

Characteristics of posttraumatic headache following mild traumatic brain injury in military personnel in Iran

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Abstract

Objectives The primary goal of this study was to evaluate the incidence and characteristics of posttraumatic headache attributed to mild brain injury in military personnel in Iran within a prospective and observational study design.

Methods A prospective observational descriptive study was conducted with a cohort of military personnel under military education during a 6-month period at the Military Education Center in Isfahan, Iran. 322 military personnel under education were selected randomly and were given a 13-item mild brain injury questionnaire accompanied with affective disorders and headache questionnaires and were reevaluated after a 3-month interval.

Results A total of 30 (9.3 %) of the 322 military personnel met criteria for a mild brain injury. Among them, 18 personnel (60 %) reported having headaches during the 3-month reevaluation. PTHs defined as headaches beginning within 1 week after a head trauma were present in

5.6 % of military personnel under study during 6 months. In total, 67 % of posttraumatic headaches (PTH) were classified as migrainous or possible migrainous features. Patients with affective disorders such as posttraumatic stress disorder and depression were at a higher risk for developing PTH following mild brain injury ($p < 0.05$). PTH did not relate to demographic factors such as age or type of trauma.

Conclusions Posttraumatic headache attributed to mild brain injury is a common disorder in military personnel. Migrainous features are predominant among them in comparison with the general population. PTH is not related to a type of trauma, but has association with affective disorders.

Keywords Posttraumatic headache · Mild traumatic brain injury · Blast injury · Migraine · Affective disorders

Abbreviations

PTH	Posttraumatic headache
ICHD-2	International classification of headache disorders
PTSD	Posttraumatic stress disorder
PHQ-9	Patient health questionnaire
NSAID	Non-steroidal anti-inflammatory drugs
APTH	Acute posttraumatic headache
CPTH	Chronic posttraumatic headache

Introduction

Headache is the most frequent symptom following mild brain injury [1]. Posttraumatic headache (PTH) attributed to mild brain injury is defined according to the

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International classification of Headache Disorders, 2nd Edition (ICHD-2) [2, 3]. Acute posttraumatic headache (APTH) is defined as a headache developing within 7 days after head trauma, and a headache persisting more than 3 months after the trauma is a chronic posttraumatic headache (CPTH) [2, 3].

The prognosis of APTH which is generally favorable in the general population occurs in nearly half of mild brain injuries and usually resolving within a few weeks [1, 4–7]. CPTH was reported in 15–50 % of those injuries [8–10]. In comparison, military troops are at risk for PTH because of head trauma sustained during combat operations [1]. Between 10 and 25 % of US military troops returning from Iraq or Afghanistan have had concussions while deployed, with explosive blast being the most common cause [11–15]. The prevalence of PTH is 37 % in returning US Army soldiers who had a concussion while serving in a combat zone in the Middle East [8]. In total, 58 % of PTHs were classified as a migraine and had a higher attack frequency and an increasing prevalence of CPTH compared with headaches not directly attributed to head trauma [8].

Previous studies have suggested that affective disorders such as posttraumatic stress disorder (PTSD) and depression also have a role in APTH [2]. It seems likely that patients with affective disorders suffering mild head injury are at a higher risk for developing chronic pain [16, 17]. In addition, they are well-known comorbidities of primary headache disorders and add up to disease-related disabilities [18, 19]. This supports a hypothesis of Saper, who said that it might not be so much what happens to the head, but whose head it happens to [20]. A brain that is already sensitized or dysfunctional because of a preexisting affective disorder may react more easily with a headache after a mild head trauma [2].

Posttraumatic headaches are typically treated like the primary headaches that they most closely resemble [21, 22]. Although practice guidelines have been developed by the US Department of Defense (DoD) and department of Veterans Affairs (VA) for managing headaches after mild brain injury [23], these treatment recommendations have not been validated by clinical studies in troops with PTH [23]. Also, no study has been conducted to determine the incidence and characteristics of PTHs and their treatment outcomes attributable to mild brain injury in military personnel in Iran.

We conducted an observational study prospectively assessing incidence and characteristics of PTH as defined in ICHD-2 for the first time in a cohort of military personnel under military operation education in Iran. It is hoped that the findings will provide preliminary evidence to guide the management of PTH in troops and military veterans.

