

Evaluation of Relationship Between Childhood Maltreatment and Medication Overuse Headache

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ABSTRACT

Introduction: We aimed to evaluate the prevalence and relationship between childhood maltreatment (CMT) among patients with medication overuse headache (MOH) and to investigate whether CMT is associated with medication overuse in patients having headaches or with headaches that become chronic. Epidemiological studies report a relationship between childhood abuse and headache. There is growing knowledge about the evidence that childhood maltreatment leads to neurobiological sequel. Medication overuse is the most important problem for migraine to become chronic. But in the literature, there was no information about the role of childhood abuse in MOH and for migraine to become chronic.

Methods: A total of 116 patients with headache, aged from 15 to 65 years, were included in the study. Patients having chronic migraine (CM), MOH and episodic migraine (EM) were selected out of patients presented to the headache outpatient clinic. Types of headache were determined according to the revised International Headache Society (IHS) criteria published in 2004. The Childhood Trauma Questionnaire, Beck Depression Inventory and Beck Anxiety Inventory were performed.

Presence of psychiatric co-morbidities was evaluated by a clinician using Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, the Fourth Edition.

Results: A total of 116 patients with headache were included in the study. Of patients, 64 had MOH, 25 had CM and 27 had EM. The prevalence of CMT, particularly emotional neglect (62%), physical neglect (44%) and emotional abuse (36.2%), was determined higher in all headache groups. There was no statistically significant difference in prevalence of childhood maltreatment between MOH, CM and EM groups. No statistically significant difference was detected between educational status, psychiatric co-morbidities and childhood trauma, except for physical neglect.

Conclusion: Childhood maltreatment was observed in MOH as in other forms of migraine and headache. However, no significant difference was observed between the three groups of patients with headache.

Keywords: Childhood maltreatment, abuse, medication overuse, psychiatric comorbidity

INTRODUCTION

Childhood maltreatment (CMT) is a major public health problem and a serious psychological and social problem both in developed and developing countries (1). In general, there are five forms of child abuse: emotional abuse, physical abuse, emotional neglect, physical neglect and sexual abuse (2). CMT is a well-known risk factor for psychiatric disorders, such as dissociative disorders, borderline personality disorder, posttraumatic stress disorder, depression, anxiety and substance and alcohol abuse (3,4). In addition to psychiatric disorders, history for CMT is associated with higher rates of physical health problems, such as bronchitis, ulcer, liver disease, inflammation, cardiovascular disease and chronic pain syndrome (3).

Epidemiological studies estimate the prevalence of CMT to be ranging from 25% to 45% (5,6). There is no large epidemiological study in Turkey. Alikasifoglu et al. (7) reported that 13.4% of female children are exposed to sexual abuse. The prevalence of physical abuse was reported between 43% and 71% in Turkish population studies (8).

Each year, headache becomes chronic in approximately 3%–4% of patients with EM (9,10,11). Transformation of migraine or progression of migraine into chronic form refers to a headache frequency that is increased to 15 or more headache days per month for at least 3 months (12,13). The risk factors for migraine to become chronic were reported to be overuse of acute attack medications for headache, frequent migraine attack pattern, combination with tension type headache, caffeine misuse, depression, hypertension, surgical menopause, obesity, smoking, snoring, sleep apnea and suicide risk. In addition, comorbidities such as vascular (Raynaud's disease, ischemic stroke, white matter lesions and acute myocardial infarction), cardiac (patent foramen ovale, mitral valve prolapse and atrial septal aneurysm), psychiatric (depression, anxiety, bipolar disorder, panic disorder and multiple substance dependence), neurological (epilepsy, Tourette's syndrome and multiple sclerosis) and miscellaneous diseases (fibromyalgia, systemic lupus erythematosus and head trauma) may play a role in progression of migraine to become chronic (12,13).



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Although there are some studies about the relationship between headache and CMT, the largest population study on headache was designed by Tietjen et al. (2,14). This study showed that CMT, particularly emotional abuse and neglect, was in the majority of participants with migraine. They also reported that physical abuse, emotional abuse and emotional neglect might be risk factors for development of chronic migraine (CM), including transformed migraine (14).

Medication overuse is the most important problem for migraine to become chronic. The understanding of factors involved in the prognosis of medication overuse headache (MOH) is a key point of the current debate. The presence of psychiatric co-morbidity is a negative prognostic factor for headache improvement. MOH has been shown to be more strongly associated with anxiety, major depression, panic disorder and social phobia (15,16). In addition, investigation of MOH personality revealed that patients with MOH had higher scores for hypochondriasis, depression (only females) and hysteria (only females). There was no knowledge whether CMT is associated with MOH or not.

