



Exercise Headache: a Review

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Abstract

Purpose of Review Exercise headache refers to headache that is triggered by exercise or exertion. Although secondary causes must be excluded, most cases of exercise headache are benign, idiopathic, and self-limited. This article reviews the revised diagnostic criteria for primary exercise headache (PEH) and discusses recent research into the clinical presentation, epidemiology, pathophysiology, suggested workup, and treatment of this condition.

Recent Findings Recent studies estimate that PEH affects from 1 to 26% of the adult population. A secondary cause is thought to be present infrequently, but should be explored in all patients with a first or atypical presentation of exercise headache. Red flags for potential secondary causes may include older age at onset and more prolonged headache duration. There is inadequate evidence to include gender as a red flag. No recent trials have been conducted, but experts suggest that avoidance of triggers coupled with short-term NSAID and/or beta-blocker treatment may be effective for patients diagnosed with PEH.

Summary Larger studies are needed to provide high-quality evidence regarding the pathophysiology and treatment of PEH. However, recent work has shed light on the characteristics of this condition, and the ICHD-3 has provided important updates to the diagnostic criteria for this relatively common and potentially treatable condition.

Keywords Exercise headache · Exertional headache · Primary headache disorders · Secondary headache disorders · Indomethacin

Introduction

Primary exercise headache (PEH), also previously entitled primary exertional or benign exertional headache, has historically been a nonspecific term used to refer to a headache that is provoked by exertion or exercise. In the most recent revision of the International Classification of Headache Disorders (ICHD) criteria, ICHD-3, this entity has been moved from the Appendix to Section 4: Other Primary Headache Disorders, indicating a shift both in the acceptance of this entity as a primary headache disorder and in the recognition that in most cases, exercise headache is not due to a sinister secondary pathology [1]. However, given the potential for an underlying fatal or debilitating secondary cause, a first presentation of exercise headache should receive prompt workup to help

guide diagnosis and treatment. The ICHD-III diagnostic criteria for PEH and probable PEH are listed in Table 1.

Of note, although up to around 50% of patients with PEH also have a history of migraine, ICHD-III stipulates that exercise-induced migraine should be coded under the heading of migraine [1, 2]. Distinguishing between exercise-induced headache and migraine may be straightforward in a patient whose headaches are exclusively triggered by exercise, which should not be the case for migraines, but it may require more careful history-taking to distinguish a migraine from an exercise headache in a patient with a history of migraines. Exercise headaches may have migrainous features such as a pulsating quality, as will be discussed in greater detail below, but if an exercise-induced headache otherwise meets diagnostic criteria for migraine, it should be considered as a migraine.

It should also be noted that the criteria for PEH require strenuous physical activity, which distinguishes this entity from others such as headaches induced by cough or Valsalva maneuver. Also specified in the diagnostic criteria is the caveat that symptomatic causes of exercise headache, including arterial dissection, reversible cerebral vasoconstriction syndrome, and subarachnoid hemorrhage, must be ruled out in a patient with a first exercise headache.

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Table 1 The ICHD-III diagnostic criteria for primary exercise headache

Primary exercise headache
A. At least two headache episodes fulfilling criteria B and C
B. Brought on by and occurring only during or after strenuous physical exercise
C. Lasting < 48 h
D. Not better accounted for by another ICHD-3 diagnosis
Probable primary exercise headache
A. Either of the following:
1. A single headache episode fulfilling criteria B and C
2. At least two headache episodes fulfilling criterion B but not criterion C
B. Brought on by and occurring only during or after strenuous physical exercise
C. Lasting < 48 h
D. Not fulfilling ICHD-3 criteria for any other headache disorder
E. Not better accounted for by another ICHD-3 diagnosis

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Clinical Presentation and Epidemiology

Most patients with PEH present with a bilateral, pulsating headache, which begins within 30 min after the onset of exercise in more than half of patients [3•, 4]. The offending exercise is usually strenuous in nature, although any form of exercise may be implicated as the definition of “strenuous” may vary with individual patient fitness levels. Duration of headache is usually 5 min to 48 h; however, the average duration may be shorter in adolescents [5]. PEH is typically thought to resolve spontaneously in months to years in the majority of patients [2, 6, 7, 8•].

