COMMENTARY

Luca Bartolini, MD, Section Editor

Practice Current

How do you diagnose and treat post-concussive headache?

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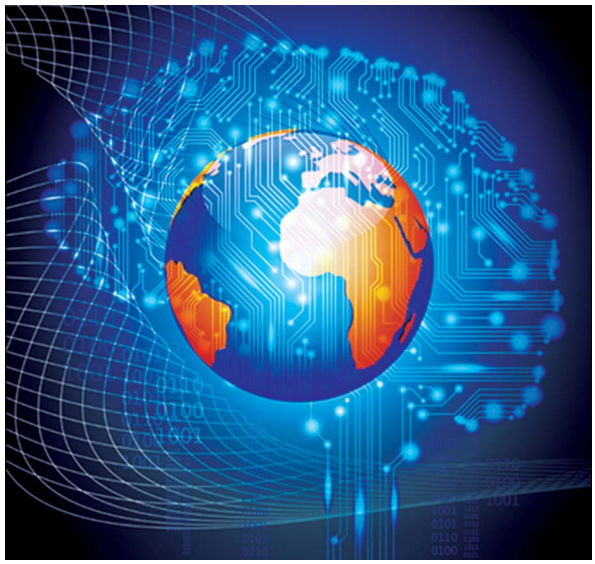
Abstract

A common complaint after concussion is the development of new or worsening headaches which can make it difficult or even impossible for patients to work or function in their day-to-day lives. Uncertainties associated with the complaints and a wide variety of approaches exist regarding the appropriate work-up and management of these patients. Areas of ongoing debate include the need for neuroimaging; optimal, acute, and preventative treatment; and proper counseling and expectation management. Given the wide variety of potential approaches and the lack of consensus, we sought expert opinion from around the globe on how to evaluate and manage patients with headache following concussion. Similar questions were posed to the rest of our readership in an online survey (links.lww.com/CPJ/A96), the results of which are also presented.



The estimated worldwide incidence of traumatic brain injury (TBI) is 69 million with 55.9 million of those cases categorized as mild TBI or concussion.[1] The vast majority of TBI occurs because of road traffic injuries and falls followed by assaults and sports-related injuries.[1–3] The most common complaint following TBI is headache, which is reported in up to 90% of cases.[4–10] The International Classification of Headache Disorders, 3rd edition defines posttraumatic headache (PTH) as a *new headache* following trauma or injury to the head and/or neck.[11] PTH attributed to mild TBI begins within 7 days or within 7 days of regaining consciousness following injury and resolves within 3 months.[11] When PTH begins after 7 days it is classified as "delayed-onset" and when the headache does not resolve within 3 months it is classified as "persistent."[11] The prevalence of PTH approaches 40% at 1 month post injury and decreases with time; however, some patients continue to have symptoms after 12 months.[12–14] A CT scan of the head is the imaging modality of choice in acute TBI.[15,16] Indications for neuroimaging include abnormal neurologic examination, progressively worsening headache pattern, or headache worsened by change in position or Valsalva maneuver.[16,17] In the subacute and chronic stage, MRI is preferred if imaging is deemed necessary.[15,16]

Patients with post-concussive symptoms are often instructed to engage in physical and cognitive rest until asymptomatic; however, there are no multisite randomized controlled trials (RCTs) to support these recommendations.[18] Active rehabilitation, which involves submaximal aerobic training, sport-specific light coordination activity, vestibular therapy, treadmill exercise, visualization, and home exercises may improve post-concussive symptoms and is an emerging area of research.[18] PTH can resemble the phenotype of primary headache disorders, with PTH most

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commonly resembling migraine followed by tension headache and cervicogenic headache.[3,13] PTH resembling migraine should be differentiated from post-concussive oculomotor disturbance, which may cause blurred vision, convergence insufficiency, diplopia, difficulty reading, dizziness, or nausea.[19]

