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SCHOLARENA

Journal of Neuroscience and Neuropsychology

REVIEW ARTICLE

2577-7890

Anxiety Affects All Aspects of Quality of Life in Medication Overuse Headache Patients

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Citation: Srdjan Ljubisavljevic (2026) Anxiety Affects All Aspects of Quality of Life in Medication Overuse Headache Patients, J Neurosci Neuropsyc 9 (1): 101.

Abstract

Anxiety among medication overuse headache (MOH) patients was assessed. The primary objective of this study was to examine the relationship between anxiety and health related quality of life among medication overuse headache (MOH) patients in group of 600 new diagnosed MOH patients. The study showed a positive correlation between the anxiety and duration of MOH. Anxiety is showed as a risk factor for development of MOH. Anxiety was singled out as a risk factor for the overall aspect of health in MOH sufferers ($p = 0.05$). The study found that the duration of the earlier chronic headache positively correlated with the impact of MOH ($r = 0.327$, $p = 0.003$). The impact of MOH as well as anxiety were on all domain of health and assessed as significant, correlating with the duration of the MOH ($p \leq 0.05$). Assessment of anxiety in MOH patients could be important for improving their quality of life.

Key words: anxiety; medication overuse headache.

Introduction

Headache disorders have been associated with anxiety. Recognizing that comorbidity is important to study their relationship, causality, shared etiology, pathogenesis, and other aspects. Psychiatric comorbidities are common, especially anxiety and depression [1]. In the COMOESTAS study, 30% met criteria for anxiety [2]. In the EUROLIGHT cross-sectional study conducted in 10 countries of the European Union, similar results were obtained, with a greater difference in the frequency of these comorbidities compared to the group with migraine without excessive use of analgesics [3]. The SAMOHA, study examined the frequency of psychopathologic comorbidities in migraine patients compared to patients with episodic migraine and healthy controls [4]. The frequency of moderate to severe anxiety was higher in both groups with headaches, whereas the frequency of addictive disorders was significantly higher in patients with migraine. Patients with migraines often had multiple psychiatric comorbidities. Obsessive-compulsive syndrome has been shown to be associated with migraine. One-third of migraine patients may have subclinical forms of obsessive-compulsive syndrome, which is a recognized risk factor for the chronicity of migraine [4-6]. Migraine may be associated with behavioral disorders related to substance use [5,6]. The daily or almost daily frequent use of symptomatic drugs in patients with high frequency or chronic migraine, and less frequently with chronic tension-type headache, leads to the development of medication overuse headache (MOH). Medication-overuse headaches (MOH), also known as analgesic rebound headache, drug-induced headache, or medication-misuse headache, are a common neurologic disorder that can cause immense disability and suffering, and can transform episodic headache disorders into chronic headache disorders [4-6].

The psychopathological profile of patients with medication overuse headache (MOH) appears to be particularly complex. Here we designed a case-control study comparing anxiety in MOH patients and matched healthy controls (HC). We enrolled 183 consecutive MOH patients and 11 HC. MOH patients showed greater difficulty in anxiety. We found a positive correlation among anxiety and HIT-6 scores. MOH patients showed a high rate of anxiety, which may negatively affect their headaches as well as health related quality of life. The ability to regulate/recognize emotions may play a central role in sustaining medication overuse [7]. Together with mood and anxiety disorders, it can be observed as tending to obsessive-compulsive disorders and the occurrence of dependence-related behavior [8,9], and it has yet been suggested that a psychological profile assessment should be included in patients' evaluation [9].

A negative prognostic value for anxiety psychiatric comorbidities has been suggested putting forward the hypothesis that these can represent a risk factor for the evolution of episodic into chronic headaches [10]. Psychopathological disturbances are also seen as a potential predictor of relapse and poor response to treatment, and this can, in turn, complicate headache management facilitating MOH development [10-12].

Materials and patients

Study population

Our database of head screen patients included more than 800 patients. For this research, we included only those with voluntary written informed consent to participate. The patients completed demographic and medical questionnaires, which included demographic information; educational level; marital status; family and work status; number of family members; residence; personal history; presence of other illnesses; presence of previous (primary and/or secondary) headaches (type, characteristics, duration, frequency, type and effectiveness of symptomatic and preventive therapy); and habits and risk factors (physical activity, cigarette smoking, use of alcohol, caffeine, etc.). The study was conducted in the Headache Center of the Neurology Clinic at the Clinical Center in Niš during 2022-2023 (January-December). The Clinical Center in Niš is a tertiary healthcare institution to which approximately 2,5 million inhabitants from the area of southeastern Serbia gravitate.

