of vision loss should be clearly explained to the patients and parents, as well as the importance of adherence to therapy.
- The possibility of medication-overuse headache, or other accompanying primary headache, should also be explored in patients with chronic daily headache.

Weight loss:

- Advice regarding weight reduction in obese patients should be offered as there is evidence of benefit in adults. (1)

Lumbar puncture (LP):

- At the initial LP, CSF pressure is brought down to 15 to 20 cm of H2O
- There is no evidence that serial lumbar punctures lead to long-term remission of IIH. LP decreases CSF pressure only temporarily. Unless there is a CSF leak, CSF reforms in six hours.
- Serial LPs could be useful as a temporary measure in fulminant IIH threatening vision, as a temporary measure as prelude to surgical treatment. (1)

Lumbar puncture - the practical aspects:

MUST ONLY BE PERFORMED AFTER SATISFACTORY NEUROIMAGING.

Ideally performed under local anaesthesia (topical anaesthetic cream followed by intradermal lignocaine) with play specialist.

a) It is important to note that nitrous oxide or general anaesthesia can affect CSF pressure due to CO2 retention. As a compromise, if nitrous oxide is being used, it is our practice to use it only until the LP needle is inserted into the CSF space. The child is then encouraged to relax and breathe without the nitrous oxide, and the pressure is measured a few minutes following this.
b) General anaesthesia can elevate CSF pressure commonly by 6–13 cm H2O. A rise of 1 kPa in end-tidal pCO2 is associated with a rise of 3.5–12 cm H2O in the CSF pressure(7). If general anaesthesia is used, the end tidal CO2 should be maintained within the normal range (4.7 – 6 kPa) and the end tidal CO2 at the time of reading the CSF pressure should be noted.

- Patient should be in the lateral decubitus position and the manometer should be connected as soon as the stylet is withdrawn. (Tip - take more than one manometer with you since pressure may be higher than the maximum reading on manometer).
- The upper end of the CSF column is read when it settles. Record the opening peak pressure, with the child as relaxed as possible.
- Opening pressures >28cm of H2O is considered abnormal in children.
- It is good practice to note the amount of CSF drained. The pressure is lowered down to 15 to 20 cm of H2O. Closing pressure should be measured and documented
- Samples should always be sent for routine biochemistry and microbiology studies.
- Patient and family should be counselled about possibility of low pressure headache following the lumbar puncture and may need short period of inpatient admission.

Surgical and interventional radiology treatments:

Indications for surgical intervention:

- IIH presenting with acute visual deterioration or loss.
- Failure of medical treatment which is reflected by recent deterioration or loss of visual acuity or fields.
- Severe debilitating headaches not responding to medical treatment

Medical treatments: (See table for details regarding each medication)