The present study aimed to compare the prevalence of CMT maltreatment between patients with MOH and those with EM and CM. In addition, we aimed to investigate whether CMT was associated with medication overuse in headache patients or progression of headache to chronic form.

METHODS

This study was approved by Baskent University Institutional Review Board and supported by Baskent University Research Fund. This is a cross-sectional study conducted in 116 patients with headache applied to the Department of Neurology in the Medical School of Baskent University.

Subjects

A total of 116 patients with headache, aged between 15 and 65 years, who met the Subcommittee of IHS were included in the study between September 2012 and August 2013. All patients gave their written informed consents after being fully informed about the objectives and methods of the study. Signed consent forms were obtained from the parents of the patients who were younger than 18 years. Subjects who had schizophrenia, schizophreniform disorder, affective disorder, mental retardation, severe neurological disorder, aged ≤ 15 years, history of any serious and progressive organic physical disease and those who were pregnant or nursing were excluded from the study.

Detailed sociodemographic data and data on clinical features (e.g. age, marital status, education level, occupation, types of migraine, disease duration, days with headache, medication overuse, medical history and family history) were obtained via a semi-structured interview. Neurological and physical examination and brain MRI were performed for differential diagnosis.

The patients who had CM, MOH and EM were selected out of patients who applied to the headache outpatient clinic. Types of headache were diagnosed according to the revised IHS criteria published in 2004. According to the International Classification of Headache Disorders (ICHD-II), diagnosis of CM could be made in individuals with at least five previous migraine attacks who currently have 15 or more headache days and eight or more migraine days and/or with headache responding to specific medications for acute migraine (compounds containing ergotamine or triptans) (17).

MOH and EM (with or without aura) were diagnosed according to revised criteria of ICHD-II. Type of overused medication was classified according to ICHD-II criteria as ergotamine, triptan, analgesic, opioid, combination analgesic, combination of medications for acute attacks, or other medication (17).

Measures

The presence of psychiatric co-morbidity was evaluated by the clinician using Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, the Fourth Edition (SCID-I). Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Childhood Trauma Questionnaire (CTQ) were applied by a psychiatrist during the second interview. After sociodemographic and clinical variables were obtained and scales were completed, headache patients were divided into three groups and compared in terms of variables and mean scores of scales.

Sociodemographic data form was performed by psychiatrists and neurologists and age, gender, marital status, occupation, psychiatric disease history and family history were recorded.

Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) is a structured clinical interview performed by the interviewer to investigate Axis-I psychiatric disorders. It consists of six modules and investigates diagnostic criteria of a total of 38 Axis-I disorders. Two modules are used for mood episodes and mood disorders, two modules are used for psychotic symptoms and psychotic disorders, one of two modules is used for anxiety disorders and the other is used for substance abuse and other disorders. It was developed in 1997 by First et al. (18). Turkish version has been validated by Ozkurkcuğil et al. under the name of structured clinical interview for DSM-IV Axis-I disorders (19).

Childhood Trauma Questionnaire (CTQ) is a 28-item self-report retrospective inventory developed by Bernstein et al (20). It is a reliable and valid self-report Likert scale that assesses abuse and neglect. CTQ contains five subscales; three abuse (emotional, sexual and physical abuse) and two neglect (emotional and physical). Each item is a 5-point Likert scale ranging from never true to very often true. The reliability and validity study for Turkish population was done by Sar et al. (21). In the present study, we used the method of Tietjen et al. The CTQ cut-off scores were as follows: physical abuse ≥ 8 , sexual abuse ≥ 6 , emotional abuse ≥ 9 , physical neglect ≥ 8 and emotional neglect ≥ 10 (2).

The Turkish version of Beck Depression Inventory (BDI) is used to assess the prevalence and severity of depressive symptoms. BDI is a self-report questionnaire developed by Beck (22). BDI items consist of four statements, scored from 0 to 3 and the total score ranges from 0 to 63. A score of 0 to 4 is considered as none/minimal, 10 to 16 as mild depression, 17 to 29 as moderate depression and 30 to 63 as severe depression. A BDI score of 14 or higher is categorized as depressive. Reliability and validity study for Turkish population was done by Hisli et al. (23) who considered a score of 17 or higher to be the indicative of major depression in the Turkish population.

Beck Anxiety Inventory (BAI) is a 21-item questionnaire developed by Beck et al. (24) and is widely used to measure the severity of anxiety. Acceptable validity and reliability has been reported in various populations. Each item is scored between 0 and 3 in the increasing order of severity. The scores for each of 21 items were summed at the end of psychological evaluation. The validity and reliability study of this inventory for Turkish society was done by Ulusoy et al. (25).