Incidence and prevalence of PEH are difficult to establish. Methods of ascertaining prevalence of exercise headache have varied widely, with some studies using ICHD-II criteria, few utilizing the updated ICHD-III criteria, and still others having much more broad inclusion criteria such as including patients with headache induced by straining or Valsalva, which under the ICHD-3 is classified under primary cough headache (PCH) as mentioned above. Even the terminology varies, with some recent articles still using the old title of primary exertional headache rather than the new moniker of primary exercise headache. The lowest PEH prevalence was found by Pascual et al. in a 2008 study, which prospectively identified a prevalence of 0.17% [7]. However, studies published around the same period reported a prevalence of up to 12.3% in adults, 26% in cyclists, or as high as 30.4% in adolescents [5, 9, 10]. Indeed, the disorder has been posited as being more prevalent in adolescents, and given its typically time-limited

course, identifying lifetime prevalence retrospectively is likely quite difficult due to recall issues. Patients who develop exercise headache when embarking upon a new exercise routine or activity often self-identify triggering activities and avoid these; thus, lifetime prevalence and point prevalence may be quite different, although many studies do not clearly draw this distinction. Furthermore, many at-risk patients may simply never perform strenuous exercise, making prevalence itself a difficult concept in this context. Prevalence estimates from studies performed over the past 5 years have ranged between 1.19 and 12.7%; these studies will be discussed in greater detail below [3•, 4, 8•].

Hanashiro et al. identified patients with PEH in the Japanese population, on screening of 2546 patients presenting to their family doctors for regular health checks targeted at those between the ages of 40 and 60 [8•]. The average patient age in their group was 44.3 years (SD 8.8 years), which excludes a significant portion of the population traditionally felt to be at highest risk of PEH. They reported a lifetime PEH prevalence of 1.19%. In their 30 patients with PEH, the majority reported bilateral rather than unilateral pain (23 vs 7 patients). Most experienced pain in the occipital region (16 patients or 53%) rather than frontal (10 patients, 30%) or diffuse (4 patients, 13%). None of the patients reporting PEH were well-trained athletes. Twenty of the 30 patients had coexisting primary headache disorders, including migraine without aura in all 20, and other triggered headaches including headache induced by sexual exertion and cough headache in 7 and 5, respectively. Since all of these activities share some features including Valsalva maneuver/straining or activity of some form, this is perhaps not surprising. However, it is important to note that this study does not clearly distinguish migrainous headache induced by exercise (which, as previously outlined, is considered under the heading of exercise-induced migraine) from PEH. This distinction may not always be practical in an individual patient. Importantly, this study followed 28 of the 30 patients over the subsequent 12 months, and all 28 reported resolution of their PEH, although details as to whether the headaches were completely resolved or simply managed with treatment strategies are not provided.

Importantly, none of the patients in the Hanashiro study had sought medical attention for their exercise headaches despite an overall mean duration of 4.5 months of the disorder. The reason for this lack of presentation to healthcare providers is not known and is especially concerning given the recommendation for workup of patients with new-onset exercise headache. It is also perhaps surprising given the high proportion of patients with migraine. Regardless, this finding has implications for future studies in that attempting to identify patients based on those presenting to physicians or headache clinics may miss a significant portion of patients with exercise headache. This may also speak to the fact that there may be a great range in severity among PEH patients, and perhaps,

patients with milder phenotypes are not seeking out medical attention. Although the methodology of the study states that brain imaging and angiography were performed in all patients to rule out secondary causes, data as to whether any such secondary causes were identified are not presented. The prevalence of secondary causes for exercise headache is generally felt to be low, but no recent studies have successfully addressed the question of how low.

