



Screening for Depression among Medication Overuse Headache Patients and Treatment Could Be Useful for Improving their Quality of Life

Ljubisavljevic Srdjan^{1,2*#}, Todorovic Stefan^{1#} and Djokovic Filip¹

¹Clinic for Neurology, Clinical Center of Niš, Niš, Serbia

²Faculty of Medicine, University of Niš, Serbia

Abstract

Background : There is no clear negative impact of Medication Overuse Headache (MOH) on Quality of Life (QoL).

Objective : The aim of this study was to identify clinical and headache-related parameters that directly affect the HRQoL of MOH patients.

Patients and methods: A total of 183 patients (111 men and 72 women) first diagnosed with MOH and 81 healthy subjects (22 men and 59 women) in the Control Group (CG) were enrolled in this study. The age of the study subjects ranged from 18 to 71 years. HRQoL was assessed using the Short Form-36 (SF-36), which includes the Physical Composite Score (PCS), Mental Composite Score (MCS) and Total Score (TS).

Results : The HRQoL of all patients (PCS, MCS, TS) was lower in the MOH than in the CG ($p < 0.001$). In the MOH, depression itself was a risk factor for all aspects of HRQoL according to the PCS ($B = -0.70$, 95% CI $-1.32 - 0.08$, $p = 0.027$); for the MCS ($B = -0.71$, 95% CI $-1.14 - -0.29$, $p = 0.001$); and for the TS ($B = -0.69$, 95% CI $-1.16 - -0.22$, $p = 0.005$), with female sex being an associated risk factor only for PCS ($B = -15.47$, 95% CI $-26.79 - -4.14$, $p = 0.008$). The results did not reveal a predictive role of anxiety, stress, or ruminative style of thinking for HRQoL in MOH patients ($p > 0.05$).

Conclusion : Screening for depression among MOH patients and treatment could be useful for improving their HRQoL.

Keywords: Medication overuse headache; Health-related quality of life

Introduction

Medication Overuse Headache (MOH) is a secondary headache caused by excessive use of therapy to stop an acute headache attack [1]. Approximately 80 million people worldwide are estimated to have MOH [2] among different populations. Additionally, in relation to place of residence, socioeconomic status, employment and level of education.

MOHs are more prevalent in urban areas (14.5% vs. 2.1%) [3]. Several studies have shown a greater incidence of MOH among people with lower socioeconomic status [4]. Some data showed the highest prevalence of MOH among those patients using social assistance (11%), among those newly retired (7.5%) and among those on extended sick leave (6%) [5]. A higher incidence of MOH is observed in migrants [6]. There is no clear

evidence of a link between these parameters and the development of MOH [4,7].

The negative impact of MOH on the quality of life of patients is undoubted. The economic costs of national and health funds related to the MOH have been assessed as very significant [8,9]. Low quality of life, a high degree of disability, sleep problems, and insufficient functional mechanisms/coping strategies have already been recognized as important parameters for the occurrence of chronic headache [10]. On the other hand, patients with chronic headaches generally have a reduced quality of life and an increased degree of disability. The results indicate that patients with chronic migraine and MOH have a greater degree of functional disability than patients with chronic migraine without MOH [11]. There is insufficient research on the relationship between quality of life and other characteristics, comorbidities and habits in patients with MOH.

The aim of this study was to assess the health-related quality of life among MOH patients regarding their different sociodemographic, clinical and headache-related parameters to identify parameters that directly affect the quality of life of MOH patients.

Patients and Methods

The study was approved by the Ethics Committee of the Faculty of Medicine at the University of Niš and was conducted as an observational, one-year cross-sectional study.

Study population

Our database of headscreens patients included more than 400 patients. For this research, we included only those with voluntary written informed consent to participate. The patients completed sociodemographic and medical questionnaires, which included demographic information; educational level; marital status; family and work status; number of

Submitted: 08 February 2024 | **Accepted:** 17 April, 2024 | **Published:** 19 April, 2024

***Corresponding author:** Srdjan Ljubisavljevic, Clinic for Neurology, Clinical Center of Niš, Faculty of Medicine, University of Niš, Serbia.
#These authors contributed equally to this work.

Copyright: © 2024 Srdjan L, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Citation: Srdjan L, Stefan T, Filip D (2024) Screening for Depression among Medication Overuse Headache Patients and Treatment Could Be Useful for Improving their Quality of Life. J Gen Med 5: 6.



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 Clinic of the Neurology Clinic at the Clinical Center in Niš during 2019 (January-December). The Clinical Center in Niš is a tertiary healthcare institution to which approximately 2 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.

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 [12].

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.