Methods

This study was approved by the Neuroscience Research Center of Baqiyatallah University of Medical Sciences. A prospective cohort study was conducted with military personnel under military education at the Military Education Center in Isfahan in Iran between 22 May 2013 and 19 Feb 2014.

All subjects were members of the same brigade consisting of approximately 2500 military personnel. According to Cochrane sample size formula the size of 333 members was calculated as the appropriate sample size for our study ($\alpha = 0.05$, $N = 2500$, $p = q = 0.5$, $d = 0.05$).

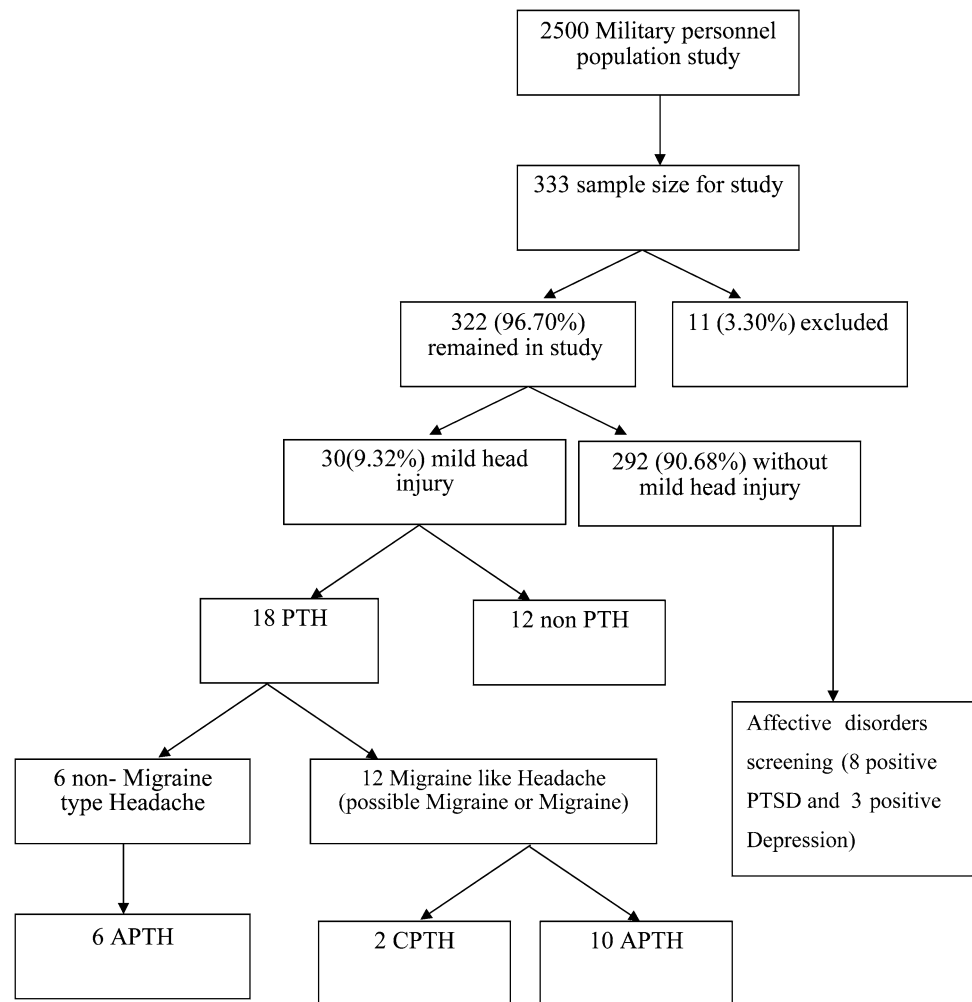
With computer-based simple randomized sampling according to military personnel codes and up to maximum capacity of our military health facilities and medical staff, 333 members were selected for entering into the study and 322 members of those (333 study subjects excluding 11 members of them) were evaluated at the emergency department of the Military Center over a 6-month period to estimate the incidence rate and characteristics of PTH.

