Pediatr Drugs (2018) 20:385–393
https://doi.org/10.1007/s40272-018-0299-8

LEADING ARTICLE

Pharmacotherapy for Persistent Posttraumatic Headaches in Children and Adolescents: A Brief Review of the Literature

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Published online: 7 June 2018

Abstract Concussion, now most often referred to as mild traumatic brain injury in recent literature, is common in pediatrics, and headache is often the most common complaint post-injury. Although most children and adolescents recover within 1–2 weeks, some develop frequent and debilitating headaches that can last for months or longer. Most clinicians would agree on the importance of managing both acute and persistent posttraumatic headaches appropriately to speed recovery, minimize disability, maximize function, and improve quality of life, but there are no well-established guidelines to instruct physicians in doing so. As this continues to be a developing field, there is much we still need to learn about concussion and the appropriate strategies to prevent and treat these injuries and their sequelae. This review is intended to help providers understand the current evidence, and sometimes the lack thereof, and ultimately to lead to improved care for children with headaches after mild traumatic brain injury.

Key Points

Although headache is the most common complaint following concussion, no guidelines exist to aid the clinician in pharmacological treatment. There are no placebo-controlled trials, and most evidence is extrapolated from few uncontrolled trials and the adult population.

Despite this, there is some evidence to suggest that posttraumatic headaches can often be classified as the primary headache disorder they most resemble and that headaches often improve when treatment is based on the primary headache type.

Many of the agents used to treat persistent posttraumatic headaches have supporting data for the management of migraine or chronic migraine, and few have been studied for the treatment of persistent posttraumatic headaches in a systematic manner, including tricyclic antidepressants, anti-epileptics, beta-blockers, and neutraceuticals.

1 Introduction

Traumatic brain injury (TBI) is one of the most common injuries in childhood and adolescence. There is evidence to suggest that one in five children will experience a mild TBI (mTBI) by the age of 10 years [1, 2]. Studies have reported that as many as 475,000 children aged 0–14 years sustain TBI annually in the USA, and most of these injuries are

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defined as mild [1]. Worldwide, mTBI represents around 75–90% of all hospital admissions for TBI [3]. An estimated 1.6–3.8 million sports-related TBIs occur each year, including those for which no medical care is pursued [4].

In youth, headache is the most common symptom of post-concussive syndrome, which is often defined as a constellation of physical, emotional, and cognitive symptoms following mTBI [5, 6]. These often include photophobia, phonophobia, dizziness, balance deficits, behavioral alterations, mood changes, and sleep disturbances. Memory, concentration, and attention deficits are also often reported [7]. The vast majority of these individuals report developing headache within a few days of injury [6, 7]. In a study of collegiate and high school football players with mTBI, as many as 86% reported headache after head trauma [8]. Eisenberg et al. [9] reported 85% of youth presenting to a pediatric emergency department (ED) reported headache following an mTBI.

2 Posttraumatic Headache

2.1 Definition

Despite being classified as a secondary headache in the *International Classification of Headache Disorders, 3rd Edition* (ICHD-3), posttraumatic headache often presents with clinical features that are seen in primary headache disorders, such as migraine and tension-type headache. Not only is headache one of the most common symptoms reported following mTBI, it is often considered the most disabling. The ICHD-3 classifies posttraumatic headache as acute if lasting less than 3 months and as persistent (term now used in the place of "chronic") if the headaches persist more than 3 months post-injury [11]. Although the ICHD-3 criteria state that posttraumatic headaches begin within 7 days after injury to the head or after regaining consciousness, it is important to note that this 7-day cut-off is subjective, and some headache specialists believe that headaches may develop after a longer interval.

2.2 Persistent Posttraumatic Headaches

Recent data from adult, pediatric, and military populations have found that posttraumatic headache may be more of a chronic problem than previously believed, with a prevalence of close to half of the injured population [11]. Although most children with mTBI recover within a few weeks, a proportion of patients continue to have persistent symptoms for weeks to months following mTBI. In a cohort study conducted in the ED setting, Babcock et al. [12] demonstrated that 29.3% of children aged 5–18 years remained symptomatic 3 months after an mTBI, with the most common symptoms being headache, fatigue, and frustration. The revised ICHD-3 [11] criteria for classifying persistent posttraumatic headaches are summarized in Table 1. The same diagnostic criteria are applied to children and adults.