Instruments

The quality of life was assessed using the Short Form (SF)-36 questionnaire. 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://eprovide.mapi-trust.org/about/about-proqolid>) [13]. 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 [14]. 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). The test was applied at the time of MOH diagnosis (MOH group) or consent to participate in the study (control group).

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 compare 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 headache-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

The study included 164 subjects (33 men and 131 women), 83 patients (11 men and 72 women) in the MOH and 81 subjects (22 men and 59 women) in the CG. The average age of the study subjects was 40.2 ± 11.9 years (min 18, max 71 years). The detailed data are described in our previous published paper [12]. All the SF-36 scores (PCS, MCS, and TS) were significantly lower in the MOH than in the CG ($p < 0.001$). Strong correlations were observed between parameters of quality of life and psychological distress parameters as well as ruminative thought style ($p < 0.05$) [15] (Table 1).

Table 1: Depressivity Kolmogorov-Smirnov test and Kronbahov α coefficient.

	CG		MOH		p
	$\bar{X} \pm SD$	Min-Max	$\bar{X} \pm SD$	Min-Max	
Depressivity†	5.78 ± 5.97	0-27	14.86 ± 10.96	1-42	$< 0.001^1$
Anxiety†	6.53 ± 5.05	0-22	16.48 ± 9.40	1-39	$< 0.001^1$
Stress†	11.81 ± 6.84	0-27	22.99 ± 10.11	1-41	$< 0.001^2$

†Mean value ± standard deviation; ¹Mann-Whitney test; ²t test
³For whole sample (MOH and CG)

The PCS was impaired in the MOH group in relation to CG, both in persons younger and in persons older than 40 years ($p < 0.001$); the PCS was impaired in women in the MOH group compared to women in the CG ($p < 0.001$); the PCS was impaired in persons with MOH (regardless of place of residence) compared to healthy persons with the same place of residence ($p < 0.001$); persons with secondary and higher education who suffer from MOH have impaired PCS compared to persons with the same education who did not suffer from MOH ($p < 0.001$); marital and unmarried people suffering from MOH have impaired PCS compared to persons of the same marital status who did not suffer from MOH ($p < 0.001$); in relation to work status (works/does not work) persons with MOH have impaired PCS compared to persons of the same work status who did not have MOH ($p < 0.001$); in relation to smoking status (smoker/nonsmoker) persons with MOH have impaired PCS compared to persons with the same smoking status who did not have MOH ($p < 0.001$); impairment of the PCS was observed in persons suffering from MOH and consuming alcohol compared to persons without MOH of the same habits ($p < 0.001$); in relation to the use of caffeinated beverages, impaired PCS was observed in persons with MOH, both in those who consume and in those who do not consume caffeinated beverages in relation to persons in CG of the same habits ($p < 0.001$); in relation to physical activity, impaired



PCS was observed in persons with MOH in relation to persons in CG of the same physical activity ($p < 0.001$). In the CG, a statistically significant impairment in the PCS was observed in patients older than 40 years ($p = 0.004$) and in patients with a lower level of education ($p = 0.004$). In the MOH group, a statistically significant impairment in the PCS was observed in women ($p = 0.002$) (Table 2).

Table 2: 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 (oženjen/a vs neoženjen/a i dr.)	3.19	1.68-6.06	< 0.001	n.s		
Place Residency (grad vs selo)	1.45	0.66-3.19	0.358			
Education (osnovna vs viša/visoka škola)	0.33	0.17-0.62	0.001	n.s		
No. of children	1.13	0.74-1.73	0.569			
Smoking	0.99	0.97-1.03	0.894			
Alcol Use (no vs yes)	3.44	1.06-11.14	0.040	n.s		
Caffeine Use (no vs yes)	0.77	0.30-1.98	0.593			
Physical Activity (no vs yes)	4.69	1.98-11.11	< 0.001	n.s		
Depresivnty	1.14	1.08-1.20	< 0.001	1.10	1.05-1.19	0.039
Anxiety	1.21	1.14-1.29	< 0.001	1.09	1.07-1.21	0.029
Stress	1.17	1.11-1.23	< 0.001			

n.s. – $p > 0.05$; OR unakrsni odnos; 95% CI – 95% interval poverenja; *Hosmer Lemeshow test – $p = 0.136$
†Mean value ± standard devijacij; †Mann-Whitney test; ‡t test

