Natural History of Headache after Traumatic Brain Injury


Abstract

Headache is one of the most common persisting symptoms after traumatic brain injury (TBI). Yet there is a paucity of prospective longitudinal studies of the incidence and prevalence of headache in a sample with a range of injury severity. We sought to describe the natural history of headache in the first year after TBI, and to determine the roles of prior history of headache, sex, and severity of TBI as risk factors for post-traumatic headache. A cohort of 452 acute, consecutive patients admitted to inpatient rehabilitation services with TBI were enrolled during their inpatient rehabilitation from February 2008 to June 2009. Subjects were enrolled across 7 acute rehabilitation centers designated as TBI Model Systems centers. They were prospectively assessed by structured interviews prior to inpatient rehabilitation discharge, and at 3, 6, and 12 months after injury. Results of this natural history study suggest that 71% of participants reported headache during the first year after injury. The prevalence of headache remained high over the first year, with more than 41% of participants reporting headache at 3, 6, and 12 months post-injury. Persons with a pre-injury history of headache ($p<0.001$) and females ($p<0.01$) were significantly more likely to report headache. The incidence of headache had no relation to TBI severity ($p=0.67$). Overall, headache is common in the first year after TBI, independent of the severity of injury range examined in this study. Use of the International Classification of Headache Disorders criteria requiring onset of headache within 1 week of injury underestimates rates of post-traumatic headache. Better understanding of the natural history of headache including timing, type, and risk factors should aid in the design of treatment studies to prevent or reduce the chronicity of headache and its disruptive effects on quality of life.

Key words: headache; natural history; traumatic brain injury

Introduction

Headache is one of the most commonly reported symptoms following traumatic brain injury (TBI; Dikmen et al., 2010; Packard, 2005). Awareness of TBI-related symptoms, including headache, has increased as attention is focused on concussion or mild TBI sustained in sports injuries (Makdissi et al., 2010; Pellman et al., 2004), and as a result of the military conflicts in Iraq and Afghanistan (Hoge et al., 2008). While the mechanism of post-traumatic headache (PTH) remains poorly understood, it is classified as a secondary headache syndrome in the International Classification of Headache Disorders, 2nd edition (ICHD; The International Classification of Headache Disorders, 2004). Classification is primarily based on time of onset after injury or regaining consciousness (within 7 days), and chronicity of headache based on duration of headache lasting less than or greater than 3 months (acute versus chronic). However, several studies have reported a longer latency between injury and PTH and a higher incidence of chronic PTH than one would expect based on the ICHD definition (Martins et al., 2009; Theeler and Erickson, 2009).

The prevalence of PTH has ranged between 30% and 90% in retrospective studies that have been reported to date. In a review of available literature, Lew and associates (2006) reported that 18–22% of PTH lasted longer than 1 year. In an

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examination of returning service members, Hoge and colleagues (2008) reported that 32% of soldiers with mild TBI that included a loss of consciousness described having headaches in the past month. Headache was the only physical symptom that remained related to mild TBI after controlling for mental disorders (Hoge et al., 2008). Some studies have reported that the prevalence of PTH in civilian injuries is higher following mild TBI than moderate to severe TBI (Couch and Bearss, 2001; Lahz and Bryant, 1996; Uomoto and Esselman, 1993; Yamaguchi, 1992). Despite its high prevalence and chronicity, the actual diagnosis of PTH and its impact on functioning remains unclear.

Retrospective and cross-sectional studies, small or biased samples, and varying definitions of TBI have contributed to the poor understanding of the natural history of PTH. More definitive studies characterizing PTH are needed to improve their recognition and ultimately optimize the design of clinical trials of interventions to facilitate return to normal function in this population. Previous attempts to characterize PTH have not included representative samples followed longitudinally, with attention to possible risk factors for the development of headache (Baandrup and Jensen, 2004; Bettucci et al., 1998; Couch and Bearss, 2001; Faux and Sheedy, 2008). In the current study we sought to describe the rate of PTH over the first year following TBI, to compare persons who develop headache to those who do not, and to examine potential risk factors for the development of PTH.