2.3 Risk Factors

Whereas most children and adolescents report headache and other post-concussive symptoms immediately following mTBI, the vast majority of patients will experience an improvement and often resolution within 2 weeks [13]. Children who continue to experience persistent posttraumatic headache are often the most disabled and most difficult for clinicians to treat [13, 14]. Among the pediatric population, predictive factors for the development of posttraumatic headache have been investigated, including age, sex, prior personal history of headaches, and family history. Blume et al. [15] reported a trend toward female sex being a risk factor for posttraumatic headaches. Younger age, defined as 5–12 years, was considered a risk factor with moderate/severe TBI; however, with regards mTBI, adolescent-aged patients demonstrated an increased risk of posttraumatic headache [15]. An earlier study reported no sex differences in reporting headache following a sports-related concussion [16]. A review of 500 adolescent patients seen for post-concussive symptoms found that females reported posttraumatic headache more often than did males (90 vs. 79%), but the authors still concluded that the role of sex was uncertain, perhaps because other potential risk factors, such as prior headache history, were not reported [17].

Prior headache history appears to also play a role in the development of posttraumatic headache. A history of migraine or other primary headache disorder or a positive family history should be noted as there may be a genetic predisposition to experience worsening of the child's pre-existing headache disorder or the initial manifestation of a primary headache disorder in a susceptible child. Many recent studies have demonstrated that patients with prior headaches are at greater risk of developing headaches following mTBI. Kuczynski et al. [18] showed that 51% of children with posttraumatic headache at 3 months after mTBI had preexisting headaches, and 31% had headaches fulfilling the ICHD-3 criteria for migraine or probable migraine prior to injury. They also found that 56% of those with headaches at 3 months post-mTBI had a family history of migraine [18]. However, Blume et al. [19] found that, while preexisting headache was not associated with headache 3 months after mTBI in a multivariate analysis, chronic pain, non-steroidal anti-inflammatory drug (NSAID) use prior to injury, and family history of

Table 1 ICHD-3 beta definition of persistent posttraumatic headaches [11]

5.2 Persistent headache attributed to traumatic injury to the head
A. Any headache fulfilling criteria C and D
B. Traumatic injury to the head[a] has occurred
C. Headache is reported to have developed within 7 days after one of the following:
1. the injury to the head
2. regaining of consciousness following the injury to the head
3. discontinuation of medication(s) that impair ability to sense or report headache following the injury to the head
D. Headache persists for > 3 months after the injury to the head
E. Not better accounted for by another ICHD-3 diagnosis
5.2.2 Persistent headache attributed to mild traumatic injury to the head
A. Headache fulfilling criteria for 5.2
B. Head injury fulfilling both of the following:
1. associated with none of the following:
(a) loss of consciousness for > 30 min
(b) Glasgow Coma Scale score < 13
(c) post-traumatic amnesia[b] lasting > 24 h
(d) altered level of awareness for > 24 h
(e) imaging evidence of traumatic head injury, e.g., intracranial hemorrhage and/or brain contusion
2. associated immediately following the head injury, with one or more of the following symptoms and/or signs:
(a) transient confusion, disorientation, or impaired consciousness
(b) loss of memory for events immediately before or after the head injury
(c) two or more other symptoms suggestive of mild traumatic brain injury: nausea, vomiting, visual disturbances, dizziness and/or vertigo, impaired memory, and/or concentration

[a]Traumatic injury to the head is defined as a structural or functional injury resulting from the action of external forces on the head. These include striking the head with or the head striking an object, penetration of the head by a foreign body, forces generated from blasts or explosions, and other forces yet to be defined

[b]The duration of posttraumatic amnesia is defined as the time between head injury and recovery of memory of current events and those occurring in the last 24 h

headache were each associated with an increased risk of developing posttraumatic headache [19].

3 Management of and Pharmacotherapy for Posttraumatic Headaches

Although controversies exist as to the etiology and pathophysiology of posttraumatic headache, there has been significant advancement in the understanding of the underlying mechanisms and neurobiology of TBI and concussion. Despite this knowledge, there have been no clear outcome improvements with regards to its management and treatments. As stated, the natural evolution of posttraumatic headache is to spontaneously resolve in a matter of weeks. When they become chronic and difficult to manage, evidences suggests that a comprehensive and multidisciplinary approach, including pharmacologic intervention, physical rehabilitation, lifestyle modifications, and cognitive behavioral therapy, may provide the most success [20].