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences software (Version 17.0, SPSS Inc., Chicago, IL, USA). If continuous variables showed normal distribution, they were described as mean \pm standard deviation [($p > 0.05$ using Kolmogorov-Smirnov test or Shapiro-Wilk test ($n < 30$))] and if continuous variables did not show normal

Table 1. Sociodemographic and clinical features of patients

	Group 1 (n=64) Median (Min–Max)	Group 2 (n=25) Median (Min–Max)	Group 3 (n=25) Median (Min–Max)	p	P _{Group 1 and 2}	P _{Group 1 and 3}	P _{Group 2 and 3}
Age	37 (17–60)	30 (17–47)	38 (20–61)	0.050	0.021	0.978	0.059
Headache duration (year)	10 (1–40)	7 (1–30)	7 (1–35)	0.377	0.182	0.557	0.400
Chronic headache duration (month)	6 (1–48)	4 (0–24)	0 (0–6)	0.0001	0.247	0.0001	0.0001
Frequency of headache (day/month)	30 (18(30))	25 (20–30)	3 (1–25)	0.0001	0.152	0.0001	0.0001
VAS	9 (1–10)	8 (5–10)	8 (7–10)	0.063	0.097	0.035	0.956
Analgesic number	30 (6–80)	5 (0–30)	3 (1–8)	0.001	0.0001	0.0001	0.092
BAI	20 (3–46)	16 (7–56)	16 (2–46)	0.784	0.823	0.563	0.521
BDI	17 (4–55)	19 (4–36)	13 (2–28)	0.520	0.815	0.265	0.428

p: Kruskal–Wallis test (p<0.05). p_{Group 1 and 2}, p_{Group 1 and 3}, p_{Group 2 and 3}: Post hoc Mann–Whitney U test (p≤0.017 Bonferroni correction). Significant data (p<0.05) are signed with bold characteristics. Group 1: Medication Overuse Headache, Group 2: Chronic Migraine, Group 3: Episodic Migraine. Max: maximum; VAS: visual analog scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory

distribution, they were described as median. Comparisons between the groups were performed using Kruskal–Wallis test for data, which were not normally distributed. Because analysis of variance was significant, comparisons were performed using Mann–Whitney U test. Categorical variables between the groups were analyzed using Chi square test or Fisher's Exact Test. Bonferroni correction test was used to adjust the P value to 0.0166 for each hypothesis. P values <0.017 were considered statistically significant.

RESULTS

Sociodemographic and clinical characteristics of the participants are summarized in Tables 1 and 2. A total of 116 patients participated in the study. Of the participants, 64 had MOH, 25 had CM and 27 had EM. There was no difference between the mean age, mean headache duration, headache severity (VAS), marital status, job and smoking status. There was also no significant difference between three groups in terms of headache-associated symptoms, nausea, vomiting, photophobia and osmophobia.

As expected, duration of chronic headache and frequency of headache were higher in MOH and CM groups with no significant difference between the groups. Simple analgesics (70%) and non-steroidal anti-inflammatory drugs were the most commonly used medications. Triptans have been used in 23.5% and ergo derivatives have been used in 15.6% of the patients.

The prevalence of CMT, particularly emotional neglect (62%), physical abuse (21.6%) and neglect (44%), was higher in all headache groups. Scores of these tests were higher but no significant differences were observed between three groups in terms of CMT. The results are summarized in Tables 3 and 4.

Results of psychiatric examination for co-morbid psychiatric conditions are demonstrated in Table 5. Psychiatric co morbidities were present in 43.1% of the patients, of which 20.7% had depression, 29.3% had anxiety and 7.8% had a somatoform disorder. The prevalence of psychiatric co-morbidities (depression and anxiety) was also higher in three groups, primarily in MOH and CM groups. However, there was no statistically significant difference between the groups (p>0.05). In addition, scores of BDI and BAI were higher in all three groups, particularly in MOH and CM groups. No statistically significant correlation was determined between psychiatric co-morbidities and childhood trauma, except for physical neglect (p<0.05).