Methods

Study participants

Four hundred fifty-two participants with TBI were enrolled in the study during acute inpatient rehabilitation hospitalization following TBI. Recruitment occurred in tandem with that of the larger model system database study at 7 TBI Model Systems (TBIMS) centers between February 2008 and June 2009. Follow-up assessments were completed by July 2010. Inclusion criteria were the same as for the TBIMS, for which participants: (1) presented to the designated TBIMS acute care hospital within 72 h of injury; (2) received both acute medical and acute rehabilitation care within the same system; (3) had sustained a TBI with at least one of the following characteristics: Glasgow Coma Scale (GCS) score <13 on emergency admission (not due to intubation, sedation, or intoxication), loss of consciousness >30 min (not due to sedation or intoxication), post-traumatic amnesia (PTA) >24 h, or trauma-related intracranial abnormality on neuroimaging; and (4) were aged 16 years or older. Participants were excluded if they were incarcerated or did not have telephone access. Informed consent was obtained as approved by the institutional review boards of all 7 institutions. If the subject was unable to consent due to persistent confusion, proxy consent was obtained from their legally authorized representative.

Initial data were collected on headache and headache characteristics following TBI. Questionnaires completed by proxies occurred with 68 patients at initial evaluation, 59 at 3 months, 70 at 6 months, and 48 at 12 months post-injury. A comparison of proxy to participant responses found no significant difference in report of headache (versus no headache) pooled over time, but underreporting of headache at 3 and 6 months post-injury by proxies compared to participants with TBI. Of the 452 enrolled patients, follow-up rates were 81% at 3 months, 90% at 6 months, and 88% at 1 year post-injury.

Measurement

As part of the overarching TBIMS study, basic demographic data were collected from participants during inpatient rehabilitation, including age at injury, sex, race (white, black, Asian/Pacific Islander, Native American, Hispanic, and other), completed high school/did not complete high school, and cause of injury (moving-vehicle-related, violence, sports, fall, hit by object, and other). Severity of TBI was obtained using duration of prospectively assessed PTA categorized as mild (0–1 day of PTA), moderate (1–7 days PTA), or severe (>7 days PTA).

A headache survey included questions about current headache at initial evaluation during inpatient rehabilitation (yes/no), history of premorbid headache prior to injury, and headache at follow-up. In the current study, PTH was defined as any headache occurring after injury, and did not follow the ICHD classification limitation based on occurring within the first 7 days post-injury or regaining consciousness. History of premorbid headache and follow-up PTH at each time point were calculated as yes/no headache in the preceding 3 months, and by frequency (less than once per month, once a week to once a month, several times a week to daily, and no headache in the past 3 months). History of headache was determined by the question “How often did you have a moderate to severe headache before your injury?” Prevalence of headache was calculated using positive endorsement of any headache at each assessment point divided by the total number of responders at each assessment. Incidence and cumulative incidence were calculated for total PTH using all possible respondents (n = 452), beginning with initial assessment during inpatient rehabilitation, with incidence showing new cases that occurred at each follow-up after the initial assessment, and the cumulative incidence being a sum of all participants who ever endorsed headache over time. Incidence and cumulative incidence were also calculated based on frequency of headache (less than one per month, one per week to one per month, and several times a week to daily) for follow-up assessments (3, 6, and 12 months). Finally, we also compared those who had no headache at all follow-ups (3, 6, or 12 months) to those who either reported headache at all 3 time points, or who reported headache at some (one or two) time points.

Statistical analysis

Chi-square analyses were used to compare those with and without a history of headache, males and females, and TBI severity across consistency of headache over time.

