MIGRAINE IN CHILDREN AND ADOLESCENTS

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DISCLOSURES

- No relevant financial relationships to disclose
OBJECTIVES

1- To demonstrate the progression of migraine from infancy to adolescence
2- To demonstrate the application of the headache classification
3- To demonstrate the use of abortive medications in children and adolescents, triptans specifically
4- To outline the use of major preventive medications in children and adolescents
5- To stress the importance of non-pharmacological approaches to headache in children and adolescents
6- Brief overview of newer treatments
CHALLENGES IN MANAGEMENT

- Difficult to make specific diagnosis. The classification is only partially helpful.
- Difficult to obtain history because children may not be able to describe and the parents could very anxious.
- Difficult to treat because of lack of the FDA approval of many of the pharmacological agents.
- “Simply”- difficult because indeed children are not small adults but it doesn’t prevent them from having headaches in general and migraine specifically.
YOUNG MIGRAINE?

- May be as young as the child is able to indicate, express her/himself
- May start even in infancy or present differently and later involve into a more “traditional” migraine pattern
Episodic syndromes that may be associated with migraine

(IHS 3b)

- Formerly known as Childhood Periodic Syndromes
Benign Paroxysmal Torticollis: International Headache Society (IHS) Classification

- **Diagnostic criteria:**
  - A: Episodic attacks, in a young child, with all of the following characteristics and fulfilling criterion B:
    - 1. tilt of the head to one side (not always the same side), with or without slight rotation
    - 2. lasting minutes to days
    - 3. remitting spontaneously and tending to recur monthly
  - B: During attacks, symptoms and/or signs of one or more of the following:
    - 1. pallor
    - 2. irritability
    - 3. malaise
    - 4. vomiting
    - 5. ataxia
  - Normal neurological examination between attacks
  - Not attributed to another disorder

- **Note:** Ataxia is more likely in older children within the affected age group.
Cyclic Vomiting: IHS Classification

- **Description:**
  - Recurrent episodic attacks, usually stereotypical in the individual patient, of vomiting and intense nausea. Attacks are associated with pallor and lethargy. There is complete resolution of symptoms between attacks.

- **Diagnostic criteria:**
  - A: At least 5 attacks fulfilling criteria B and C
  - B: Episodic attacks, stereotypical in the individual patient, of intense nausea and vomiting lasting from 1 hour to 5 days
  - C: Vomiting during attacks occurs at least 4 times/hour for at least 1 hour
  - D: Symptom-free between attacks
  - E: Not attributed to another disorder

- **Note:** History and physical examination do not show signs of gastrointestinal disease.
Abdominal Migraine: IHS Classification

- **Diagnostic criteria:**
  - A: At least 5 attacks fulfilling criteria B-D
  - B: Attacks of abdominal pain lasting 1-72 hours (untreated or unsuccessfully treated)
  - C: Abdominal pain has all of the following characteristics:
    - 1. midline location, periumbilical or poorly localized
    - 2. dull or "just sore" quality
    - 3. moderate or severe intensity
  - D: During abdominal pain at least 2 of the following:
    - 1. anorexia
    - 2. nausea
    - 3. vomiting
    - 4. pallor
  - E: Not attributed to another disorder

- **Note:** In particular, history and physical examination do not show signs of gastrointestinal or renal disease or such disease has been ruled out by appropriate investigations.

- **Comments:** Pain is severe enough to interfere with normal daily activities
Benign Paroxysmal Vertigo: IHS Classification

- **Description:**
  - A heterogeneous disorder characterized by recurrent brief episodic attacks of vertigo occurring without warning and resolving spontaneously in otherwise healthy children.

- **Diagnostic criteria:**
  - **A:** At least 5 attacks fulfilling criterion B.
  - **B:** Multiple episodes of severe vertigo, occurring without warning and resolving spontaneously after minutes to hours.
  - **C:** Normal neurological examination; audiometric and vestibular functions between attacks.
  - **D:** Normal electroencephalogram.
  - **Note:** Often associated with nystagmus or vomiting; unilateral throbbing headache may occur in some attacks.
Two major categories of headaches:

- **Primary** - migraine, tension-type headaches, cluster headaches and other trigeminal autonomic cephalgias, and other primary headaches

- **Secondary** - attributed to the other underlying disorder
EPIDEMIOLOGY OF MIGRAINE

- Up to 7 years of age - prevalence 2% to 3.2%
  - males > females

- Between 7 and 11 years of age - 4% to 11%
  - males = females

- Adolescents above 11 years - 8% to 23
  - females > males
DIAGNOSE!