MOH group

This group included all patients in whom MOH was first diagnosed during the period of this study after their voluntary consent to participate in the study. The diagnosis of MOH was made according to the diagnostic criteria of the Headache Classification Committee of the International Headache Society (2018). The secondary etiology of the headache was ruled out after complete diagnostic processing (computed tomography/magnetic resonance imaging of the endocranium, etc.). For all patients, the diagnosis of MOH was made by the same doctor, a specialist in neurology and pain medicine, who manages the Headache Center at the Clinical Center Nis. At this clinic, patients were referred for examination by primary care physicians or specialists in neurology, internal medicine, or related specializations. This group consists from 183 patients (72 men and 111 women).The study cohort was 40.5 ± 11.6 years.

The following data related to MOH and previous chronic headache were collected from these patients: duration of headache; frequency (number of days with headache in one month); location of pain (frontal, temporal, parietal, and occipital); lateralization (unilateral and diffuse); character of pain (muffled and pulsating pain); intensity of pain (using a numerical scale for pain assessment); presence of related symptoms and signs (nausea/vomiting, photophobia, phonophobia, diplopia, neck and shoulder stiffness, blurred vision, tinnitus, and hypoxia); type of analgesic therapy used; use of preventive therapy; frequency of use of this therapy (number of days in one month); and therapeutic efficacy (assessment of pain intensity reduction/associated symptoms). Detailed data regarding headache characteristics are presented in our previous paper [13].

Control group

The control group (CG) was selected from among the companions (relatives, friends) of all patients who were examined at the Headache Center during the period of this study after their voluntary consent to participate. These individuals were included consecutively (in order) up to the predicted number (according to the number of patients in the MOH group). The preconditions for their inclusion were that they did not have a headache in their personal life history (at least in the last two years), that they did not have serious somatic or mental illnesses and that they did not use any chronic therapy. This group consisted of 129 respondents (82 women and 47 man).

Instruments

The quality of life was assessed using the Short Form (SF)-36 questionnaire6. The SF-36 questionnaire has previously been approved for use in the Serbian language and has shown good internal consistency (ranging from .80 to .90) (https://e-provide.mapi-trust.org/about/about-proqolid). The SF-36 consists of 36 questions that evaluate eight dimensions of health: physical functioning, role functioning physical, bodily pain, general health, vitality, social functioning, role functioning emotional, and mental health. In each domain, higher scores (range 0–100) reflect better self-perceived health per unit. The physical composite score (PCS) represents the mean value of the scores in the first four domains, and the mental composite score (MCS) represents the mean value of the scores in the last four domains. The total score (TS) was calculated as the mean physical composite score (PCS) and the mean mental composite score (MCS) [6]. The test was applied at the time of MOH diagnosis (MOH group) or consent to participate in the study (control group).The study was performed in strict accordance with the Declaration of Helsinki after informed consent was obtained from each participant in the study. The study was approved by the local ethics committee.

Statistical analysis

No power calculations were conducted to determine the sample size for this particular study. The data are presented as the mean±standard deviation or as counts and percentages. Unpaired Student's t test or the Mann–Whitney test was used to com-

pare continuous data, as appropriate. Analysis of variance (ANOVA) or the Kruskal–Wallis test was performed for continuous data among three or more groups, as appropriate. The chi-square test or Fisher's test was used for analysis of categorical data. An exploratory logistic regression analysis (entry method) was also conducted to further assess the significant associations between demographic, clinical and headche-related characteristics and quality of life. From these analyses, those variables with $p< 0.10$ were retained for the subsequent multivariable model (backward Wald method). Logistic and linear regressions were performed, and the Hosmer–Lemeshow test was performed to estimate the calibration ability of the models. A complete case analysis was performed. A p value was set at $p<0.05$. All the statistical analyses were performed using R software, version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Our study showed a high rate of anxiety in MOH group. Moreover, we found a positive correlation among anxiety and HIT-6 questionnaires as well as reduction in mental, physical and total health aspects ($p\leq0.05$). Patients showed a mean of 24±6 of headache per month and a median of 40 symptomatic medications taken per month (IQR: 76; minimum 22 and maximum 155). The mean HIT-6 score was 67 (± 6), the mean of MIDAS total score was 78.8 (± 61.3), MIDAS score was 65.2 (± 22.3). We found no significant difference between men and women. Also, we found that anxiety appear as a risk factor for mental as well as physical aspect of health related quality of life as well total aspect of quality of life.

