



Pharmacological treatment of migraine headache in children and adolescents

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Why ?



Migraine headaches are common in children

By ages	Preschool	Elementary school	High school
Prevalence (%)	1.2-3.2	4-11	8-23
Gender ratio	boys > girls	boys = girls	girls > boys

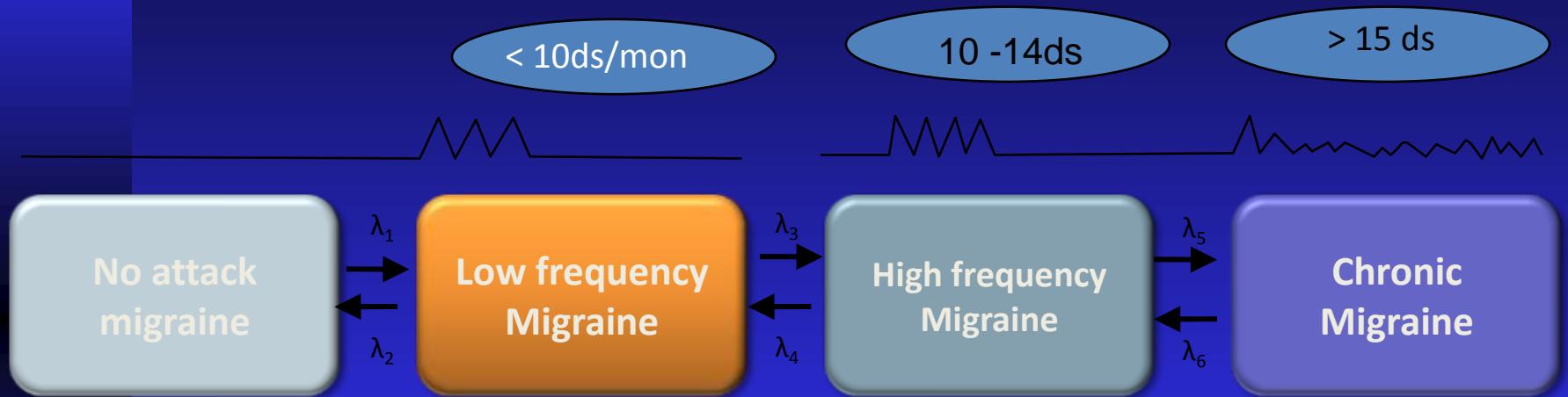
J Pediatr Pharmacol Ther 2008 Vol. 13 No. 1

The mean age at onset: **7.2 years (boys),**
10.9 years (girls)



Diagnosis- Treatment ???

Progressive migraine



2004 ICHD: Criteria for pediatric migraine



Migraine without aura	Migraine with typical aura
A. 5 attacks or more	A. 2 attacks or more
B. Headache attacks lasting 4-72 hours	B. Aura (no motor weakness): <ol style="list-style-type: none">1. Fully reversible visual symptoms2. Fully reversible sensory symptoms3. Fully reversible dysphasic speech disturbance
C. Headache characteristics (2 of the following): <ol style="list-style-type: none">1. Unilateral location2. Pulsating quality3. Moderate or severe pain intensity4. Aggravated by or causing avoidance of routine physical activity	C. At least 2 of the following: <ul style="list-style-type: none">- homonymous visual symptoms- unilateral sensory symptoms- aura symptom develops gradually over ≥ 5 minutes
D. Associated symptoms: <ol style="list-style-type: none">1. Nausea and/or vomiting2. Photophobia and phonophobia	D. Headache (migraine without aura) begins during the aura or follows aura within 60 minutes