The American Headache Society's goal in the acute treatment of migraine is to provide rapid and consistent freedom from pain and its associated symptoms without recurrence.[20] A retrospective cohort study showed that patients with non-blast-related PTH responded well to the triptan class of medications, but, beyond that, there is a paucity of data to guide acute headache treatment in PTH. Patients who are experiencing more than 3–4 headache days per month at 2 months post injury are good candidates for starting a preventative agent.[21–24] Medications used for primary headache disorders are often used "off label" for PTH, but there is variability in the medications chosen. There are a few retrospective and prospective cohort studies, which have shown that adolescent and adult PTH patients may benefit from topiramate or amitriptyline.[25–29] Cohort studies have indicated that adult patients with PTH may benefit from divalproex sodium and adolescent patients with PTH may benefit from melatonin.[26,30] Patients with PTH who are refractory to 2 or more headache preventative medications are another management challenge. Retrospective studies have shown onabotulinum toxin A to be beneficial in adult PTH[31] and have shown greater occipital nerve (GON) block to be beneficial in both adult and adolescent PTH.[32–36] Transcranial magnetic stimulation has been shown to be safe and effective in the treatment of migraine and 2 RCTs have shown its benefit in PTH.[37–40]

Given the variability, and only a few cohort studies and RCTs in the literature to guide treatment, we sought expert opinion on how to best evaluate, counsel, and manage patients with PTH. By soliciting expert opinion, we hope to both validate and modify current practice habits in addition to potentially shaping how future trials examine this challenging topic.

Expert opinion

Questions were posed to experts from 3 different continents, representing differing medical systems and patient populations. The following summary addresses their approaches to PTH and their opinion regarding imaging as well as acute and preventative treatment. Similar questions were posed to the rest of our readership in an online survey using representative cases with the results presented following the expert commentaries.

In alphabetical order:

Karen M. Barlow MSc, MB,ChB, MRCPCH, RACP (Australia)

Evaluation of post-concussive headache

In my practice, I treat children or young adults, and when they present with post-concussive headaches, they are usually quite severe in intensity and have been occurring for between 1 month and several years after the traumatic event, and first-line therapies tried by emergency or other frontline providers have not been effective. I normally avoid imaging patients with convincing post-concussive headache unless I am suspicious of an alternative cause or note something atypical in the history or examination. I find that there are many options we can try for these children, provided we are guided by the phenotype and take care to delineate the cause of the pain. A careful assessment of the cause of the headache is especially important because headaches in these patients due to other causes may be misattributed even to a very mild injury. As part of this process, it is also important to understand what the patient's pre-injury headaches were like; for example, some patients may have suffered migraine headaches previously or other types, such as exertional or traction headaches. Patients themselves may be dismissive of prior headaches, perceiving the post-concussive headaches as a new phenomenon rather than an exacerbation of a preexisting issue.

Patients themselves may be dismissive of prior headaches, perceiving the post-concussive headaches as a new phenomenon rather than an exacerbation of a preexisting issue. (K. Barlow)

Approach to analgesic treatment

In a prospective cohort study, we found that migraine was the most common headache type seen after mild TBI, followed by other types, including tension-type, cervicogenic headaches, and occipital neuralgias, and that 64% of patients responded to phenotypically guided treatment.[26] When patients present with severe acute pain, I find it helpful to use a "SKIP protocol," consisting of a saline infusion, ketorolac, and an anti-emetic, which has been shown to be efficacious in the emergent setting in an RCT.[41] Although patients can present acutely with symptoms similar to status migrainosus, I avoid using triptans in the first few weeks post concussion, given concerns about alterations in cerebral blood flow. Occipital nerve blocks can be very helpful, especially in patients with cervicogenic or occipital neuralgia-like pain; about 60% of patients seem to have a long-term benefit with these blocks, which I prefer to perform bilaterally.[35] I also caution patients and their parents against overusing analgesics and encourage them to reduce regular use quickly and to use these agents only for rescue from headache exacerbations. In children, nonpharmacological strategies, such as cold cloths and short rest periods, are often effective in my

experience. Rarely, in patients suspected to have C2 or C3 facet-related pain, we have tried facet joint injections with help from our radiology colleagues.

