Headache
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ISSN 0017-8748
doi: 10.1111/j.1526-4610.2011.01946.x
Published by Wiley Periodicals, Inc.

Research Submission

Prevalence and Treatment of Headaches in Veterans With Mild Traumatic Brain Injury

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Objectives.—To report the prevalence and characteristics of headaches in veterans with mild traumatic brain injury (TBI) and to describe most common treatment strategies after neurological evaluation.

Methods.—We conducted a retrospective cohort study. The setting was a United States Veterans Healthcare Administration Polytrauma Network Site. The study participants consisted of 246 veterans with confirmed diagnosis of mild TBI. The main outcome measures were: Self-reported head pain occurring 30 days prior to initial mild TBI screening; headache severity measured by the Neurobehavioral Symptom Inventory; headache characteristics; and treatment prescribed by neurologists.

Results.—The majority (74%) of veterans with a confirmed diagnosis of mild TBI (N = 246), due largely to blast exposure, reported headaches in the 30 days preceding the initial mild TBI evaluation. Thirty-three percent of these veterans (N = 81) were referred to neurology for persistent headaches. Of the 56 veterans attending the neurology evaluation, 45% were diagnosed with migraine headaches and 20% with chronic daily headaches. The most commonly used abortive agents were triptans (68%) and the most common preventive medications were anticonvulsants (55%) and tricyclics (40%).

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Disclaimers: Part of the materials found in this manuscript was presented as a poster at the American Headache Society 52nd annual meeting, June 24-27, 2010.

Funding: This study was supported by the Department of Veterans Affairs, Office of Research and Development, Health Services Research and Development Service as grant IIR 07-188-3, Locally-Initiated Project 42-533 and the Edward Hines Jr. VA Hospital, Center for Management of Complex Chronic Care (CMC3). The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

Reprints will not be available from the authors.

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Accepted for publication April 19, 2011.

Author Financial Disclosure and Conflicts of Interest: We certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on us or on any organization with which we are associated AND, if applicable, we certify that all financial and material support for this research (eg, NIH or NHS grants) and work are clearly identified in the title page of the manuscript.

Conclusion.—There was an increased prevalence of headaches in veterans with mild TBI. Most of the TBI veterans in our study group were exposed to blast injury and findings indicate that the nature of head trauma may be contributing to headaches. Findings highlight the need for developing effective headache prevention and treatment strategies for all persons with mild TBI and in particular for veterans with blast-related mild TBI.

Key words: headache, brain injury, veteran, blast injury

(*Headache* 2011;51:1112-1121)

Traumatic brain injury (TBI) has emerged as the "signature wound" among US troops since Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) began in 2001 and 2003, respectively.[1-3] TBI-related somatic symptoms vary from person to person and reported symptoms include pain, sleep problems, balance difficulties, irritability, sensitivity to light as well as difficulty with concentration and memory.[4,5] Headaches are, however, the most commonly reported symptom.[6]

The prevalence of headaches subsequent to mild TBI in the civilian population is 54%,[7] and preliminary prevalence reports indicate that 22% to 47% of OEF/OIF combat veterans report headaches related to mild TBI events.[8-10] Evidence also indicates that 80% to 90% of civilians incurring mild TBI report headache resolution within a few weeks of injury[11] with about 10-20% of persons reporting persistent headaches for months and years following injury.[12-14] While we know that 7.6-36.7% of OEF/OIF combat veterans have incurred a mild TBI[8,15-17] and that reports of acute somatic symptoms include headaches, we do not know the prevalence of persistent headaches for combat veterans.

Given the high prevalence of mild TBI and headaches related to mild TBI events for combat veterans, the goal of our study was to determine the prevalence and characteristics of persistent headaches and the commonly prescribed headache treatment strategies for OEF/OIF combat veterans seeking care at a US Veterans Health Administration Polytrauma Network Site (VA PNS).