Nonspecific manifestations

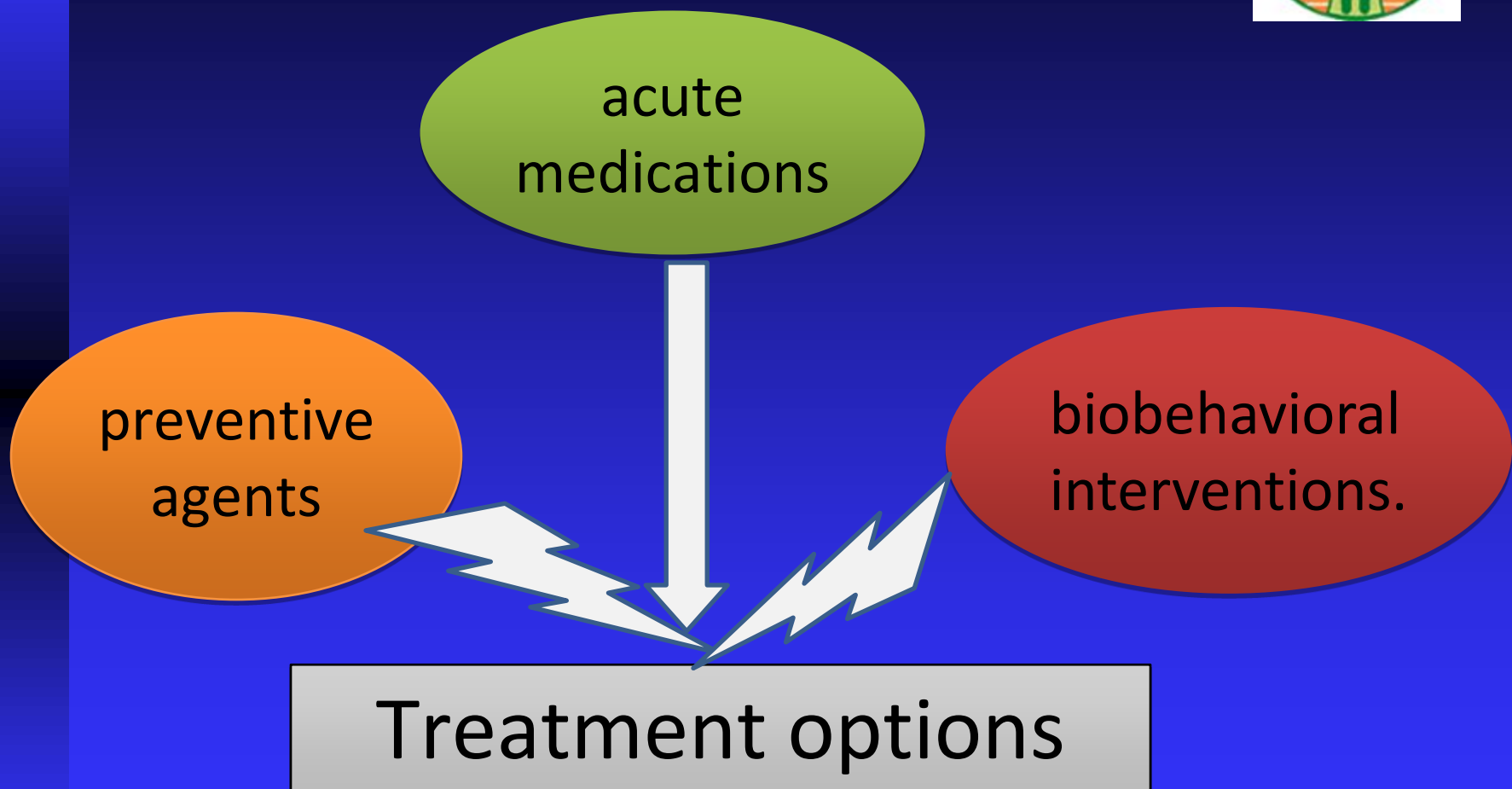


- Only episodic “head banging”
- Preschool children: ill appearance, abdominal pain, vomiting, and the need to go to sleep; they may exhibit pain by irritability, crying, rocking, or seeking a dark room...
- 5-10 years typically have bifrontal, bitemporal, or retro-orbital headache; nausea; abdominal cramping; vomiting; photophobia; phonophobia; a need to sleep; migraine facies; tearing, swollen nasal passages; thirst; edema; excessive sweating; increased urination; or diarrhea

Aims ?



