



Pediatric Specialists
of Virginia

 Children's National.  INOVA

Migraine in Children and Adolescents



©1991, Novartis Pharmaceuticals Corporation. All rights reserved.

William M. McClintock, MD

October 5, 2018

Pediatric Specialists
of Virginia

Children's National. INOVA

Pediatric Migraine Disclosures I have none



Pediatric Migraine Objectives

- Understand how often children get headaches
- Understand how migraine criteria differ in pediatrics
- Treatment approaches for pediatric headaches.
- (Be aware of some of the unusual ways migraine can present in young children)

Pediatric Migraine

Introduction

- Kids get headaches
 - Primary headaches
 - Secondary headaches
- Children are not just small adults
- There is a parent in the equation
- Worry is that the child has a brain tumor or worse

Pediatric Migraine Epidemiology

- Prevalence of headache throughout childhood varies greatly across studies between 5.9 to 82%
 - The vast majority are primary headaches
 - Prevalence by age 3 is 3 to 8%, by age 5 19.5%, and by age 7 - 21 to 37%, and by age 15 – 21 to 82%
 - Regular migraine is about 5% by 5 years, 7 to 10% by 10 years, and 7 to 15% by 15 years.

Pediatric Migraine Epidemiology

- Migraine headaches are more frequent in boys than girls before age 10 years
- Girls affected 1.5 times more than boys after puberty.
- Chronic daily headache occurs in 2 to 3% of adolescence
- 8% of children miss 6 days or more of school per year because of headache.
- Headache is probably the most common complaint seen in a pediatric neurology practice.

Pediatric Migraine

Definitions

- Primary headaches
 - Genetic disposition, with secondary influences
 - Migraine
 - Tension
 - Chronic daily headache
- Secondary headaches

Primary vs. Secondary Headache

- Course of headaches
- Red flags

Temporal Profile of Primary and Secondary Headaches

Rothner AD. The evaluation of headaches in children and adolescents. *Semin Pediatr Neurol* 1995;2:109-118.

1. Acute Headache
- Primary or Secondary

Acute headache

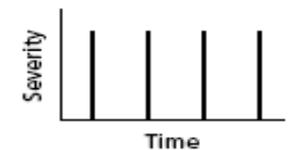
Single episode of head pain without history of previous events



2. Acute recurrent
- Primary

Acute-recurrent headache

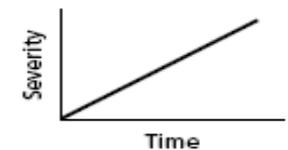
Pattern of head pain separated by symptom-free intervals



3. Chronic Progressive
- Secondary

Chronic-progressive headache*

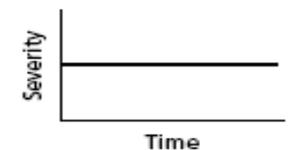
Gradual increase in frequency and severity



4. Chronic non-progressive
- Primary

Chronic-nonprogressive (or chronic-daily) headache

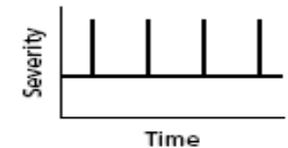
Frequent or constant headache



5. Mixed
- Primary

Mixed headache

Acute-recurrent headache (usually migraine) superimposed on a chronic-daily background pattern (represents a variant of chronic-daily headache)



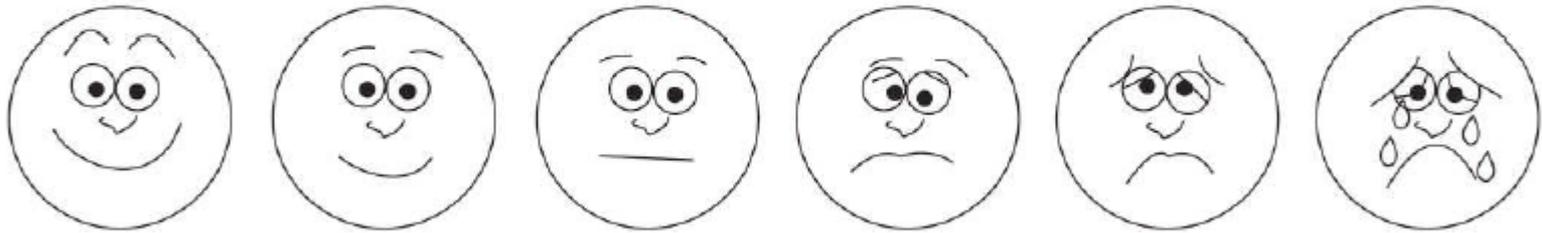
Red Flags

- Headache upon awakening, or wakes child up in sleep
- Ataxia or dizziness
- Alteration of consciousness
- Focal neurological findings
- Associated stiff neck
- Double vision
- Persistent headache after head injury
- Positional component of headache
- Very young children with headache
- Worsening headache
- Severe, acute headache

Pediatric Migraine Diagnostic Criteria

- How different from adult criteria – studies are in adults primarily, and for the most part the same criteria are used.
 - Pediatric headache are often shorter
 - Observation is often needed instead of getting verbal history
 - Family history becomes very important
 - Children have difficulty describing their pain
 - Visual pain scales
 - Observation of function
 - Many of the symptoms of the full migraine criteria develop later, often after age 12 years.

Faces Pain Scale



0	2	4	6	8	10
Very happy, no hurt	Hurts just a little bit	Hurts a little more	Hurts even more	Hurts a whole lot	Hurts as much as you can imagine (don't have to be crying to feel this much pain)

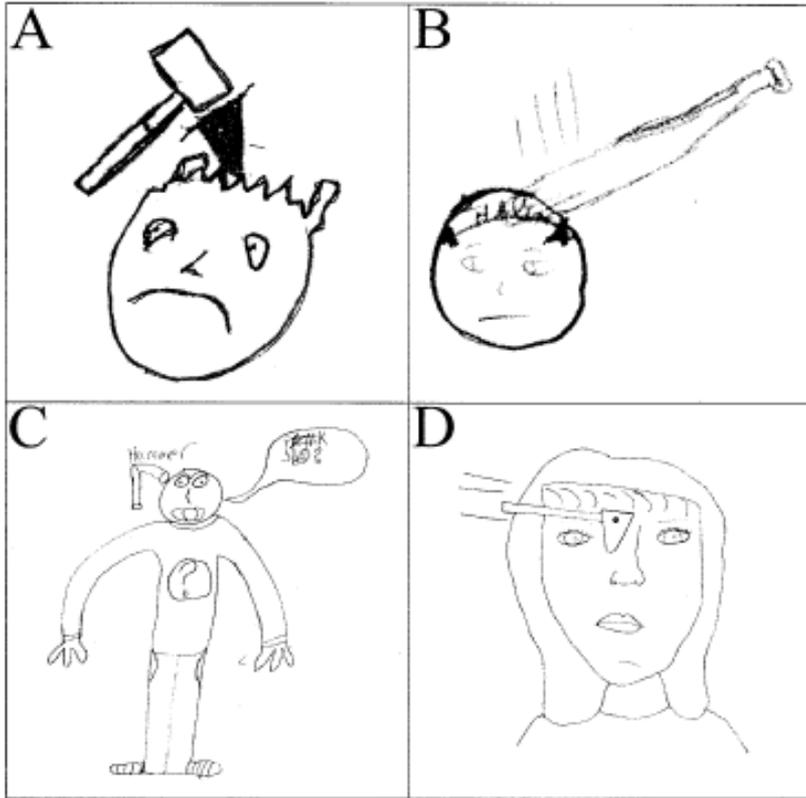
Unilateral or Bifrontal Location



Moderate to Severe Intensity



Pounding or Throbbing “Variable like heartbeat”

