

Alternative and Complementary Therapy for the Treatment of Adolescent Migraine

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1.1 Migraine without aura

- A. At least 5 attacks fulfilling criteria B-D**
- B. Headache attacks lasting 4-72 h (untreated or unsuccessfully treated)**
- C. Headache has ≥ 2 of the following characteristics:**
 - 1. unilateral location
 - 2. pulsating quality
 - 3. moderate or severe pain intensity
 - 4. aggravation by or causing avoidance of routine physical activity (eg, walking, climbing stairs)
- D. During headache ≥ 1 of the following:**
 - 1. nausea and/or vomiting
 - 2. photophobia and phonophobia
- E. Not attributed to another disorder**

1.5.1 Chronic migraine

New entrant to classification

- A. Headache fulfilling criteria C and D for
1.1 *Migraine without aura* on ≥ 15 d/mo for >3 mo**

- B. Not attributed to another disorder**

1.5.1 Chronic migraine

Notes

- **When medication overuse is present, this is the most likely cause of chronic symptoms**
 - code according to antecedent migraine subtype +
1.6.5 *Probable chronic migraine* +
8.2.8 *Probable MOH*
- **Post-withdrawal, code as:**
 - 1.5.1 *Chronic migraine* + antecedent migraine subtype if symptoms persist beyond 2 mo
 - 8.2 *Medication-overuse headache* + antecedent migraine subtype if, before 2 mo, improvement occurs and these criteria are no longer fulfilled

Chronic daily headache in adolescence

- Chronic daily headache (CDH) affects up to 4% of adults
- CDH affects up to 1 to 2% of middle school children
- Children with CDH often have a history of episodic migraine or a family history of migraine
- The headache characteristics in patients with CDH may vary between patients as well as within a given individual patient
- Their headaches may present as severe intermittent migraine attacks, intermittent low severity headaches, continuous headache pain, or as a combination of these headache types
- This variation continues to make this headache type remarkably challenging to understand and treat

Quality of life in adolescents with headache: Results from a population-based survey

- N=1047, aged 13-17 years
- QOL questionnaire, Munich, Germany
- Adolescents with migraine reported higher reductions in physical wellbeing and total QOL than subjects with tension-type headache (TTH)
- The size of the reduction in QOL scores was small but similar to that observed for other chronic conditions in adolescents.
- Headache prevention programs might therefore have an impact on QOL in adolescents.

