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GREATER FREQUENCY OF DEPRESSION ASSOCIATED WITH CHRONIC PRIMARY HEADACHES THAN CHRONIC POST-TRAUMATIC HEADACHES

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Abstract

Objective—To compare the prevalence of co-morbid depression between patients with chronic primary headache syndromes and chronic post-traumatic headaches.

Method—A prospective cross-sectional analysis of all patients presenting sequentially to a community-based general neurology clinic during a 2-year period for evaluation of chronic headache pain was conducted. Headache diagnosis was determined according to the International Headache Society's Headache Classification criteria. Depression was determined through a combination of scores on the clinician administered Hamilton Rating Scale for Depression and patients' self-report. An additional group of patients who suffered traumatic brain injuries (TBI) but did not develop post-traumatic headaches was included for comparison.

Results—A total of 83 patients were included in the study: 45 with chronic primary headaches (24 with chronic migraine headaches, 21 with chronic tension headaches), 24 with chronic post-traumatic headaches, and 14 with TBI but no headaches. Depression occurred less frequently among those with chronic post-traumatic headaches (33.3%) compared to those with chronic migraine (66.7%) and chronic tension (52.4%) headaches (Chi-Square = 7.68; $df = 3$; $p = 0.053$),

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and did not significantly differ from TBI patients without headaches. A multivariate logistic regression model using depression as the outcome variable and including headache diagnosis, gender, ethnicity, and alcohol and illicit substance use was statistically significant (Chi-Square = 27.201; $df = 10$; $p < 0.01$) and identified primary headache (migraine and tension) diagnoses (Score = 7.349; $df = 1$; $p = 0.04$) and female gender (Score = 15.281; $df = 1$; $p < 0.01$) as significant predictor variables. The overall model accurately predicted presence of co-morbid depression in 74.7% of the cases.

Conclusions—Co-morbid depression occurs less frequently among patients with chronic post-traumatic headaches and TBI without headaches than among those with chronic primary headaches.

Keywords

chronic pain; depression; headache

INTRODUCTION

The pathophysiology of co-morbid depression among chronic post-traumatic headache sufferers remains poorly understood and its relationship to primary headaches is currently not clearly defined. Chronic post-traumatic headaches may develop as a direct consequence of intracranial derangement and neuronal injury resulting from trauma, or trauma may trigger the same processes that cause primary headaches in susceptible individuals. Previous studies have reported no difference in the clinical characteristics between primary headaches and post-traumatic headaches, suggesting that the same underlying mechanisms may be responsible for both types of headaches [1]. However, the frequency of co-morbid depression has not been directly compared between people suffering from chronic primary headaches and chronic post- traumatic headaches.

Depression is a common co-morbidity among chronic pain sufferers, including those with chronic primary headaches, and also is a common sequelae of traumatic brain injuries [2–5]. However, while common among both disorders, previous studies suggest that prevalence rates of depression may differ between chronic primary headache sufferers and those who have sustained traumatic brain injuries [2–5]. Consequently, we wanted to determine if patients with chronic post-traumatic headaches would exhibit depression rates more similar to those with chronic primary headaches or traumatic brain injury patients without chronic headaches. If depression among chronic primary headache sufferers and those with chronic post-traumatic headache are caused by the same or similar brain mechanisms, then prevalence rates of depression would also be expected to be similar between these populations. Conversely, significant differences in prevalence rates of co-morbid depression between those with chronic primary headaches and chronic post-traumatic headaches would support the existence of differences in the underlying brain mechanisms causing depression in these patients.

In this study we assessed prevalence of co-morbid depression among all patients presenting prospectively to a community based neurology clinic during a 2-year period for evaluation of chronic headache pain or for evaluation of traumatic brain injury without chronic

headaches. We hypothesized that rates of co-morbid depression would be similar between the primary and post-traumatic headache groups and that co-morbid depression would occur more frequently among all the headache groups compared to the reference group of TBI patients that did not develop chronic headaches.