- For reassurance - this is NOT a brain tumor
- Make sure that headache is not secondary
- Primary headaches (migraine, tension type, cluster, etc.) are the diagnoses by themselves
- Most HA in children are benign (in less than 1% of children with brain tumors HA was the only symptom)
WAYS TO FIND OUT

- Obtain a GOOD history
- Don’t forget to ask about the triggers, emotional status, school performance, etc.
- Exam - both physical and neurological
  Special attention - fundoscopy
FOR PRIMARY HEADACHES NO NEED TO PERFORM ANY STUDIES
WHEN TO IMAGE?

- New onset severe headache
- Pattern changes dramatically in < 1 month in a child under 12 y, and especially 7 y of age
- Progressive headache
- Nocturnal and/or early morning headaches/emesis
- Valsalva provokes headache
- Fever, seizures
- Altered sensorium
WHEN TO IMAGE?

- Abnormal neurologic signs: focal weakness, abnormal eye movements, head tilt, diplopia, imbalance, confusion, incoherent speech, seizure

- Headache is exclusively in one location, especially occipital
WHEN TO IMAGE?

- Abnormal neurologic exam: papilledema, focal motor or sensory changes (objective)
- Patient with cancer, HIV, immunosuppression
WHICH STUDY?

- MRI is ideal
- CT if suspect bleeding or fracture or MRI is not feasible
- LP if suspect SAH or increased ICP
MIGRAINE

Two major categories:

- **Migraine without aura**
  - previously common

- **Migraine with aura**
  - previously classical
MIGRAINE WITHOUT AURA

Diagnostic criteria:

A. At least five attacks fulfilling criteria B–D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated). Pediatric- 1-48 hours

C. Headache has at least two of the following four characteristics:
   1. unilateral location. Pediatric- uni- or bilateral
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine physical activity

D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis
MIGRAINE WITH AURA

Previously used terms:
- Classic or classical migraine; ophthalmic, hemiparesthetic,
- hemiplegic or aphasic migraine; migraine accompagnée; complicated migraine

Diagnostic criteria:

A. At least two attacks fulfilling criteria B and C

B. One or more of the following fully reversible aura symptoms:
1. visual
2. sensory
3. speech and/or language
4. motor
5. brainstem
6. retinal

C. At least two of the following four characteristics:
1. at least one aura symptom spreads gradually over 5 minutes, and/or two or more symptoms occur in succession
2. each individual aura symptom lasts 5-60 minutes
3. at least one aura symptom is unilateral
4. the aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded
COMPLICATED MIGRAINE??

- Term is not in use

- Classified as migraine with aura - migraine presents significant neurologic deficits that may persist beyond the conclusion of headache pain
HEMIPLEGIC MIGRAINE

- Aura consists of fully reversible motor weakness and visual, sensory, and speech and language symptoms

- Familial – three types

- Sporadic
MIGRAINE WITH BRAINSTEM AURA

- Fully reversible speech and language, sensory or visual auras, but NO retinal or motor symptoms
- Spread over 5 min
- Last 5-60 min
- HA within 1 hour
- **Must** have at least 2 “brainstem” features: dysarthria, vertigo, tinnitus, hypoacusis, diplopia, ataxia, decreased level of consciousness
- Most common clinical features - vertigo, nausea/vomiting, ataxia, visual field defects
ACUTE CONFUSIONAL MIGRAINE

- Rare. Incidence unknown. Paucity of data. Unclassified
- Acute onset of confusion manifesting as agitation, memory deficit, disorientation, increased alertness, dysarthria, perceptual disturbance
- HA may occur before, during or after
- Duration min to hours, usually no longer than 24 h
- Probably linked to migraine with brainstem aura
- Imaging, CSF normal
- EEG- diffuse slowing
RETINAL MIGRAINE

- Rare

- 2 attacks of fully reversible MONOCULAR visual disturbance with positive or negative visual phenomena

- HA – during or within 60 min

- Term commonly misused in cases of migraine with visual aura where typical aura occurs in a hemifield
COMPLICATIONS OF MIGRAINE

- Status migrainosus
- Persistent aura without infarction
- Migrainous infarction
- Migraine aura-triggered seizure
TENSION TYPE HEADACHE

- Bilateral location
- Non-pulsating quality
- Mild to moderate intensity
- Lack of aggravation by routine physical activity
- Not accompanied by nausea, although just one of photo or phonophobia doesn’t exclude the diagnosis
TENSION TYPE HEADACHE

- The distinction between TTH and migraine may, therefore, be difficult, especially in children.