Unfortunately, studies regarding the safety and efficacy of treatments for persistent posttraumatic headaches are sparse [15, 21]. As most clinicians who manage concussion and posttraumatic headaches can attest, these headaches may be arduous to treat. No guidelines have been established for the treatment of posttraumatic headaches, especially when persistent, and practices vary widely from one clinician to the next. Making management more challenging, no randomized controlled trials have evaluated the efficacy of therapies for posttraumatic headaches in children and adolescents. Most algorithms proposed have been inferred from the primary headache literature and small non-controlled trials of posttraumatic headache [22] (Table 2).

Headaches developing after mTBI often resemble a primary headache disorder, including most commonly migraine without aura, tension-type headache, and occipital neuralgia; some may even be considered "unclassifiable", not fitting ICHD-3 criteria for any other headache type. It is crucial to ask about the specific headache features, including location, quality, severity, and associated

symptoms, to accurately categorize the child's headache type. For example, in a questionnaire-based study of US soldiers post-deployment, Theeler et al. [23] reported that 58% met ICHD-3 criteria for migraine. This may highlight the importance of identifying which primary headache type the headache resembles to offer the optimal treatment options. [16, 20, 22]. As seen with the primary headache disorders, posttraumatic headache can substantially effect a child's life, leading to lost school days and withdrawal from social interactions with both family and peers. Management should subsequently be relevant to the headache type in addition to the clinical needs of the child. A referral for bio-behavioral therapy may also be necessary [16, 19–22].

Adherence should be optimized by educating both the child and their family about the proper use of acute and prophylactic medications. Establishing realistic expectations, including expected recovery and compliance, should be emphasized at initiation of treatment [15, 16, 22]. Ponsford et al. [24] demonstrated that education regarding the injury and expected clinical course are some of the few interventions that may significantly improve outcome following mTBI. Adherence can further be optimized by educating families about lifestyle modifications, including maintenance of good sleep hygiene, a regular and balanced diet, and the importance of hydration, as these factors are commonly identified as headache triggers [25, 26].

3.1 Acute Headache Treatment

Although, to date, no studies have investigated the safety and effectiveness of over-the-counter (OTC) analgesics for the treatment of headaches after head trauma, they are often recommended as the initial outpatient treatment strategy. The goal of acute treatment in children with persistent posttraumatic headaches should be a consistent response with minimal side effects and a rapid return to normal function. The treatments should be properly dosed and used as quickly as possible while minimizing the potential for analgesic overuse. Abortive treatments should be incorporated into the child's life with the possibility of receiving these treatments in school or at home without having to miss school or social activities [26, 27]. Adequate hydration with non-caffeinated fluids is always encouraged. Use of NSAIDs is advised no more than 3 days per week, with a maximum of two doses in the same day to avoid exceeding maximum daily doses and medication-overuse. If this initial attempt fails to abort a headache with migraine qualities, the use of triptans may be warranted. In general, triptans are well tolerated in children and can be used safely. To avoid overuse, their use should be restricted to less than 9 days per month [27].

3.2 Medication Overuse Headache

Medication overuse headache (MOH) is defined as a progressive increase in headache frequency, paralleled by an excess in analgesic consumption [28]. It has been thought that susceptible patients who use analgesics (either OTC or prescription) excessively to abort headaches acutely after mTBI risk developing a medication-overuse pattern that may lead to the transformation from an acute to a chronic headache syndrome [28, 29]. Very few pediatric studies have looked at the relationship between analgesic overuse and the development of persistent posttraumatic headache. Babcock et al. [12] reported that adolescents with post-concussive symptoms 3 months after TBI, including those with headache, were more likely to have used analgesics to treat their symptoms at home than were patients with resolution of symptoms at 3 months post-mTBI. As discussed earlier, Theeler et al. [23] surveyed 196 US soldiers with chronic daily headaches post-deployment and found that 49% self-reported using analgesics to treat their headaches on $\geq$ 15 days per month for 3 consecutive months, meeting ICHD-3 criteria for MOH. In a retrospective chart review of 104 post-concussive adolescents, Heyer and Idris [29] reported that 77 (74%) met criteria for persistent posttraumatic headache of 3–12 months duration. Of these 77 adolescents, 70% met criteria for MOH, with simple OTC analgesics acting as the overused agents in all these patients. It therefore appears imperative that clinicians discuss the potential for MOH from the initial encounter. Patients should be instructed to use analgesics no more than 3 days per week to avoid the development of MOH. When prescribed, triptans should be used fewer than nine times per month [14, 26, 27].