Approach to chronic and preventative treatment

My choice of chronic prophylactic agents is often guided by the objective of also treating comorbidities; for example, I will often choose amitriptyline to achieve sedative benefits in patients with poor sleep or, sometimes, nortriptyline for better tolerability. I will try propranolol if the pain is exacerbated by exercise or indomethacin if it is purely exercise induced. I do not tend to use topiramate as it often exacerbates cognitive complaints in post-concussive patients, although I might make an exception in the case of an overweight patient without depression. Flunarizine is another option in children younger than 10 or 11 years[26] We have also had success with melatonin 1–10 mg, which we are testing in an RCT.[42] Nutraceutical agents, such as magnesium and folate, may be favored by parents not keen to try other medications, but they may have limited efficacy. When there is a cervicogenic component, I encourage patients to get neck physiotherapy with exercises aimed at getting the neck moving properly again. Psychological management is often an important adjunct to medical therapy. Cognitive-behavioral therapy (CBT) can be especially helpful if headaches seem related to anxiety or stress—quite common among these children—or bullying. Biofeedback can be a nonpharmacological alternative; it can be helpful for patients to bring in schoolwork to train them to control their responses to pain when dealing with a cognitively demanding task. With this strategy, we see a response in about half of our patients with medication-refractory headaches. Repetitive transcranial magnetic stimulation has been studied in adults and may be an effective treatment option for some patients.[40]

Case discussion

Whereas I usually avoid brain imaging for typical cases, for case 1, I would consider brain MRI, ideally within 2 weeks, including contrast to evaluate the venous sinuses, owing to the patient's atypical story of the headache starting only 1 week after the head trauma. In such a scenario, we must be careful not to misattribute the headache to the trauma, particularly if the patient did not have a history of migraine-like headaches. In our experience, most children with post-concussive headaches develop their headache within 72 hours of the injury. I would not start any new medications while awaiting the MRI but would encourage the patient to maintain a headache diary to better characterize the phenotype. As part of my counseling, I would also ensure that the patient is not over-resting in the aftermath of the injury and tries some gentle exercise such as an exercise bike. If the MRI is reported as normal, I would choose a preventative agent on the basis of his comorbid complaints, triggers, and the work that he does. My usual choice would be amitriptyline or nortriptyline to help with sleep, which, in turn, can itself help with pain control. My approach would not differ if the patient was a 14-year-old, unless the headache started closer to the trauma, in which case I would not order neuroimaging. I would also emphasize the importance of minimizing analgesic use (e.g., naproxen) to avoid overuse/rebound headaches. If the patient returns with poor headache control despite trying amitriptyline/nortriptyline, then I would consider propranolol, especially if there is an exercise-induced component. Botulinum toxin injections may be another option, although I find that male patients are less tolerant of the injection-related pain.

For case 2, I would certainly change her headache treatment as she is experiencing a disabling frequency of headaches. I would consider increasing the topiramate to 100 mg twice daily at least for a short trial to see whether this improves headache control. Because this patient clearly has mood complaints and other hallmarks of a chronic pain syndrome that will be hard to control medically, I would certainly refer her to a psychologist for supportive counseling and/or CBT.