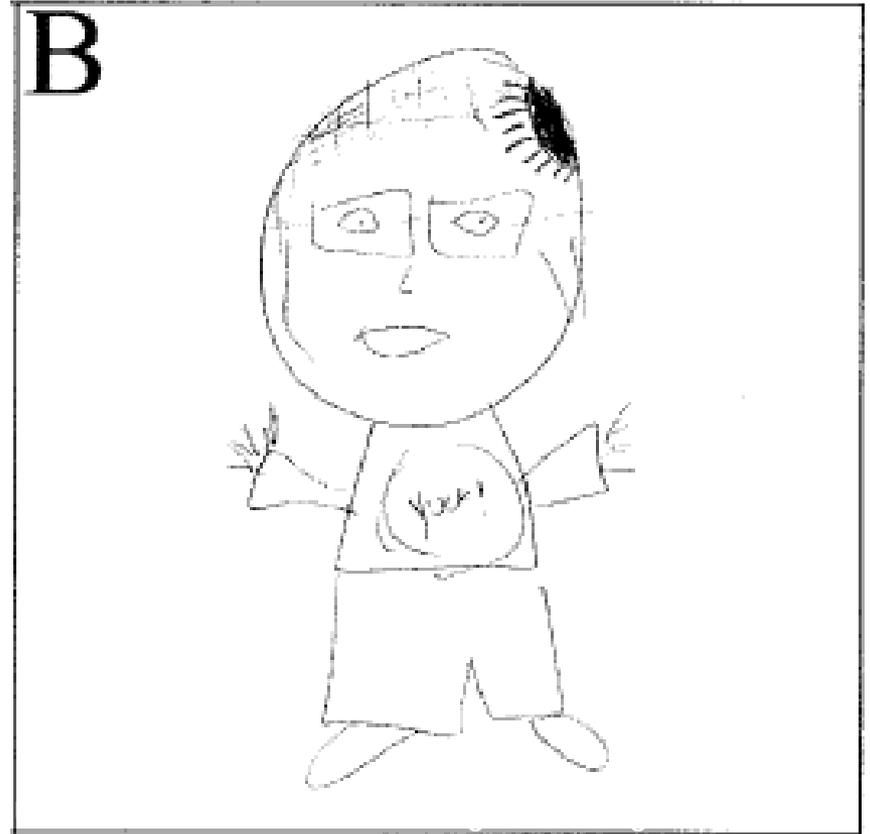


Pediatrics 2002;109;460-472

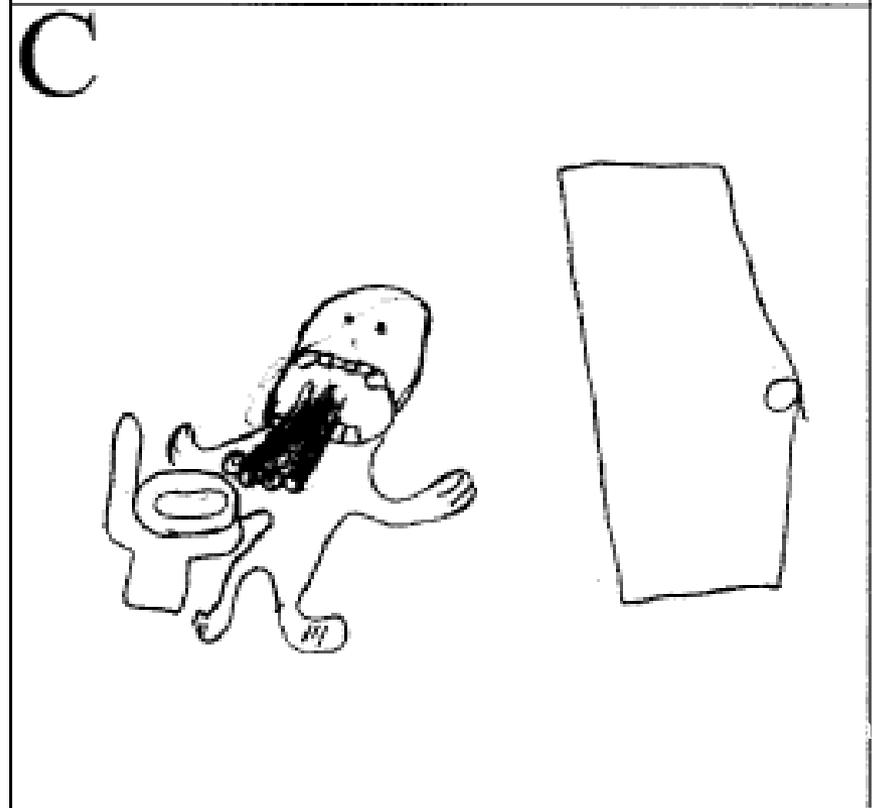
Pediatric Specialists
of Virginia

Children's National. INOVA

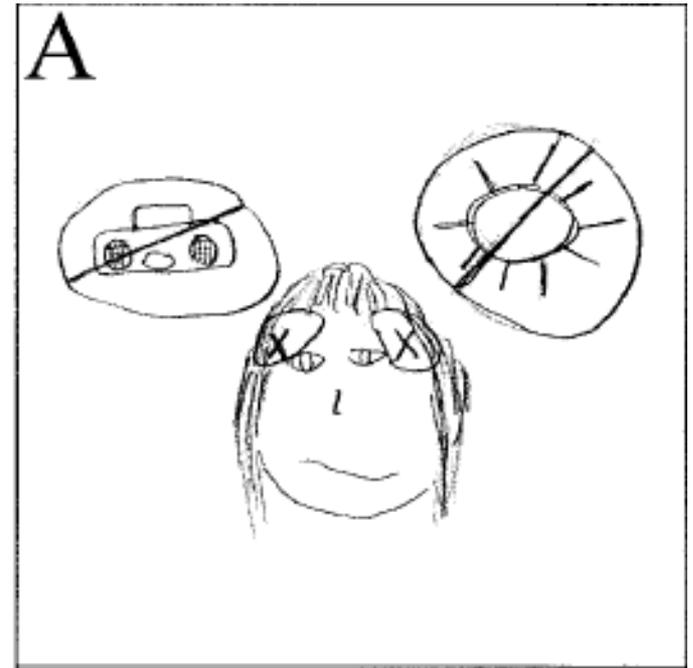
Nausea



Vomiting



Photophobia



Phonophobia



Pediatric Specialists
of Virginia

 Children's National.  INOVA

What Type of Headache Do Migraineurs *Think* They Have?

American Migraine Prevalence and Prevention Study. *Headache*
2007;47:355

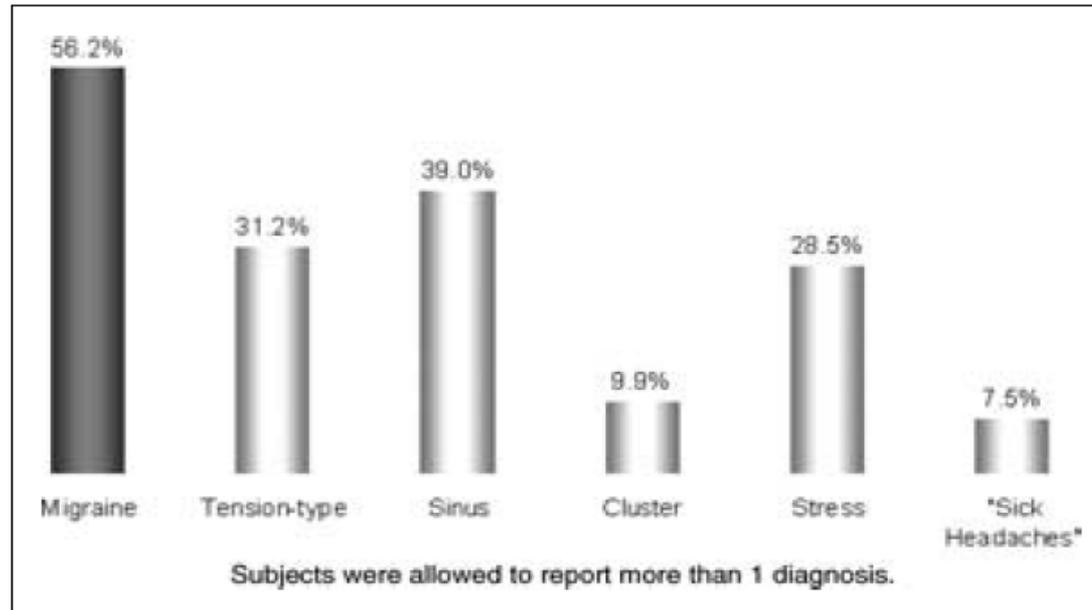


Fig 1.—Proportion of persons with ICHD-2 migraine reporting specific headache diagnosis.

Pediatric Migraine Definitions

- Status migrainosus
- Chronic migraine
 - New onset persistent daily headache
 - Transformed migraine

Prevalence of Pediatric Migraine

Pediatric Migraine. Neurol Clin 2009;27;481–501

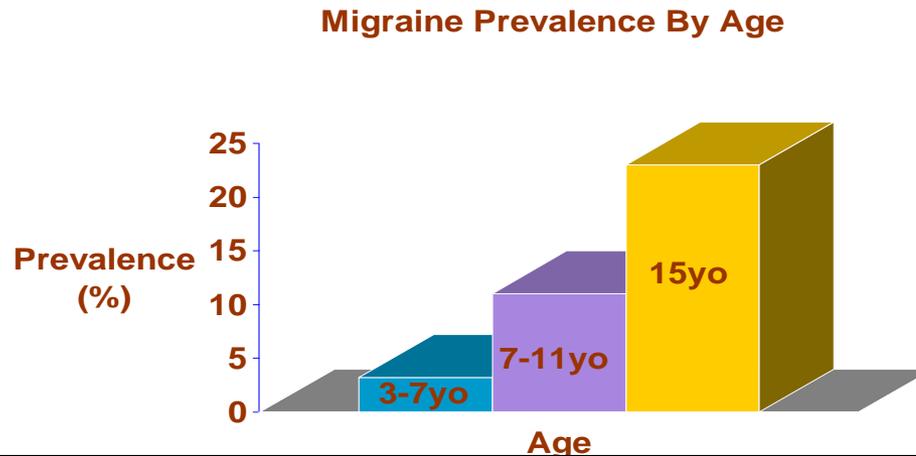


Table 1
Prevalence of migraine headache through childhood

	Age		
	3–7 Years	7–11 Years	15 Years
Prevalence	1.2%–3.2%	4%–11%	8%–23%
Gender ratio	Boys > girls	Boys = girls	Girls > boys

Chronic Migraine in Pediatrics

Guidetti V. Chronic daily headache in childhood and adolescence: clinical aspects and a 4-year follow-up. *Cephalalgia* 2004; 24:850-858.