In contrast to the fairly low prevalence of PEH reported by Hanashiro et al., a cross-sectional descriptive study from Iran using ICHD-II criteria for exertional headache identified 38/300 (12.7%) male conscripts who reported ever experiencing exertional headache [4]. It should be noted that this population was entirely male, which excludes a significant portion of migraine sufferers given the female preponderance of migraine. This study agreed with previous reports in that most patients (73%) experienced bilateral exercise headaches, but in contrast to the previous study, the majority were frontal at 34.2%, with lower percentages of patients experiencing temporal (16.8%), holocephalic (13.2%), occipital (10.5%), vertex (7.9%), or non-localizable (18.4%) exercise headaches. They reported predominantly pulsating (47.4%) or squeezing (44.7%) headache phenotypes. Exercise headaches in this population typically occurred fairly rapidly after the onset of exercise, with 55.3% occurring within 30 min from onset and 81.5% with headache onset within the first hour of exercise. Exercise headaches were typically short, with only 5.3% lasting longer than 24 h. They lasted < 5 min in 13.2%, 5–60 min in 39.5%, and 1–24 h in 42.1% of patients. This would support the prevailing idea that longer duration exercise headaches are unusual and should be treated with greater concern for an underlying secondary cause. This study identified hot weather as an aggravating factor, with 81.6% of patients reporting this as a factor. Other aggravating factors identified included high altitude (7.9%), light (5.2%), sound (2.6%), and coughing (2.6%).

An Iranian study from 2015, using ICHD-II criteria (with the subsequent inclusion of both pulsating and compressive-type headaches after the publication of the ICHD-III during the study period) in a face-to-face, questionnaire-based survey of 2076 randomly identified community-dwelling adults, found a 1-year prevalence of exercise headache of 7.3% (152 patients) [3••]. The age range of patients in this study was 12–69 years. Although the methods for this article state that migraine and secondary causes of headache were excluded in patients diagnosed with exercise headache, data as to the workup performed and the numbers of patients were again not included in the publication. Unfortunately, the prevalence of comorbid migraine and other primary headache disorders was not assessed in this study. The authors identified bilateral headaches in 78% of patients, but found essentially equal numbers of patients with temporal (30%) and frontal (29.3%) locations for their headaches, versus holocephalic (14.3%), occipital (13.6%), vertex (10%), or non-localizable

less commonly. Similarly to the previous study, patients reported a mixture of pulsating (55.3%) and compressive (44.7%) pain, supporting the revision of ICHD-III to remove the requirement for headaches to be pulsating in nature. Other noteworthy findings of this study are the replication of time of onset as most commonly within 30 min of beginning exercise, with 60.3% occurring in this timeframe, 14.9% in 30–60 min of exercise onset, 15.7% after 1–2 h, and only 9.1% more than 2 h after exercise onset. Duration once again was relatively brief, at 5–60 min in 41.8%, 1–24 h in 50%, and a mere 8.2% of patients reporting exercise headaches lasting 24–48 h. Also of interest is the finding that exercise does not consistently trigger headache in a given patient, with only 26.9% of patients reporting headache more than five times out of ten exercise sessions. Precipitants and aggravating factors identified include hot weather (48%), high altitude (13.2%), sounds (5.3%), and coughing (2%), with other factors such as ongoing exercise, menstruation, specific foods, heavy lifting, and dehydration also reported by some patients. It is important to note that this questionnaire captured 424 patients (20.4%) who reported bodybuilding and lifting as their headache trigger. The ICHD-III states that weight lifter's headache is a recognized, but not individually classified, subtype of primary exercise headache; however, weight lifting may be felt to be closer to a Valsalva maneuver, which would place it under the category of PCH [1]. Although many patients with true PEH may also have headaches induced by cough or Valsalva, including up to 47% of the adolescents in the 2008 Chen study, this data should be interpreted with caution and further research is needed to clarify the specific characteristics of weight lifter's headache [5].

Gender estimates for exercise headache vary. Studies from the twentieth century identified a higher prevalence in men, but more recent studies found a higher prevalence in women than men at a ratio of 1.38 in adults and 1.49 in adolescents [5, 9]. The Rabiee study from 2015 also supported a higher prevalence in women, with a general prevalence of 7.3% of all subjects and 10% in females versus 5.5% of males, for a ratio of 1.82 [3••]. Similarly, Hanashiro and colleagues reported a higher prevalence in women than in men at 1.77 versus 0.82%, respectively, for a female:male ratio of 2.1 [8•]. It may be hypothesized that women do likely have a higher prevalence of exercise headache given the reported association between migraine and exercise headache, but further studies are needed to confirm this hypothesis.

