

# Management Approaches of Pediatric Migraine: Review

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**Abstract:** This review was aim to focus on the treatment option strategies for pediatric migraine, including prevention methods and acute treatment of migraine. The current evidence for these treatments will be reviewed. We conducted a literature search through Scopus, Medline, and PubMed databases independently for all English language publish studies up to December 2016, search was performed using the terms “(headache OR migraine) AND (child OR pediatric OR teen OR adolescent) AND (pediatric headache treatment). Cited references within selected articles were also searched to identified more relevant studies, only human subject articles were included in this review. Migraine headache is the most common repeating pain syndrome in youth and teenage years. Stereotyped attacks of bitemporal or frontal pounding, nauseating headache lasting 1 to 48 hours represent the frustrating proportion of migraines. The treatment philosophy now embraces a well balanced approach with both bio-behavioral interventions and pharmacological steps. Essential to treatment choices is the degree of impairment produced by the headaches. In general, the effect of prophylactic therapy is not instant, frequently taking as long as 6-8 weeks before enhancement happens. Offering this details to the patient and his/her parents results in improved compliance and more sensible goals. Giving a suitable trial before trying a new treatment is very important.

**Keywords:** Pediatric Migraine, Prevention Methods and Acute Treatment of Migraine.

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## 1. INTRODUCTION

Migraine is common in childhood and happens in up to around 11% of children between the ages of 5 to 15 yrs and 28% in children aged 15 to 19 yrs. Headache is a typical reason for pediatric patients to provide to the emergency situation department (ED), with national price quotes of 250,000 visits occurring every year <sup>(1)</sup>. At the time of pediatric discussion in ED, a lot of pediatric headaches have been ongoing for 2-3 days, <sup>(2,3,4)</sup> and most patients have currently used more than one abortive treatment <sup>(2)</sup>. The headache history is essential to making the diagnosis. In a potential study <sup>(5)</sup> of 500 paediatric neurology patients, the function of the history (through letter of recommendation and at the time of evaluation), the health examination and investigations in both identifying and managing a variety of conditions were evaluated. Amongst 150 children with headaches, the history provided the proper medical diagnosis and management in 100% <sup>(5)</sup>.

Most children have main headaches; the International Headache Society criteria for migraine and tension-type headaches exist in (Table 1) <sup>(6)</sup>. In 2004, the International Headache Society presented the modified headache diagnostic criteria, which now acknowledge special functions of paediatric migraine (Table 1) (6). Paediatric migraineurs commonly report bilateral headaches that resolve within 2 h to 4 h, in contrast with adult migraines. Tension-type headaches and migraines may become part of a spectrum instead of distinct diagnostic entities. A typical pathophysiological mechanism might discuss the regular co-occurrence of these headache types and advancement with time from one to the other <sup>(7)</sup>.

There is variation in pediatric severe migraine management throughout institutions <sup>(2,4,8)</sup>, and evidence-based treatment is not always administered. A retrospective, observational research study across four states discovered that near half (46%) of pediatric patients providing with migraine are not recommended or suggested medication, while a much larger portion (84%) are not prescribed or recommended evidence-based medication <sup>(9)</sup>.

**Table 1: International Headache Society diagnostic criteria for paediatric migraine without aura <sup>(6)</sup>**

A. At least five attacks fulfilling criteria B–D (below)
B. Headache attacks lasting 1 h to 72 h
C. Headache has at least two of the following characteristics:
list-behavior=unordered prefix-word= mark-type=disc
• Unilateral location, may be bilateral, frontotemporal (not occipital)
• Pulsating quality
• Moderate or severe pain intensity
• Aggravation by or causing avoidance of routine physical activity (eg, walking, climbing stairs)
D. During the headache, at least one of the following:
list-behavior=unordered prefix-word= mark-type=disc
• Nausea, vomiting or both
• Photophobia and phonophobia, which may be inferred from behaviour
E. Not attributed to another disorder

This review was aim to focus on the treatment option strategies for pediatric migraine, including prevention methods and acute treatment of migraine. The current evidence for these treatments will be reviewed.