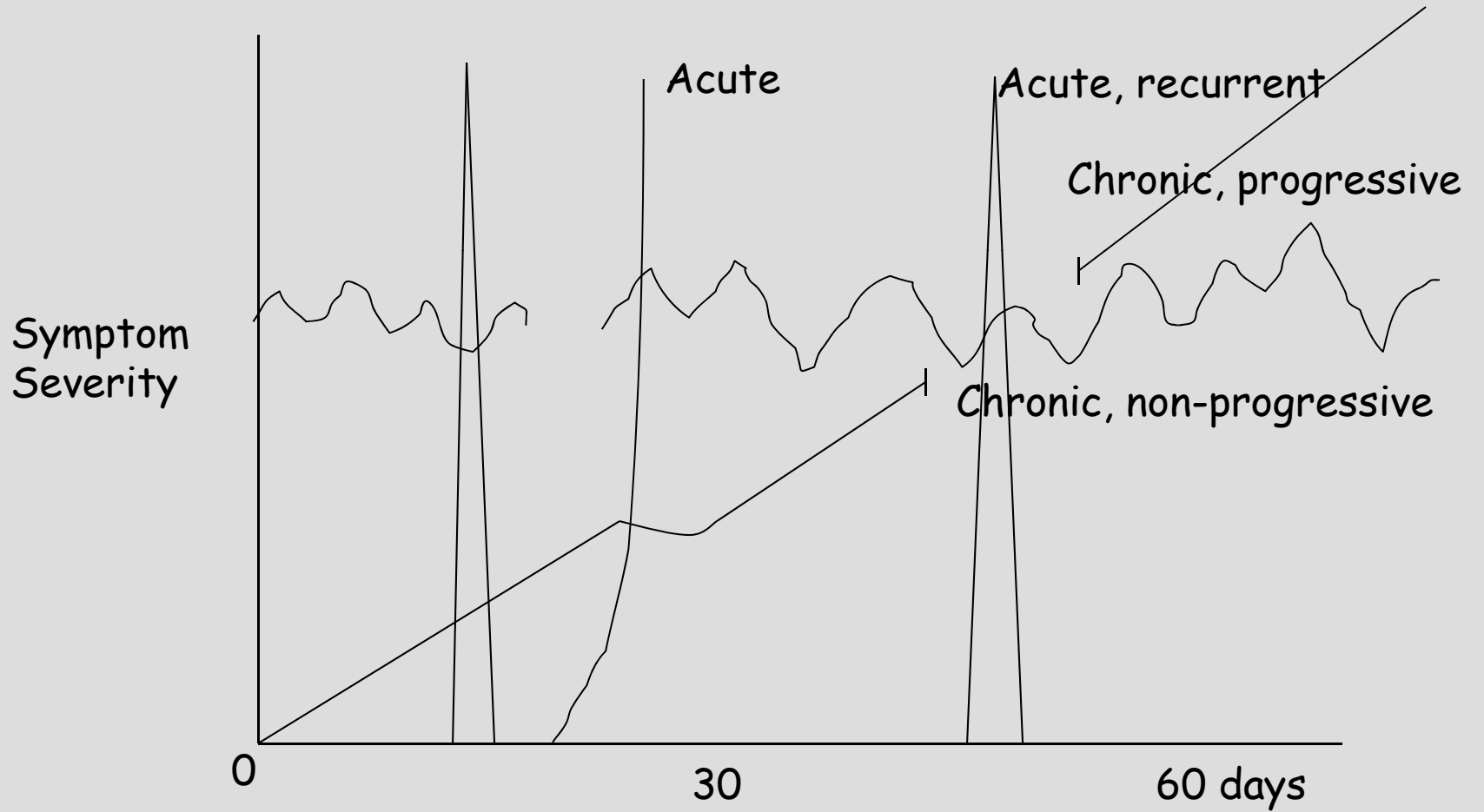
Chronic Daily Headaches

- Recurring daily headaches
- At least 15 days per month
- No serious underlying pathology
- May mask depression