- Probably, the most important distinction is the severity. Migraine is severe. Tension type is mild to moderate.
CHRONIC DAILY HEADACHE

- Collective term, not diagnosis

- Presence of headache for at least 15 days in a one-month period over a period of three consecutive months and with no underlying organic pathology
PRIMARY HEADACHE

- Transformed or chronic migraine
- Chronic tension type headache
- New daily persistent headache
- Hemicrania continua

Silberstein et al.
NEW DAILY PERSISTENT HEADACHE

- Abrupt development of HA that does not remit
- Develops over <3 days
- Persists >15 days/month for > 1 month
- Frequently caused by viral illness
- Absence of past history of HA
- Often resistant to treatment
RISK FACTORS

- High HA frequency
- Female gender
- Obesity (BMI>30)
- Snoring
- Stressful life events
- Migraine
RISK FACTORS

- High caffeine consumption
- Acute medication overuse
- Depression
- Head or neck injury
- Less than high school education
MEDICATION OVERUSE HEADACHE: HOW MUCH IS TOO MUCH?

5-8 days per month of use of opiates and barbiturates associated with migraine progression
OTHER PRIMARY HEADACHE DISORDERS

- Primary Stabbing Headache
- Neck-Tongue Syndrome
- Red Ear Syndrome
- Hypnic Headache
TREATMENT
GOALS

- Early, rapid treatment
- Use of proper formulation and dose based on the child’s weight
- Limited use of rescue medications to avoid MOH
- Optimization of self-care
- Minimal to no adverse effects
- Cost effectiveness
TREATMENT

- Pharmacological
- Non-pharmacological
PHARMACOLOGICAL TREATMENT

FEW MEDICATIONS THAT ARE USED IN TREATMENT OF PEDIATRIC HEADACHE HAVE FDA APPROVAL FOR THE TREATMENT OF PEDIATRIC HEADACHE
MIGRAINE NONSPECIFIC TREATMENT

Acetaminophen  15 mg/kg/dose Q 4-6h
max  75 mg/kg in 24 h in children up to 12 years

Ibuprofen  10 mg/kg/dose Q6-8h
max  800mg

ASA, acetaminophen, caffeine  1-2 tab

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The Michael J. Bresnan Child Neurology Course
MIGRAINE NONSPECIFIC TREATMENT

Ketorolac
- IV 0.5 mg/kg; max 15 mg
- IM max 60 mg
  with subsequent 5 day total oral every 8 hours course

Steroids
- ER- to prevent recurrence
- Medrol dose pack- inconsistent data

Naproxen
MIGRAINE NONSPECIFIC TREATMENT

Acetaminophen + codeine 0.5-1 mg/kg/dose Q 6-8h

Fioricet 1 tab Q 6 hours

Fiorinal

Oxycodone
JUST SAY ‘NO’ TO NARCOTICS!

- All efforts must be made to avoid narcotic-containing medications
- No evidence of superiority versus triptans or NSAIDs
- Risk of clinical and psychological dependency
- May contribute to MOH
ANTIEMETICS

Prochlorperazine 0.15 mg/kg IV, max 10 mg PO- 5-10 mg

Metoclopramide 0.2 mg/kg IV max 10 mg

Ondansetron 4-8 mg PO/IV
ANTIEMETICS

- Side effects: postural hypotension, drowsiness, extrapyramidal, akathisia

- Antiemetics could be combined both with other migraine non-specific and migraine specific medications
TRIPTANS

- FDA approval

- rizatriptan (Maxalt) for 6 y and older
- almotriptan (Axert) for 12 y and older

- zolmitriptan (Zomig) for 12y and older

- sumatriptan/naproxen combination–sumatriptan
  10 mg with naproxen 60 mg with option to increase to 85 mg sumatriptan with 500 mg naproxen- for 12y and older
TRIPTANS: CONTRAINDICATIONS

- risk of coronary artery disease
- cerebrovascular syndromes
- peripheral vascular syndromes or other significant underlying cardiovascular disease
- uncontrolled hypertension
- hemiplegic and migraine with brainstem aura
- Pregnancy- category C
- Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders
TRIPTANS

- Well absorbed
- No significant adverse events were noted
- AE – tingling, dizziness, warm/hot sensations, chest or jaw discomfort, and injection site reactions
TRIPTANS

- Give at onset. If onset missed, still give expecting a lesser effect.

- The initial dose may be repeated in two hours.

- The triptans should NEVER be combined. Must be 24 h apart.
TRIPTANS

- Should not be used for more than 6 headaches per month to avoid medication overuse
- Failure of one doesn’t predict the failure of others
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# TRIPTANS

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<tr>
<td>Frova</td>
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DHE
Nasal Spray

0.1 mg/dose 6-9 yr
0.5 mg/dose 9-12 yrs
0.75 mg 12-16 yrs

Can be used IM, or IV with a concomitant antiemetic
Combining Abortives? 