The prevalence of childhood and adolescent CDH ranges from 0.2 to 0.9%.

– The prevalence in the adult population varies between 1.5 and 7%

- The prevalence of CDH in clinical practice ranges from 15 to 20% of patients with headache
- Chronic migraine defined in adults as >15 headache days per month for a 3 month period

Psychopathology in Children and Adolescence with Migraine: A Review

Pediatrics December, 2010, 126:323-332

- Systematic review and meta-analysis
 - Seven studies met their criteria and they found:
 - Strong evidence of no increased withdrawn behavior, thought problems, social problems, delinquent or aggressive behaviors
 - Strong evidence of more somatic complaints and internalizing behaviors (?nature of their disease)
 - Limited evidence they are more often diagnosed with ODD, ADHD, conduct disorder, dysthymia or depression

Pediatric Migraine

Case 1

- A five-year old boy comes to you for the evaluation of episodes of persistent vomiting and headache that lasts for 24 hours. He has had about one episode every month for the past 6 months, but had 3 episodes this past month. He also complains of being “dizzy” at the onset of the episodes. He seems well in between these episodes. He has started Kindergarten, and is doing well.
- He has no other medical problems.
- Physical and neurologic examinations are normal.
- What else would you like to know about the history?
- What is your differential diagnosis?
- What other testing would you do?
- What treatments would you suggest?

Pediatric Migraine

Case 2

- A 10 year-old girl come to see you because of intermittent headaches for the past 2 years. The headaches have slowly increased in frequency to the point they occur two to three times per week. About half of the headaches are severe enough that she needs to lie down in bed for a few hours. She takes ibuprofen with minimal relief. With some headaches there is mild nausea and light sensitivity. There are no visual symptoms. The headaches are bi-temporal, aching or pounding, and 5 to 8 out of 10 intensity. She has missed 3 to 4 days of school each month, and her grades are slipping.
- She has mild asthma, but no other medical problems.
- Physical and neurologic examinations are normal.
- What else would you like to know about the history?
- What is you differential diagnosis?
- What other testing would you do?
- What treatments would you suggest?

Pediatric Migraine

Case 3

- 15 year old girl comes to see you because of headache that have been present for the past 5 years, but have been daily for the past 1 year. She has all but dropped out of school. Most days her headache is steady and 6 out of 10 in severity. About once a week she has a worse headache, which is 10 out of 10, associated with nausea, visual blurring, and mild vertigo. She is usually upbeat, but she admits to becoming a little depressed with all the headaches that none of the doctors can fix, her pediatrician has treated her multiple times for sinus HA. She takes ibuprofen most days with a little relief. She has tried many other over the counter and some prescription pain medications, without much help.
- There are no other major health problems.
- Physical and neurologic examinations are normal.
- What else would you like to know about the history?
- What is your differential diagnosis?
- What other testing would you do?
- What treatments would you suggest?

Pediatric Migraine

Case 4

- A 15-year-old girl began having headaches 2 weeks ago. They are generalized and throbbing and moderately severe. They come about an hour after she gets up in the morning. They are relieved almost immediately upon lying down.
- What is your differential diagnosis, and how would you proceed with evaluation and treatment?

Pediatric Migraine

Case 5

- A 6-year-old girl has recurrent headache with vomiting. She describes unusual visual phenomenon before the headaches in which she sees in her left visual field a clown figure. This may go on for 45 minutes. The headache and vomiting follow. These episodes started two years ago, and occur once or twice per week.
- She has a history of several febrile seizures.
- She has normal development and examination.
- What is your differential diagnosis, and how would you proceed with evaluation and treatment?

Pediatric Migraine

Case 6

- A 16-year-old boy comes to see you because of headache that occurs during weight lifting. The headaches are severe and have sudden onset. He stops exercising and the headache last for 30 to 60 minutes. This has happened 4 times in 6 months, and not every time he exercises. On further questioning he has had a similar headache with coughing, and once with sexual activity.
- His examination is normal.
- What is your differential diagnosis, and how would you proceed with evaluation and treatment?

Pediatric Migraine

Case 7

- A 12 year old girl is in the ER and you are called to help. She had a severe headache with photophobia, nausea and some vomiting for the past 5 days. She has been unable to eat, but is taking fluids. Her mother has been giving her ibuprofen at the appropriate doses. She has had occasional bad headache in the past and there is a positive family history of migraine headache.
- Your physical and neurological examinations are normal.
- How would you proceed with evaluation and treatment.

Goals of Migraine Treatment

Quality of life in paediatric migraine: characterization of age-related effects using PedsQL 4.0.
Cephalalgia 2004;24:120–7.

1. Reduction of headache frequency, severity, duration, and disability
2. Reduction of reliance on poorly tolerated, ineffective, or unwanted acute pharmacotherapies
3. Improvement in the quality of life
4. Avoidance of acute headache medication escalation
5. Education and enablement of patients to manage their disease to enhance personal control of their migraine
6. Reduction of headache-related distress and psychological symptoms

Pediatric Migraine Treatment

- We tend to rely on lifestyle modification more than medications in children
 - Concern about side effects in the young
 - There are really no good studies in young children showing safety and efficacy of most of the abortive or preventive medication for migraine.
 - Information is extrapolated from adult literature which is not always valid

Pediatric Migraine Treatment

- Lifestyle changes:
 - Regular sleep and meals
 - Fluids
 - Certain foods
- Psychosocial factors
 - Identify drug use
 - Identify school issues
 - Identify home or abuse issues

Pediatric Migraine Treatment

- Psychosocial
 - Identify barriers to improvement
 - Factors that can amplify pain
 - Parental input
 - Cognitive behavioral therapy