We informed our study members to visit to emergency department after any symptoms following head trauma which were described for them. Figure 1 summarizes our study flow chart. Informed consent from each member has been obtained.

All the sample members were evaluated for PTH with a standardized baseline evaluation that included a comprehensive clinical history, physical examinations, and a battery of screening questionnaires during the 6 months of observation examined 2 times at least 3 months apart.

At the initial visit, occurring within 48 h after head trauma, headache-related disability was assessed using the Migraine Disability Assessment scale (MIDAS) and brain injury was assessed using the Rivermead Post Concussion Symptoms Questionnaire [24, 25]; posttraumatic stress disorder (PTSD) symptoms were assessed using the PTSD checklist (PCL) using a score of ≥ 50 as a positive screen, and depression was screened using the Patient Health Questionnaire-9 (PHQ-9) using a score ≥ 15 as a positive screen [1, 26, 27] in Persian language translated format. The same set of questionnaires was also performed 3 months later at the second call between days 90 and 100. These questionnaires were chosen because they allow a quick and valid screening for the corresponding affective disorders. Patients underwent a detailed telephone interview between days 7 and 10 and between days 90 and 100 after the injury.

Headaches were classified according to the ICHD-2 as migrainous, possible migrainous and non-migrainous features [3], (Table 1). The headache questionnaires sought the presence, frequency, severity, duration and the time since onset of headaches occurring in the previous

Fig. 1 Study flow chart**Table 1** Diagnostic criteria of PTH attributed to mild brain injury according to ICHD-2

Headache, no typical characteristics known, fulfilling criteria C and D

Headache trauma with all the following:

Either no loss of consciousness, or loss of consciousness of less than 30-min duration

Glasgow Coma Scale (GCS) ≥ 13

Symptoms and/or signs diagnostic of concussion

Headache develops within 7 days after head trauma

One or other of the following:

Headache resolves within 3 months after head trauma

Headache persists but 3 months have not yet passed since head trauma

3 months. The following features of migraines were also asked in the questionnaires: (1) pain that was worse on one side of the head; (2) throbbing or pulsating pain; (3) pain exacerbated by physical activity; (4) pain severe enough to disrupt normal activities; (5) pain accompanied by nausea

or vomiting; (6) pain exacerbated by light and sound. Headaches with all the above criteria were classified as migrainous features. Headaches with at least three features of migraine, which did not fulfill the above criteria, were classified as possible migrainous features. Headaches with only 0, 1 or 2 migraine features were classified as other headaches [28].

Posttraumatic headaches were classified into blast PTH and non-blast PTH. Blast PTH was defined as PTH precipitated by an explosive blast of any type. Blast injuries were not further subdivided into primary, secondary or tertiary blast injuries. Non-blast PTH refers to PTH precipitated by a traumatic mechanism without blast exposure [1].

Inclusion criteria were men aged between 18 and 65 years with mild head injury according to criteria of ICHD-2 [3] for diagnosis of APTH and CPTH (Table 1). Patients were excluded for medication overuse and substance abuse. We further excluded patients with a history of preexisting chronic headache, as we aimed to avoid mingling of APTH with another daily or nearly daily

headache for a first characterization of APTH [2]. This study was carried out after approval by the local ethics committee.

Characteristics of headaches were described as frequencies or mean values ± standard deviation (SD), as applicable. Binary logistic regression analysis was used for comparing patients with and without PTH. For calculating the differences between unpaired groups, Fisher exact test was used. Alpha level significance was set at 5 %. All analyses were carried out using SPSS 18.0.

Results

30 cases with mild brain injury that were diagnosed during the 6-month study period met study inclusion–exclusion

Table 2 Baseline characteristics of 30 patients with mild brain injury

Age, years (mean ± SD)	27.36 ± 4.82
Gender, 100 % male [n (%)]	30 (100)
Family status [n (%)]	
Single	8 (26.7)
Married	22 (73.3)
Education [n (%)]	
Elementary	1 (3.3)
High school	11 (36.7)
University	18 (60)