Results

Demographics of the 452 participants enrolled in the study are presented in Table 1. The majority of participants were
male, white, had completed high school, and were injured in vehicle-related incidents. Table 1 also shows that the prevalence of headache remained consistently high across the first year after injury. While only 18% of the participants reported a history of headache prior to injury, more than 41% of individuals reported headaches at initial evaluation, and at 3, 6, and 12 months post-injury. Inpatient headache (fewer than 1 per month) was less prevalent than frequent headaches (several times per week or daily), 16% compared to 22% at 12 months, respectively. Finally, of those participants who completed all assessments, the majority reported headache at one or two time points after injury, with 23% reporting headache at all three post-injury time points.

Incidence and cumulative incidence of PTH over time

During the first year after TBI, the cumulative incidence of headache was 71% (Fig. 1). The highest incidence of headache occurred at baseline, when 44% of participants endorsed headache. However, while new headache reports decreased over time, the incidence of new headache remained close to 20% from 3–12 months after injury. Figure 1 also shows the incidence and cumulative incidence for the subset of participants who endorsed frequent headaches, or headaches that occurred several times per week or daily. Eighteen percent of participants reported frequent headache at 3 months post-injury, with a total cumulative incidence of 31% over the first year after injury. In contrast, participants with less frequent headaches reported incidences of 5% (infrequent headache), and 13% (between 1 per week and 1 per month), at 3 months post-injury (data not shown).

Potential risk factors in the development and maintenance of PTH

Demographic factors including age and sex were examined as potential risk factors for the development of PTH, along with prior history of headache before TBI, cause of injury, and severity of TBI. History of headache and being female were found to be significantly related to higher rates of headache over time; 81 of the 452 (18%) participants reported a history of headache. We compared the population of participants who reported having a history of headache prior to injury with those who did not. The results are shown in Figure 2 for participants with complete data at 3, 6, and 12 months post injury (n = 333). Individuals with a history of headache were significantly more likely to report headache at all time points compared to those without a history of headache (45% versus 19%; chi-square = 25.1; p < 0.001). While the majority of those with a history of pre-injury headache reported at least one headache over 1 year, there were 5 participants (9%) with pre-injury headache who reported no headaches over the entire first year after injury. For those with a pre-injury headache, 91% continued to report at least one headache over time compared to those without a history of pre-injury headache (62%). Though the participants were primarily male (71%), females were more likely to report any headaches over time (74% versus 63%), and were much more likely to report headache at all time points (37%) compared to males (18%; chi-square = 13.5; p < 0.01; Fig. 3).

We examined severity of TBI as a determinant of PTH (Fig. 4). The incidence of headache reported across 3, 6, and 12 months post-injury was not significantly different whether TBI severity was mild (0–1 day), moderate (1–7 days), or severe (>7 days), as determined by length of PTA (77%, 68%, and 65%, respectively; chi-square = 2.3, p = 0.67). Examination of age and cause of injury showed no relationship with change in headache over time (data not shown).

Discussion

The prevalence of PTH was over 40% at all time points over the first year after TBI, which suggests that PTH is a frequent problem that continues long after the initial TBI. In addition, PTH is a widespread problem, with a cumulative incidence reaching 71% in this prospectively collected sample of participants. This high rate of headache over time has not been previously reported. Prior research has suggested lower prevalence rates of headache at 1 year, between 18% and 33% (van der Naalt et al., 1999; Walker et al., 2005), with only one study of veterans (who were mostly male), with rates of headache at 1 year of 40% (Walker et al., 2005).