Pathophysiology

The pathophysiology of PEH is not well understood. Some investigators feel that it represents a vascular disorder, with decreased venous return and/or arterial distension leading to traction on pain-sensitive cerebral structures. In support of

the venous congestion, a theory is work by Doepp et al. showing that patients diagnosed with PEH are more likely to have internal jugular vein valve incompetence compared with age-matched controls, at 14/20 (70%) vs 8/40 (20%), respectively [11]. In contrast, a small radiological study did not find an increased preponderance of transverse sinus and/or internal jugular vein stenosis in patients with PEH [12]. This study included 36 patients and used magnetic resonance (MR) venography in patients with ICHD-II criteria PEH (10 patients), PCH (7 patients), or primary headache associated with sexual activity (PHASA) (19 patients), with 16 controls from patients undergoing MR venography for non-headache reasons. They found a significant increase in transverse sinus and/or internal jugular vein stenosis in the PCH (5/7 patients) and PHASA groups (12/19 patients), but not in the group with PEH (2/10 patients) or in controls (0/16 patients). This is especially notable given the fact that more than half of their patients classified under PEH also had headaches triggered by cough (six patients), sneezing (one patient), or sexual activity (one patient). Unfortunately, not all patients completed assessment of both the transverse sinus and the internal jugular vein, with 4/10 PEH patients having imaging of only the transverse sinus, which may limit the interpretation of their results.

Given our recent shift in classifying many other primary headache disorders as non-vascular in origin, whether a vascular origin for PEH will be borne out by future studies remains to be seen. Of note, the patients in the studies described above were identified when they presented to medical attention for their headaches. As previously mentioned, a significant number of patients with PEH do not seek medical attention, and thus, potential differences in their underlying pathophysiological characteristics cannot be excluded.

Although not directly assessing the pathophysiology of exercise headache, a recent Norwegian study examined the effects of physical fitness level, as measured by peak oxygen uptake (VO₂peak) and headache [13]. They reported that headaches in general, including migraine, tension-type headache, and nonspecific headaches, increased with worsened physical fitness as measured by decreased VO₂peak and that VO₂peak was also lower in patients who reported worsening of their migraines by exercise. This is of particular interest in light of reports that PEH tends to occur more in non-trained athletes [8•]. However, a Dutch study identified a PEH prevalence of 26% among endurance cyclists, and the relationship of physical fitness level to the development of PEH therefore remains unclear [10].

Of further interest is a recent report of two patients with headache induced by laughing, one of whom also had headaches induced by playing basketball [14]. Unfortunately, this patient declined investigations for a secondary cause of their headaches. The authors posit commonality between the pathogenesis of laugh-induced headache, PCH, and PEH.

It is fascinating to speculate as to why this disorder presents and then (in most cases) vanishes as it came, one of the few primary headache disorders with a typically time-limited course. Perhaps these patients give up exercise or headache-triggering activities, or perhaps as their fitness level increases, their susceptibility to exercise-induced headaches decreases. The pathophysiology of PEH and other potentially related disorders such as PCH remains a fruitful area for further study.

Investigations

As with any new, exertional headache, patients presenting with a first episode of exercise-induced headache should undergo a directed workup to exclude secondary causes. Such secondary causes typically include subarachnoid hemorrhage, reversible cerebral vasoconstriction syndrome (RCVS), and cervical artery dissection. Other less common etiologies include space-occupying lesions, sinusitis, Chiari malformation, and pheochromocytoma [15]. Previous authors have suggested that gender may be used as a factor for risk stratification regarding a possible secondary cause of exercise headache, but given conflicting data in this area, we suggest investigating both females and males with a first presentation of exercise headache [16]. We agree with previous recommendations to consider later age of onset and longer duration of headache as a red flag for a secondary cause.