METHODS

Study Design and Setting.—A retrospective cohort study was conducted of OEF/OIF combat veterans seen for an initial mild TBI screening at a large Mid-western VA PNS. PNS provide specialized, post-acute rehabilitation in consultation with rehabilitation centers in a setting appropriate to the needs of veterans, service members, and families. OEF/OIF veterans sign up for VA benefits post deployment and these benefits include VA health care. If an OEF/OIF veteran seeks care at a VA center, a mild TBI screening is one required element of the initial visit.

Traumatic Brain Injury Screening and Evaluation Procedures.—The mild TBI screening is administered to all OEF/OIF veterans at the time of their initial VA visit, regardless of the reason for this initial visit. Therefore, all clinics in the VA can administer this systematic nationwide screening. The screening includes a series of 4 questions regarding exposure to a mild TBI event(s), immediate or acute symptoms, changes in symptoms and symptoms at time of screening (ie, current symptoms; see Appendix I). The screen is positive if the patient responds positively to 1 or more possible answers in each of the 4 questions. A more detailed review of the VHA mild TBI screening process is described by Donnelly et al.[18] Veterans with a positive screening, at the participating VA PNS site, are referred by the screening administrator for a comprehensive TBI evaluation by a multidisciplinary PNS team.

The comprehensive mild TBI evaluation includes self-reports regarding mild TBI (eg, blast, fall, vehicular), distance from blast (if applicable), other non-brain-related injuries, pain within preceding 30 days by region (eg, head, back), mental health diagnoses and the Neurobehavioral Symptom Inventory (NSI).[19] The NSI is a 22-item self-report rating scale examining affective, cognitive, somatic and sensory areas following mild TBI. Symptoms such as headaches, sleep disturbances, and sensitivity to light are included in the NSI.[20] On the NSI, patients use a

Table 1.—Department of Defense/VA Consensus-Based Classification of Closed Traumatic Brain Injury (TBI) Severity

	Severity Indices		
	Mild TBI/Concussion	Moderate TBI	Severe TBI
Initial GCS	13-15	9-12	<9
Loss of consciousness	0-30 minutes	>30 minutes and <24 hours	>24 hours
Length of alteration of consciousness	A moment up to 24 hours	>24 hours	>24 hours
Length of post-traumatic amnesia	0-1 day	>1 and <7 days	>7 days

GCS = Glasgow Coma Scale.

5-point scale to rate the extent to which a symptom disturbs them. This rating scale ranges from "Not at all" (0 = None: rarely if ever present; not a problem at all) to "Almost always" (4 = Very severe: almost always present and I have been unable to perform at work, school or home due to this problem; I probably cannot function without help). A more detailed review of the VHA TBI evaluation process is described by Ruff et al.[10]

After completion of this comprehensive TBI evaluation, the presence or absence of symptoms corresponding to mild TBI is confirmed. The criteria used for mild TBI diagnosis are based on Department of Defense/VA Consensus-Based Classification of Closed TBI Severity[21] (see Table 1). The criteria for the diagnosis of mild TBI are that duration of loss of consciousness was less than 30 minutes, the length of alteration of consciousness (mental state) following the TBI was less than 24 hours, and the length of post-traumatic amnesia was less than 24 hours. Veterans are also provided with appropriate referrals to specialists as needed to assist with current and/or unresolved medical conditions.

Selection of Participants: Study Sample.—Data were extracted from electronic medical records of 250 consecutive OEF/OIF veterans receiving a confirmed diagnosis of mild TBI between June 15, 2007 and July 15, 2009. Four veterans were subsequently excluded for the following reasons: 1 veteran had actually incurred a moderate to severe TBI while another veteran did not discuss headache symptoms upon arrival to neurology clinic and 2 veterans were excluded due to TBI etiology (ie, anoxic injury and electrocution). Therefore, the final sample for the study includes 246 OEF/OIF combat veterans seeking care at the participating VA PNS site (see the Figure). This study was approved by the local Human Subjects Institutional Review Board.

