# 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
- $\succ$  E: Not attributed to another disorder<sup>1</sup>

Note: History and physical examination do not show signs of gastrointestinal disease.

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### **Abdominal Migraine: IHS Classificaiton**

#### **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

### CLASSIFICATION

 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 accompagnee; 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



# 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**



- 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</li>
  > Persists >15days/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

Ibuprofen

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

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

ASA, acetaminophen, caffeine 1-2 tab

# MIGRAINE NONSPECIFIC TREATMENT

Ketorolac

Steroids

Naproxen

IV 0.5 mg/kg; max 15 mg IM max 60 mg with subsequent 5 day total oral every 8 hours course ER- to prevent recurrence Medrol dose pack- inconsistent data

#### MIGRAINE NONSPECIFIC TREATMENT

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

Fioricet

#### Fiorinal Oxycodone

1 tab Q 6 hours

# 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

Metoclopromide

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

#### 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—sumatiptan 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

#### > Well absorbed

No significant adverse events were noted

AE –tingling, dizziness, warm/hot sensations, chest or jaw discomfort, and injection site reactions

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

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

NAME	FORMULATION	DOSE
Sumatriptan	Tablets	<50 kg – 25 mg
Imitrex	25mg, 50mg	>50 kg- 50 mg
	100 mg	
	Nasal Spray	>50 kg, >9 y- 5mg
	5 mg, 20 mg	>10-11 y- 10 mg
	5 3 3	>50 kg, >12 y- 20 mg
Zolmitriptan	Tablets	<12 y- 2.5 mg
Zomig,	Tablets dispersible	>12 y – 5mg
Zomig ZMT	2.5mg, 5 mg	
	Nasal Spray	
	2.5 mg, 5 mg	
Rizatriptan	Tablets	<40 kg-5 mg
Maxalt,	Tablets dispersible	>40 kg- 10 mg
Maxalt MLT	5 mg, 10 mg	

NAME			
Almotriptan	Tablets	>12 yo -6.25 mg	
Axert	6.25 mg, 12.5 mg		
Elitriptan	Tablets		
Relpax	20 mg, 40 mg	×//	
Naratriptan	Tablets		
Amerge	1 mg, 2.5 mg		
Frovatriptan	Tablets		
Frova	2.5 mg		



Nasal Spray

0.1 mg/dose0.5 mg/dose0.75 mg

6-9 yr 9-12 yrs 12-16 yrs

# Can be used IM, or IV with a concomitant antiemetic

### **COMBINE 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 easilyprotriptyline 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

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#### **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**

➤ Acupuncture

≻ CBT

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

# > Erenumab (Aimovig)- CGRP receptor blocker

Fremanezumab (Ajovy)- CGRP antagonist

Galcanezumab (Emgality)-CGRP antagonist

Eptinezumab (Vyepti)- CGRP receptor blocker, 1<sup>st</sup> 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!

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