David W. Dodick, MD, FRCP (C), FACP (United States)

Evaluation of post-concussive headache

In my practice, I will order imaging if the patient has focal findings on their neurologic examination or focal neurologic complaints. If the patient is over age 65, I would order imaging because older patients are at higher risk of subdural hemorrhage.[43] I do not order head CT imaging because that will expose the patient to radiation and an MRI can identify a skull fracture and acute or aged blood products. Intracranial contusions can enhance in the acute or subacute period; however, I do not order a contrast-enhanced MRI as it does not provide me with any additional useful information.[16]

Approach to analgesic treatment

I instruct patients to use medication as needed when their headache severity is greater than 5/10. I will use a triptan if the headache has migrainous features, such as light and sound sensitivity. If the patient is having severe nausea, I will use an anti-emetic such as ondansetron; however, often a patient's nausea is most severe at the peak of their headache, so simply treating their headache can reduce nausea.

Approach to chronic and preventative treatment

If a patient is presenting to me with PTH more than 1 month following injury, I will start them on a headache prophylactic medication, as 40% of these patients will have a headache 3 months after injury and 40%–60% will have a headache 12 months post injury.[13,14] I offer the patient either a tricyclic antidepressant (TCA) or topiramate and keep them on it for at least 3–4 months. I prefer a TCA at night if they are not sleeping well. I will use either amitriptyline or nortriptyline, although nortriptyline will have fewer anticholinergic side effects. If the patient is sleeping too much, I would prefer topiramate. I do not use topiramate if the patient has cognitive complaints or a job where they are required to speak frequently. If their blood pressure can tolerate it, propranolol is an option in patients who have anxiety and symptoms of

postural orthostatic tachycardia syndrome. I counsel the patient regarding proper sleep hygiene, and I have an exercise physiologist individually counsel the patient regarding activity. I do not bother with hydration or diet. I try to minimize the burdens on the patient to encourage them to get back to their lives.

Case discussion

For the patient in case 1, I see no need to order imaging. He has a normal neurologic examination without any focal neurologic complaints. I would offer him either a TCA or topiramate. My strategy would not change if the patient in case 1 was replaced with a 14-year-old presenting after a soccer-related injury. I do not like cyproheptadine as it has no evidence in PTH and can cause weight gain and sedation. I prefer not to use melatonin as I have low confidence in its effectiveness. For the patient in case 2, switching them to a TCA could address her sleep and depressed mood. In patients with persistent PTH resembling migraine, I have had success with anti-CGRP monoclonal antibodies. Botulinum toxin is another option. A nerve block could provide days to weeks of relief.[32] If the patient is anxious, CBT, biofeedback, and relaxation therapy are options. Physical therapy can be useful if there is significant myofascial neck pain. If they are experiencing more than mild depression, I would refer them to a psychologist.

Mohammad Wasay, MD, FRCP (Pakistan)

Evaluation of post-concussive headache

In my patient population, tension, cervicogenic, and migraine are the most common headaches after mild TBI. I treat mainly adults. Children constitute 10% of my clinical practice. I see post-concussive headache primarily in young adults who have previously been in motorcycle collisions, which is a common mode of transportation for them. Typically, I order brain MRI without contrast as initial imaging if the patient is over 60 years of age, has focal neurologic deficits, severe headache, or history of a loss of consciousness.

Approach to analgesic treatment

I generally do not wait for imaging results before starting treatment for convincing post-concussive headache. For milder pain severity, I prefer reassurance and nonsteroidal antiinflammatory pain medication as needed. In my patients with post-concussive headache, I have rarely observed medication overuse headache because patients generally avoid taking medications in this part of the world. In severe cases, I start preventive medication at the same time.

Approach to chronic and preventive treatment

My choice of prophylactic agent is directed by other comorbidities, and I try to kill 2 birds with 1 stone. I have seen the best results with amitriptyline and flunarizine. I offer amitriptyline to patients with sleep problems and depression. If a low dose of amitriptyline is not working for a patient, increasing the dose can help achieve the goal. I don't use propanol because of the side-effect profile, particularly sexual dysfunction and exacerbation of underlying depression and asthma. I also do not use topiramate because it exacerbates cognitive complaints in post-concussive patients. In my experience, the combination of nonsteroidal antiinflammatory pain medication, preventive treatment (amitriptyline or flunarizine), CBT, and counseling regarding sleep and hydration works best for my patients. Occasionally, I see refractory cases, for which I will use botulinum toxin injection and nerve blocks.