1. ↓ frequency, severity, duration, disability
2. ↓ reliance on poorly tolerated, ineffective, or unwanted acute pharmacotherapies
3. ↑ 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. ↓ headache-related distress and psychological symptoms





AMERICAN ACADEMY OF
NEUROLOGY

Practice Parameter: Pharmacological treatment of migraine headache in children and adolescents

Report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society

D. Lewis, MD; S. Ashwal, MD; A. Hershey, MD; D. Hirtz, MD; M. Yonker, MD; and S. Silberstein, MD

NEUROLOGY 2004;63:2215–2224



Methods

The authors reviewed, abstracted, and classified relevant literature. Recommendations were based on a four-tiered scheme of evidence classification. Treatment options were separated into medications for acute headache and preventive medications.

Results

The authors identified and reviewed 166 articles. For acute treatment, five agents were reviewed. Sumatriptan nasal spray and ibuprofen are effective and are well tolerated vs placebo. Acetaminophen is probably effective and is well tolerated vs placebo. Rizatriptan and zolmitriptan were safe and well tolerated but were not superior to placebo. For preventive therapy, 12 agents were evaluated. Flunarizine is probably effective. The data concerning cyproheptadine, amitriptyline, divalproex sodium, topiramate, and levetiracetam were insufficient. Conflicting data were found concerning propranolol and trazodone. Pizotifen, nimodipine, and clonidine did not show efficacy.

RESULTS:



SUMMARY OF RECOMMENDATIONS FOR THE ACUTE TREATMENT OF MIGRAINE IN CHILDREN AND ADOLESCENTS

Strong evidence supports

- Ibuprofen is effective and should be considered for the acute treatment of migraine in children. (Class I*, Level A**)
- Sumatriptan nasal spray is effective and should be considered for the acute treatment of migraine in adolescents. (Class I, Level A)

Good evidence supports

- Acetaminophen is probably effective and should be considered for the acute treatment of migraine in children. (Class I, Level B)

Evidence is insufficient to support or refute

- There is no supporting data for the use of any oral "triptan" preparations in children or adolescents. (Class IV, Level U)
- There is inadequate data to make a judgment on the efficacy of subcutaneous sumatriptan. (Class IV, Level U)

RESULTS:



SUMMARY OF RECOMMENDATIONS FOR PREVENTIVE THERAPY OF MIGRAINE IN CHILDREN AND ADOLESCENTS

Good evidence supports

- Flunarizine is probably effective for preventive therapy and can be considered for this purpose but it is not available in the United States. (**Class I, Level B**)
- Pizotifen and nimodipine (**Class I, Level B**) and clonidine (**Class II, Level B**) did not show efficacy and are not recommended.

Evidence is insufficient to support or refute

- There is insufficient evidence to make any recommendations concerning the use of cyproheptadine, amitriptyline, divalproex sodium, topiramate, or levetiracetam. (**Class IV, Level U**)
- Recommendations cannot be made concerning propranolol or trazodone for preventive therapy as the evidence is conflicting. (**Class II, Level U**)



New advances in prevention of migraine

Review of current practice and recent advances

Khalid W. Al-Quliti, MBBS, MD, Ekblaz S. Assaedi, MBBS.

Neurosciences 2016; Vol. 21 (3)

Acute treatment:



Table 2 - Summary of medications used in treatment of acute attacks of migraine.

First line medications			Second line medications		
Specific Rx	Dose	Side effects	Drug	Dose	Side effects
Triptans			Ergot derivatives		
Almotriptan	12.5 mg, max 25 mg/day	Dizziness, weakness, Hot flushes, nausea, and vomiting	Ergotamine	2 mg, max 6 mg/day	Nausea, vomiting, rebound headache
Eletriptan	40 mg, max 5 mg/day	Pins and needles sensation, elevated blood pressure	Dihydro-ergotamine	1 mg IM or IV, max of 2 mg/day	Nausea, leg cramps at site of injection
Frovatriptan	2.5 mg, max 5 mg/day				
Naratriptan	2.5 mg, max 5 mg/day				
Rizatriptan	5 or 10 mg, max 20 mg/day				
Sumatriptan	50 mg, max 200-300 mg/day				
Zolmitriptan	2.5 mg, max 10 mg/day				
NSAID			Other classes		
Non-specific Rx	Dose	Side effects		Dose	Side effects
Diclofenac	50 mg, max 150 mg/day	GI upset	Butalbital	Max 4 tablets/day	Weakness, addictive potential
Ibuprofen	400 mg, max 2400 mg/day		Opioids	Limits for each individual drug	Addiction or drug dependency
			Steroids	Limits for each individual drug	Usual steroid adverse effects
Rx = prescription, max = maximum, IM = intramuscular, IV = intravenous, GI = gastrointestinal					