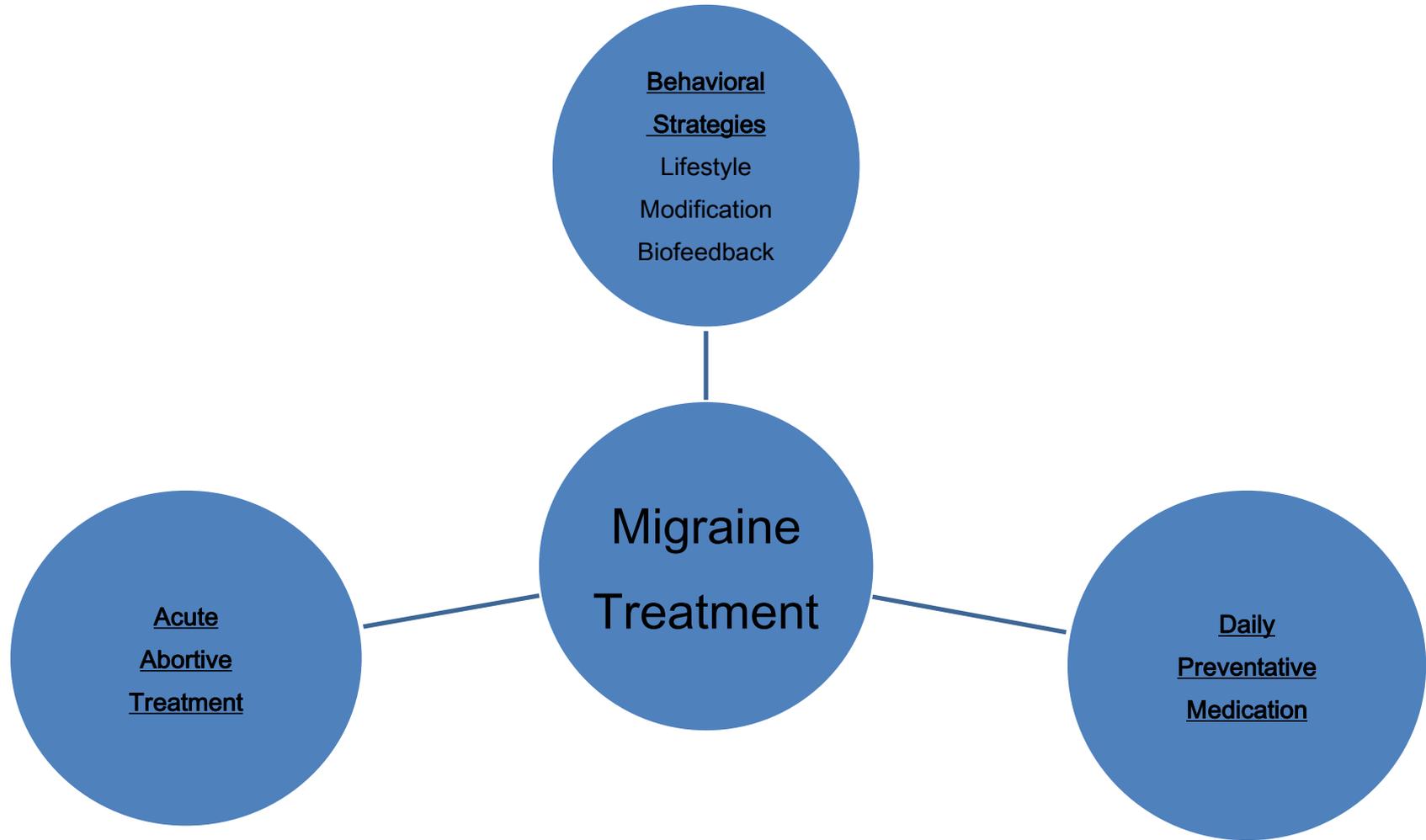
Pediatric Migraine Management

- Treatments meant to abort headaches once they start
- Treatments meant to prevent headaches from occurring

Pediatric Migraine Treatment

- Preventive medications
 - We use the same medications as are used in adults
 - Cyproheptadine in the very young
 - No good controlled studies in the pediatric population
 - Topiramate, amitriptyline, nortriptyline, and beta blockers used most often

Treatment Arms in Migraine



Headaches

Initial Management

- Education
 - Frequency of headaches in children
 - Genetic component of headache syndromes
 - Lifestyle influences
- Stress management
- Reassurance

Pediatric Migraine

Initial Management

- Stress management
 - Biofeedback
 - Stress reduction exercises
 - Cognitive behavioral therapy
- Treat co-morbid anxiety and depression
- Coping techniques when headaches continue
- Identify school and family stressors
- Identify drug and alcohol use

Pediatric Migraine

Initial Management

- Trigger factors
 - Some are out of our control, i.e. weather
 - Sleep
 - Regular meals, hydration
 - Odors
 - Bright lights, sun, florescent
 - Prolonged concentration
 - Medications, drugs, alcohol

Pediatric Migraine

Initial Management

- Food triggers – common ones mentioned
 - **Chocolate**
 - Processed meats (**nitrites or nitrates**)
 - Aged and cheddar cheese (tyramine)
 - **MSG** in high levels
 - Alcohol
 - Aspartane
- Not good evidence for their effect
 - But clinically in some patients these are a definite trigger

Pediatric Migraine Initial Management

- Alternative treatments
 - Massage therapy
 - Ice mask
 - Acupuncture
 - Botulium toxin injections
 - Now FDA approve for migraine treatment for over 18 years

Pediatric Migraine

Medical Treatments

- Abortive medication
 - More effective if used early in the headache
 - Use proper dose
 - Acetaminophen – 10 to 15 mg/kg/dose
 - Ibuprofen – 10 to 15 mg/kg/doses
 - Naproxyn – 5 mg/kg/dose

Pediatric Headaches Treatment

- Abortive therapy – medicines I rarely use
 - Narcotics
 - Butalbital
 - Ergotamines

Pediatric Migraine

Abortive medications

- Triptans
 - Designed specifically for migraine treatment
 - Several now are approved by the FDA for children under 18 years, and have been used quite frequently
 - Axert recently approved for 12 to 17 years.
 - Zomig for 12 years and older
 - Maxalt for 8 years and older
 - Selective 5HT_{1D} agonists
 - 5HT felt to be important neurotransmitter of the trigemino-vascular network, thought to be important in the pathogenesis of migraine

Pediatric Migraine

Abortive medications

- Dihydroergotamine
 - Migrainol
 - DHE-45
- Toradol
- Depacon IV
- Phenothiazines
 - Dopamine antagonist
- Oxygen

Medical Treatment of Migraine Emergency Room

- Headache pathway
 - Fluids
 - Dopamine agonist
 - NSAIDs
 - Ketorolac
 - Headache cocktail
 - Anticonvulsants
 - Other

Pediatric Migraine Treatments

- Treatment of Status migrainosus
 - Headache Pathway
 - Ketorolac
 - Metaclopramide or prochlorperazine
 - diphenhydramine
 - IV valproic acid
 - Other
 - IV magnesium
 - DHE

Medical Treatment of Migraine Emergency Room

- Dopamine agonist
 - Prochlorperazine IV – has been shown to be effective
 - Dose 0.15 mg/kg max dose 10 mg
 - In a controlled blinded study the response rate was 82%
 - Akathisia in about 5%
 - Metoclopramide – less effective when compared to prochlorperazine
 - Dose 0.1 mg/kg max dose 10 mg
 - Side effects akathisia and dystonic reactions
 - Addition of diphenhydramine 1 mg/kg, max 50 mg
 - Brousseau, D, et.al. *Ann Emerg Med.* 2004;43:256-262
 - Trottier, ED, et.al. *J Emerg Med.* 2010;39:166-17

Medical Treatment of Migraine Emergency Room

- Ketorolac
 - 0.5 mg/kg max dose 30 mg
 - Often combined with dopamine antagonist
- Headache cocktail
 - Fluids
 - Prochlorperazine or metoclopramide
 - Ketorolac
 - Diphenhydramine
 - Some indication more effective in retrospective studies.

Medical Treatment of Migraine Emergency Room

- IV valproic acid
 - Small uncontrolled studies in pediatrics
 - Sheridan, D, et.al. J of Emerg Med 2015;49:541-545
 - Appears to be effective
 - 10 mg/kg, may be repeated

Medical Treatment of Migraine Emergency Room

- Other treatments
 - Other NSAIDs
 - Imitrex as NS, SQ, IV

Medical Treatment of Migraine

Home Abortive Treatments

- Principles of treatment
 - Treatment as soon as possible
 - Use proper dosages for age and weight
 - Often taken with oral fluid bolus
 - Sometimes caffeine can potentiate their benefit
 - Avoid opioids, butalbital and benzodiazepines
 - Life style and psychosocial issues should be addressed
 - Avoid medication overuse

Medical Treatment of Migraine

Home Abortive Treatments

- Acetaminophen
 - 15 mg/kg/dose max 1000 mg
- NSAIDs
 - Ibuprofen 10 to 15 mg/kg
 - Naprosyn 5 mg/kg
- In recent studies the effectiveness of ibuprofen and acetaminophen was equal, and ibuprofen and zolmitriptan were equal
 - Damen, L, et.al. Pediatrics 2005;116:e295-e302
 - Evers, S, et.al. Neurology 2006; 67:497-499

Medical Treatment of Migraine

Home Abortive Treatments

- Triptans
 - 5HT 1D agonist
 - Many studies over the years showing safety and efficacy in adults
 - Many studies show safety in Pediatrics
 - Hard to prove efficacy in Pediatric population due to high placebo rate.
 - Most are used off label in pediatrics
 - Avoid rebound headache

Medical Treatment of Migraine

Home Abortive Treatments

- Triptans
 - Each triptan has some unique property, so that one might work even if another one had failed
 - Different delivery systems may also be important for efficacy:
 - tablets
 - orally disintegrating tablets
 - nasal spray
 - injection subcutaneous

Medical Treatment of Migraine

Home Abortive Treatments

- Sumatriptan (Imitrex)
 - First, only injectable, nasal spray (bad taste)
- Rhizotriptan (Maxalt)
 - Orally disintegrating tables, higher bio-availability
- Naratriptan (Amalg)
 - Longer half-life
- Zolmotriptan (Zomig)
 - Oral disengaging tablet, nasal spray (ok taste)
- Almotriptan (Axert)
 - Less side effects, better bio-availability
- Eletriptan (Relpax)
 - Less side effects, better bio-availability
- Frovatriptan (Frova)
 - Longest half-life (menstrual migraine)
- Sumatriptan/naproxen

Medical Treatment of Migraine

Home Abortive Treatments

- Triptans
 - Side effects
 - “triptan effect”
 - Ischemia
 - Drowsiness
 - Bad taste
 - GI upset
 - Worsening of headache
 - Rebound headache

Medical Treatment of Migraine

Home Abortive Treatments

- Triptans
 - Contraindications
 - Complicated or basilar migraine
 - Ischemic heart disease
 - Obesity (relative)
 - Hypertension - uncontrolled
 - Use within 24 hours of DHE

Medical Treatment of Migraine

Home Abortive Treatments

- Triptans
 - There are now three triptans FDA approved with positive controlled studies
 - Rizatriptan for 6 to 17 years
 - 5 mg for <40 kg and 10 mg for >40 kg
 - Ho TW, et.al. *Cephalalgia*. 2012;32:750-765
 - Hewitt DJ, et.al. *Headache*. 2013;53:104-117
 - Almotriptan for 12 to 17 for headache over 4 hours
 - Zolmatriptan for 12 and over
 - Controlled studies showing the effectiveness of the combination medication sumatriptan and Naprosyn in adolescents
 - Formulations of 10/60, 30/180, and 85/500
 - McDonald SA, *Headache*. 2011;51:1374-1387.