4 Preventive Therapy for Posttraumatic Headache

Many agents are being used to treat persistent posttraumatic headaches; most have supporting data for management of migraine or chronic migraine and few have been studied for the treatment of persistent posttraumatic headaches in a systematic manner. These include tricyclic antidepressants, such as amitriptyline and nortriptyline; anti-epileptics, including topiramate, valproic acid, gabapentin, and zonisamide; and beta-blockers, such as propranolol. Supplements, such as melatonin and magnesium, have also been studied. Although limited, evidence regarding their use is discussed in this section.

As yet, no clear guidelines exist to assist the clinician on the timing of initiation of prophylactic therapy in children and adolescents to reduce the likelihood of developing persistent posttraumatic headaches [22, 30, 31]. In general, preventive medications should be limited to children whose

Table 2 Commonly used preventive agents for childhood and adolescent headache prophylaxis Adapted from Kacperski and Hershey [32]

Agent	Dosing	Available formulations	Commonly encountered AEs
Antidepressants			
Amitriptyline	10–150 mg qhs (max 1 mg/kg/day)	Tablets—10, 25, 50, 75, 100, 125, 150 mg	Sedation, dizziness, constipation, decreased GI motility, increased appetite, weight gain, urinary retention
Nortriptyline	10–75 mg qhs	Capsules—10, 25, 50, 75 mg Liquid suspension—10 mg/5 ml	Drowsiness, dizziness, constipation, increased appetite, orthostatic hypotension, QT prolongation
Antiepileptics			
Topiramate	1–10 mg/kg/day (typical dose 50 mg bid)	Tablets—25, 50, 100, 200 mg Sprinkle capsules—15, 25 mg	Paresthesia, somnolence, dizziness, anorexia, metabolic acidosis, cognitive/memory dysfunction, abdominal pain
Valproic acid	15–30 mg/kg/day	Tablets DR—125, 250, 500 mg Tablets ER—250, 500 mg Sprinkle capsules—125 mg Liquid suspension—250 mg/5 ml	Somnolence, nausea/vomiting, thrombocytopenia, tremor, alopecia, increased appetite, weight gain, emotional lability, lymphopenia, hyperammonemia, elevated pancreatic enzymes
Levetiracetam	500–1500 mg bid	Tablets—250, 500, 750, 1000 mg Liquid suspension—100 mg/ml	Somnolence, fatigue, irritability, mood/behavioral changes
Zonisamide	100–600 mg/day	Tablets—25, 50, 100 mg	Somnolence, dizziness, anorexia, nausea, irritability
Gabapentin	300–1200 mg tid	Tablets—100, 300, 400, 600, 800 mg Liquid suspension—50 mg/ml	Dizziness, sedation, ataxia, fatigue, peripheral edema
Antihistamines			
Cyproheptadine	0.25–1.5 mg/kg/day	Tablets—4 mg Liquid suspension—2 mg/5 ml	Drowsiness, fatigue, increased appetite, weight gain, dizziness
Antihypertensives			
Propranolol	2–4 mg/kg/day	Tablets—10, 20, 40, 60, 80 mg Tablets ER—60, 80, 120, 160 mg Liquid suspension—20, 40 mg/5 ml	Fatigue, dizziness, constipation, hypotension, depression, exercise-induced asthma
Verapamil	4–10 mg/kg/day tid	Tablets—40, 80, 120 mg Tablets ER—120, 180, 240 mg	Constipation, dizziness, nausea, hypotension

AE adverse effect, *bid* twice daily, *DR* delayed release, *ER* extended release, *GI* gastrointestinal, *qhs* at bedtime, *tid* three times daily

headaches occur with ample frequency and/or severity to justify a daily agent. Reducing headache frequency, reducing the progression to chronic daily headache, and lessening associated disability should remain the goals of therapy for all children and adolescents. Similar to criteria for patients who have frequent primary-type headaches, most clinicians necessitate that a child experience a minimum of one headache per week or three to four headaches per month to rationalize initiating a daily prophylactic medicine. Preventive treatments should also be considered

if abortive medications are ineffective, poorly tolerated, contraindicated, or overused [32, 33]. The long-term treatment plan should be carefully discussed so families recognize that the response will not occur rapidly. The dose of medication should be titrated gradually to minimize side effects, and—once an effective dose is attained—relief must be sustained for 2–3 months before considering weaning off medication if the headaches are sufficiently controlled. Three to four headaches per month is recommended for a sustained period of 4–6 months. If not, an alternative medication may be considered [25, 27, 32–34].