## 2. METHODOLOGY

We conducted a literature search through Scopus, Medline, and PubMed databases independently for all English language publish studies up to December 2016, search was performed using the terms “(headache OR migraine) AND (child OR pediatric OR teen OR adolescent) AND (pediatric headache treatment). Cited references within selected articles were also searched to identified more relevant studies, only human subject articles were included in this review.

## 3. RESULTS

### • *Prevention procedures of pediatric migraine:*

One review study <sup>(10)</sup> discussed the prevention methods of pediatric migraine and revealed that there are a varied group of medications that utilized to prevent migraine attacks <sup>(10)</sup>. Their usage, nevertheless, ought to be restricted to those patients whose headaches accompany adequate frequency (at least 3 headaches per month), severity, and functional special needs to require an everyday treatment program. It is likewise useful to determine the presence of comorbid conditions (e.g., depression, weight problems, sleep conditions) which may suggest the relative advantage of one agent over another <sup>(10)</sup>. Preferably, daily migraine avoidance representatives ought to be used for a limited period of time. The general recommendation is to offer treatment through all or part of the school year, then gradually remove everyday representatives during summertime getaway. Another choice in younger children is to use a much shorter course (e.g., 6 to 8 weeks) followed by a slow wean <sup>(10)</sup>.

While there is an unfortunate absence of controlled information regarding drug therapies for migraine prophylaxis in children, information is starting to emerge. Using the many of these agents is based upon anecdotal info or theorized adult experiences where Level I information exists for amitriptyline, disodium valproate, propranolol, and timolol with a growing body of literature regarding topiramate <sup>(11,12)</sup>. For preventive treatment in the population of children and adolescents with regular, disabling migraine, flunarizine (not offered in the United States) has been the most carefully studied representative and has the best efficacy (vs. placebo) information <sup>(13,14)</sup>. Presently, the normal first-line choices for migraine prophylaxis are cyproheptadine, non-steroidal anti-inflammatory representatives (NSAIDs), antiepileptic medications (topiramate and disodium valproate) and amitriptyline (**Table 2**) <sup>(10)</sup>.

**Table 2: Preventive treatment options for pediatric migraine<sup>(10)</sup>**

Drug	Dose	Available	Toxicity
Cyproheptadine	0.25-1.5 mg/kg/day to a maximum of 12 mg divided tid	Tablet 4 mg Syrup 2 mg/5 mL	Sedation; weight gain
Beta-blockers*			
Metoprolol	2-6 mg/kg/day	Tablets 50 mg, 100 mg	Hypotension; sleep disorder; decreased stamina; depression
Nadolol	0.5-2.5 mg/kg/day	Tablets 20 mg, 40 mg, 80 mg	
Propranolol	2-4 mg/kg/day	Tablets 10 mg, 20 mg, 40 mg, 60 mg, 80 mg Long-acting capsule 60 mg, 80 mg, 120 mg, 160 mg	
Anticonvulsants			
Gabapentin	10-40 mg/kg/day	Tablets 600 mg, 800 mg Capsules 100 mg, 300 mg, 400 mg Syrup 250 mg/5 mL	Fatigue; ataxia; tinnitus
Levetiracetam	250 bid starting dose	Tablets 250 mg, 500 mg, 750 mg, 1000 mg	Drowsiness; dizziness
Topiramate	1-10 mg/kg/day	Tablets 25 mg, 100 mg Sprinkle capsule 15 mg, 25 mg	Sedation; paresthesias; weight loss; glaucoma; kidney stones
Valproic acid	20-40 mg/kg/day (usual 250 mg bid)	Tablets 250 mg, 500 mg Sprinkle capsule 125 mg Syrup 250 mg/5 mL	Weight gain; bruising; hair loss; hepatotoxicity; ovarian cysts
Antidepressants			
Amitriptyline	10-25 mg q hs	Tablets 10 mg, 25 mg, 50 mg	Sedation
Fluoxetine	10-40 mg q am	Capsules 10 mg, 20 mg	Insomnia, anxiety, weight gain
Nortriptyline	10-75 mg q hs	Tablets 10 mg, 25 mg, 50 mg, 75 mg	Weight gain
Non-steroidal anti-inflammatory drugs			
Naproxen sodium	250-500 mg bid	Tablets 220 mg, 250 mg, 375 mg, 500 mg	Gastric upset
Calcium channel blockers			
Verapamil	4-10 mg/kg/day tid	Tablets 40 mg, 80 mg, 120 mg Sustained release tablets 120 mg, 180 mg, 240 mg	Hypotension, nausea, AV block, weight gain