Table 2. Demographic features of patients

	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Total n (%)	p
Sex					
Male	11 (17.2)	4 (16.0)	1 (3.7)	16 (13.8)	0.219
Female	53 (82.8)	21 (84.0)	26 (96.3)	100 (86.2)	
Job					
House-wife	27 (42.2)	12 (48.0)	12 (48.0)	51 (44.7)	0.333
Worker	12 (18.8)	2 (8.0)	4 (16.0)	18 (15.8)	
Retired	2 (3.1)	0 (0.0)	1 (4.0)	3 (2.6)	
Student	5 (7.8)	5 (20.0)	1 (4.0)	11 (9.6)	
Clerical	11 (17.2)	4 (16.0)	6 (24.0)	21 (18.4)	
Self-employment	6 (9.4)	0 (0.0)	0 (0.0)	6 (5.3)	
Unemployed	1 (1.6)	1 (4.0)	1 (4.0)	3 (2.6)	
Other	0 (0.0)	1 (4.0)	0 (0.0)	1 (0.9)	
Marital Status					
Single	49 (76.6)	15 (60.0)	17 (68.0)	81 (71.1)	0.474
Married	13 (20.3)	9 (36.0)	6 (24.6)	28 (24.6)	
Divorced	2 (3.1)	1 (4.0)	2 (8.0)	5 (4.4)	
Cigarette					
Smoking	2 (3.1)	3 (12.0)	5 (18.5)	10 (8.6)	0.093
No Smoking	5 (7.8)	4 (16.0)	2 (7.4)	11 (9.5)	
Ex-Smoker	57 (89.1)	18 (72.0)	20 (74.1)	95 (81.9)	

p: Kruskal–Wallis test (p<0.05). Group 1: Medication Overuse Headache, Group 2: Chronic Migraine, Group 3: Episodic Migraine

The correlations between CTQ and educational and psychiatric co-morbidity states were analyzed. There was no significant difference between education level and childhood trauma, except for physical neglect. Primary school graduates had higher scores than high school or university graduates. Physical neglect was determined in 88.9% of primary school graduates and in 11.1% of high school graduates. There was no patient with childhood physical trauma among university graduates (p<0.05).

Table 3. The association of childhood maltreatment types in patients with MOH, CM and EM

	Group 1 (n=64) Median (Min–Max)	Group 2 (n=25) Median (Min–Max)	Group 3 (n=25) Median (Min–Max)	p	P _{Group 1 and 2}	P _{Group 1 and 3}	P _{Group 2 and 3}
Childhood maltreatment	36 (25–85)	43 (25–68)	36 (25–60)	0.417	0.244	0.676	0.181
Emotional abuse	6 (5–20)	8 (5–15)	6 (5–17)	0.238	0.138	0.996	0.102
Physical abuse	5 (5–17)	5 (5–15)	5 (5–15)	0.752	0.469	0.924	0.560
Physical neglect	7 (5–18)	7 (5–14)	7 (5–13)	0.487	0.565	0.248	0.583
Emotional neglect	11 (5–25)	12 (5–25)	11 (5–22)	0.621	0.321	0.938	0.502
Sexual abuse	5 (5–17)	5 (5–24)	5 (5–13)	0.268	0.336	0.315	0.112

p: Kruskal–Wallis test (p<0.05), data are provided as median (minimum–maximum), P_{Group 1 and 2}, P_{Group 1 and 3}, P_{Group 2 and 3}: Post hoc Mann–Whitney U test (p≤0.017 Bonferroni correction).
Group 1: Medication Overuse Headache, Group 2: Chronic Migraine, Group 3: Episodic Migraine. MOH: medication-overuse headache; CM: chronic migraine; EM: episodic migraine

Table 4. The prevalence of childhood maltreatment subscales between groups

Childhood maltreatment	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Total n (%)
Emotional abuse	23 (35.9)	12 (48.0)	7 (25.9)	42 (36.2)
Physical abuse	11 (17.2)	7 (28.0)	7 (25.9)	25 (21.6)
Sexual abuse	10 (15.6)	6 (24.0)	2 (7.4)	18 (15.5)
Emotional neglect	36 (56.3)	20 (80.0)	16 (59.3)	72 (62.1)
Physical neglect	30 (46.9)	12 (48.0)	9 (33.3)	51 (44.0)

Group 1: Medication Overuse Headache, Group 2: Chronic Migraine, Group 3: Episodic Migraine. The percentage of study participants based on CTQ cut off scores (physical abuse ≥8, sexual abuse ≥6, emotional abuse ≥9, physical neglect ≥8, emotional neglect ≥10)

Table 5. The prevalence of psychiatric disorders in groups

	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Total n (%)
Psychiatric comorbidity	22 (34.4)	12 (48.0)	16 (59.3)	50 (43.1)
Depressive disorder	14 (21.9)	6 (24)	4 (14.8)	24 (20.7)
Anxiety disorder	23 (35.9)	6 (24)	5 (18.5)	34 (29.3)
Somatiform disorder	5 (7.8)	1 (4)	3 (11)	9 (7.8)

Chi-square test: n (%). Group 1: Medication Overuse Headache, Group 2: Chronic Migraine, Group 3: Episodic Migraine