METHOD

Participants

Permission to perform this study was obtained from the Ventura County Medical Center Institutional Review Board. Participants were adults, over the age of 18 years, who presented sequentially to a community-based general neurology clinic during a 2-year period from July 1, 2009 to June 30, 2011 for assessment of either traumatic brain injury (TBI) occurring at least 3 months prior to evaluation and with no reported headaches, or who presented for evaluation of headache pain of 3 months or greater duration. Initial review of our Neurology database containing diagnosis and clinical information for all 1,964 patients seen by the neurology outpatient clinic service during the study period identified a total of 89 patients possibly meeting the inclusion criteria. Further review of patient records and chart notes resulted in six patients being excluded from the study either because they did not meet ICHD-2 criteria for chronic migraine headaches (four patients, three with insufficient duration and one with insufficient clinical characteristics), chronic tension headaches (one patient with insufficient duration) or chronic post-traumatic headaches (one patient with no headaches and no documented history of head trauma). Participants underwent a standardized workup including a history and physical examination by a board certified neurologist. The presence of co-morbid hypertension and diabetes were determined by self-report. Use of tobacco, alcohol, and illicit substances was determined by self-report and categorized as current, past, or none. All study participants were referred to the neurology outpatient clinics either from their primary care physicians or from the hospital trauma service.

Headache Classification

Headaches were classified according to the International Headache Society's Headache Classification (ICHD-2) criteria by a board certified neurologist [6], ICHD-2 criteria for chronic migraine headache, chronic tension headache, and chronic post-traumatic headache were used. Headache severity was determined by use of a 5-point scale ranging from 0 to 4.

Depression Diagnosis

All participants underwent assessment for depression using the clinician administered Hamilton Rating Scale for Depression [7]. Depression was determined to be present if either of the two following criteria were fulfilled:

1. Hamilton Rating Scale for Depression score of greater than seven; or
2. self-report of a previous depression diagnosis made after headache onset and date of traumatic brain injury, and resulting in treatment with an antidepressant medication.

Statistical Analysis

Continuous demographic factors and other continuous variables were compared between groups using analysis of variance (ANOVA). Non-parametric data was compared between groups using the independent samples Kruskal-Wallis test. Frequency of occurrence of categorical variables was compared between groups using chi-square analysis or Fisher's exact test as appropriate. A multivariate logistical regression model was constructed using depression as the dependent variable, and including headache diagnosis as well as all potentially confounding variables that displayed significant differences between headache groups on ANOVA or chi-square analyses. All statistical calculations were performed using SPSS version 21.0 [8].

RESULTS

A total of 83 patients were assessed, including 45 females and 38 males. Chronic migraine headaches were present in 24 of the patients, chronic tension headaches were present in 21, chronic post-traumatic headaches were present in 24, and 14 patients were included who presented during the same time period for evaluation of TBI without development of headache. Overall, the groups displayed similar demographic characteristics (see Table 1). No difference in mean age was noted between the groups. A trend toward greater male to female ratios was noted in the TBI groups compared to the primary headache groups (Chi-Square = 6.62; $df = 3$; $p = 0.085$). There was greater frequency of Hispanic ethnicity and lesser frequency of Asian ethnicity among the TBI groups compared to the primary headache groups (Chi-Square = 15.17; $df = 6$; $p = 0.019$).

Duration of headaches was greater for the patients with chronic migraine headaches (mean = 133.75 months, $SD = 131.58$) compared to those with chronic tension (mean = 66.86 months, $SD = 54.51$) and chronic post-traumatic (mean = 71.6, $SD = 95.9$) headaches ($F = 3.280$; $df = 2.66$; $p = 0.04$). The groups did not differ in frequency of self-reported tobacco use. Self-reported alcohol use was significantly less frequent among the primary headache groups (migraine headaches: current = 4.2%, past = 4.2%; tension headaches: current = 4.8%, past = 4.8%) compared to those who sustained traumatic brain injuries (post-traumatic headaches: current = 20.8%, past = 25.0%; head trauma without headaches: current = 42.9%, past = 7.1%; Chi-Square = 21.128; $df = 6$; $p < 0.01$). A trend toward greater frequency of self-reported current illicit substance use among TBI groups compared to primary headache groups (Chi-Square = 12.23; $df = 6$; $p = 0.057$) was noted. Self-reports of co-morbid hypertension and diabetes did not differ significantly between groups. No significant differences were detected between the groups for mean pain severity.

Depression was present less frequently among those with traumatic brain injuries compared to those with primary headaches (31.6% versus 60.0% respectively; Chi-Square = 6.681; $df = 1$; $p = 0.010$), Additionally, comparison of depression frequency between headache diagnostic groups showed a trend toward lower rates of depression among those with post-traumatic headaches (33.3%) compared to those with chronic migraine (66.7%) and chronic tension (52.4%) headaches (Chi-Square = 7.679; $df = 3$; $p = 0.053$). The multivariate logistic regression model using depression as the outcome variable and including headache diagnosis, gender, ethnicity, and alcohol and illicit substance use was statistically significant

(Chi-Square = 27.201; $df = 10$; $p < 0.01$) and identified headache diagnosis (Score = 7.349; $df = 1$; $p = 0.04$) and gender (Score = 15.281; $df = 1$; $p < 0.01$) as significant predictor variables. The overall regression model accurately predicted presence of co-morbid depression in 74.7% of the cases.