Case discussion

For the patient in case 1, I would consider ordering brain MRI because the headache started 1 week after trauma. I would choose nonsteroidal antiinflammatory pain medication as needed and amitriptyline, since his headache improves after sleep. My approach will be the same if the patient is a 14-year-old. If the patient returns with poor headache control despite trying amitriptyline, then I would consider increasing the dose of amitriptyline before considering botulinum toxin injections.

For case 2, I would consider adding amitriptyline, as this will help her sleep issues and depression. Propranolol exacerbates depression so I would taper it down and eventually discontinue it. In this case, because of chronic disabling headaches, I would consider referring her to a psychologist for counseling and CBT before considering botulinum toxin injections.

Lower-/middle-income country challenges

Concussion and post-concussion syndrome are common in our part of the world. It is largely related to motorcycle collisions. Almost 41% of Pakistani households own a motorcycle. More than 90% of motorcycle users do not wear a helmet. Sport-related concussion is rare in cricket, which is the most popular sport in Pakistan. Poor concussion awareness is a major problem. Most individuals with concussion never go to a hospital or get neuroimaging. Concussion after mild motorcycle-related accidents is considered normal, and most people will not seek medical advice unless they develop a post-concussion syndrome. Use of painkillers other than paracetamol or nonsteroidal antiinflammatory drugs is uncommon, especially narcotic analgesics. In our culture, kids are taught to tolerate pain and take medications only if it becomes severe. Pain is not considered a fourth vital sign. In my opinion, this is why analgesic abuse and analgesic-abuse headache is not common in this part of the world.

Preliminary survey results (April 16, 2019): Section Editor: Luca Bartolini, MD

We collected a total of 302 complete questionnaires between March 25 and April 16, 2019. Respondents were primarily adult neurologists (n = 224; 74%) who did not designate themselves as headache or TBI specialists (n = 253; 83%). The majority of survey takers had been in practice for less than 10 years (n = 128; 42%) and had treated more than 10 patients with post-concussive headache in the 12 months preceding the survey (n

= 153; 51%). Eighty-one respondents were physicians in training and 32 were advanced care providers. Approximately half of responses came from people practicing in the US (n = 144; 48%). A total of 62 from other countries participated, with Brazil (n = 11), United Kingdom (n = 10) and Canada (n = 9) being the most represented.

For case 1, of a young adult with headache developing 1 week after hitting his head on a sidewalk with no loss of consciousness, normal neurologic examination and symptomatic relief with sleep and naproxen, half of respondents (n = 195; 55%) would obtain brain imaging, especially a noncontrast head CT on the same day (n = 115; 60%) or brain MRI without contrast within 2 weeks (n = 34; 18%). For treatment, the majority of survey takers would recommend different combinations of the following options: reassurance and naproxen (54%), antiemetics (39%), triptan for severe headache (23%), counseling on lifestyle modifications (58%), daily headache preventative medication (37%), and nonpharmacologic treatments (32%) (figure 1). Of all options for daily preventative medication, the majority chose amitriptyline (n = 63; 48%), followed by nortriptyline (n = 23; 18%).

When presented with a similar scenario in a 14-year-old following concussion during football or soccer, responses did not differ significantly, except for choice of daily preventative medication: 26% chose amitriptyline, 18% propranolol, and 15% topiramate (figure 2). These choices were similar for those who initially did not opt to start a preventative and were then told that the child came back after 1 month for persistent headache.