Pediatric Migraine Preventative Medications

- If the frequency and severity warrant
- Meant to decrease frequency and severity
- Not curative
- Use headache diary
- Start low, increase every 2 to 4 weeks
- Use maximum dose for at least 2 months
- Most common reason for failure is inadequate dose and duration of treatments
- End point?
- Should we use them?

Pediatric Migraine Preventative Medications

- CHAMP study published in the NEJM
January 2017

CHAMP Study

Table 2. Primary and Secondary Outcomes.*

Outcome	Amitriptyline (N=132)	Topiramate (N=130)	Placebo (N=66)
Primary outcome†			
≥50% Relative reduction in headache frequency — no. (%)	69 (52)	72 (55)	40 (61)
98.3% CI	42 to 63	45 to 66	45 to 75
P value for pairwise comparison with placebo	0.26	0.48	—
Secondary outcomes			
PedMIDAS score‡			
At baseline	41.3±27.9	41.2±25.0	42.0±27.0
At wk 24	18.8±25.3	14.4±17.3	19.4±20.8
Observed absolute difference (95% CI)	-22.5 (-27.6 to -17.4)	-26.8 (-32.2 to -21.5)	-22.6 (-30.2 to -15.0)
P value for pairwise comparison with placebo	0.91	0.13	—
Headache days per 28-day period§			
At baseline	11.3±6.0	11.3±5.7	11.1±6.5
At wk 24	4.6±4.6	4.6±5.3	5.2±6.5
Observed absolute difference (95% CI)	-6.7 (-7.9 to -5.5)	-6.7 (-7.6 to -5.7)	-5.9 (-7.7 to -4.1)
P value for pairwise comparison with placebo	0.36	0.41	—
Completion outcomes¶			
Patients who completed the trial — no. (%)	106 (80)	102 (78)	59 (89)
95% CI	73 to 86	71 to 85	80 to 95
Patients who withdrew owing to side effects — no. (%)	7 (5)	8 (6)	1 (2)
95% CI	3 to 11	3 to 12	<0.5 to 8

* Plus-minus values are means ±SD. No pairwise comparisons met the criteria for statistical significance. CI denotes confidence interval.

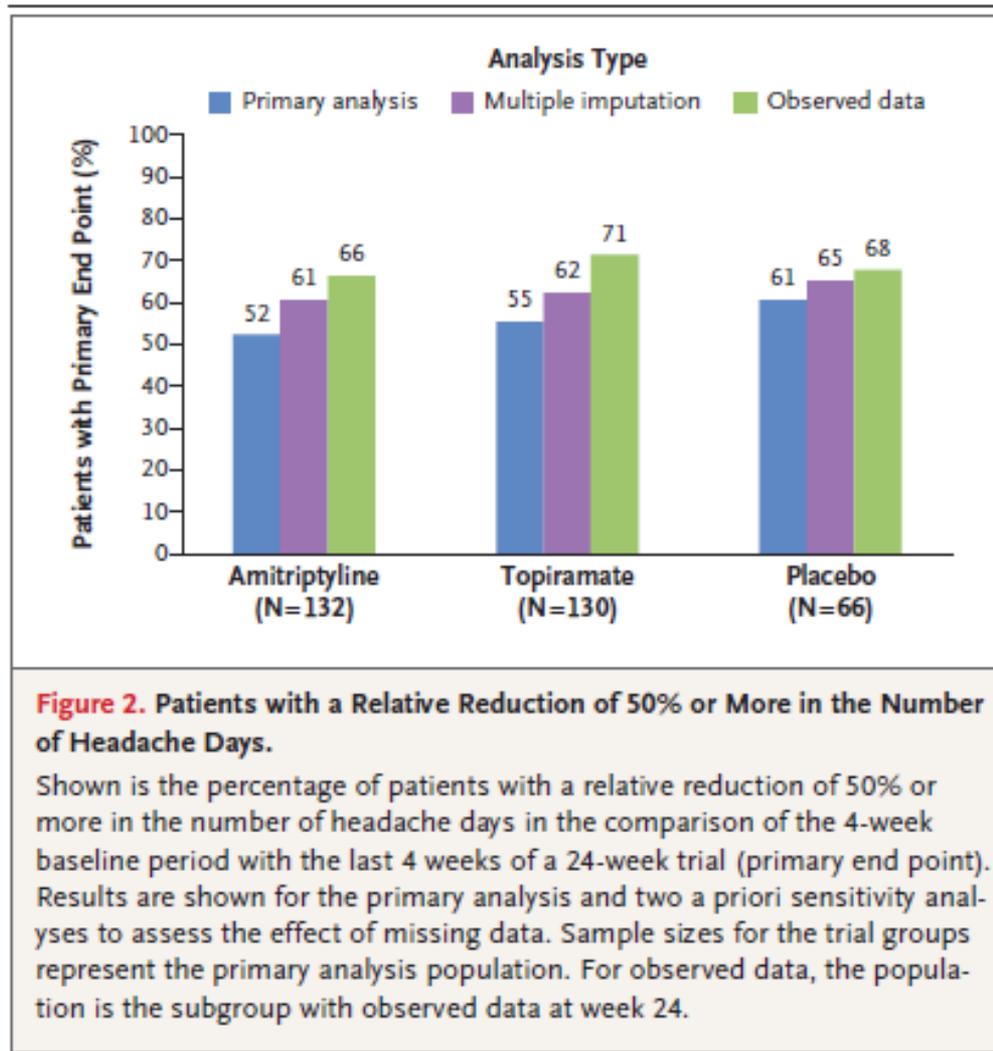
† The primary efficacy analysis population included all the patients who either had an observed end-point visit with complete headache-diary data or had a target date for an expected end-point visit on or before the target date for completion of the last weaning visit in the original closeout plan (February 4, 2015).

‡ The analysis population included all the patients who had observed end-point data: 107 in the amitriptyline group, 104 in the topiramate group, and 60 in the placebo group.

§ The analysis population included all the patients who had observed end-point data: 104 in the amitriptyline group, 101 in the topiramate group, and 59 in the placebo group.

¶ According to the statistical analysis plan, a concern about side effects was defined as a percentage of patients who complete the 24-week treatment period for the two active-treatment groups that was significantly lower than the percentage among patients receiving placebo or a percentage that was significantly less than 65%.

Champ Study



Indications for Migraine Prophylaxis

- **1) At least 3-4 severe migraines per month**
- **2) Migraines that limit daily activities**
 - Missing school, extracurricular activities
 - Adverse effect on grades, ability to pay attention
 - Disrupting sleep
 - Secondary psychiatric symptoms - depression
- **3) Migraines with interfering neurologic function**
 - Visual loss
 - Weakness
 - Confusion
 - Vertigo



Pediatric Migraine Preventative Medications

- Cyproheptadine (Periactin)
 - In younger patients with migraine
 - 2 to 8 mg, given all at night
 - Weight gain and drowsiness
 - Moderately effective
 - Might be helpful if sleep or allergies are also a problem

Pediatric Migraine Preventative Medications

- Tricyclic antidepressants
 - Amitriptylline (10 to 100 mg qhs)
 - Nortriptylline (10 to 100 mg qhs)
 - Use very low doses given all at night
 - Good for chronic daily headache
 - Very effective if tolerated in adult studies

Pediatric Migraine Preventative Medications

- Tricyclic antidepressants
 - Side effects
 - Drowsiness
 - Dry mouth
 - Weight gain
 - Orthostatic hypotension
 - Tachycardia
 - Do EKG at initiation?
 - Constipation, urinary retention

Pediatric Migraine Preventative Medications

- Tricyclic antidepressants
 - Contraindications
 - Glaucoma
 - Urinary retention
 - Pregnancy
 - MAO's