\* Avoid in those with asthma or diabetes

The antihistamine cyproheptadine has anti-serotonergic and calcium channel blocker properties. While not subjected to controlled trials, clinical experience has discovered cyproheptadine to be effective in decreasing headache frequency and intensity, and has been utilized extensively in more youthful children. Side effects might include sedation and increased hunger<sup>(15)</sup>.

Naproxen salt, an NSAID, has actually been revealed to be efficient in teen migraine in one little series. Gastrointestinal upset limitations its use as a prophylactic medication to 2 months' period or less<sup>(16)</sup>.

Antidepressants have actually ended up being the mainstay of migraine prophylaxis in grownups, nevertheless, there are couple of studies in children. The tricyclic antidepressants amitriptyline, nortriptyline, and desipramine are common pediatric options. Research studies show statistically significant headache decrease using amitriptyline, with very little adverse effects (primarily sedation)<sup>(17)</sup>. Selective serotonin reuptake inhibitors (SSRI) might also be efficacious, particularly if there is coexistent depression; sadly, there are no studies in children. Of note, the system of action of antidepressants for preventing migraine headaches is reported to be separate from their developed antidepressant result. Nevertheless, as awareness of the typical comorbidity of affective conditions and migraine expands, the antidepressant residential or commercial properties might play a more vital function<sup>(17)</sup>.

Antiepileptic drugs such as topiramate, disodium valproate, gabapentin, and levetiracetam might have expanding functions for pediatric migraine in the future. The present understanding of migraine pathophysiology shows a moving wave of regional cortical excitation followed by an extended period of neuronal depression, which might be modified by antiepileptics. Many retrospective research studies show a reduction in headache seriousness with antiepileptic drugs<sup>(18,19)</sup>.

- **Treatment options for pediatric migraine:**

**Non-pharmacological treatment of migraine;**

Behavioural interventions, especially biofeedback and relaxation treatment have shown their effectiveness in the treatment of both adults and older children with migraine in controlled trials. The physiological basis for their efficiency is unclear, but information from one trial recommend that levels of plasma beta-endorphin can be changed by relaxation and biofeedback treatments. The information supporting the efficiency of behavioural treatments are less specific in children than in grownups, but that is likewise real for the information supporting medical treatment. This is due in part to methodological issues, particularly the lack of specific tests for migraine, which has actually hindered research and helped leading to an inappropriate de-emphasis on look after youth headache. In addition, migraine headaches in children are typically briefer and have a higher rate of spontaneous remission than those experienced by adults, making it tough to separate reliable from inefficient treatments<sup>(20,21)</sup>.

Beginning with the consideration that children and adolescents with headache reveal greater indices of psychopathology<sup>(22,23)</sup> and reveal higher risk of establishing psychological disorders in the adult years than healthy controls<sup>(24)</sup>, various psychotherapeutic techniques are often supplied in clinical practice. Relaxation and cognitive-behavioural strategies have been discovered to reduce the intensity and frequency of headache in adolescents and children<sup>(25,26)</sup>.

Prospective, randomized, partly double-blind, placebo-controlled, parallel-group trial showed that Butterbur root extract and music therapy might be superior to placebo and may represent appealing treatment approaches in the prophylaxis of paediatric migraine<sup>(27)</sup>.