Data Abstraction.—Electronic medical records were reviewed and data were collected using a data

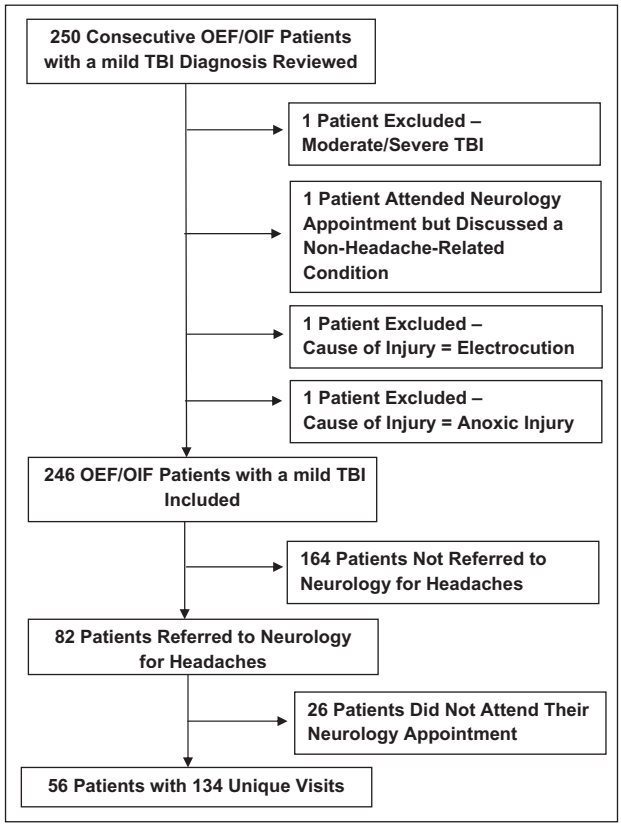

Figure.—Patient inclusion/exclusion. OEF = Operation Enduring Freedom; OIF = Operation Iraqi Freedom; TBI = traumatic brain injury.

collection tool developed for the study. Abstracted data elements included demographics, injury type, responses to each mild TBI screening question, mild TBI screening results (ie, positive or negative), referrals, diagnoses and prescribed treatments from neurology clinic visits, responses to each item in the comprehensive TBI evaluation as well as final diagnosis of presence/absence of mild TBI.

Abstracted data regarding headaches included duration, onset, location, frequency, pain quality and intensity, associated symptoms and triggers, past medical/family history and duration since injury (ie, in years). Duration since injury was calculated as the difference between injury date (recorded during the comprehensive mild TBI evaluation) and first neurology clinic presentation. Treatment data were also abstracted and categorized as abortive and prophylactic medications. If head computed tomography (CT) or magnetic resonance imaging (MRI; ie, 1.5 Teslar clinical scanner) were completed, then the findings were abstracted from radiology reports.

Data Analyses.—Associations between headache symptoms and veteran characteristics were examined using *t*-tests for continuous variables and chi-square tests for categorical variables. Comparisons were made according to veteran demographics for the total sample (gender, race, etc) and between the groups of veterans receiving or not receiving a referral to neurology for headaches. All analyses were conducted using SAS 9.2 software and statistical significance was considered at the $P < .05$ level.

RESULTS

Sample Description.—The majority of the 246 veterans were young (age at time of initial comprehensive evaluation = 27.9 years, ±6.3 standard deviation [STD]) men (92.3%). Most of the veterans were either currently employed (56.1%) or enrolled students (18.9%) who reported being single or never married (46.8%) and had a high school diploma or equivalent (>99%).