Table 1. Demographics and Headache Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total participants</td>
<td>452</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.7 ± 19.7</td>
</tr>
<tr>
<td>Male</td>
<td>322 (71%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>332 (73%)</td>
</tr>
<tr>
<td>Black</td>
<td>74 (16%)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>13 (3%)</td>
</tr>
<tr>
<td>Native American</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>28 (6%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (0%)</td>
</tr>
<tr>
<td>Completed high school</td>
<td>314 (69%)</td>
</tr>
<tr>
<td>Cause of injury</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>238 (53%)</td>
</tr>
<tr>
<td>Violence</td>
<td>44 (10%)</td>
</tr>
<tr>
<td>Sports</td>
<td>16 (4%)</td>
</tr>
<tr>
<td>Fall</td>
<td>124 (27%)</td>
</tr>
<tr>
<td>Hit by object</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>23 (5%)</td>
</tr>
<tr>
<td>TBI severity</td>
<td></td>
</tr>
<tr>
<td>Mild (&lt;1 day PTA)</td>
<td>25 (6%)</td>
</tr>
<tr>
<td>Moderate (1–7 days PTA)</td>
<td>75 (17%)</td>
</tr>
<tr>
<td>Severe (&gt;8 days PTA)</td>
<td>346 (77%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Headache characteristics</td>
<td></td>
</tr>
<tr>
<td>Overall prevalence of PTH</td>
<td></td>
</tr>
<tr>
<td>Pre-injury (n = 446)</td>
<td>81 (18%)</td>
</tr>
<tr>
<td>Inpatient rehabilitation (n = 342)</td>
<td>201 (47%)</td>
</tr>
<tr>
<td>3 Months post-injury (n = 362)</td>
<td>167 (46%)</td>
</tr>
<tr>
<td>6 Months post-injury (n = 402)</td>
<td>166 (41%)</td>
</tr>
<tr>
<td>12 Months post-injury (n = 392)</td>
<td>173 (44%)</td>
</tr>
<tr>
<td>Headache consistency (n = 333)</td>
<td></td>
</tr>
<tr>
<td>No headaches at any time</td>
<td>112 (34%)</td>
</tr>
<tr>
<td>Headaches at all time points</td>
<td>78 (23%)</td>
</tr>
<tr>
<td>Headaches at intermittent points</td>
<td>143 (43%)</td>
</tr>
</tbody>
</table>

*333 participants completed questionnaires at all 3 follow-up time points (3, 6, and 12 months post-injury). PTA, post-traumatic amnesia; TBI, traumatic brain injury; PTH, post-traumatic headache; SD, standard deviation.
Our findings show that 28% of new headaches are reported after the initial evaluation, occurring at 6 and even 12 months-post injury. The ICHD criteria for a diagnosis of acute or chronic PTH requires that onset of headache must occur within 1 week of regaining consciousness after TBI; therefore, the issue of any temporal relationship is important. Individuals with more moderate or severe TBI may not be responsive or able to verbalize pain due to headache within the first week after injury (Sherman et al., 2006). Even the authors of the ICHD diagnostic criteria acknowledge the difficulty in distinguishing a high general population prevalence tension-type headache from PTH occurring weeks or months after trauma (The International Classification of Headache Disorders, 2004). Our results are similar to those found by Theeler and Erickson (2009), who examined the temporal association of headaches following mild head or neck trauma in a military population, and found that only 27% of headaches developed within a week post-trauma. Whether such classification, or misclassification, of headache after TBI is important is under debate. In its present form, a diagnosis of PTH does not rely on symptom criteria or provide direction for treatment. However, misclassification or missed diagnoses may underestimate the true incidence and prevalence of PTH, which could negatively impact treatment decisions as well as interfere with medico-legal issues in securing financial support for ongoing management of TBI.

In our sample, rates of PTH were high in all three severity groups, with no significant differences as a function of length of PTA. Further studies need to be conducted to confirm this finding in representative and prospectively studied groups of participants with a broad range of TBI severity. Our sample of “mild TBI” (i.e., PTA less than 1 day) contained only 25 participants (6% of the total participants) who were admitted for inpatient rehabilitation. These participants may be classified as having complicated mild traumatic brain injuries, as 24 of the 25 had GCS scores of 13–15, and 23 of the 25 had head CT
abnormalities (Williams et al., 1990). However, the presence of CT scan abnormalities would classify these injuries in the moderate-to-severe category in some classification systems (Malec et al., 2007), making this sample more homogeneous and possibly limiting the extent to which differences in PTH incidence differ between injury severity classes. Prior research that has supported the idea of higher rates of headache in individuals with mild TBI has often focused on individuals presenting to outpatient clinics with a wide variation in time since injury and with varying presenting problems (Couch and Bearss, 2001; Uomoto and Esselman, 1993). While our mild group is likely more severely injured than those with mild TBI referred to in the literature, our rates of PTH with varying levels of severity of brain injury are similar and high. Our finding is consistent with the findings of a prior study which reported on rates of post-traumatic symptoms that included headache at 1 year in a prospectively studied group of participants with TBI with a broad range of TBI severity (Dikmen et al., 2010). Future studies will need to include similar definitions of TBI severity as well as headache in representative and non-select cases.