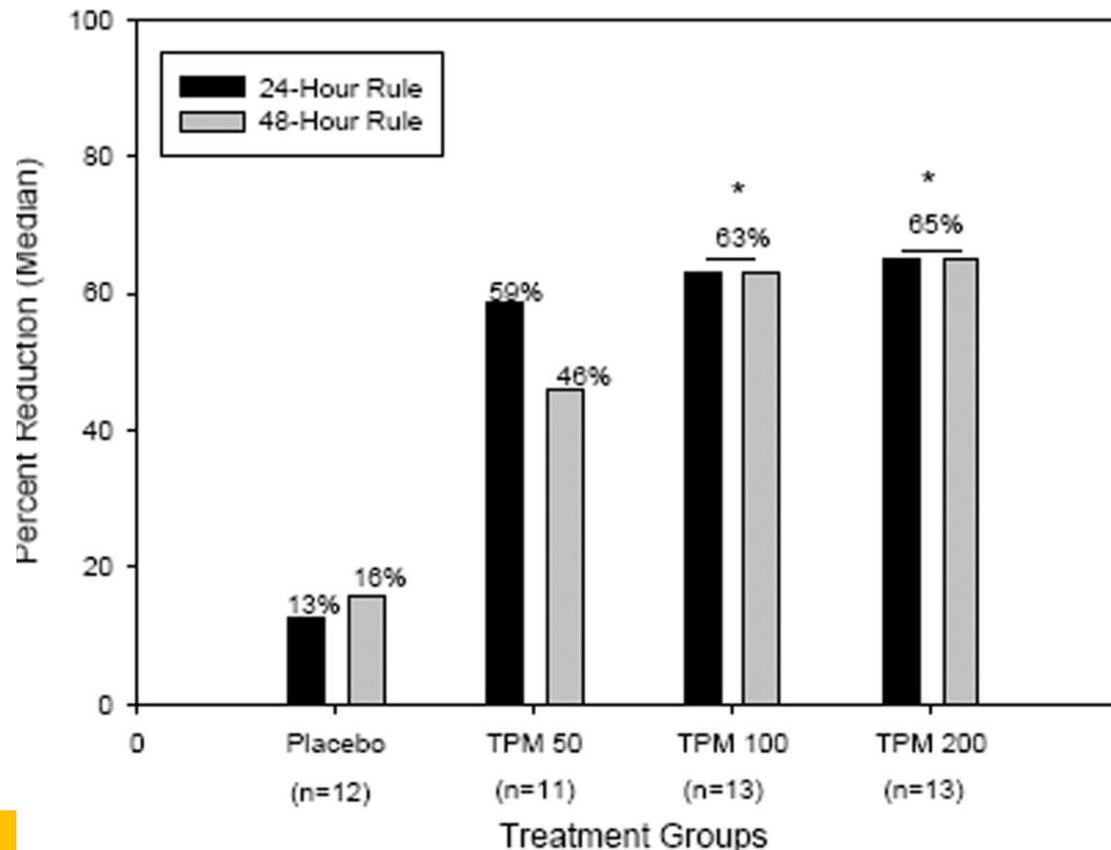
Pediatric Migraine Preventative Medications

- Anticonvulsants
 - Topiramate (Topamax)
 - Very effective in adult studies
 - 25 to 100 mg given all at night

Topiramate for Migraine Prevention in Adolescents: A Pooled Analysis of Efficacy and Safety

Headache 2006;46:1503-1510

Percent Reduction From Baseline in Migraine Frequency
Using 24-Hour and 48-Hour Rule



Pediatric Migraine Preventative Medications

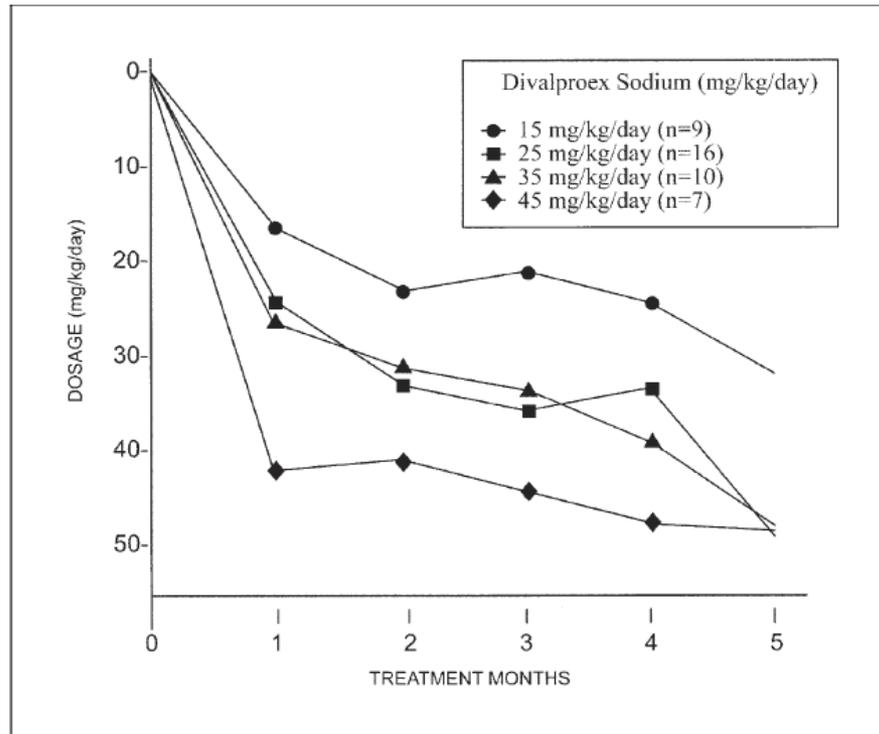
- Topiramate
 - Side effects
 - Weight loss
 - Word finding difficulties, lethargy
 - Acidosis
 - Stomach upset
 - Paresthesias
 - Rare acute glaucoma

Pediatric Migraine Preventative Medications

- Anticonvulsants
 - Valproic acid (Depakote)
 - Very effective in adult studies
 - Comes in ER form which should be used for migraine
 - Effective for chronic daily headache
 - 250 to 1500 mg daily

The Efficacy of Divalproex Sodium in the Prophylactic Treatment of Children With Migraine

Headache, 2000;40:672-676



Cumulative reduction in headache frequency over a 4-month treatment period with divalproex sodium.

The Efficacy of Divalproex Sodium in the Prophylactic Treatment of Children With Migraine

Headache, 2000;40:672-676

Table 2.—Adverse Effects With Use of Divalproex Sodium in Children

Adverse Effect	No. (%) of Patients			
	15 mg/kg/day (n = 9)	25 mg/kg/day (n = 16)	35 mg/kg/day (n = 10)	45 mg/kg/day (n = 7)
Gastrointestinal upset	2 (22)	1 (6.3)	4 (40)	7 (100)
Weight gain	1 (11)	0	1 (10)	1 (14.3)
Somnolence	1 (11)	1 (6.3)	2 (20)	2 (28.6)
Dizziness	0	1 (6.3)	2 (20)	1 (14.3)
Tremor	0	0	1 (10)	1 (14.3)

n indicates the number of patients receiving each final dose of divalproex sodium.

Pediatric Migraine Preventative Medications

- Valproic acid
 - Side effects
 - Weight gain
 - Liver function abnormalities
 - Thrombocytopenia
 - Hair loss
 - Tremor
 - Neuro-toxicity

Utilize Side Effects to Advantage

- Amitriptyline – sleep problems
- Topiramate – obesity
- Valproic acid – rapid relief, underweight
- Cyproheptadine – younger child, underweight
- Beta-blocker – POTS, hypertension



Avoid Harmful Side Effects

- Amitriptyline – cardiac rhythm problems, hypertension
- Topiramate – kidney stones, underweight
- Valproic acid – obesity, liver dysfunction, teenage female/PCOS
- Cyproheptadine – obesity
- Beta-blocker – asthma, depression

Headaches

Preventative Medications

- **Beta blockers**
 - Not all beta blockers work
 - Propranolol (10 to 60 mg TID) (use LA form)
 - Atenolol (25 to 100 mg daily)
 - Nadolol (10 to 20 mg daily)
 - Metoprolol, timolol
 - High degree of individual bio-availability
 - Moderately to very effective in adult literature
 - Pediatric literature is mixed

Headaches

Preventative Medications

- Beta-blockers
 - Contraindications:
 - Asthma
 - Chronic obstructive lung disease
 - Congestive heart failure
 - Atrial-ventricular heart block
 - Brittle diabetes
 - Reynaud's disease
 - Depression

Headaches

Preventative Medications

- Beta-blockers
 - Side effects
 - Fatigue
 - Dizziness
 - Cold extremities
 - Vivid dreams, nightmares, insomnia
 - Depression

Pediatric Migraine Preventative Medications

Pediatr. Rev. 2010;31:e17-e23

Current Pain and Headache Reports 2008, 12: 379 – 383

- Magnesium
 - 200 to 400 mg
- Riboflavin
 - 200 to 400 mg
- Coenzyme Q 10
 - 1 to 3 mg/kg
 - In patients with CDH and measured deficiency