When veterans were asked if they experienced pain within the 30 days preceding the initial TBI evaluation, headache/head pain was reported by 74% of the veterans during the comprehensive TBI evaluation. Sixty-five percent of veterans reported at least 1 blast exposure as the etiology for the mild TBI. On average, the veterans rated headaches as moderately affecting their lives (mean = 2.3, ±1.0 STD) based on the NSI tool. This score differed significantly by gender with women reporting greater life interference (mean = 3.3, ±0.7 STD) than men (mean = 2.2, ±1.0 STD; $t = 4.9$, $P < .01$). Non-whites also reported greater life interference (mean = 2.78, ±0.94 STD) than white/Caucasian veterans (mean = 2.2, ±1.0 STD, $t = 3.1$, $P < .05$). Headache ratings did not differ by ethnicity (ie, Hispanic/Latino vs non-Hispanic/Latino) or marital status (ie, married vs non-married).

Regarding other symptoms, the majority (92%) of veterans also reported some level of sleep disturbances. The average NSI sleep difficulty was rated as 2.6 (±1.2 STD) meaning that sleep difficulties are often to frequently present. The majority of the sample (74%) also had suspected or confirmed post-traumatic stress disorder (PTSD) at the time of the comprehensive mild TBI evaluation. Confirmed PTSD is when the patient has had a previous mental health evaluation by a psychiatrist and has been given a diagnosis of PTSD. Suspected PTSD is when patients self-report symptoms suggestive of PTSD and are awaiting mental health evaluation at the time of comprehensive TBI evaluation.

Referrals to Neurology Clinic.—Eighty-two of the 246 veterans (33.3%) examined with the comprehensive mild TBI evaluation were provided with referrals to the neurology clinic due to persistent headaches (Figure). Veterans with (n = 82) or without (n = 164) a referral to neurology were equally likely to report headache/head pain within the 30 days preceding the comprehensive mild TBI evaluation (74%). However, veterans not receiving a referral to neurology for headaches rated headaches significantly less severe than those receiving a referral ($t = 7.6$, $P < .01$; see Table 2). There were no significant differences ($P > .05$) in reports of sleep disturbances, or suspected or confirmed diagnosis of PTSD between veterans receiving and not receiving a neurology referral. Veterans with or without a referral to neurology did not differ by etiology of injury (vehicular, falls, bullet, or blasts).

Veterans Evaluated in Neurology Clinic.—Of the 82 veterans provided with neurology referrals, 26

Table 2.—Patient Demographics

	No Referral (n = 164)	Referral (n = 82)	*P* value
Age† (STD)	27.54 (6.28)	28.64 (6.22)	.19
Gender (% male)	96.34%	84.15%	<.01
Race: White/Caucasian	86.47%	81.33%	.32
Ethnicity: Hispanic/Latino	19.05%	19.75%	.90
Single or never married	46.95%	46.34%	.93
Employed‡ or student	75.48%	73.98%	.38
Headache rating (STD)§	1.97 (0.91)	2.87 (0.80)	<.01
Sleep disturbances (STD)§	2.53 (1.17)	2.78 (1.12)	.11
PTSD¶	70.7%	80.5%	.10

†Age at time of second-level evaluation.
‡Employed includes both full and part time.
§Using Neurobehavioral Symptom Inventory scale.
¶Post-traumatic stress disorder (PTSD) includes patients diagnosed with or suspected of having disorder.
STD = standard deviation.

(30.6%) did not attend the neurology appointment resulting in a final cohort of 56 OEF/OIF combat veterans evaluated in neurology clinic. For this group of veterans attending their neurology appointment, about two-thirds (62%) reported no family history of headaches.