Consistent with prior research, we found that a history of premorbid headache is significantly related to headache after TBI. This highlights the importance of assessment of premorbid headache as a risk factor for PTH, and may guide treatment options for physicians caring for individuals with TBI. In

FIG. 3. Gender as a determinant of post-traumatic headache (PTH). All time points category includes reports of headache (HA) at 3, 6, and 12 months post-injury. Some time points category includes reports of HA at one or two, but not all three time points (chi-square = 13.5; $p < 0.01$).

FIG. 4. Severity of traumatic brain injury (TBI) as a determinant of post-traumatic headache (PTH). All time points category includes reports of headache (HA) at 3, 6, and 12 months post-injury. Some time points category includes reports of HA at one or two, but not all three time points (chi-square = 2.3; $p = 0.67$).
addition, females were found to have higher rates of headache, similar to the rates seen in the general headache literature (Jensen and Thulstrup, 2001). In the current study, females were not only found to have higher rates of PTH overall, but also reported headache at all time points significantly more frequently than males. Whether this was related to hormonal changes or to other sex characteristics was not assessed, since such data were not collected. Future research is needed to examine whether these potential risk factors of sex and history of headache prior to injury may influence the treatment or diagnosis of PTH.

The current study does have limitations. First, all information about headache was collected by trained examiners using a standardized questionnaire in person (initial assessment), or over the phone (for follow-ups), and there was no physician evaluation. However, the headache questionnaire was developed by experts in headache and TBI to include relevant data similar to that which would be collected in a physician’s office. Second, only participants who were hospitalized for rehabilitation were eligible for our study; therefore the sample may not be entirely representative of patients with TBI within this severity range in general. However, it is important to point out that subject selection was not related to pre- or post-injury headache.

Third, we cannot determine the effect of TBI as compared to injuries to other body parts with respect to headache, as we did not have a non-head-injured trauma control group. Finally, information about the headaches was collected from proxies that knew the patient well pre- and post-injury in a fraction of the cases (15%), either due to the degree of neuropsychologic impairment precluding valid testing at baseline, or lack of availability of the subject at follow-up evaluations. However, proxies tended to report headache less frequently than participants, and therefore our estimates of headache represent an underestimation of the likely rates of headache in our sample.

In summary, our data show that PTH is a frequent consequence of TBI and occurs in a much larger percentage of persons than previously reported. We found that 23% of participants reported headache at all time points over 1 year after injury, with 22–29% reporting frequent headaches (multiple times per week/daily). In contrast only 4–5% of persons with headaches in the general population endorse chronic daily headache (>15 days per month; Castillo et al., 1999; Scher et al., 1998; Silberstein and Lipton, 1994). Finally, the severity of TBI, at least within the range represented in our sample, does not appear to determine the incidence of PTH. We found a similar rate of PTH across a range of PTA durations.

Future research is needed to determine the clinical characteristics of PTH. Our findings and future findings of clinical characteristics may have relevance for the development of a new classification scheme for PTH. Better understanding of the characteristics and natural history of PTH may provide us with a framework on which to study early, aggressive treatments to prevent or reduce the frequency of chronic PTH, and to alleviate suffering.

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Dr. Hoffman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Author Disclosure Statement

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References


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