Silberstein Classification of CDH

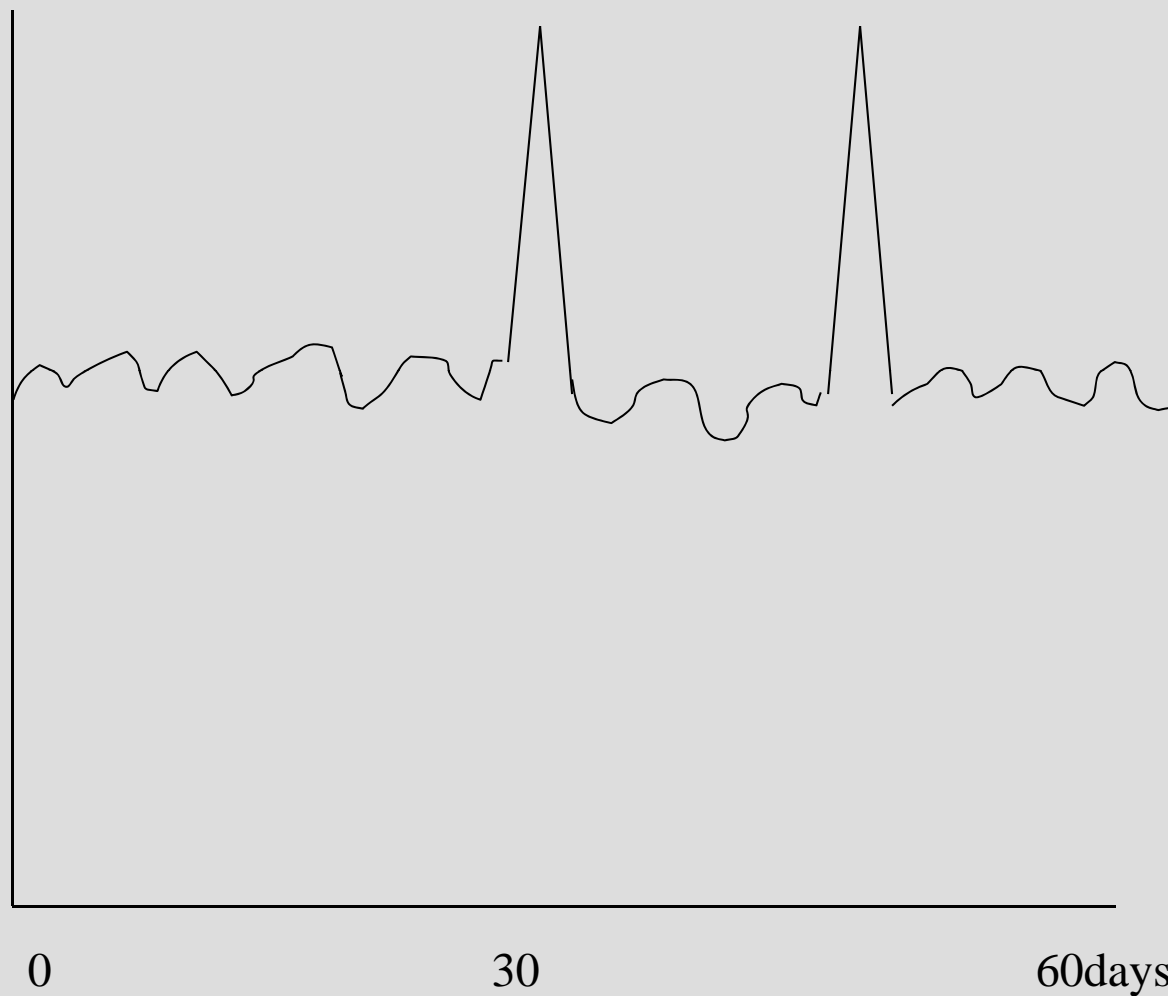
- “Transformed” migraine
 - History of episodic migraine that is now a daily or near daily experience
 - Headache duration typically > 4 hrs per day
- Chronic tension-type headache
 - HA has 2 of the following pain characteristics: pressing/tightness, bilateral, mild to moderate, aggravated by mod exercise and no autonomic sx
- New persistent daily headache
 - Acute onset, constant, unremitting headache
- Hemicrania continua
 - Unilateral, continuous with fluctuations in intensity.
 - Female preponderance
 - Autonomic features with pain exacerbations
 - Treated with indomethacin