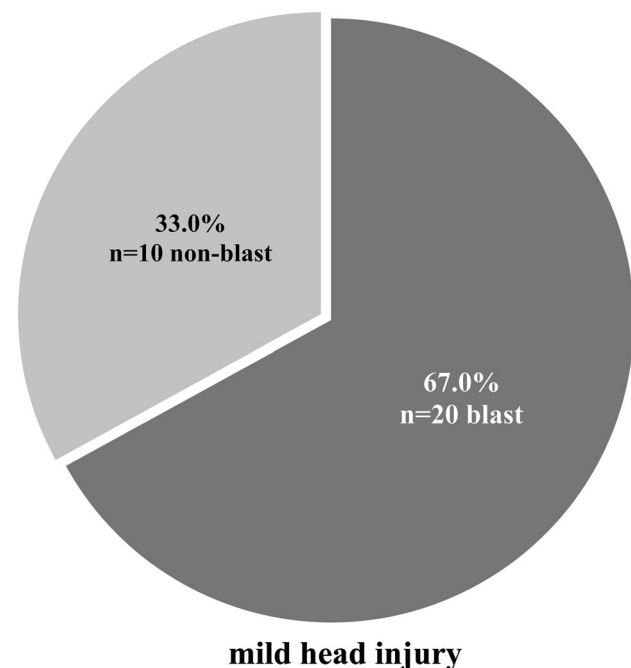


Fig. 2 Mechanism of mild brain injury n = 30 out of 322 sample size

criteria. Among the 333 study subjects, 11 members were excluded and among the remaining 322 members, 30 of them had mild brain injuries including 18 with PTH and 12 without headaches. Of these 30 (9.3 %) patients, all were men with mean age 27.4 ± 4.8 years. Further details of the patients are summarized in Table 2.

Causes of trauma were blast in 20 patients and were non-blast in 10 of them. The causes of non-blast were fall, motor vehicle accident, sports and fist fight/assaults [4, 7, 13] (Fig. 2).

Headache after trauma was experienced by 18 (60 %) patients. Headache developed in an acute pattern that lasted less than 3 months in the majority (16/18, 88.9 %) and occurred in 2 patients with a chronic pattern (11.1 %). 12 patients (40 %) did not have any headaches at all. APTH resembled migrainous or possible migrainous in 10 patients and CPTH resembled migrainous in 2 patients (Table 3).

The most frequent medications used were over-the-counter medications, including acetaminophen (83.3 %), non-steroidal anti-inflammatory medications (44.4 %) and a combination of both (33.3). 1 patient (5 %) did not use any medications. The medications used to treat headaches did not differ significantly (*p* > 0.05) between migraine-like headaches and non-migraine-like headaches (Table 4).

Comparisons of patients with and without PTH are summarized in Table 5. Age did not differ between the groups, whereas the number of posttraumatic symptoms did differ with statistical significance (*p* < 0.001). Out of a total of 13 posttraumatic symptoms, patients with PTH reported a mean of 4.1, but patients without PTH only 1.8 symptoms. Furthermore, the PTSD score and PHQ-9 score which measure affective and somatic symptoms of a PTSD disorder and depression, respectively, were significantly higher in patients with PTH (*p* < 0.001 PTSD score, *p* = 0.002 PHQ-9 score).

At 6 months of study after trauma with at least two episodes of interviews 3 months apart for each military personnel, 30 (9.3 %) patients out of 322 could be identified with mild brain injury. PTH had been present in 18 (60 %) patients and absent in 12 (40 %). In only 2 patients initially reporting PTH, the headache had not abated and

Table 3 Classification of PTH by clinical appearance according to the ICHD-2 criteria of Migraine—Madigan Army Medical Center [4]

	PTH (n = 18) ^a	
	APTH (n = 16) (%)	CPTH (n = 2) (%)
Migrainous features	5/30 (16.7)	2/30 (6.6)
Possible migrainous features	5/30 (16.7)	0 (0)
Non-migrainous features	6/30 (20)	0 (0)