The types of headaches most frequently diagnosed by the neurologists were migraine headaches (44.6%) followed by chronic daily headaches (19.6%) and post-traumatic headache (7.14%; see Table 3). The majority of veterans could not identify a triggering factor (78.4%) although stress (18.9%) and food triggers (2.7%) were reported by some. The most commonly reported associated symptoms were photophobia (29.9%), phonophobia (25.0%), and nausea (19.6%). Most (78%) of the veterans reported moderate to severe headaches, at least once a week, lasting several hours. The mean duration between the first mild TBI event, as reported in the comprehensive mild TBI evaluation, to first neurology visit was 3.1 years, although 24 (42.9%) veterans did not report or remember the date of first injury. While 26 of the 56 veterans (46.4%) were missing data regarding time between headache onset and TBI event, 7 (12.5%) veterans reported headache onset within 7 days of injury and 23 (41.0%) veterans had headache onset more than 7 days after the injury. At initial neurology visit, the mean frequency of headaches per month was 17.0 (median, 15 headaches per month) and 12 (21.4 %) patients were missing the frequency information. Of the 24 veterans who attended their follow-up visit, the mean frequency of headaches was 11 headaches per month (median, 8 headaches per month).

Table 3.—Diagnosed Headache Types†

Headache Type	n (%)
Migraine‡	25 (44.64)
Chronic daily	11 (19.64)
Mixed	8 (14.29)
Tension	6 (10.71)
Post-traumatic	4 (7.14)
Cluster	1 (1.79)
Other§	1 (1.79)
Total	56 (100)

†Diagnoses are mutually exclusive. Veterans with more than 1 type of headache occurring are classified as "mixed."
‡One patient had migraine with aura.
§Patient reported "ice-pick" type headache.

The majority of veterans evaluated in neurology received head CT or MRI orders (52/56; 92.9%) with 80% completing either head CT, MRI or both. Almost half of the veterans receiving neuroimaging had abnormal/non-specific findings. The findings included largely white matter changes (40%) and

Table 4.—Medications Prescribed at First Visit (n = 56)

Abortive		Preventive	
Medication	n (%)	Medication	n (%)
Acetaminophen	2 (8.33)	Gabapentin	6 (22.22)
Ibuprofen	2 (8.33)	Levetiracetam	1 (3.70)
Tramadol	1 (4.17)	SSRI	1 (3.70)
Triptan	17 (70.83)	Topiramate	4 (14.81)
Other†	2 (8.33)	Tricyclics	11 (40.74)
		Valproic acid	4 (14.81)

†Other includes flexeril and methocarbamol.
SSRI = selective serotonin reuptake inhibitor.

other incidental findings of sinus polyps/cysts (30%), arachnoid cysts, vascular malformation or masses (25%), and atrophy (5%).

Self-Administered and Prescribed Treatments.— During initial neurological evaluation (n = 56), 50% of veterans reported taking acetaminophen to abort headaches and 29% reported taking ibuprofen. Less frequently, veterans reported taking opiates or triptans (5.6% each) to abort headaches prior to their neurology appointment. During the initial neurology visit, a small number of veterans (5.4%) reported using gabapentin, topiramate or valproic acid to prevent headaches prior to initial visit. Additionally, veterans reported using a number of medications known to ameliorate headaches, but for reasons other than headaches. For example, 12 veterans (21.4%) reported taking ibuprofen regularly for body pain such as back or knee pain and 34.3% of veterans were taking selective serotonin reuptake inhibitors for psychiatric reasons.

During the initial neurology appointment, 70.8% of medications prescribed for abortive purposes were triptans (30.4% of veterans). The primary preventive medications prescribed were anticonvulsants (55.5%) followed by tricyclics (40.7%). Gabapentin was the most common anticonvulsant prescribed as a preventive medication at the first visit (22.2%, Table 4).

Sixty-eight percent of veterans attended their first neurology visit and, of those attending, 40% of patients did not return for the second follow-up visit. The mean interval for follow-up appointment was 5.4 months. Change in headache frequency was difficult to interpret given the poor compliance with follow-up.