The MCS in relation to gender, age and other sociodemographic variables, the following statistically significant differences were observed: the MCS was impaired in the MOH group in relation to CG, both in persons younger and in persons older than 40 years ($p < 0.001$); the MCS was impaired in both women and men in the MOH group compared to women and men in the CG ($p < 0.001$); the MCS is impaired in persons with MOH (regardless of place of residence) compared to healthy persons with the same place of residence ($p < 0.001$, $p = 0.001$); persons with secondary and higher education who suffer from MOH have impaired MCS compared to persons with the same education who did not suffer from MOH ($p < 0.001$); marital and unmarried people with MOH have a MCS disorder compared to people of the same marital status who did not have MOH ($p < 0.001$); in relation to work status (works/does not work) persons with MOH have impaired MCS compared to persons of the same work status who did not have MOH ($p < 0.001$); in relation to smoking status

(smoker/nonsmoker) persons with MOH have impaired MCS compared to persons of the same smoking status who did not suffer from MOH ($p < 0.001$); impaired MCS was observed in people suffering from MOH who consume and in those who do not consume alcohol compared to people without MOH of the same status ($p = 0.008$, $p < 0.001$); in relation to the use of caffeinated beverages, impaired MCS was observed in persons with MOH who consume and do not consume caffeinated beverages in relation to persons in CG of the same habits ($p < 0.001$, $p = 0.001$); in relation to physical activity, impaired MCS was observed in persons with MOH in relation to persons in CG of the same physical activity ($p < 0.001$). In the CG, a statistically significant impairment in the MCS was observed in individuals older than 40 years ($p = 0.010$) and in physically less active people ($p = 0.044$) (Table 3-3b).

Table 3: Risk factors for quality of life in MOH (physical aspect of health).

	Univarijantni Model			Multivarijantni Model*		
	B	95% CI	p	B	95% CI	p
Gender (female)	-21.61	-33.79 - -9.43	0.001	-15.47	-26.79 - -4.14	0.008
Depresivnty	-0.93	-1.28 - -0.57	< 0.001	-0.70	-1.32 - -0.08	0.027
Anxiety	-1.04	-1.45 - -0.62	< 0.001	0.07	-0.73 - 0.87	0.861
Stress	-0.86	-1.26 - -0.46	< 0.001	-0.30	-0.87 - 0.27	0.297

B-coefficient of regression; 95% CI – 95% confidential interval; *Adjusted $R^2 = 0.340$

Table 3a: Risk factors for quality of life in MOH (mental aspect of health).

	Univarijantni Model			Multivarijantni Model*		
	B	95% CI	p	B	95% CI	p
Gender (female)	-3.02	-13.02-6.97	0.549			
Age	-0.16	-0.45-0.13	0.285			
Depresivnty	-0.95	-1.18 - -0.72	< 0.001	-0.71	-1.14 - -0.29	0.001
Anxiety	-0.96	-1.25 - -0.66	< 0.001	-0.01	-0.53-0.51	0.967
Stress	-0.90	-1.17 - -0.62	< 0.001	-0.33	-0.71-0.05	0.090

B-coefficient of regression; 95% CI – 95% confidential interval; *Adjusted $R^2 = 0.446$

Table 3b: Risk factors for quality of life in MOH (total aspect of health).

	Univarijantni Model			Multivarijantni Model*		
	B	95% CI	p	B	95% CI	p
Depresivnty	-0.94	-1.19 - -0.68	< 0.001	-0.69	-1.16 - -0.22	0.005
Anxiety	-1.00	-1.31 - -0.69	< 0.001	-0.02	-0.61 - 0.56	0.942
Stress	-0.88	-1.18 - -0.58	< 0.001	-0.28	-0.70 - 0.14	0.184

B-coefficient of regression; 95% CI – 95% confidential interval; *Adjusted $R^2 = 0.409$

The TS in relation to gender, age and other sociodemographic variables showed the following statistically significant differences: the TS was impaired in the MOH group in relation to CG, both in same place of residence ($p < 0.001$); persons with secondary and higher education who suffer from MOH have impaired TS compared to persons with the same education who did not suffer from MOH (p persons younger and in persons older than 40 years ($p < 0.001$); TS was impaired in both women and men in the MOH group compared to women and men in the CG ($p <$



0.001, $p = 0.001$); the TS was impaired in persons with MOH (regardless of place of residence) compared to healthy persons with the < 0.001 ; marital and unmarried people with MOH have impaired TS compared to people of the same marital status who did not have MOH ($p < 0.001$); in relation to the work status (works/does not work) persons with MOH have impaired TS compared to persons of the same work status who did not have MOH ($p < 0.001$); in relation to smoking status (smoker/nonsmoker), persons with MOH have impaired TS compared to persons of the same smoking status who did not suffer from MOH ($p < 0.001$); impairment of the TS was observed in persons suffering from MOH who do not consume alcohol compared to persons without MOH of the same status ($p < 0.001$); in relation to the use of caffeinated beverages, impairment of the TS was observed in persons with MOH who consume and do not consume caffeinated beverages in relation to persons in CG of the same habits ($p < 0.001$); in relation to physical activity, impairment of the TS was observed in persons with MOH in relation to persons in CG of the same physical activity ($p < 0.001$). In the CG, a statistically significant impairment in TS was observed in individuals older than 40 years ($p = 0.002$) and in individuals with a lower level of education ($p = 0.015$). In the MOH group, impaired TS was observed in women ($p = 0.023$) (Table 4,4a).