^a Twelve cases [12/30 (40 %)] without any headache

Table 4 Medication used for migraine-like and non-migraine headaches

	All PTH (<i>n</i> = 18) ^a (%)	Migraine like (possible or definite) (<i>n</i> = 12) (%)	Non-migraine like (<i>n</i> = 6) (%)	<i>p</i> value*
Triptans	0 (0)	0 (0)	0 (0)	–
Non-Triptans				
NSAID	8/18 (44.4)	6/12 (50)	2/6 (33.3)	0.44
Acetaminophen	15/18 (83.3)	11/12 (91.7)	4/6 (66.7)	0.24
Combination drugs	6/18 (33.3)	5/12 (41.7)	1/6 (16.7)	0.31
Any medication	1/18 (5.5)	0/12 (0)	1/6 (16.7)	0.33

* Fisher exact test

^a Some patients may be present in multiple classified groups**Table 5** Comparison of patients with mild brain injury with and without PTH

	Mild head injury (<i>n</i> = 30)			<i>p</i> value*
	PTH (<i>n</i> = 18)	Non-PTH (<i>n</i> = 12)	OR (CI 95 %)	
Age (mean ± SD)	28.05 ± 4.63	26.33 ± 5.12	0.87 (0.48–1.59)	0.347
PTSD score (mean ± SD)	52 ± 19.01	22.33 ± 10.36	0.96 (0.87–1.06)	<0.001
PHQ-9 score (mean ± SD)	10 ± 7.99	1.83 ± 2.25	0.92 (0.67–1.28)	0.002
Post traumatic symptoms (mean ± SD)	4.11 ± 1.87	1.83 ± 0.71	0.10 (0.01–1.12)	<0.001
Blast trauma [<i>n</i> (%)]	10/18 (55.6 %)	10/12 (83.3 %)	0.16 (0.01–4.95)	0.236

* Binary logistic regression

led to a diagnosis of CPTH. In the majority of patients with PTH, the headache had abated and did not happen in recurrent episodes. PTHs defined as headaches beginning within 1 week after a head trauma were present in 5.6 % of military personnel under study.

Among rest of members under study without any brain injury (*n* = 292), 8 patients with PTSD positive and 3 patients with depression-positive results were identified during 6 months of study. They were referred for further psychiatric evaluations.

Discussion

This is the first study in Iran to prospectively assess the characteristics of PTH as defined in ICHD-2 in military personnel. During 6 months of observation of a sample size of 333 military personnel, 11 members were excluded from the study and 30 patients with mild brain injury were diagnosed. All patients were male between 19 and 37-year old with mild brain injury and without substance abuse and chronic daily headache. After 6 months of follow-up, the major findings were (1) 60 % of patients experienced headache following trauma; (2) PTH was usually acute and self-limiting except in 2 patients (6.7 %) and frequently characterized by migrainous features; (3) explosive blast was the leading cause of the trauma; (4) the headache was

not related to demographic factors, such as age or type of trauma (blast or non-blast); otherwise, it was higher in patients with affective disorders such as PTSD or depression; and (5) the type of medications used for treatment did not differ in distinguished classified headache groups.

The yearly incidence of head trauma is 350 per 100,000 in the general population in Europe [29]. Mild head trauma accounts for the majority (80 %) cases [30, 31]. PTHs in the civilian population often resemble primary headaches with 34 % resembling tension-type headaches and 29 % resembling migraines with 15–50 % of them was reported as chronic posttraumatic headache according to ICHD-2 [21, 32]. Theeler et al. [8], using a questionnaire-based study of US soldiers with a history of concussion during deployment to Iraq or Afghanistan, found that 97 % of returning troops with deployed-related concussions reported headaches in the final 3 months of deployment and in addition, 58 % of PTHs attributed to military-related mild brain injury in troops can be classified as having migrainous features with an additional 31 % classified as possible migrainous. That migrainous type is the most common military PTH has been confirmed by a large-scale post-deployment survey and smaller clinical samples [8, 15, 28, 33, 34]. Our study supports their findings that incidence of mild brain injury was higher than in the general population (18.6 % yearly) and migrainous type was the most common feature of PTHs among military personnel.