Chronic migraine

Chronic migraine is a common condition, affecting approximately 1 in 50 people. The diagnosis of chronic migraine implies that a patient has a history of migraine headaches and is now experiencing headaches at least 15 days per month. Effective management of chronic migraine involves a multifaceted approach, including the prescription of a daily preventive medication to reduce headache frequency, aggressive acute treatment of headaches that occur despite the preventive medication, and the identification and treatment of any underlying conditions that may be contributing to chronic headaches. The medical conditions that most commonly exacerbate chronic migraines are sleep disorders, mood disorders (typically depression, anxiety, or both), hormonal influences (pregnancy, recent childbirth, use of oral contraceptives), and overuse of pain medications [14]. An analgesic is any medication used to relieve pain, whether it be a simple over-the-counter (OTC) medication like acetaminophen or a strong opioid ("narcotic"). Patients with chronic headaches often take analgesics frequently to relieve their pain and enable them to carry out their daily activities. Unfortunately, virtually all medications—whether prescription or OTC—taken by migraine sufferers to treat acute headaches can exacerbate headaches if taken too frequently over a period of weeks or months. Some of the most commonly used are acetaminophen, compounds containing acetaminophen plus caffeine, butalbital-containing compounds, and hydrocodone. Even the triptans, which are commonly used to treat acute migraine, can also cause medication overuse headache (MOH) [3,15].

The interplay of chronic migraine and medication overuse headache can significantly impact a person's quality of life [14-16]. The constant presence of headaches and the need for frequent medication use can lead to physical and emotional distress, decreased productivity, and limitations in daily activities [14,17]. Both chronic migraine and medication overuse headaches are believed to stem from the same underlying pathophysiology of altered pain processing in the brain. In both conditions, there is a deregulation of pain signals, leading to an increased sensitivity to pain and a decreased ability to modulate pain. This shared mechanism is what makes medication overuse headache a common consequence of treating chronic migraines with frequent analgesic use. It is essential for healthcare providers to address both the chronic migraine and medication overuse headache to improve the overall well-being of the patient [9,14,17].

Aim of the study

The primary objective of this study was to examine the relationship between anxiety and health related quality of life among medication overuse headache (MOH) patients in group of 600 new diagnosed MOH patients. The primary objective of this study was to examine the relationship between chronic migraine as a previous headache disorder and the subsequent development of MOH. By elucidating the connection between these two conditions, the researchers sought to gain valuable insights that could inform more effective prevention and management strategies for patients at risk of experiencing this debilitating secondary headache. Detailed data are presented in Tables 1-5.

Table 1. Basic data about MOH patients

	Broj	%
Marrital status		
married	79	68,7
divorced	7	8,4
Unmarried	1	1,2
Unmarried	18	21,7
City	65	78,3
Village	12	21,7
Education		
Elementary	16	7,2
High	46	53,0
Faculty	16	14,5
PhD	9	22,9
Working status		
work	55	6,3
No work	25	30,1
Retaired	3	3,6
N famillty members	3,39±1,05	1-7
N of child		
0	21	25,3
1-2	56	67,5
3	6	7,2
Smoking		
Yes	34	41,0
No	49	59,0
Alcol use		
Yes	4	4,8
No	79	95,2
Coffeine use		

Yes	74	89,2
No	9	10,8
Physical activity		
Yes	8	9,6
No	75	90,4

Table 2. Basic data about MOH patient

Dg comborbodity		
endocrinological	7	8,4
psychiatric	2	2,1
neurological	1	1,2
cardiological	10	12,0
respiratory	7	8,4
musculo skeletal	9	10,8
MOH duration (years)	5.08±5.52	1-30
MOH –N of days per month	19.40±6.07	10-30
MOH - duration (h)	10.71±1.90	5-12
MOH – pain (VAS)		
5	16	19,3
6	17	20,5
7	7	8,4
8	38	45,8
9	3	3,6
10	2	2,4
MOH localisation		
F	14	16,9
O	5	6,0
P	10	12,0
T	54	65,1
MOH -lateralisation		
Bilateral	57	56,6
Unilateral	46	43,4
MOH		
Yes	41	49,4
No	42	50,6
MOH -associated symptoms		