Nonpharmacological approaches remain the first-line approach to all headache management, including chronic daily headache. A headache diary may be remarkably therapeutic. It allows the child and parent to explore the headache patterns and identify precipitating factors. It provides an outlet for the child to express both the headache symptoms and associated triggers. Headache precipitants vary for each child and may include overtiredness, missed meals, changes in physical activity, hormonal changes, bright lights, food and stress<sup>(28)</sup>. Stresses that induce headaches may be either 'good' (excitement, such as a sleepover) or 'bad'. Bad stressors are often relatively minor, and the parents may be unaware of them. Focusing on headache precipitants will also, hopefully, teach the child lifelong strategies for managing headaches<sup>(29)</sup>. The headache diary must be the responsibility of the child and not the parents.

Other nonpharmacological approaches include appropriate sleep hygiene, regular physical activity, limiting caffeine intake, relaxation techniques, biofeedback and self-hypnosis. Elimination diets are seldom beneficial. Behavioural therapies, such as relaxation techniques and biofeedback, have demonstrated efficacy in the treatment of paediatric headache with improvements reaching 80%<sup>(30)</sup>. While most paediatricians refer patients who require these therapies to a psychologist, it is possible for paediatricians to receive training in these areas from the Society of Developmental and Behavioral Pediatrics (USA).

**Pharmacological treatment of pediatric migraine:**

The medicinal treatment of migraine consists of symptomatic and/or prophylactic treatment. The previous is aimed at eliminating or ameliorating the signs of a severe attack, whereas prophylactic treatment, which needs the day-to-day consumption of medication for a particular period of time, reduces the frequency of the attacks and the intensity of pain.

**Symptomatic drug treatment:**

The objective of treatment should be a fast action with go back to normal activity and without relapse. A number of essential principles must be made understood to patients. Medication usage should be restricted to avoid medication overuse headache. It is essential that a suitable dose is utilized. Medications should be taken shortly after onset of migraine headache to enhance the impact, despite the fact that clinical evidence supporting this suggestion is doing not have. The medication should be offered to the patients likewise at school. Allodynia throughout a migraine in adult's correlates with action to treatment of severe migraine with triptans and the progressive nature of migraine. This has actually highlighted the significance of early recognition of headache and appropriate treatment. Allodynia has recently been revealed to be present in 37% of children during their migraine. Allodynia is typically not consistently assessed throughout a headache history even though there may be possible healing ramifications. Popular scalp signs include level of sensitivity to touch and difficulty brushing hair<sup>(31,32,33)</sup>.

**Acetaminophen and ibuprofen have been studied for the treatment of acute migraine:**

A randomized, double-blinded, placebo-controlled crossover research study of 4 to 16-year olds examined acetaminophen 15 mg/kg, ibuprofen 10 mg/kg, and placebo<sup>(34)</sup>. The main endpoint was 2-hour reduction in moderate or serious headache by a minimum of 2 grades on a 5-point scale. Private investigators found that at 2 hours, ibuprofen had almost 3 times the chances of efficacy as placebo (OR 2.9, 95% CI 1.0-8.1), and two times the chances as acetaminophen (OR 2.2, 05% CI 1.1-4.0). Acetaminophen was, however, superior to placebo. Another randomized, double-blind, placebo-controlled, parallel group research study assessed the efficacy of dealing with one migraine attack with a single dosage of ibuprofen 7.5 mg/kg vs placebo<sup>(35)</sup>. The primary endpoint of 2- hour decrease in headache from serious or moderate to moderate or none on a 4-point scale was reached in 76% of responder's vs 53% of placebo (p 5.006). They discovered an interaction with sex, with 84% of boys treated with ibuprofen experiencing relief vs 65% of ladies; the latter being closer to the placebo action rate which was 53% (p 5.8). These research studies show the effectiveness of ibuprofen and, to a lower degree, acetaminophen in the treatment of acute migraine in children.