Table 4: Risk factors for quality of life in MOH (physical aspect)

	Univarijantni Model			Multivarijantni Model*		
	B	95% CI	p	B	95% CI	p
Depresivnty	-1.01	-1.34 - -0.69	< 0.001	-0.70	-1.13 - -0.27	0.002
Anxiety	-1.02	-1.43 - -0.60	< 0.001	-0.20	-0.75 - 0.33	0.452
Stress	-0.50	-0.83 - -0.17	0.003	-0.12	-0.46 - 0.22	0.491

B-coefficient of regression; 95% CI – 95% confidential interval; *Adjusted $R^2 = 0.363$

Table 4a: Risk factors for quality of life (total aspect) in CG

	Univarijantn Model			Multivarijant Model*		
	B	95% CI	p	B	95% CI	p
Depresivnty	-1.16	-1.42 - -0.89	< 0.001	-0.90	-1.23 - -0.54	< 0.001
Anxiety	-1.12	-1.48 - -0.76	< 0.001	-0.17	-0.61 - -0.27	0.434
Stress	-0.61	-0.90 - -0.31	< 0.001	-0.25	-0.52 - 0.03	0.077

B-coefficient of regression; 95% CI – 95% confidential interval; *Adjusted $R^2 = 0.543$

In relation to the clinical characteristics of MOH and previous headaches, a statistically significant impairment in the PCS was observed in persons with MOH who used antidepressant therapy for preventive purposes compared to persons who used another type of preventive therapy ($p = 0.029$). No other statistically significant differences in PCS, MCS, or TS impairment were observed compared to the tested variables ($p > 0.05$) (data not shown).

By including all variables with a significance level of $p < 0.1$ from the univariate model in the analysis of the multivariate model, the following risk factors for health-related quality of life were identified for MOH patients: for PCS, female sex ($B = -15.47$, 95% CI -26.79-4.14, $p = 0.008$) and depression ($B = -0.70$, 95% CI -1.32-0.08, $p = 0.027$); for MCS, depression ($B = -0.71$, 95% CI -1.14-0.29, $p = 0.001$); and for TS, depression ($B = -0.69$, 95% CI -1.16-0.22, $p = 0.005$) (Table 5). Additionally, by including all variables with a significance level of $p < 0.1$ from the univariate model in the analysis of the multivariate model, the following risk factors for health-related quality of life were identified for CG: for PCS, depression ($B = -0.70$, 95% CI -1.31-0.27, $p = 0.002$); for MCS, smoking ($B = -10.25$, 95% CI -19.13—1.38, $p = 0.024$), smoking length ($B = -0.52$, 95% CI -0.92-0.13, $p = 0.009$) and depression ($B = -0.96$, 95% CI -1.40-0.52, $p < 0.001$); for TS, age ($B = -0.16$, 95% CI -0.32-0.01, $p = 0.046$); and depression ($B = -0.90$, 95% CI -1.23-0.54, $p < 0.001$) (Table 5).