Thus, migraine-like headaches appear to have association with military-related mild brain injury. The reason for discrepancy in headache patterns observed in military and general populations is unknown. One possibility is that the pathogenesis of headaches caused by military-related trauma, which is frequently precipitated by an explosive blast, may be different than the mechanisms responsible for headaches after trauma in civilians that tend to be caused by acceleration–deceleration injury or blunt impact [8, 29, 35–38]. Explosive blasts are the leading cause of head trauma in deployed US military troops, whereas motor vehicle accidents, falls, assaults and sports are the common causes of concussion in civilians [11–15]. In our study, 67 % of mild brain injuries were due to explosive blasts during military operation training, which is consistent with the results of previous studies [1, 8].

Previous studies have suggested that affective disorders such as PTSD and depression were more frequent in patients with PTH [2, 19, 25, 39, 40]. Our study found that patients with PTSD or depression showed higher incidence of PTH after mild brain injury in military personnel. PTH was neither related to demographic factors such as age nor the type of the head trauma (blast or non-blast) (Table 5).

The finding that the number of posttraumatic symptoms was significantly higher in patients with PTH than in those without confirms other studies that were conducted only on civilians [2, 41–43]. Our study contributes another aspect to this issue about military personnel. High levels of depression or PTSD in posttraumatic patients increase both the risk of PTH and evolving acute PTH to chronic pattern. Further longitudinal studies are needed to explore the complex interactions between affective disorders and PTH.

Our findings show that the most frequent medications prescribed by our military health physicians for patients with PTH are over-the-counter medications including acetaminophen (83.3 %), NSAID (44.4 %) and a combination of both (33.3 %) with no patients using triptans, narcotics, muscle relaxants or any other medications. Other studies support the current DoD/VA treatment guidelines for mild brain injury which lists triptan medications as a treatment choice for PTH [1, 18, 37, 44, 45]. Triptan medications may improve the function and quality of life of troops with moderate to severe PTH who do not experience reliable relief with simple analgesics [1]. In our study, medications used to treat PTH did not differ significantly ($p > 0.05$) between different types of PTH (migrainous features vs non-migrainous features) and this shows that treatment plans were not evidence based according to current guidelines for PTH related to mild brain injury complications [3, 23, 38].

As recently discussed by Evans [22], and other studies [2, 8] indicated, the ICHD-2 diagnostic criteria for PTH and its classification are somewhat arbitrary, particularly the requirement that the headache must begin within 7 days

of trauma. Also Criterion A cannot be specified more accurately. The screening criteria we used for migraines were similar but not identical to ICHD-2 according to Madigan Medical Center questionnaires used for screening PTH in US army soldiers returning from deployment to Iraq and Afghanistan [8] perhaps resulting in misclassification of headaches in some of them.

This study has multiple limitations related to questionnaire-based prospective observation design. Military personnel were asked to recall events and symptoms that occurred during military operations which probably resulted in some recall bias. The main shortcoming of this study is the sample size. The findings of this study may not be applicable to all military personnel under military education in Iran.

Strengths of the study include performance of a careful clinical evaluation to accurately detect and classify patients with mild brain injury, comparison of PTH subgroups with regard to blast or non-blast injury and a prospective observation of military personnel that makes the study different from previously published studies examining PTH in military personnel as well as it occurring for the first time in Iran.

The primary aims of this study were to determine the incidence and characteristics of posttraumatic headache (PTH) after mild brain injury among military personnel in Iran. PTH, defined as headaches beginning within 1 week after mild brain injury, was present in 60 % of patients with mild brain injury during the 6 months of study on military personnel in Iran whom presented in military operation education. Migrainous feature was the predominant headache feature among patients with PTH. Patients with affective disorders such as PTSD and depression were at a higher risk of developing PTH. However, occurrence of PTH after mild brain injury was not related to the type of injury (blast vs non-blast). Recommendations for treating PTH attributable to mild brain injury in Iran military personnel can be reasonably drawn from findings of this study, including changing the current symptomatic treatment medications to a comprehensive treatment approach that utilizes pharmacologic and non-pharmacologic treatments and addresses co-morbid conditions such as PTSD and depression in our military troops and veterans with PTH. Controlled trials are greatly needed to validate the findings of this observational study and additional studies are also needed to fully understand the interrelationship of mild brain injury and PTH in our military personnel.

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Conflict of interest The authors declare that there is no conflict of interest.

Ethical standard This study was carried out after approval by the local ethics committee. Also, participants' consent was received through questionnaires.

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