- Three are approved for use the pediatric population: **sumatriptan**, **rizatriptan**, and **almotriptan**.
- Sumatriptan has been the most widely studied medication from the class, and the AAN has recognized that there is sufficient evidence to support the use of **intranasal sumatriptan** in the acute treatment of episodic
- migraine in children

Prophylactic treatment:



Table 3 - Level of recommendation and evidence for prophylactic medication used for migraine according to the U.S.,^{13,16,25} Canadian,¹³ French⁴ and EFNS²⁵ guidelines.

Drug	2012 U.S. guidelines	Canadian guidelines	French guidelines	EFNS
<u>Valproate*</u>	Level A	Weak recommendation, HQE	DE, Grade A methodology	Level A
<u>Topiramate*</u>	Level A	Strong recommendation, HQE	DE, Grade A methodology	Level A
Carbamazepine*	Level C	Not rated	Not rated	Not rated
Gabapentin*	Level U	Strong recommendation, MQE	Doubtful efficacy, Grade B or C methodology	Level C
Lamotrigine*	Ineffective	Not rated	Not rated	Not rated
Amitriptyline [†]	Level B	Strong recommendation, HQE	PE, Grade B or C methodology	Level B
Venlafaxine [†]	Level B	weak recommendation, LQE	PE, Grade B or C methodology	Level B
Fluoxetine [†]	Level U	Not rated	Not rated	Not rated
Pizotifen [†]	Not rated	Weak recommendation, HQE	PE, Grade B or C methodology	Not rated
<u>Metoprolol[‡]</u>	Level A	Strong recommendation, HQE	DE, Grade A methodology	Level A
<u>Propranolol[‡]</u>	Level A	Strong recommendation, HQE	Not rated	Level A
<u>Timolol[‡]</u>	Level A	Not rated	PE, Grade B or C methodology	Not rated
Atenolol [‡]	Level B	Not rated	PE, Grade B or C methodology	Not rated
Nadolol [‡]	Level B	Strong recommendation, MQE	PE, Grade B or C methodology	Not rated
Nebivolol [‡]	Level C	Not rated	Probable efficacy, Grade B or C methodology	Not rated
Acebutolol [‡]	Ineffective	Not rated	Not rated	Not rated
Verapamil [§]	Level U	Weak recommendation, LQE	Not rated	Not rated
Candesartan [§]	Level C	Strong recommendation, MQE	PE, Grade B or C methodology	Level C
Lisinopril [§]	Level C	Weak recommendation, LQE	Not rated	Level C
Naproxen [§]	Level B	Not rated	PE, Grade B or C methodology	Level B
Aspirin ^{**}	Level U	Not rated	Not rated	Level C
Feverfew ^{**}	Level B	Not recommended	Not rated	Not rated
<u>Petasites^{**}</u>	Level A	Not rated	Not rated	Level B
Butterbur ^{**}	Not rated	Strong recommendation, MQE	Not rated	Not rated
Coenzyme 10 ^{**}	Level C	Strong recommendation, LQE	Not rated	Level C
Riboflavin ^{**}	Level B	Strong recommendation, LQE	Not rated	Level C
Magnesium ^{**}	Level B	Strong recommendation, LQE	Not rated	Level C

HQE - high quality evidence, LQE - low quality evidence, MQE - moderate quality evidence, DE - demonstrated efficacy, PE - probable efficacy, EFNS - European Federation of Neurological Societies, U.S. - United States of America, symbols represent different groups of medications



TIME?

1. **Episodic migraine:**
 - **6 months** in children and younger adolescents
 - **a year** in older adolescents and adults
2. **Chronic migraine: 2 or more years**



Conclusion:

- Frequency but unknown clearly
- Disability but not complete treatment

Thank for your attention!