Headache Types



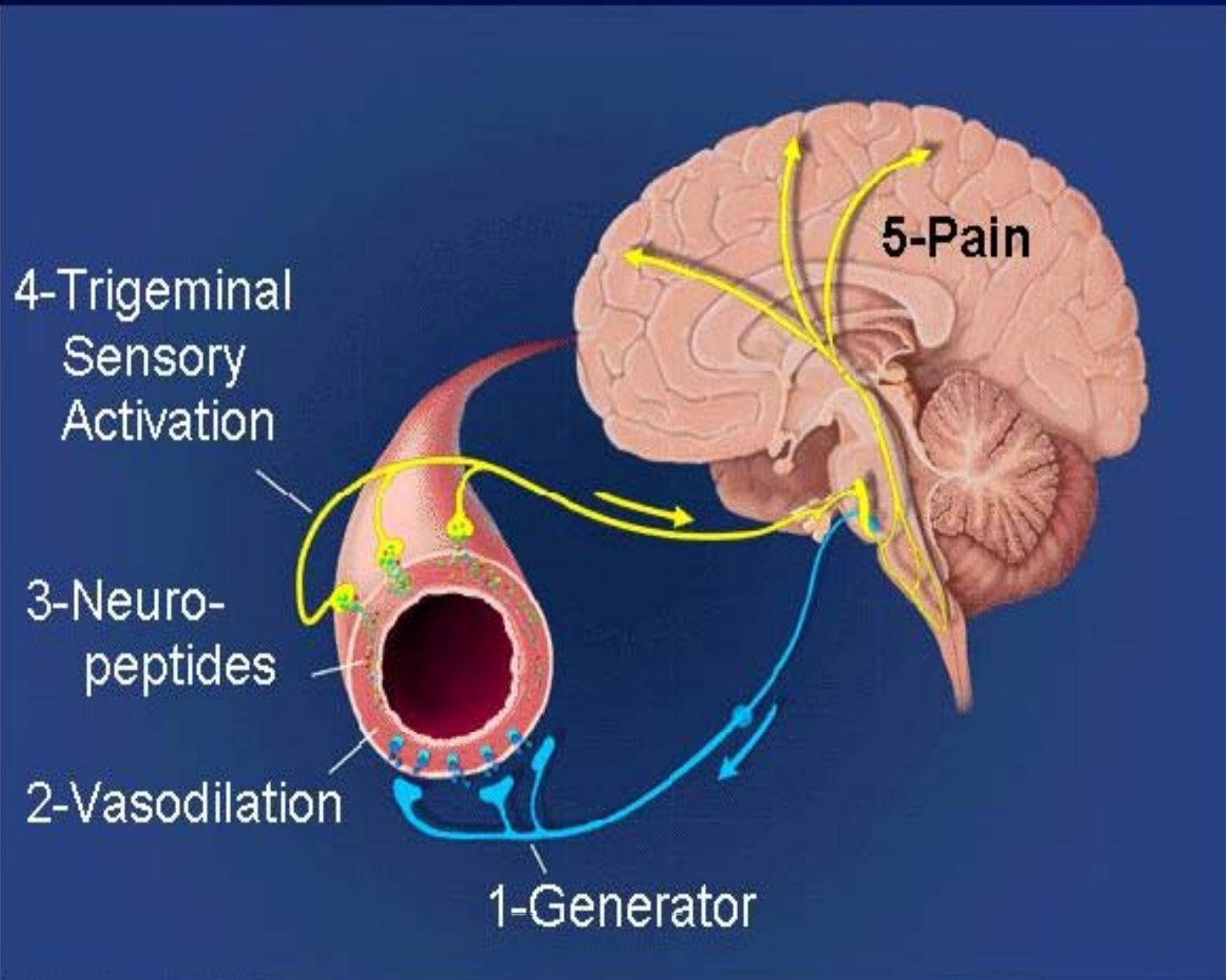
Types of Headache according to temporal progression

Symptom
Severity



The **Mixed Headache Syndrome**: Chronic, non-progressive

Pathogenesis of Migraine



(Hargreaves, Shephard 1999)

Migraine is Associated with Other Medical Disorders (Comorbidity)

- **Neurologic Disorders**

- Stroke (esp. in women under 45)
- Epilepsy
- Positional vertigo
- Essential tremor
- Tourette's?

- **Medical Disorders**

- Raynaud's syndrome
- Asthma
- Hyper- or hypotension
- Mitral valve prolapse
- Irritable Bowel syndrome
- Interstitial Cystitis

- **Psychiatric Disorders**

- Depression
- Anxiety disorders
- Panic disorder
- Bipolar illness
- Phobias

Adapted from Lipton RB et al, *Neurology*, 2000

Adapted from Stewart WF et al, *Psychosocial Medicine* 1989.

Adapted from Swartz KL et al, *Arch Gen Psych* 2000.

Adapted from Van Manen JG et al, *J Clin Epidemiol* 2001.

Biobehavioral Strategies for Chronic Daily Headache

- Lifestyle changes
 - Weight loss, if indicated
 - Regular sleep schedule
 - Daily exercise
- Dietary measures
 - Caffeine avoidance/limitation
 - Regular meal schedule
- Psychological interventions
 - Stress management
 - Cognitive behavioral therapy
 - Psychotherapy
 - Biofeedback training
 - Relaxation training
- Complementary and alternative interventions
 - Vitamins: riboflavin, CoQ10
 - Minerals: magnesium oxide
 - Meditation
 - Yoga