1	4	4,8
2	1	1,2
10	3	3,6
11	68	81,9
12	7	8,4

Table 3. Risk factors for MOH

	Univarijant model			Multivarijant model*		
	OR	95%CI	p	OR	95%CI	p
Gender (female)	2,44	1,10-5,44	0,029	n.s		
Age	1,00	0,98-1,03	0,745			
Marrital status (married vs unmarried and ectr,)	3,19	1,68-6,06	<0,001	n.s		
Residency place (city vsvillage)	1,45	0,66-3,19	0,358			
Education (elementary vs high/faculty)	0,33	0,17-0,62	0,001	n.s		
N of child	1,13	0,74-1,73	0,569			
Smoking	0,85	0,45-1,59	0,606			
Alcol using (no vs yes)	3,44	1,06-11,14	0,040	n.s		
Coffeine using (no vs yes)	0,77	0,30-1,98	0,593			
Physical activity (ne vs da)	4,69	1,98-11,11	<0,001	n.s		
Anxiety	1,14	1,09-1,19	<0,001	1,12	1,07-1,18	<0,001

Tables 4. Health related quality of life

SF-36 physical aspect	67,22	10,60	40	91,25	0,084	0,200
SF-36 mental aspect	69,53	11,80	41,75	93,75	0,111	0,015
SF-36 total aspekt	68,38	16,22	45,63	88,25	0,109	0,019

Table 5. Correlation between different parameters and MOH

	Univariant model			Multivariant model*		
	B	95%CI	p	B	95%CI	p
Gender (female)	-12,32	-22,47 - -2,16	0,018	-8,72	-17,90 – 0,47	0,063
Age	-0,20	-0,50 - - 0,11	0,204			
Marrital status (married vs unmarried and ectr,)	-0,23	-0,72 – 7,45	0,952			
Residency place (city vsvillage)	-3,80	-12,41 – 4,80	0,382			
Education (elementary vs high/faculty)	4,73	-2,48 – 11,93	0,196			
N of child	-3,75	-8,57 – 1,07	0,126			
Smoking	-3,32	-10,54 – 3,88	0,362			

Alcol using (no vs yes)	-0,06	-0,38 – 0,26	0,713			
Coffeine using (no vs yes)	14,79	-1,52 – 31,11	0,075	0,22	-14,12 – 14,56	0,976
Physical activity (ne vs da)	-2,80	-14,24 – 8,65	0,628			
Migraine	-0,94	-1,19 – -0,68	<0,001	-0,69	-1,16 - -0,22	0,352
Anxiety	-1,00	-1,31 - -0,69	<0,001	-0,02	-0,61- - 0,56	0,005
Stress	-0,88	-1,18 - -0,58	<0,001	-0,28	-0,70 – 0,14	0,184

Discussion

The impairment of the MCS is more pronounced in people suffering from MOH and are independent of gender and alcohol-related habits. In this study, the TS was impaired in patients with MOH compared to healthy subjects regardless of gender and in patients who did not consume alcohol, compared to healthy subjects of the same status. Previous research has shown a deterioration in the quality of life in patients with MOH compared to healthy subjects. It has also been shown that anxiety is of particular importance in this impairment of quality of life as frequent comorbidities of MOH. In the observational research, it was noticed that with the discontinuation of overused medications in hospital settings, there is a significant improvement in the quality of life of patients with MOH and a reduction in the level of their psychological distress. It has also been shown that patients with greater MCS disorders and a higher degree of anxiety have a less favorable outcome in reducing the number of days with monthly headaches and improving quality of life after discontinuation of excessive medication [8,9]. There is a study that examined the quality of life in patients with MOH after discontinuation of excessive medication in relation to different modalities of secondary prevention and rehabilitation in hospital settings. In these patients, the PCS was not significantly changed in relation to the expected values after discontinuation of excessive medication, while the MCS was significantly impaired after discontinuation of excessive medication for a long period [9,14,17]. Previous research has shown that strengthening coping strategies play a key role in improving the quality of life, especially the MCS, in adolescents suffering from chronic headaches [15,16,18]. There is research on the impact of stress control on the intensity of pain and quality of life of people with chronic headaches. The results of this study confirm the effectiveness of mindfulness-based stress reduction in improving all aspects of quality of life and suggest the application of this method in combination with traditional pharmacotherapy [12]. There are suggestions that the application of combined models of acceptance and the type of cognitive-diffusion-related process can influence the improvement of the PCS and MCS in people with chronic pain [11,12,16,18].The results of previous research indicate the complexity of the mechanisms that mediate impaired quality of life in patients with chronic pain. These mechanisms especially emphasize the importance of the ruminative style of thinking, the tendency to disaster and strengthen the feeling of helplessness [13]. Other studies have compared the effectiveness of mindfulness-based cognitive therapy and the quality of life-based therapy to the ruminative style of thinking in patients with chronic headaches. The results indicate a significant efficacy in reducing the number of days with headache on a monthly basis and improving the quality of life when applying both therapeutic interventions [2,6,19]. This type of association was observed at the beginning of the study only in the population of the elderly, but at the end of the study [19,20].