4.1 Tricyclic Antidepressants

Antidepressants have been demonstrated as an effective prophylactic medication in children with primary headache disorders [35–38]. Kuczynski et al. [18] prospectively followed a cohort of 39 children (mean age 11 years) presenting with headache after mTBI to the ED and found that, 3 months post injury, 7.8% of children continued to report headaches as their primary complaint. Of those children, 56% had pre-existing headaches (prior to TBI) and 18% had experienced migraine before the injury. Of these, 55% met the criteria for migraine. A family or past medical history of migraine was present in 82% of cases. Among the treatment cohort, medications included amitriptyline, flunarizine, topiramate, and melatonin, with an overall response rate of 64%. Amitriptyline produced a good response in 13 of 18 children [39]. A randomized controlled trial of preventive medications for persistent posttraumatic headache in US military personnel revealed that amitriptyline, propranolol, and topiramate were similarly tolerated and associated with improvements in both headache frequency and disability. However, none of these treatments were superior to placebo [40].

4.2 Anti-Epileptics

Anti-epileptics have been the most widely studied prophylactic agents for the treatment of migraine in both adults and children. These include topiramate, valproic acid, gabapentin, levetiracetam, and zonisamide. Both topiramate and valproic acid are approved by the US FDA for migraine prevention in adults. Data from several studies suggest that topiramate is effective in the preventive treatment of pediatric migraine, leading to its FDA approval for children aged $\geq$ 12 years.

In an observational study, Erickson [41] reported that treatment with topiramate was associated with a significant reduction in headache frequency after mTBI. Of note, 57% of subjects had chronic daily headache with migrainous features and 31% were in medication overuse. The author proposed that the positive response to topiramate among this cohort suggested that cortical hyperexcitability may possibly contribute to persistent posttraumatic head pain [41]. However, caution should be employed when considering topiramate for posttraumatic headache prevention given its tendency for perceived cognitive slowing, a common complaint in many patients after mTBI [31].

Valproic acid is considered a first-line therapy for preventive therapy in adult migraineurs. Several open-label and retrospective studies have suggested that it may also be effective in the pediatric migraine population [42]. No studies have evaluated its effectiveness in the pediatric posttraumatic headache population, and scant evidence exists for the adult posttraumatic headache population. Packard [43] performed a retrospective review of 100 patients treated with divalproex for persistent posttraumatic headache and found that about 60% of patients with persistent posttraumatic headaches had mild to moderate improvement in their headaches after at least 1 month of treatment, whereas 40% either showed no response (26%) or discontinued treatment because of adverse effects (14%). Of those who reported a response, 58% had a change in headache pattern from daily to episodic. The author concluded that divalproex sodium appears to be safe and effective for treatment of patients with persistent posttraumatic headaches [43].

Several other anti-epileptic agents have been investigated in pediatric migraine, including levetiracetam, zonisamide, and gabapentin. However, no studies have evaluated their utility in treating posttraumatic headache in adult or pediatric patients.

4.3 Anti-Hypertensives

Beta-blockers, most commonly propranolol, have long been used for the prevention of migraine in both adults and children. While often viewed amongst clinicians as a first-line agent in pediatrics, this class of agents has failed to consistently demonstrate effectiveness in randomized, double-blind studies [44, 45]. Prescribers should be mindful of using beta-blockers to treat posttraumatic headache in conditioned athletes to avoid exercise intolerance [31].

4.4 Melatonin

Melatonin is considered a safe and well-tolerated agent with some purported neuroprotective effects that may be useful following mTBI. It may be considered for those who report significant insomnia, a common complaint in patients after concussion. There are reports of melatonin being used to treat chronic daily headaches in teenagers in an attempt to aide and manage sleep disruption [13]. Kuczynski et al. [18] reported on the use of melatonin in

children with persistent posttraumatic headache. In this study, melatonin was started at 3 mg and titrated to a maximum of 10 mg. The authors found that melatonin improved headache frequency significantly in 9 of 12 children (75%) [18].