Case 2 was a 37-year-old woman presenting for persistent headache after a low-speed motor-vehicle accident where she hit her head on the headrest and had negative head CT in the emergency room. Her headache was associated with insomnia and depressed mood and had little relief with ibuprofen and sumatriptan. Treatment with propranolol for 3 months did not help; topiramate 50 mg BID for 5 months also failed, too. She had a normal brain MRI and normal examination. Most survey takers would change the regimen and consider primarily the following options: nonpharmacologic treatments, such as cognitive behavioral therapy (59%), counseling on lifestyle modifications (57%), adding a second agent (31%), and increasing topiramate dose (29%). Seventy-five per cent of respondents would also refer her to a mental health specialist.

These preliminary results highlight the extremely important role of nonpharmacological interventions and lifestyle modification in the management of post-concussive headache. The pathophysiology of this condition is complex and multifaceted, with no easy one-size-fits-all solution. We look forward to a continued participation in this survey and to see the final results on a larger worldwide scale.

Discussion

With expertise in both concussion and headache, neurologists will continue to be called upon to diagnose and manage PTH. The management of PTH is complicated because there are few RCTs on which to base the decisions . The 3 experts agreed that routine neuroimaging was not necessary

Figure 1 Initial headache treatment recommendations

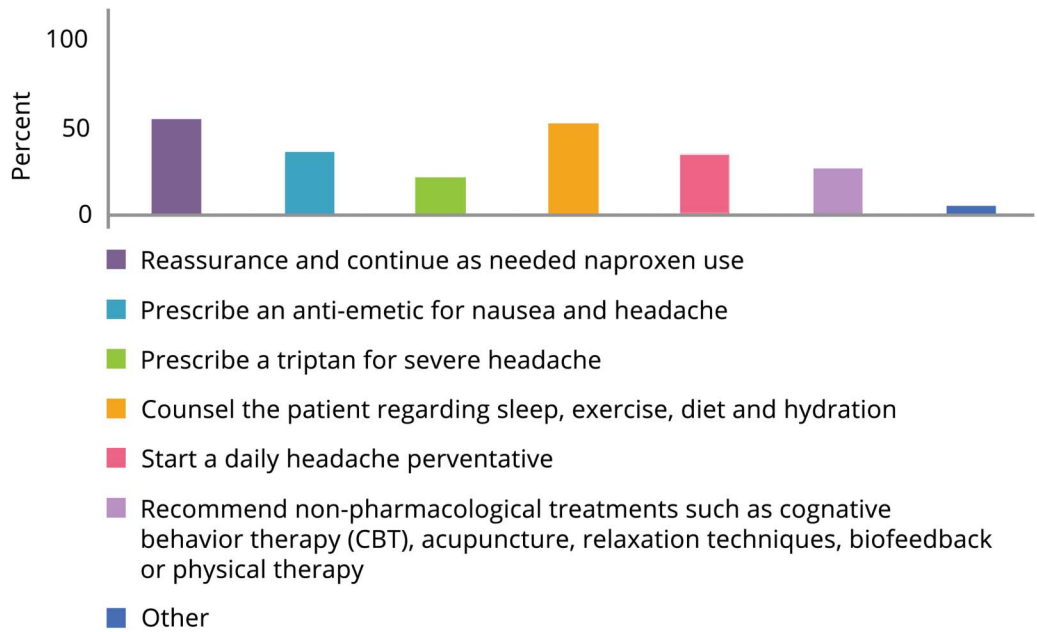
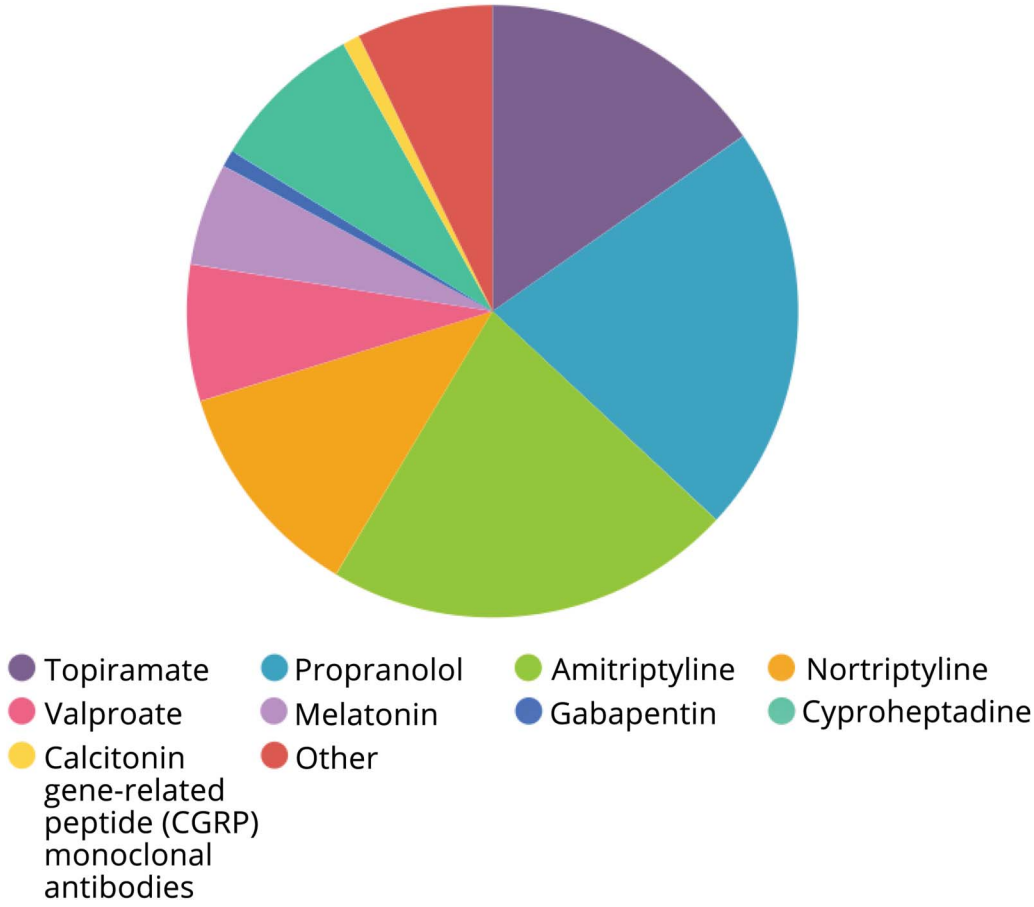