1. The study cohort revealed that MOH was predominantly caused by the transformation of chronic migraine, with a staggering 74% of cases showing this association. This emphasizes the strong relationship between these two conditions, where the excessive use of acute headache medications to manage chronic migraine can result in the development of MOH.

2. The data from the study indicated that MOH often goes undiagnosed and untreated for an average duration of 6.1 ± 5.5 years. The impact of MOH on patients' daily lives was found to be significant, as reflected by a high Headache Impact Test (HIT) score of 65.4 ± 5.5. This underscores the profound effect that MOH can have on an individual's quality of life, emphasizing the importance of early recognition and proper management.

The study showed a positive correlation between the duration of chronic migraine and the impact of MOH, suggesting that the longer a person experiences chronic migraine, the more severe the consequences of medication overuse can be. This highlights the crucial role of healthcare providers in educating patients about the risks of medication overuse and the significance of adhering to preventive therapy to prevent the development of this secondary headache disorder.

As we found here MOH was most commonly generated by the transformation of chronic migraine, affecting 74% of the patients. The study found that common (51%) and combination analgesics (48.2%) were the medications most frequently overused, with patients consuming them 15 to 25 days per month. Importantly, the impact of MOH on the patients' daily life was assessed as significant, with a HIT score of 65.4 ± 5.5. Furthermore, the duration of the earlier chronic headache correlated with the impact of MOH, as indicated by the moderate positive correlation ($r = 0.327$, $p = 0.003$).

The potential for developing MOH appears to vary based on the individual patient's unique biology and the specific medication in question. Some studies have suggested that triptans have the highest potential for causing MOH, while non-steroidal anti-inflammatory drugs (NSAIDs) have the lowest risk. Importantly, over-the-counter analgesics can be particularly "insidious" in this regard, as their ready availability and perceived safety can tempt patients to steadily increase their intake, ultimately leading to the entrapment of MOH. By including all variables with a significance level of $p<0.1$ in the univariate model in the analysis of the multivariate model, anxiety was singled out as a risk factor for the overall aspect of health in MOH sufferers (B= -0.69, 95%CI -1.16 - - 0.22, p=0.005). This suggests that the longer an individual has been suffering from chronic migraine, the more severe the consequences of medication overuse can be. Therefore, clinicians must be vigilant in educating patients with chronic migraine about the risks of medication overuse and the importance of adherence to preventive therapy, in order to prevent the development of this secondary, and potentially more disabling, headache disorder. The data revealed that the average duration of MOH until diagnosis was 5.1 ± 5.5 years, indicating that this secondary headache disorder often goes unrecognized and untreated for an extended period. Interestingly, the impact of MOH on the patients' daily lives was assessed as significant, with a high Headache Impact Test (HIT) score of 65.4 ± 5.5. This underscores the profound and debilitating effect that MOH can have on an individual's quality of life, and highlights the need for early recognition and appropriate management of this condition. Notably, the study found that the duration of the earlier chronic headache (migraine) was positively correlated with the impact of MOH ($r = 0.327$, $p = 0.003$). This suggests that the longer an individual has been suffering from chronic migraine, the more severe the consequences of medication overuse can be. Common (41%) and combination analgesics (48.2%) were the most frequently used medications, taken 15 to 25 days per month, contributing to the overuse that leads to MOH. Importantly, the impact of MOH on daily life was assessed as significant, correlating with the duration of the earlier chronic headache, Table 3. Anxiety has been rolled out as a predictor for all aspects of health related quality of life [21-26].

Conclusion

In summary, the close relationship between anxiety and medication overuse headache underscores the importance of vigilant patient education, early recognition, and a comprehensive management approach that includes preventative medication, acute treatment, and the avoidance of analgesic overuse. By addressing both the primary and secondary headache disorders, as well anxiety can useful for MOH patients quality of life.

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