Riboflavin prophylaxis in pediatric and adolescent migraine

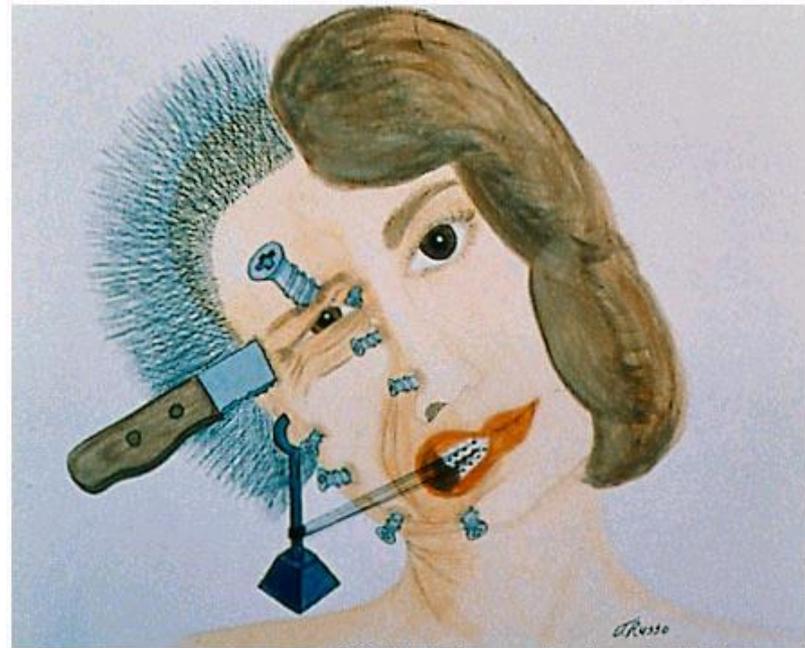
J Headache Pain (2009) 10:361–365

- Retrospective study of 41 patients
- 200 – 400 mg/day
- During follow up 68% had 50% or greater in HA frequency and 21% decreased HA intensity
- Few or no side effects
- Low cost
- Needs blinded controlled studies to confirm

Headache Migraine Treatments

What's new

- CGRP inhibitors
- Botox injections for pediatric age group
- Cefaly



©1991, Novartis Pharmaceuticals Corporation. All rights reserved.

Pediatric Migraine

Who to refer?

- Diagnostic dilemmas
- Initial management fails
- Parental anxiety
- Abnormal neurological findings

Pediatric Headaches

Migraine variants

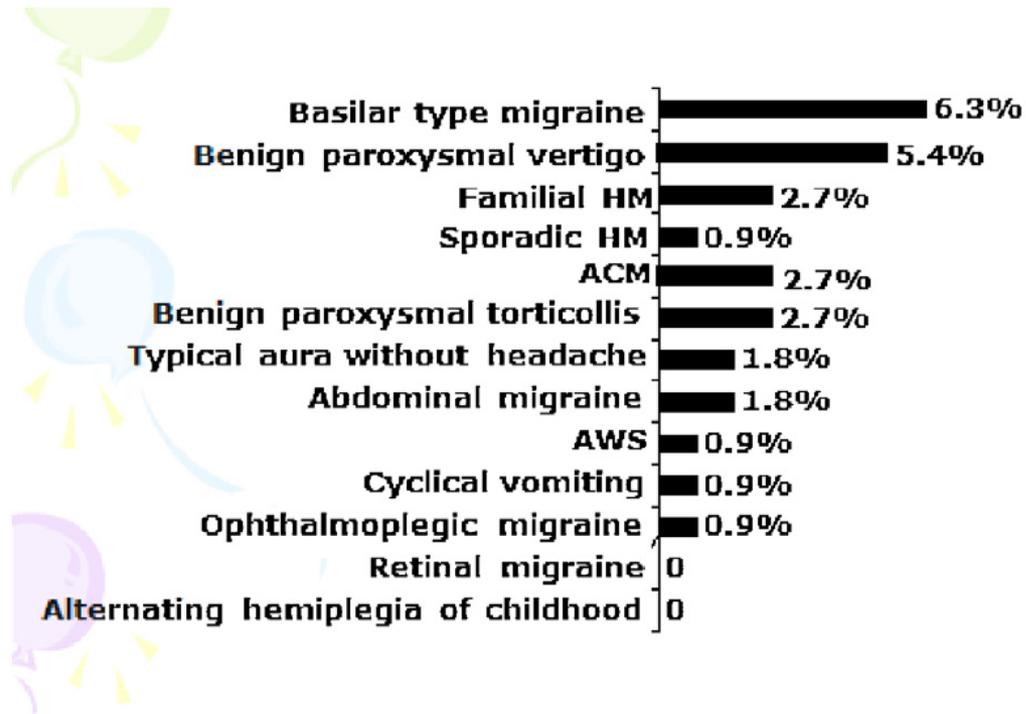


Fig. 2. Occurrence of migraine variants among migrainous patients ($n = 111$).

Pediatric Headaches

Migraine variants

- Infant colic and migraine
 - Studies use parental recall
 - Crying for at least 3 hours, at least 3 times per week before the age of 3 months.
 - Much higher incidence of colic in migraine group as compared to controls
 - Mother's higher incidence of migraine
 - Earliest periodic syndrome

Gefland, AA, et.al., Neurology 2012; 79:1392

Table 1. Patient Characteristics

Child Characteristics	Migraine Group ^a (n = 208)	Control Group ^a (n = 471)	P Value	Tension-Type Headache (n = 120) ^a	P Value ^b
Boys, No.	122	280	.85	65	.30
Girls, No.	86	191		55	
Age at evaluation, median (IQR), y	10.1 (8.2-13.7)	9.0 (7.0-12.0)	.001	10.1 (8.0-12.0)	.01
Aged 6-11.9 y	129 (62.0)	337 (71.5)		84 (70.0)	
Aged 12-18 y	79 (38.0)	134 (28.5)		36 (30.0)	
Gestational age at birth, median (IQR), wk	40 (38-40)	40 (38-40)	.25	40 (39-40)	.02
Birth weight, median (IQR), g	3345 (3000-3640)	3310 (2980-3640)	.61	3370 (3005-3595)	.56
Breastfeeding			.002		.001
Exclusive	106 (50.9)	295 (62.6)		55 (45.8)	
Mixed	44 (21.2)	70 (14.9)		32 (26.7)	
Formula feeding	58 (27.9)	106 (22.5)		33 (27.5)	
Conditions Reported in Infancy and Childhood					
Diagnosis of infantile colic	151 (72.6)	125 (26.5)	<.001	42 (35.0)	.07
Recurrent abdominal pain during childhood	38 (18.3)	22 (4.7)	<.001	13 (10.8)	.01
Coexisting chronic medical conditions ^c	16 (7.4)	39 (8.3)	.80	8 (6.6)	.56
Repeated a grade in school	12 (5.8)	23 (4.9)	.63	3 (2.5)	.26
Sleep disorders ^d	20 (9.6)	9 (1.9)	<.001	14 (11.7)	<.001
Family history					
Parental consanguinity	7 (3.4)	25 (5.3)	.27	1 (0.8)	.03
Primary headache in first-degree relatives	165 (79.3)	157 (33.3)	<.001	79 (65.8)	<.001
Migraine with aura ^e	38 (23)	28 (17.8)		17 (21.5)	
Migraine without aura ^e	89 (54)	49 (31.2)		41 (51.9)	
Tension-type headache ^e	38 (23)	77 (49)		21 (26.6)	
Other types ^e	0	3 (0.6)		0	
Infantile colic in first-degree relatives	53 (25.5)	47 (10)	<.001	26 (21.7)	<.001

Abbreviation: IQR, interquartile range.

^aData are reported as No (%) of participants unless otherwise indicated.

^bP values compare tension-type headache with control participants.

^cThe most common chronic medical conditions were asthma, diabetes, recurrent urinary tract infections, and sickle cell anemia.

^dAs diagnosed by *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision) criteria.

^eHeadache subtypes are among first-degree relatives with primary headache.

Romanello, S, et.al., JAMA. 2013;309(15):1607-1612

Pediatric Headaches

Migraine variants

- Benign paroxysmal torticollis
 - Onset of episode of torticollis
 - In infancy, often before 6 months of age
 - Last from hours to several days
 - Self limited and improves by age 2 years
 - Associated pallor, irritability, ataxia or tortipelvis
 - May be associated with CACNA1A or PRRT2 genes
 - Treatment with cyproheptadine?
 - Diagnosis of exclusion

Rossman, NP, et.al. J Child Neurol 2009; 24:155

Pediatric Headaches

Migraine variants

- Benign paroxysmal vertigo
 - Recurrent attacks of vertigo, short lived
 - With ataxia and nystagmus
 - Seconds to minutes
 - Age of onset between 2 and 5 years
 - Most outgrow, but some persist
 - A few with genetic link to FHM (CACNA1A)
 - Rule out seizure and vestibular dysfunction

Krams, B et.al., Cephalalgia 2011; 31:439

Pediatric Headaches

Migraine variants

- Cyclic vomiting
 - Stereotyped episodes of frequent vomiting
 - At least 4 episodes in one hour
 - Predictable intervals
 - Average age of onset was 5 years
 - Average 0.8 episodes per month
 - Mean duration of 3.4 days

Lee, L, Eur J Gastroenterol Hepatol 2012; 24:1001

Pediatric Headaches

Migraine variants

- Cyclic vomiting
 - 40% have headache
 - 1/3 have family history of migraine
 - Rule disorders of fatty acid metabolism and intermittent volvulus
 - Treatment with rehydration and anti-emetics
 - Migraine preventives in severe cases?