Figure 2 Recommended daily headache preventative



unless there are abnormalities in the history or neurologic examination. However, 2 of our experts would order a brain MRI if headache started at or after 7 days to evaluate for other secondary causes. They prefer using a nonsteroidal antiinflammatory drug as their abortive of choice. They also prefer to tailor their choice of headache preventative medication based on the side-effect profile and ability to treat other comorbidities. All 3 experts use amitriptyline as their first-line therapy, but they differed on some of the other preventative medications they prefer to use. In refractory PTH, all 3 experts would consider botulinum toxin injections or GON block. They would also utilize referral to a mental health professional with experience in CBT when managing PTH in a depressed or anxious patient. They differed on what specific counseling, if any, they considered vital when treating PTH.

Our survey results indicated a general feeling of uncertainty regarding how newly developed treatments for migraine headache may apply in PTH. This uncertainty may help shape the design of future RCTs. Future RCTs will need to take into account currently accepted practice strategies in order to recruit patient cohorts that can yield a new and better understanding of how to best manage PTH.

Karen M. Barlow, MSc, MB, ChB, MRCPCH, RACP (Australia), is Chair of Paediatric Rehabilitation and Associate Professor at the University of Queensland in Australia. She completed studies at the universities of Edinburgh, London, and British Columbia. She has published extensively on epidemiological and outcome studies of children with mild and severe TBI. Her current work focuses on the assessment, outcome, and treatment of children with acquired brain injury and concussion. She has conducted clinical trials using nutraceuticals and noninvasive brain stimulation in children with persistent post-concussion symptoms. She serves as an Attending Consultant Paediatric Neurologist at Children's Health Queensland and as Adjunct Associate Professor of Clinical Neurosciences and Paediatrics at the University of Calgary. She is a fellow of the Royal Australasian College of

Physicians, Alberta College of Physicians and Surgeons, and the Royal College of Paediatrics and Child Health (London). Renowned for her work in paediatric neurology, Dr. Barlow has been the recipient of several honors and awards, such as the Clinician of the Year (University of Calgary, 2017) and Best Original Research Article (National Academy of Neuropsychology, 2014). Current studies include the use of eHealth technologies to improve uptake to clinical pathways following a concussion, and noninvasive neuromodulation to enhance recovery after traumatic brain injury.

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Mohammad Wasay, MD, FRCP, is currently Professor of Neurology at Aga Khan University. Dr. Wasay is Past President of Pakistan Society of Neurology and Pakistan Stroke Society, President of Neurology Awareness and Research Foundation, Chairman of an advocacy and awareness task force of World Federation of Neurology, Editor of *Pakistan Journal of Neurological Sciences,* Chief Editor of *Jahan e Aasab* (a neurology public awareness magazine), and Chair of FHS research committee at Aga Khan University. Dr Wasay has received several national and international awards for educational, research and advocacy activities, including Teachers Recognition Award (American Academy of Neurology), Distinguished Teacher Award (Pakistan Society of Neurology), Outstanding Teacher Award (Aga Khan University), Gold medal for research (Pakistan Academy of Medical Sciences), Advocacy Leader of the Year Award (American Academy of Neurology), Victor Rivera Award (UT Southwestern Medical Center), and Lester R. Bryant Founders Award (Marshall University, Huntington, WV, USA). He was awarded fellowship of Pakistan Academy of Medical Science and Gold Medal in Health Sciences by Pakistan Academy of Sciences. Recently, he was elected as Fellow, Pakistan Academy of Sciences.Dr. Wasay has held a number of leadership positions at prestigious forums. At the international level, these include World Federation of Neurology Advocacy Task Force (Chair); International Subcommittee, American academy of Neurology (Member); Board of Directors, World Stroke Organization (Director); and Public Relations Committee, World Federation of Neurology (Chair) and Executive committee member Asia Pacific Stroke Organization. He is also serving as member of the technical advisory committee for Pakistan Health and Research Council (PMRC). He has trained 33 neurologists (Fellows College of Physicians and Surgeons) under his supervision (as CPSP supervisor). He has received 24 grants from various national and international agencies as Principal Investigator or Co-Principal Investigator. His publication bibliography includes 166 papers in peer-reviewed medical journals. The combined impact factor of his scientific publications is more than 423 and the collective citations exceed 2100. He has been an invited speaker and presenter at more than 95 international conferences, with more than 100 presentations and lectures. He is an active reviewer of research grants and scientific papers for more than 25 journals and granting agencies. His book *Fasting and health* is translated into Sindhi and English. He has traveled to 58 countries in all 6 continents. He has more than 70 media interviews at TV channels, newspapers, and web channels.

Author contributions

A. Dave was involved in the conception and design of the study, acquired data, and wrote and revised the paper. A. Ganesh was involved in the design of the study and data acquisition, and wrote and revised the paper. M. M. Adil was involved in the design of the study and data acquisition, and wrote and revised the paper. J. W. Tsao supervised the study, was involved in the conception and design of the study, and revised the paper.

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Health Analytics (AHA Health Ltd). He is a Section Editor for *Neurology Clinical Practice*. M. M. Adil is an editorial team member of the Resident and Fellow Section of *Neurology*. J. W. Tsao is on the editorial boards of *Neurology* and *Neurology: Clinical Practice* and is the editor of *Traumatic Brain Injury: A Clinician's Guide to Diagnosis, Management, and Rehabilitation*. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

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