Alternative and Complementary Medications

- Riboflavin
- Butterbur
- Magnesium oxide
- Coenzyme Q 10

High-dose riboflavin for migraine prophylaxis in children

- N=48; age 5-15 years; 2-8 migraine per month
- Riboflavin 200 mg vs placebo
- Primary efficacy measure was number of patients achieving greater than or = 50% reduction in number of migraine attacks per 4 weeks
- Other outcome measures were mean severity of migraine per day, mean duration of migraine, days with nausea or vomiting, analgesic use and adverse effects
- A 50% or greater reduction in headaches was seen in 14/21 patients in the placebo group and 12/27 patients in the riboflavin group (ns $P = .125$)
- Results suggest riboflavin not an effective treatment for prevention of migraine; high placebo responder rate seen

Medium-dose riboflavin as a prophylactic agent in children with migraine:
A preliminary placebo-controlled, randomised, double-blind, cross-over trial


- N=42 children
- Age 6-13 years
- Riboflavin 50 mg/day
- Carotene “placebo”, turns urine orange
- No significant difference in the reduction of mean frequency of migraine attacks in the last month of treatment was found between the riboflavin and placebo groups ($P=0.44$)
- Significant reduction in headaches with a tension-type phenotype in the riboflavin treatment group ($P=0.04$)

Migraine prevention in children and adolescents: results of an open study with a special butterbur root extract.

- N=108, children and adolescents, aged 6-17
- IHS migraine > 1 year
- Dose 50mg per day to 150 mg per day, depending upon age
- 77% of patients reported a reduction in frequency of migraine attacks of at least 50%
- Attack frequency reduced by at least 63%
- AE's included mostly eructation (7.4%)

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Migraine prevention in children and adolescents: results of an open study with a special butterbur root extract.

Table 2.—Descriptive Analysis of Primary Efficacy Variables (Attack Frequency, Therapy Responders, Attack Duration) After 4 Months of Treatment in Relation to Baseline

	Patients 6-9 Years (n = 29)		Patients 10-17 Years (n = 79)		Total		
Attack frequency (n)	4.0 ± 3.9	(1 2 15)	21	5.8 ± 16.2	(0 2 124)	59	5.3 ± 14.0
Relative reduction of attack frequency (%)	-67.0 ± 28.3	(37 78 92)	21	-61.9 ± 53.3	(187 80 100)	58	-63.2 ± 47.7
Responder	18 (85.7%)			43 (74.1%)		61 (77.2%)	
Non responder	3 (14.3%)			15 (25.9%)		18 (22.8%)	
Duration of migraine attacks (h)	7.3 ± 9.8	(1.0 3.7 35.0)	16	6.4 ± 6.2	(1.0 5.0 35.0)	37	6.5 ± 7.3
Shortened attack	10 (66.7%)			22 (61.1%)		32 (62.7%)	
Unchanged attack	1 (6.7%)			5 (13.9%)		6 (11.8%)	
Prolonged attack	4 (26.7%)			9 (25.0%)		13 (25.5%)	

Values followed by brackets are means ± SD, with minimum, median, and maximum in brackets, and valid cases after the brackets.

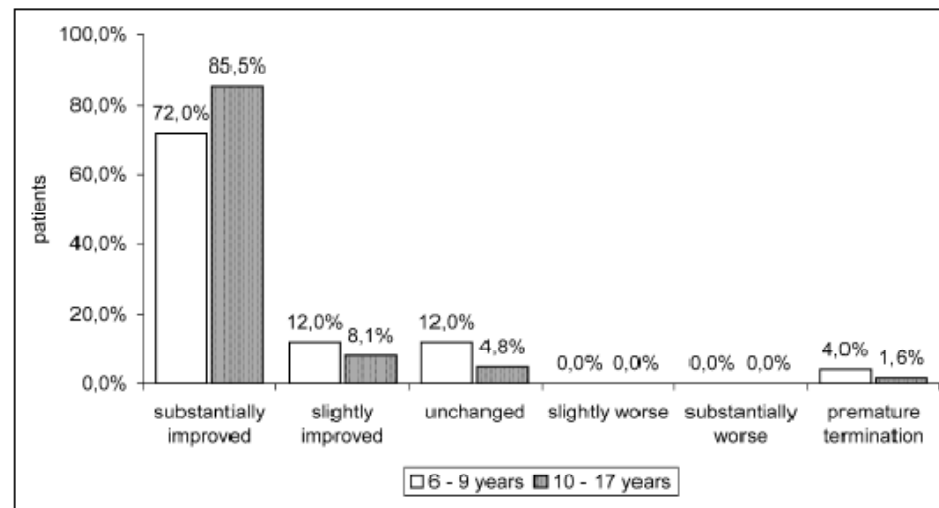


Fig 1.—Global judgment of efficacy of prophylactic butterbur treatment by patients: current status of migraine in comparison to the prestudy situation.