DISCUSSION

Chronic primary headache syndromes and secondary chronic post-traumatic headaches are common conditions that affect quality of life for many people. In this study, co-morbid depression occurred at greater frequency among patients suffering from chronic primary headaches than chronic post-traumatic headaches. Additionally, co-morbid depression was found to occur at approximately the same frequency among TBI patients regardless of headache status. These results suggest that development of depression after TBI is more likely related to central nervous system dysfunction resulting from the traumatic injury than to underlying mechanisms related to development of chronic headache pain. Additionally, the lower rate of co-morbid depression among those with chronic post-traumatic headaches compared to chronic primary headaches supports the existence of different pathophysiologic mechanisms underlying headache development after TBI compared to primary headaches.

The frequencies of co-morbid depression in the chronic migraine and chronic tension headache groups in this study were similar to previously published values which typically range from about 29% to 60% [2, 9]. The rates of co-morbid depression determined in this study are among those at the higher end of the reported spectrum. This is likely related to several factors including: the high female to male ratio comprising our primary headache population, the chronic nature of the headache pain, and the population being drawn from a general neurology clinic rather than a population sample or primary care clinic, all of which are factors known to increase frequency of co-morbid depression among headache sufferers [2, 9, 10]. Additionally we used both a clinician administered, standardized depression rating scale as well as self-report for diagnosis of depression, which could also have increased detection of this condition in our sample.

Co-morbid depression was found to be present in approximately the same percentage of TBI patients in this study regardless of headache status. These values are also consistent with previously published reports indicating that approximately 22% to 47% of TBI survivors will develop depression, depending on factors such as gender, ethnicity, and chronic pain severity [11, 12].

Other psychiatric conditions reported to occur at increased rates among chronic migraine sufferers include anxiety and bipolar disorders [2, 13, 14]. A recent report by Teixeira et al. compared rates of anxiety and bipolar disorders among chronic migraine patients from community and tertiary care clinics, finding anxiety to be present in 34.9% of patients evaluated at a headache center and 39.0% of patients evaluated in the community [2]. In their study, bipolar disorder was identified in 4.7% of patients presenting to a headache center and no cases were identified in the community sample [2]. Another recent report by Chen et al., evaluated rates of anxiety and bipolar disorders among headache sufferers in Taiwan using a national database [13]. In their study, anxiety disorders were found to be

present in 15.57% of patients with chronic migraine, resulting in relative risk of 1.48 compared to episodic migraine and 2.89 compared to a non-migraine population; and bipolar disorder was found to be present in 2.35% of patients with chronic migraine, resulting in a relative risk of 1.81 compared to episodic migraine and 3.88 compared to a non-migraine population [13]. The chronic migraine patients included in this study self-reported anxiety disorder at a rate within the range of previously reported values, and also which was not significantly different from our reference group comprised of TBI patients with no headaches. Because the rates of anxiety disorder in the reference group are also consistent with previously published reports [15, 16], we feel the relationship between chronic migraine and anxiety was likely obscured by the use of a reference group which was itself at elevated risk for anxiety and consequently masked detection of any increased risk associated with chronic migraine headaches.

In this study no cases of bipolar disorder were identified among the chronic migraine sufferers and only one case was identified among the other headache groups. The lack of detection of bipolar disorder is likely related to the relatively small sample size and reliance on self-report for detection of bipolar disorder rather than use of a standardized assessment tool. In particular, the lack of use of a formal assessment tool for detection of bipolar disorder likely caused a measurement bias, resulting in under-reporting of this condition across all headache categories.

Self-reported alcohol and illicit substance use rates among the primary headache sufferers and TBI survivors in this study were also within the range of previously reported values [17–19]. The frequency of self-reported alcohol and illicit substance use were greater among TBI patients compared to those with primary headaches. This is consistent with previous reports of decreased alcohol use among both migraine and non-migraine headache sufferers possibly due to alcohol being a trigger for headaches in these populations, and increased risk among TBI patients [17–19]. We did not detect any significant difference in the rates of self-reported alcohol and illicit substance use between TBI patients with and without chronic headaches, suggesting that the lower rates of alcohol use observed among primary headache sufferers may not directly translate to TBI patients with chronic headaches.