Cardiac cephalalgia is another important mimic of PEH [17]. A recent case report identified a 40-year-old man with multiple vascular risk factors, including hypertension, smoking, and a previous non-ST-elevation myocardial infarction (NSTEMI) [18]. He presented to the authors' attention with a 4-year history of fairly severe headaches provoked by exertion, cold, and sexual activity, sometimes associated with worrisome features such as chest pain and palpitations, and which were relieved by nitrates. Cardiac workup revealed significant coronary artery disease. Interestingly, the authors performed MRI during one such headache and reported diffuse cerebral hypoperfusion intra-ictally. The patient's headaches resolved with cardiac angiography and stenting. Older patients (typically those over 50), patients with vascular risk factors, and those with unusual associated symptoms such as chest pain or sweating should undergo cardiac workup, including ECG, echocardiography, and consideration of referral to cardiology for more invasive testing. It may also be worthwhile investigating for cardiac etiologies in those patients with typical PEH who progress or who do not resolve as expected.

The European Headache Federation guidelines from 2015 recommend that patients with a new presentation consistent with PEH (i.e., a headache precipitated by physical activity) undergo investigations including brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA), carotid and vertebral MRA, and lumbar puncture

and cardiological evaluation in specific conditions [19••]. Depending on institutional protocols, scanner availability, and patient characteristics, we feel that CT angiogram may be a reasonable substitute for MRA in select cases. Magnetic resonance venography is recommended in the evaluation of PHASA but not included in the PEH workup suggestions; this may be included at the physician's discretion, especially in patients with overlap syndromes and headache provoked by both sexual activity and exercise. The guideline mentions other possible entities to be investigated at the physician's discretion, including pheochromocytoma, carcinoid syndrome, intracranial hypertension, spontaneous intracranial hypotension, and cerebral venous sinus thrombosis.

Treatment

No good-quality evidence regarding treatment of PEH exists. However, studies indicate that PEH is self-limited, resolving in most individuals within months to years [2, 6, 7, 8•]. For this reason, avoidance of triggers may be of benefit. Some experts recommend an extended warm-up period prior to any exercise, or a gradual increase in activity level over weeks to months. Conservative measures that may be of use in minimizing or preventing exercise headaches include ensuring that equipment is not exacerbating headaches, for example that headgear is not restrictively tight. PEH also seems more frequent in hot weather and at high altitude, so avoiding these potentially aggravating factors may also be prudent when feasible [3••, 4, 10].

From a pharmacological perspective, small studies have suggested a role for indomethacin 25 mg tid, while other experts recommend indomethacin 25–50 mg, or other NSAIDs such as naproxen, taken as needed 30–60 min prior to exercise [20, 21]. Caution should be taken to avoid potential side effects of NSAIDs, such as gastric upset and/or bleeding with excessive use. Other medication classes of potential use in PEH include beta-blockers such as nadolol or propranolol at 1–2 mg/kg/day [7]. Pharmacological prevention of PEH with ergotamine tartrate or flunarizine has also been proposed, but further studies are needed on the topic of both acute and prophylactic treatment of PEH [15]. Given the typical natural history of the disorder, we suggest a trial of discontinuing such treatments every 6 months, with resumption of treatment if needed.

Conclusions

Previous studies on PEH are limited by their methodology, including many with questionnaire-based retrospective data, the potential for recall bias, small sample sizes, and varying definitions of PEH. This makes studying PEH somewhat of a

moving target. Likewise, PEH appears to have overlap or at the very least is comorbid with other primary headache disorders, and thus, studying it in isolation presents a major problem. Identifying patients with PEH is fraught with difficulty as many of these patients may not present to medical attention, or the typically self-limited course of the condition may influence patient recall and reporting. Furthermore, most survey-based studies have not included investigation of potential secondary causes or have not documented secondary causes identified, and thus, secondary causes of exercise headache may have been included in some studies. Further research is needed to better delineate the epidemiology and natural history of this condition, as well as to ascertain the optimal treatment strategy for PEH.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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