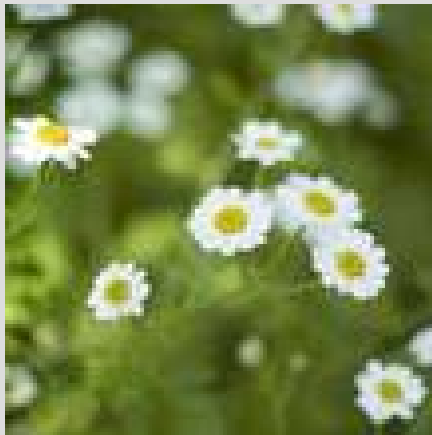
Oral Magnesium Oxide Prophylaxis of Frequent Migrainous Headache in Children: A Randomized, Double-Blind, Placebo-Controlled Trial

- N=118
- Ages 3-17
- Statistically significant decrease over time in headache frequency in the magnesium oxide group ($P=.0037$) but not in the placebo group ($P=.086$), although the slopes of these 2 lines were not statistically significantly different from each other ($P=.88$)
- The group treated with magnesium oxide had significantly lower headache severity ($P=.0029$) relative to the placebo group
- This study does not unequivocally determine whether oral magnesium oxide is or is not superior to placebo in preventing frequent migrainous headache in children

Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine

- N=1550
- Measure CoQ10 levels, found that 33% had values less than the reference range
- Received CoQ10 supplementation 1 to 3 mg/kg/d
- Headache frequency improved from 19 (+/-10) to 12 (+/- 11) per month, $P < .001$
- These investigators proposed that CoQ10 deficiency may be a common phenomenon in children with frequent migraine
- This clearly warrants further study

Not tested in adolescents, but safe
and effective in RCT in adults



Feverfew
(*Tanacetum parthenium*)
Active ingredient: parthenolide

Problems with RCT for prevention of migraine in children

- High placebo responder rate (therapeutic gain = % reduction vs. placebo)
- Most trials involve small numbers, therefore, lesser impact/power
- Study design issues

Conclusions

- Biobehavioral strategies should be considered in the management of every adolescent with chronic migraine
- Butterbur (Petadolex), magnesium oxide and Coenzyme Q10 may be recommended on the basis of scientific evidence for prophylaxis in adolescents
- There is insufficient evidence to recommend riboflavin
- Feverfew has not been tested in the adolescent age group

References

- Andrasik F, Schwartz MS, Behavioral Assessment and Treatment of Pediatric Headache, *Behavior Modification*, 2006, 30 (1): 93-113.
- Mack KJ and Gladstein J, Management of Chronic Daily Headache in Children and Adolescents, *Pediatr Drugs*, 2008, 10 (1): 23-29.
- Mack KJ and Hershey AD, Chronic daily headache in adolescence: a continuing problem, *Neurology*, 2009; 73: 412-413.
- MacLennan SC et al, High-dose riboflavin for migraine prophylaxis in children: A double-blind, randomized, placebo-controlled trial, *Journal of Child Neurology*, 2008; 23 (11): 1300-1304.
- Milde-Busch A et al, Quality of life in adolescents with headache: Results from a population-based survey, *Cephalalgia OnlineFirst*, published on March 10, 2010 as doi:10.1177/0333102409354389
- Bruijn J et al, Medium-dose riboflavin as a prophylactic agent in children with migraine: A preliminary placebo-controlled, randomised, double-blind, cross-over trial, *Cephalalgia OnlineFirst*, published on March 26, 2010 as doi:10.1177/0333102410365106
- Wang F et al, Oral Magnesium Oxide Prophylaxis of Frequent Migrainous Headache in Children: A Randomized, Double-Blind, Placebo-Controlled Trial, *Headache*, 2003; 43: 601-610
- Hershey AD, et al. Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine. *Headache* 2007;47:73–80.