DISCUSSION

A substantial proportion of veterans with mild TBI, diagnosed via a comprehensive TBI evaluation, reported headache pain in the 30 days preceding the comprehensive mild TBI evaluation. This finding is similar to previous reports of chronic persistent headaches in OEF/OIF combat veterans with mild TBI.[22] Given that the prevalence of persistent headaches in the mild TBI civilian population ranges from 10% to 20%, the prevalence of headaches in OEF/OIF combat veterans with mild TBI treated at the participating VA PNS is high. This finding suggests that the nature of head trauma sustained by combat veterans may be different from that by civilian population. This may be supported by the finding that the most common cause of mild TBI in our study sample is exposure to blast(s), which is similar to other studies of military personnel.[9,22]

The high prevalence of PTSD and sleep problems with mild TBI in our sample is consistent with reports of increased prevalence of PTSD and sleep problems in other studies of military populations with mild TBI.[10,23,24] Collectively, the findings regarding etiology of mild TBI, high prevalence of co-occurring PTSD, and sleep problems may together serve to exacerbate headaches and/or increase the frequency. These findings highlight the need for research to elucidate the role of psychological factors and sleep disturbances in persistent headaches after mild TBI in combat veterans and the role of blast exposure as a contributing factor.

Women in our study had more severe headaches than men. This finding is consistent with previously reported higher prevalence of migraines and post-traumatic headaches in women in both the civilian and military population.[25-27] Given the small number of women in our sample, we could not stratify analyses by gender. Therefore, the underlying reasons for more severe post-traumatic headache in women continues to be poorly understood.[25,28,29]

Almost one-half of patients were diagnosed with migraine-type headache followed by chronic daily

headaches. Of the patients with migraine headaches, only 1 patient had migraine with aura. Cervicogenic headache was not diagnosed in our sample although many injuries experienced in combat are whiplash-like in nature. Such infrequent diagnosis of cervicogenic headache could be related to the fact that they were not referred to a neurologist and the treatment was provided by a physiatrist who performed the comprehensive evaluation.

While our study indicates that the most common type of headaches were migraine-type headaches, a different previous study of veterans showed a predominance of tension-type headache with mild TBI[30] and another study reported a predominance of migraine-like headaches in veterans with mild TBI and residual neurocognitive deficits on neuropsychology testing.[10] We did not collect neuropsychology results in our group of veterans, because all of them did not receive neuropsychology testing. We could not, therefore, examine the relationship between headaches and neurocognitive function. Our findings, together with previously reported findings in the literature, suggest that migraine and tension-type headaches are the most common types of headaches after mild TBI.

A small proportion of our cohort with chronic headaches were diagnosed as post-traumatic headaches (7.1%). This rate is smaller than previous studies[31,32] and might be an under-representation due to insufficient or missing documentation regarding the timing of the headache onset relative to timing of the mild TBI event as well as the long interval between the mild TBI event and presentation to the VA for comprehensive mild TBI evaluation.

A majority (80%) of the veterans in the sample completed either head CT or MRI. We abstracted findings from radiology reports and we did not collect or review original images according to location of white matter changes because this was beyond the scope of the study. Our imaging findings of white matter changes, however, are consistent with previous reports of non-specific imaging abnormalities with conventional imaging modalities.[33] Imaging findings of white matter changes suggest that research using more advanced imaging techniques may shed light on pathophysiology of blast-related mild TBI. Future studies should look at correlating cognitive function in those with or without white matter lesions on MRI.

Given the paucity of prospective blinded randomized trials examining the efficacy of different treatment modalities in this population, the treatment of persistent headaches is complex and poses many clinical challenges. Although VA has developed an algorithm for mild TBI treatment, there are no specific clinical practice guidelines for headache treatment in the mild TBI population. The recommended treatment is extrapolated from the treatment of primary headaches. Abortive pharmacologic therapies for headaches include the use of analgesic medications (eg, NSAIDs, acetaminophen) and triptans. Non-pharmacologic therapy includes sleep hygiene education, physical therapy, biofeedback and relaxation techniques. The focus of treatment should be to prevent chronicity by using prophylactic medications and to decrease the risk of medication-overuse headache associated with analgesic overuse.