- NSAIDs + antiemetics (DOPA receptor antagonists)
- Triptans + NSAIDs
- Triptans + NSAIDs + antiemetics
PREVENTIVE TREATMENT
PREVENTIVE TREATMENT

- After adequate trial of acute treatment if frequent disabling attacks persist
- Headache interferes with daily function
- Acute medication is insufficient or ineffective
- Specific contraindication to using abortive treatment
- Acute medication is overused
COMMON MISTAKES

- Starting dose too high → side effects, medication discontinued

- Starting dose low, staying low and not titrating up to therapeutic benefit → frustration, medication discontinued
COMMON MISTAKES

- Not scheduling regular visits
- Not offering non-pharmacologic modalities
- Not recognizing associated comorbidities, such as depression and anxiety
- The fair trial is not given
CYPROHEPTADINE

- 5 HT-2 antagonist
- Usually used in children younger than 9 years of age
- A nightly dose 4-12 mg is used, or 0.25 mg/kg/day 1/3 AM-2/3PM
- Common SE- fatigue, weight gain, appetite stimulation
ANTIDEPRESSANTS

- **Nonsedating** are used in patients who initiate and maintain sleep easily—protriptyline and desipramine

- **Sedating**—amitriptyline, nortriptyline, imipramine—tolerated better by patients who have difficulties to initiate and maintain sleep
ANTIDEPRESSANTS

- Anticholinergic side effects - dry mouth, blurred vision, urinary retention, constipation, sedation, weight gain

- Start low - 10 mg

- Gradual increase is usually well tolerated and effective

- Obtain a baseline EKG to rule out prolonged QTc
BETA BLOCKERS

- May also have anxiolytic effects

- Propranolol and timolol

- Dose — start 1mg/kg/day up to 3-4mg/kg/day divided bid

- Contraindicated in patients with bronchospastic disease, diabetes, and WPW syndrome, CHF

- Side effects—depression, fatigue, and decreased athletic endurance
CALCIUM CHANNEL BLOCKERS

- Verapamil, diltiazem, flunarizine (not available in US), nimodipine, and nicardipine

- May be useful in hemiplegic migraine

- Should be avoided in second or third-degree AV block, hypotension, ventricular dysfunction, Duchenne muscular dystrophy

- Dose- 80 mg-240 mg

- The most common side effects are daytime sedation, weight gain, depression, and constipation
TOPIRAMATE

- Initiate at 15 mg/day and titrate over 8 weeks to a dose approximately 2-3mg/kg/day, or the maximum tolerated dose

- Side effects: weight loss, cognitive, paresthesias, metabolic acidosis, glaucoma

- Pregnancy- category D
VALPROATE

- FDA indication in adults
- Monitor blood work
- Pregnancy - category D
OTHER ANTICONVULSANTS

- Gabapentin up to 2400mg/day
- Zonisamide 200-400 mg/day
- Levetiracetum 500-3000mg/day

There are limited studies to support their use. The antiepileptic doses are usually prescribed.
HOW LONG TO TREAT?

- No definite recommendations
- Generally 3-6-12 months
- Individual approach
**ALTERNATIVES**

- Vitamin B2
- Magnesium
- Melatonin

- I have yet to see the effectiveness, but some parents are more open to these measures rather than medications.
ALWAYS IN STYLE!

- Healthy life style: sleep (not too little, not too much, consistent time frame), hydration, regular meal schedule, exercising.

- STRESS!!!- school – academics, desire to achieve, social dramas, bullying.

- Home- parental divorce, parental pressure, death in the family, sibling rivalry and jealousy
UNFORTUNATELY, IN STYLE OFTEN

- Anxiety
- Depression
- Other emotional problems
NON- PHARMACOLOGICAL

- CBT
- Acupuncture
- Biofeedback
IN ADULT WORLD...

- Last two years several acute and preventive medications have been approved for patients over 18 yo
- Some - work as antagonists of CGRP which released during a migraine attack
- One - agonist of serotonin 5HT 1F receptor
- Advantage - no constriction of blood vessels as opposed to triptans
- Few side effects
- No pregnancy within 6 months of use
ACUTE TREATMENT

- Ubrogepant (Ubrelvy)- CGRP receptor antagonist
- Rimegepant (Nurtec)- blocks CGRP receptors
- Lasmiditan (Reyvow)- serotonin (5HT) 1F receptor agonist
PREVENTIVE TREATMENT

- Erenumab (Aimovig)- CGRP receptor blocker
- Fremanezumab (Ajovy)- CGRP antagonist
- Galcanezumab (Emgality)-CGRP antagonist
- Eptinezumab (Vyepti)- CGRP receptor blocker, 1st IV preventive
CONCLUSIONS

- Do your best to make a diagnosis, but don’t “kill yourself” if it doesn’t strictly fit into the IHS criteria
- Use abortive meds at appropriate time and at appropriate dose
- Don’t be afraid to use triptans in children
- Always start prevention with addressing the triggers and healthy life style
- Give each medication fair chance to work
- Always set up realistic expectations, involve child and parents in decision making. MAKE A TEAM!