Kothare, Eur J Paediatr Neurol 2005; 9:23

Pediatric Headaches

Migraine variants

- Abdominal migraine
 - School age children
 - Moderate to severe abdominal pain lasting 1 to 72 hours
 - Dull, midline and poorly localized
 - May have nausea, vomiting, anorexia, or pallor
 - Well in between with no GI symptoms
 - Incidence in GI practice with idiopathic abdominal pain is 4 to 15%
 - Treatment with IN sumatriptan or preventives?

Carson, L, et.al., Headache 2011; 51:707

Pediatric Headaches

Migraine variants

- Alice in wonderland syndrome
 - Both hallucinations and illusions occur
 - Altered sensation of size, form or movement
 - Reports of auditory hallucinations
 - Olfactory and gustatory illusions have been reported
 - Can occur before onset of intermittent headache and can cause a diagnostic challenge

Todd J. The syndrome of Alice in wonderland. Can Med Assoc J 1955;73:701–4.

Pediatric Headaches

Migraine variants

- Alice in wonderland – other sensory phenomenon
 - Achromatopsia
 - Prosopagnosia, metamorphosia
 - micropsia and macropsia
 - macrosomatognosia and microsomatognosia
 - depersonalisation, derealisation
 - illusions of time and a dreamy confused state
 - alexia

Table 1 Symptoms reported from questionnaire based study

Nine subjects	Mean
Age at interview	12.7 years
Gender	
Male	4
Female	5
Age onset illusions	8.4 years
Age onset headaches	9.4 years
Hearing voices when no-one is around (hallucination)	6 (67%)
Hearing noise with nothing to explain it (hallucination)	4 (44%)
Seeing things that no-one else can see (hallucination)	7 (78%)
Smelling things with no explanation (hallucination)	0
Feeling things touch you when there is nothing to explain it (hallucination)	4 (44%)
Seeing things that become distorted (illusion)	7 (78%)
Things seeming much bigger than they really are (illusion)	5 (55%)
Things seeming much smaller than they really are (illusion)	3 (33%)
A sensation that time is going very slowly (illusion)	3 (33%)
A sensation that time is going very quickly (illusion)	5 (55%)
A sensation that colours are much brighter than they should be (illusion)	4 (44%)
A sensation that colours are much dimmer than they usually are (illusion)	4 (44%)

Smith RA, et al. Arch Dis Child 2015;100:296–298.

A sensation that colours are much dimmer than they usually are (illusion)	4 (44%)
A sensation that you are outside your body (illusion)	6 (67%)
A feeling that the world is not real (illusion)	5 (55%)
A feeling that you are not real (illusion)	4 (44%)
A feeling of fear for no reason	6 (67%)
A feeling that people are being sarcastic when you don't really think they are	2 (22%)
A feeling that parts of your body change in size (illusion)	55%
Have you experienced any other unusual symptoms	44%
Hyperacusis (illusion)	55%
Object moving (illusion)	78%
Number of different illusions	10.5 (range 7–15)
Full fills ICH diagnostic criteria for migraine	100%
First degree relative with migraine	78%
First degree relative with AIWS like symptoms	22%
Normal CNS examination	100%
EEG (all normal)	44%
MRI (all normal)	55%

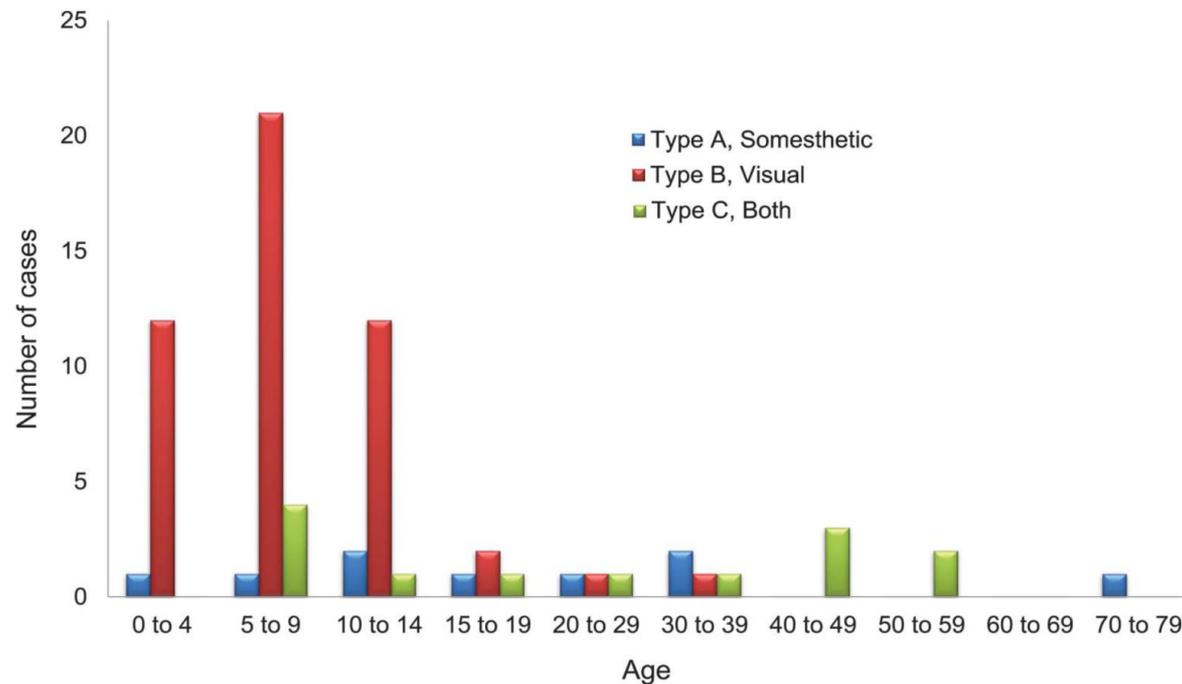
AIWS, Alice in Wonderland Syndrome; CNS, central nervous system.

Smith RA, et al. Arch Dis Child 2015;100:296–298.

Pediatric Headaches

Migraine variants

Figure Distribution of reported Alice in Wonderland syndrome cases by age and type



From Lanska, JR, Neurology 80:1262 March 26, 2013

Pediatric Headaches

Migraine variants

- Alice in wonderland syndrome
 - Pathophysiology still not completely understood, due to rarity of this disorder
 - Most studies just a few case reports
 - Abnormal VEP's and SPECTS studies leading to the idea of decrease cerebral perfusion and cerebral depression.

Pediatric Headaches

Migraine variants

- Alice in wonderland – differential diagnosis
 - Infection – EBV
 - Rule encephalitis
 - Seizures
 - Drug intoxication – Topamax, cough syrup, stimulants.
 - Psychosis
 - Narcolepsy

Weidenfeld, A, Childs Nerv Syst (2011) 27:893–896

Pediatric Headaches Migraine Equivalents

Table I. Characteristics of Patients in Each Group of Migraine Equivalent.

Type of Migraine Equivalent	No.	Age (Mean)	Gender (F/M)	Family History	Lost to Follow-Up	Prophylaxis	Good Outcome
Paroxysmal torticollis	2	1	0/2	–	0	–	2
Benign paroxysmal vertigo	12	3.6	6/6	9	3	6	9
Abdominal migraine	15	6.8	8/7	10	3	12	12
Cyclic vomiting	1	8	1/0	1	0	1	1
Aura without migraine	3	8.3	1/2	2	1	2	2
Confusional migraine	5	10.2	1/4	3	3	2	2
Total	38	6.1	17/21	25	10	23	28

Teixeira, KCS, et. Al., Journal of Child Neurology 2014, Vol. 29(10) 1366-1369

Pediatric Headaches

Migraine Equivalents

Table 2. Treatment of Migraine Equivalents.

Migraine equivalents	Prophylaxis	
Paroxysmal torticollis	–	–
Benign paroxysmal vertigo	Flunarizine	4
	Ciproheptadine	2
Abdominal migraine	Flunarizine	3
	Ciproheptadine	7
	Imipramine	1
	Valproic acid	1
Cyclic vomiting	Cyproheptadine	1
Aura without migraine	Flunarizine	2
Confusional migraine	Cyproheptadine	2
Total		23

Teixeira, KCS, et. Al., Journal of Child Neurology 2014, Vol. 29(10) 1366-1369