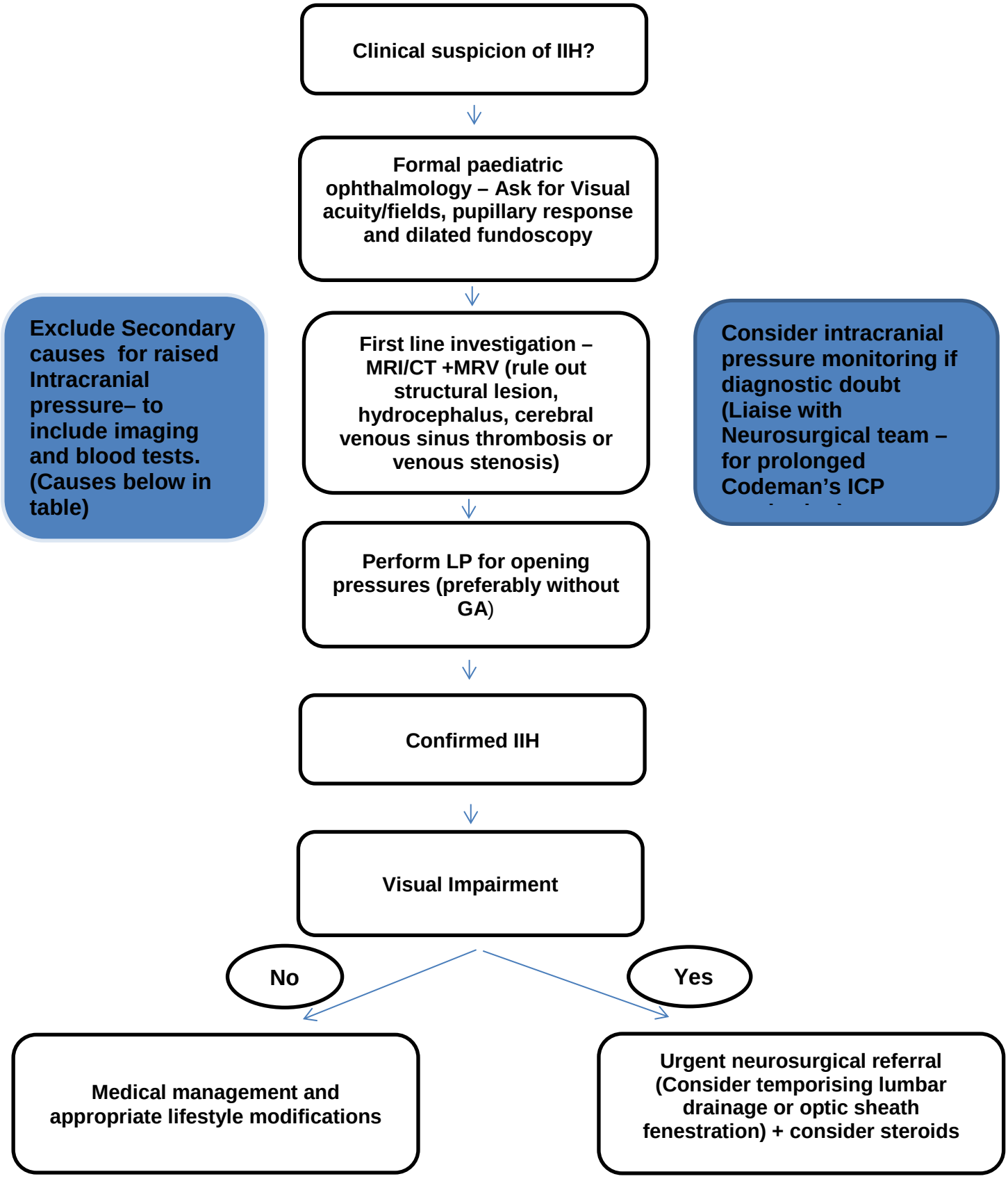
Name	Mechanism of action	Dose	Side effects	Other comments
Acetazolamide	Carbonic anhydrase inhibitor and may reduce CSF production by reducing sodium ion transport from the choroid plexus cells	Prepubertal children: start at 25 mg/kg/day in 2–3 divided doses and increase by 25mg/kg/day to a maximum of 100 mg/kg/day. 250mg tablets available, doses should be rounded to the nearest quarter or half of a tablet e.g. 62.5mg, 125mg as tablets are only slightly soluble in water. Adolescents: start at 1 g/day in 2–3 divided doses and if needed increase by 250 mg/day till a maximum of 4 g/day. (1)	Metallic taste, tingling sensation in the mouth, paraesthesia and nausea. Routine urea and electrolytes and bicarbonate recommended if on high doses (> 1 g/day) or symptomatic.	Used as first line treatment. Start sodium bicarbonate* or potassium citrate** if levels fall below 18mmol/L. Consider weaning as soon as improvement is evident.
Name	Mechanism of action	Dose	Side effects	Other comments
Topiramate	Weak carbonic anhydrase inhibitor	Children 6 to < 12 years and weight ≥ 20kg: 15mg od for 1 week; then increase to 15mg bd for 1 week; then increase to 25mg bd for 1 week; continue to gradually titrate to effect up to target dose of 2 to 3mg/kg/day in two divided doses; maximum daily dose: 200mg/day (6) Children ≥ 12 years: Initially 25mg at night for 1 week and increase by 25mg weekly. Usual dose 50 – 100mg daily in two divided doses. Maximum 200mg/day (8,9)	Word finding difficulties, psychomotor slowing, impaired concentration, anorexia, weight loss and sedation	Available as tablets and sprinkle capsules
Furosemide	Probably by diuresis and reduction of sodium transport into the brain	1–2 mg/kg/day with or without Acetazolamide (1)	Electrolyte disturbances, postural hypotension	Usually reserved as second-line therapy due to risks of electrolytes disturbance on prolonged use.

*Sodium bicarbonate: initially 1-2 mmol/kg daily in divided doses, adjusted according to response (9)

**Potassium citrate: 0.5-1mmol of citrate/kg/day. 1mmol of citrate is approximately equivalent to 3mmol of bicarbonate. Potassium levels should be monitored. Potassium Citrate mixture BP, each 1ml provides 2.8mmol of potassium, 0.9mmols of citrate and equivalent to 2.8mmol of bicarbonate (10)

Summary:

An algorithmic approach to management of IIH



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QUERIES Contact Neurology registrar on bleep 6734