In our study, the most commonly prescribed abortive medications were triptans and the most common preventive medications prescribed were anticonvulsant medications followed by tricyclics. The medications for preventive therapy were chosen based on the veterans' comorbid conditions and other concomitant medications. Given the high frequency of patients not attending follow-up appointments and missing frequency data, the sample size was too small to assess the efficacy of the treatment. This highlights the need for future randomized controlled trial studies assessing the effectiveness of different treatment strategies specific to headaches in mild TBI. Furthermore, strategies to improve the compliance with follow-up care and treatment need to be considered. A multidisciplinary approach in treating patients with post-traumatic headaches might better address the complex psychological and cognitive problems in these patients in addition to headache treatment. Future studies should also examine the role of non-pharmacological intervention (ie, yoga, acupuncture, etc) for the treatment of headaches in this patient population.

Living with chronic headaches may result in absenteeism from work and maladaptive chronic pain behavior with associated loss of quality of life both of which may become significant public health issues.[32] One European study reported an average of 35% loss of productivity for persons working with migraines.[34] These observations highlight the importance of preventing and adequately managing persistent and chronic headaches. This is especially imperative in our OEF/OIF combat veterans, who face the additional stress of transitioning from combat environment to reintegrating into civilian life. Our veterans also face associated psychological issues like depression, PTSD, and sleep problems that are likely to exacerbate headache pain and increase the frequency of headaches.

Our study is limited by the retrospective study design with a small sample size. During the comprehensive mild TBI evaluation, the prevalence of headaches was based on self-report data. The evaluation was performed at long time intervals from the original injury, contributing to the difficulty of accurately diagnosing post-traumatic headaches as required by the International Classification of Headache Disorders definition.[35] Additionally, a validated instrument for measuring headache-related disability was not used in this retrospective study design. The headache frequency information was missing in some of the patients charts. These issues in addition to poor follow-up visits add to the difficulty of assessing treatment efficacy.

CONCLUSIONS

Our findings indicate a high prevalence of persistent headaches in OEF/OIF combat veterans with mild TBI. Since most of the veterans in our study sample were exposed to a blast injury, the nature of head trauma may be contributing to headaches and should be further investigated. Our findings also suggest that frequently co-occurring sleep problems and PTSD may exacerbate headache frequency and/or severity. The sample size of the veterans who attended their follow-up neurology appointments was too small to assess the efficacy of headache treatment. These findings highlight the need for developing effective headache prevention and treatment strategies, including increasing follow-up visits, for all veterans with blast-related mild TBI.

Acknowledgment: We would like to thank Ms. Catherine Gruener for her assistance in the chart review process and staff in Dr. Pape's lab, Department of Veterans Affairs (VA), Spinal Cord Injury Quality Enhancement Research Initiative, Center for Management of Complex Chronic Care, Edward Hines Jr. VA Hospital, Hines, IL, USA, for their assistance with this project.

APPENDIX I

The four questions, administered as initial mild TBI screening administered to OEF/OIF veterans. Veterans with a positive screen are referred for comprehensive evaluation.

Question 1. During any of your OEF/OIF deployment(s) did you experience any of the following events? (check all that apply)
- blast or explosion;
- vehicular accident/crash (including aircraft);
- fragment wound or bullet would above shoulders;
- fall.

Question 2. Did you have any of these symptoms IMMEDIATELY afterwards? (check all that apply)
- losing consciousness/"knock out;"
- being dazed, confused or "seeing stars;"
- not remembering the event;
- concussion;
- head injury.

Question 3. Did any of the following problems begin or get worse afterwards? (check all that apply)
- memory problems or lapses;
- balance problems or dizziness;
- sensitivity to bright light;
- irritability;
- headaches;
- sleep problems.

Question 4. In the past week, have you had any of the symptoms from Question 3? (check all that apply)
- memory problems or lapses;
- balance problems or dizziness;
- sensitivity to bright light;

- irritability;
- headaches;
- sleep problems.

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