4.5 OnabotulinumtoxinA

OnabotulinumtoxinA was approved by the FDA in 2010 and is commonly used for the treatment of intractable chronic migraines in patients aged > 18 years. Although experience with it is limited in the pediatric population, it is often reserved for conditions deemed intractable, often defined as failing at least two oral preventive agents. Kabbouche et al. [46] conducted a retrospective review of pediatric patients receiving onabotulinumtoxinA for chronic migraine and reported that monthly headache frequency improved, with statistical significance. A 30-point improvement in the pediatric disability scoring between first injection and follow-up injection was also observed, with a change from severe disability to moderate disability on the Pediatric Migraine Disability Assessment Score (PedMIDAS) [46]. There are several reports in the literature regarding onabotulinumtoxinA as an effective and well-tolerated treatment in adults with persistent posttraumatic headaches [47]. In a retrospective consecutive case series of US soldiers treated with onabotulinumtoxinA for chronic headaches after head injury (n = 64), 40.6% had at least 15 headache days per month with migrainous features and 41 (64%) reported getting better [48].

4.6 Peripheral Nerve Blocks

Benefits from peripheral nerve blocks of the scalp have been reported for adults with posttraumatic headaches. A retrospective case series of 28 patients aged < 18 years assessed the efficacy of scalp peripheral nerve blocks using 2% lidocaine with epinephrine for the treatment of persistent posttraumatic headaches. The authors reported that 71% of patients experienced immediate complete relief of their headaches; the mean percent headache reduction was 94%. Of these, 91% reported they would recommend a nerve block for posttraumatic headaches [49]. Seeger et al. [50] performed a retrospective chart review, including adolescent patients with posttraumatic headache (mean age 15 years; n = 14) who received occipital nerve blocks, and found that 64% reported long-term response to the occipital nerve blocks, with associated improved quality of life and decreased post-concussion symptom scores ($p < 0.05$).

5 Discussion

Posttraumatic headache in pediatric patients remains a frequent health problem for children and their families, yet many gaps in our knowledge remain with regards to its pathophysiology and treatment. Our understanding of primary pediatric headache disorders is improving with increased recognition of the features and associated symptomology. This should further guide individualized treatment approaches for improved outcome and reduction of headache progression into adulthood. The management of migraine headaches in pediatrics demands an individualized therapeutic approach that considers the developmental stage of the child as well as psychiatric and other comorbidities. As described, numerous agents have limited data in this population, and many agents lack efficacy. Although the most data are available for amitriptyline, topiramate, and valproic acid as prophylaxis in children, controlled studies on the pharmacological treatment of chronic headaches in children remain seriously lacking, and consequently, the need for new studies and evidence is urgent.

A survey by Brown et al. [51] demonstrated that clinicians who treat patients with posttraumatic headache use a variety of approaches to diagnosis and treatment. These findings indicate that additional research is needed to establish the most effective management strategies based on headache phenotype. They also suggest a unique opportunity to bring together the continuum of medical specialists who treat individuals with headache after TBI in a collaborative effort to use established headache diagnostic classifications and measures of associated disability as part of a consistent, effective model of care [51].

As described, several trials investigating the efficacy of various therapeutic treatments for posttraumatic headache have been conducted in recent years or are currently underway, and much has already been inferred from pediatric migraine studies. As mentioned, migraines and posttraumatic headache share many pathophysiological similarities. Potential new approaches for the treatment of acute migraine include antibodies against calcitonin gene-related peptide (CGRP) or the CGRP receptor. CGRP is thought to be pro-inflammatory and a potent vasodilator that is produced in both peripheral and central nervous system neurons. CGRP is implicated in the transmission of pain signals and is released during severe migraine attacks. Some have suggested that, as with migraine, activation of the trigeminovascular system in posttraumatic headache is also associated with the release of pro-inflammatory factors such as CGRP [52]. Given its pathophysiologic resemblances, posttraumatic headache may similarly benefit from this future treatment option.

6 Conclusion

Headaches are a common complaint following mTBI in children and adolescents. While acute posttraumatic headaches resolve within a few weeks for the majority of individuals, some may go on to develop persistent headaches that can cause significant disability and interfere with academic activities and family and peer-related interactions. Making matters more challenging for clinicians, there continues to be lack of consensus regarding management of headaches within this population. Despite this, it is judicious to complete a thorough evaluation and exclude other secondary causes of headache and to provide each child with an individualized and multidimensional treatment plan comprising lifestyle changes, psychological support, and pharmacological treatments. Because these headaches can be disabling and difficult to treat, new evidence-based approaches to this long-neglected field of research are urgently needed to improve outcomes for affected children.

Compliance with Ethical Standards

Funding No funding was received for the preparation of this review.

Conflict of Interest Joanne Kacperski has no conflicts of interest to report.

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