**Dopamine receptor antagonists are used frequently for acute migraine treatment:**

Various categories of dopamine receptor antagonists consist of the phenothiazines, butyrophenones, and metoclopramide. The butyrophenones include droperidol and haloperidol, which are not commonly utilized in children due to the risk of torsade de pointes observed in the adult population<sup>(36,37)</sup>. Metoclopramide is used in pediatric EDs for acute migraine management, nevertheless, is not as well studied for migraine as the phenothiazines. The phenothiazines include prochlorperazine, chlorpromazine, and promethazine. Potential negative effects include akathisia and dystonic reactions. Chlorpromazine can likewise trigger orthostatic hypotension. All medications in this class have the possible to extend the QTc, hence electrocardiogram (ECG) evaluation prior to administration might be prudent in children. 2 research studies looked particularly at prochlorperazine efficiency in pediatric migraine<sup>(36,37)</sup>.

**Prophylactic treatment of pediatric migraine:**

Pharmacological approaches to headache treatment include both intense symptomatic and prophylactic medications (Table 3)<sup>(5)</sup> Nonprescription analgesics are effective for severe headache relief in the majority of patients if they are offered early and in appropriate doses. Ibuprofen has been revealed to be safe and efficacious in the management of paediatric migraine in two double-blind, placebo-controlled trials<sup>(34,35)</sup>. One study<sup>(34)</sup> compared the effectiveness of 15 mg/kg of acetaminophen with 10 mg/kg of ibuprofen and discovered no substantial differences in outcome. Both ibuprofen and acetaminophen were more efficient than the placebo in offering pain relief. Lewis et al<sup>(35)</sup>, however, have revealed that the result of ibuprofen at the main end point of 2 h worked in young boys only. Amongst the kids, a response at 2 h was seen in 84% of those treated with ibuprofen compared to 43% of the placebo-treated group. For girls, the numbers were less impressive, with 65% reacting to ibuprofen and 67% to the placebo<sup>(35)</sup>.

**Table 3: Pharmacological treatment options for headaches in childhood<sup>(5)</sup>**

Acute abortive medications	Paediatric dosage	Evidence
Ibuprofen	10 mg/kg/dose	Class I
Acetaminophen	10–15 mg/kg/dose	Class I
Nasal sumatriptan	5 or 20 mg dose	Class I
Prophylactic medications	Paediatric dosage	Evidence
Flunarizine	5 mg/day	Class I
Propranolol	2–4 mg/kg/day	Class II (conflicting results)
Cyproheptadine	0.25–1.5 mg/kg	Class IV
Amitriptyline	10–25 mg/day at bedtime	Class IV
Topiramate	1–10 mg/kg/day	Class IV
Valproate	20–40 mg/kg/day	Class IV
Gabapentin	10–40 mg/kg/day	Class IV

In 2004, the American Academy of Neurology and the Child Neurology Society published practice specifications, which advised ibuprofen and nasal sumatriptan as tested treatments for youth migraine, and specified that acetaminophen was

'probably reliable' <sup>(38)</sup>. Damen et al <sup>(39)</sup> evaluated 10 trials with an overall of 1575 patients four to 18 years of age. They concluded that there was moderate evidence that both acetaminophen and ibuprofen were more reliable in the decrease of headache symptoms after 1 h and 2 h than the placebo. Among the nonanalgesics, there was moderate proof that nasal sumatriptan was more effective than the placebo, but was connected with significantly more side effects. They reported no differences in effect in between oral triptans and the placebo <sup>(39)</sup>.

#### 4. CONCLUSION

Migraine headache is the most common repeating pain syndrome in youth and teenage years. Stereotyped attacks of bitemporal or frontal pounding, nauseating headache lasting 1 to 48 hours represent the frustrating proportion of migraines. The treatment philosophy now embraces a well balanced approach with both bio-behavioral interventions and pharmacological steps. Essential to treatment choices is the degree of impairment produced by the headaches. In general, the effect of prophylactic therapy is not instant, frequently taking as long as 6-8 weeks before enhancement happens. Offering this details to the patient and his/her parents results in improved compliance and more sensible goals. Giving a suitable trial before trying a new treatment is very important.

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