This study has several limitations. First, our study population was a convenience sample of patients who presented to a community-based neurology clinic rather than a randomly selected population sample. Because the patients included in the study were obtained from the local clinic, their demographic characteristics followed local population characteristics and were lacking in representation of people of African-American and other minority ethnicities. This study relied on a subjective pain severity scale and no objective method, such as determination of pain thresholds, was used. Diagnosis of depression was made by a combination of self-report and use of a standardized scale rather than through a detailed assessment by a qualified psychiatrist, however, any detection bias resulting from this would be expected to affect all groups equally and therefore would be unlikely to change the results. This study did not include an assessment of quality of life and consequently this potential confounding factor was not able to be accounted for in the analysis. Additionally, results of brain neuroimaging studies were not included in this analysis and were not available for all study participants. Consequently, it is possible that changes in brain

structures related to perception of pain (thalamus) or emotion (limbic system) may be present in the patients with traumatic brain injuries and could account for some of the observed differences. Another limitation of the study is that information regarding headache frequency was not collected or included in the analysis. Finally, this was a cross-sectional study with no follow-up or long-term information and consequently causality is not able to be determined from these results.

The results of this study identify gender and headache diagnosis as significant predictors for prevalence of depression among chronic headache sufferers. An improved understanding regarding the relationship between chronic primary headaches and chronic post-traumatic headaches may help to explain the differences in rates of co-morbid depression identified in this study between headache types. The difference in rates of co-morbid depression identified in this study do support different neuropathological factors underlying the development of chronic primary and chronic post-traumatic headaches. Further study, including neuroimaging assessment of cortical and subcortical structures related to emotion and pain sensation, is needed to identify and characterize any structural and/or functional differences that may underlie development of depression in primary and post-traumatic headaches.

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Table 1

Subject Characteristics and Psychiatric Co-morbidities

	Migraine Mean/*SD* No. (%)	Tension Mean/*SD* No. (%)	Post-traumatic Mean/*SD* No. (%)	TBI without headaches Mean/*SD* No. (%)	Sig.
Age	42.9/11.8	48.4/8.5	42.1/12.0	43.2/16.0	$p = 0.30$
Duration (months)	133.8/131.6	66.9/54.5	71.6/95.9	N/A	$p = 0.04$
Severity	3.13/0.99	3.14/0.91	2.92/0.93	N/A	$p = 0.09$
Gender					
Male	7 (29.2)	8 (38.1)	14 (58.3)	9 (64.3)	$p = 0.09$
Females	17 (70.8)	13 (61.9)	10 (41.7)	5 (35.7)	
Ethnicity					
Asian	5 (20.8)	8 (38.1)	2 (8.3)	0 (0.0)	
Caucasian	15 (62.5)	12 (57.1)	13 (54.2)	10 (71.4)	$p = 0.02$
Hispanic	4 (16.7)	1 (4.8)	9 (37.5)	4 (28.6)	
Tobacco use					
Current	3 (12.5)	5 (23.8)	4 (16.7)	5 (35.7)	
Past	0 (0.0)	0 (0.0)	2 (8.3)	0 (0.0)	$p = 0.23$
Noner	21 (87.5)	16 (76.2)	18 (75.0)	9 (64.3)	
Alcohol use					
Current	1 (4.2)	1 (4.8)	5 (20.8)	6 (42.9)	
Past	1 (4.2)	1 (4.8)	6 (25.0)	1 (7.1)	$p < 0.01$
None	22 (91.7)	19 (90.5)	13 (54.2)	7 (50.0)	
Illicit substance use					
Current	1 (4.42)	0 (0.0)	2 (8.3)	2 (14.3)	
Past	0 (0.0)	3 (14.3)	0 (0.0)	0 (0.0)	$p = 0.06$
None	23 (95.8)	18 (85.7)	22 (91.7)	12 (85.7)	
Co-morbid condition					
Diabetes	3 (12.5)	0 (0.0)	1 (4.2)	0 (0.0)	$p = 0.18$
Hypertension	5 (20.8)	10 (47.6)	7 (29.2)	3 (21.4)	$p = 0.21$
Depression	16 (66.7)	11 (52.4)	8 (33.3)	4 (28.6)	$p = 0.05$
Anxiety	3 (12.5)	2 (9.5)	1 (4.2)	2 (14.3)	$p = 0.42$
Bipolar disorder	0 (0.0)	1 (4.8)	0 (0.0)	0 (0.0)	$p = 0.39$