DISCUSSION

To the best of our knowledge, this is the first Turkish study in the literature investigating the correlation of childhood maltreatment and MOH in adult patients. The current study suggested that the prevalence of CMT, particularly emotional neglect (62%), physical abuse (21.6%) and physical neglect (44%), was higher in all headache groups. Second notable finding was absence of statistically significant difference in CMT between the three groups (MOH, CM and EM groups). Third, there was no statistically significant correlation between the education level and childhood trauma, except for physical neglect. Physical neglect was most frequently observed in primary school graduates compared with other groups and finally, BDI and BAI scores were higher in three groups, particularly in MOH and CM groups, but no statistically significant correlation was determined between psychiatric co-morbidity and childhood trauma, except for the physical neglect.

Childhood maltreatment is a serious problem, which may have long-term consequences. It is known that psychiatric or systemic disorders may be associated with CMT. The overall prevalence of CMT in our study group was 36.2% for emotional abuse, 44% for physical abuse, 15.5% for sexual abuse, 62% for emotional neglect and 44% for physical neglect. The prevalence rates of physical neglect, physical abuse and emotional abuse were higher than those reported by Tietjen et al. They reported the prevalence rates of CMT types as follows: physical abuse, 21%; sexual abuse, 25%; emotional abuse, 38%; physical neglect, 22%; and emotional neglect, 38%. In particular, the prevalence rates of physical abuse, emotional neglect and physical neglect were higher than those reported by Tietjen et al. (14). Although there was no literature about CMT in Turkish population with migraine, these rates may also be reasonable for Turkey (8,26,27,28). In developing countries, physical abuse is particularly reported at higher prevalence (1). In Turkey's traditional life, the prevalence of physical and emotional neglect may be higher because of crowded family life as well as cultural and religious beliefs (8,26,27). The most commonly preferred ways of child punishment are verbal and physical maltreatment and abuse. These high rates may be associated with these factors.

The nature of the relationship between CMT and migraine remains speculative. It is not definitely known how CMT affects the brain functions and structure. However, there are some evidences that CMT leads to neurobiological sequelae. There is considerable clinical evidence that chronic early life stress results in long term changes in the function of hypothalamic–pituitary–adrenal axis and is regulated by the hypersecretion of CRH and ACTH. CMT causes cortisol hypersecretion in early lifetime but results in cortisol hyposecretion in time (5). It was shown that the function of hypothalamic–pituitary–adrenal axis was normal in EM but abnormal in CM. Early stress also results in a number of other functional changes that may play a role in migraine. Preclinical studies showed that stress increases dopamine levels and decreases serotonin levels in the amygdala and in nucleus accumbens. The expression of serotonin-1b receptors and density of central benzodiazepine receptors are decreased (29,30). In addition, early stressful experiences are associated with left prefrontal cortex amygdala and hippocampus (31). Other theories correlated with all CMT types are linked to re-victimization in the adulthood (3).

According to our hypothesis, patients with MOH may experience CMT, which may cause migraine to become chronic. Although the prevalence of CMT was higher among overall participants of the present study, there was no statistically significant difference between three groups. Despite the insignificant results, CMT should be investigated in patients with migraine.

In our study, no statistically significant correlation was reported between education level and childhood trauma, except for physical neglect. Physical

neglect was most frequently observed in primary school graduates compared with other groups. It is known that low education level is associated with CMT. Physical neglect consists of not having enough to eat, being forced to wear dirty clothes, not receiving medical care and not being taken care of or protected. Low education level may accompany low socioeconomic level, which can cause physical neglect (6,32,33).

Scores of BDI and BAI were high in all groups. In addition, depression and anxiety co-morbidities determined according to DSM-IV were also high with no statistically significant difference between three groups. Depression and anxiety are known to be associated with migraine and they are acceptable risk factors for transformation to chronic migraine from episodic migraine (34,35).

Relatively small sample size was the limitation of this study. Large group of patients with headache may lead to the evaluation of differences between MOH and other groups. By the virtue of cross-sectional design, this study does not allow a good inference about causal relationship. Another limitation of the study is the fact that our participants were selected from specialized services; therefore, the results may not reflect the general population. In addition, the study included no group without headache and we did not know the cut-off values of CTQ for Turkish population.

It is known that psychiatric co-morbidities are predictive for severe headache. CMT scores were higher in our patient population with headache. We hope that our study will inspire others to plan further studies that would be conducted in large populations with headache, particularly with MOH. We recommend that CMT should be considered in patients with headache.

Conflict of Interest: No conflict of interest was declared by the authors.

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