Table 5: Depressivity in MOH regarding different parameters

Parameter	Depressivity				
	KG		GPUM		p-vrednost ¹
	N	$\bar{X} \pm SD$	N	$\bar{X} \pm SD$	
Age (years)					
<40	45	4.64 ± 5.35		13.50 ± 10.65	< 0.001
≥40	36	7.19 ± 6.46		16.38 ± 11.12	< 0.001
p-vrednost ¹		0.106		0.176	
Gender					
Male	22	6.27 ± 6.82		12.00 ± 9.81	0.069
Female	59	5.59 ± 5.68		15.29 ± 11.06	< 0.001
p-vrednost ¹		0.868		0.354	
Residency					
City	68	5.10 ± 5.54	65	14.82 ± 11.30	< 0.001
Village	13	9.31 ± 7.06	18	15.00 ± 9.63	0.115
p-vrednost ¹		0.030		0.686	
Education					
Elementary			6	9.04 ± 3.69	
High	27	8.44 ± 7.71	44	15.05 ± 11.23	0.009
Faculty	54	4.44 ± 4.39	33	14.73 ± 11.06	< 0.001
p-vrednost ²		0.035		0.976	
Marrital Status					
Married	33	5.39 ± 5.93	57	14.82 ± 10.93	< 0.001
Divorced	13	8.69 ± 7.11	7	15.14 ± 13.55	0.311
Widower	5	0.71 ± 0.32	1	16.00	0.333
Non Married	30	5.67 ± 1.04	18	14.78 ± 10.72	< 0.001
p-vrednost ²		0.190		0.968	
Working Status					
Work	56	5.23 ± 5.56	55	14.82 ± 1.50	< 0.001
No work	24	6.67 ± 6.70	25	14.90 ± 10.82	0.004
Retired	1	15.00	3	14.67 ± 12.06	1.000
p-vrednost ²		0.252		0.991	
Comorbidities					
Yes			36	18.89 ± 12.17	
No			47	11.77 ± 8.76	
p-vrednost ¹				0.007	
Type					
Cardiovascular			10	16.40 ± 12.01	
Pulmological			7	21.14 ± 14.31	
Reumatological			9	22.44 ± 12.10	
Endocrinological			7	12.29 ± 7.20	
Neurological/ Psyschiatrical			3	26.67 ± 15.50	
p-vrednost ²				0.383	



Smoking					
Yes	30	7.43 ± 7.29	34	16.15 ± 11.04	0.001
No	51	4.80 ± 4.85	49	13.96 ± 10.84	< 0.001
<i>p</i> -vrednost ¹		0.174		0.301	
Alcol Use					
Yes*	12	6.50 ± 7.54	4	4.75 ± 3.50	0.953
No	69	5.65 ± 5.71	79	15.37 ± 10.91	< 0.001
<i>p</i> -vrednost ¹		0.841		0.028	
Caffeine Use					
Yes*	70	5.80 ± 6.19	74	14.65 ± 10.96	< 0.001
No	11	5.64 ± 4.59	9	16.56 ± 10.88	0.025
<i>p</i> -vrednost ¹		0.647		0.603	
Physical Activity					
Yes [†]	27	3.70 ± 3.9	8	19.50 ± 11.98	< 0.001
No	54	6.81 ± 6.55	75	14.36 ± 10.75	< 0.001
<i>p</i> -vrednost ¹		0.080		0.225	

¹Mann-Whitney test; ²Kruskal Wallis test; [†] ≥ 3 days per week

Discussion

The results presented here indicate that impairments in the PCS, MCS, and TS are present in patients suffering from MOH. All examined aspects of health were impaired in patients with MOH, compared with healthy subjects, regardless of age, regardless of place of residence, in patients with higher education, in patients who are married and unmarried, regardless of work status, regardless of smoking status, regardless of the habit of drinking caffeinated beverages and regardless of physical activity. It has been shown that impairment of the PCS is more pronounced in women with MOH and in patients with MOH who do not consume alcohol than in healthy women and healthy subjects who do not consume alcohol. The impairment of the MCS is more pronounced in people suffering from MOH and is independent of sex and alcohol-related habits. In this study, the TS was impaired in patients with MOH compared to healthy individuals, regardless of sex or alcohol consumption, compared to healthy individuals with the same status.

Previous research has shown a deterioration in the quality of life in patients with MOH compared to healthy subjects. Depression and anxiety are also of particular importance in this impairment of quality of life as frequent comorbidities of MOH [16]. In observational research, it was noted that with the discontinuation of overuse of medications in hospital settings, there was a significant improvement in the quality of life of patients with MOH and a reduction in the level of psychological distress. Patients with greater incidence of MCS disorders and a greater degree of depression and anxiety have a less favorable outcome in reducing the number of days with monthly headaches and improving quality of life after the discontinuation of excessive medication [17]. One study examined the quality of life of 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 score did not significantly change in relation to the expected value after the discontinuation of excessive medication, while the MCS score was significantly impaired after the discontinuation of excessive medication for a long period [18].

Previous research has shown that strengthening coping strategies, especially MCSs, plays a key role in improving quality of life in adolescents suffering from chronic headaches [19]. Research has evaluated the impact of stress control on the intensity of pain and quality of life in 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 [20]. The application of combined models of acceptance and the type of cognitive-defusion-related process may influence the improvement of the PCS and MCS in people with chronic pain [21].

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 and the tendency to disaster and strengthen feelings of helplessness [22]. Other studies have compared the effectiveness of mindfulness-based cognitive therapy and quality of life-based therapy to the ruminative style of thinking in patients with chronic headaches. The results indicate significant efficacy in reducing the number of headache days on a monthly basis and improving quality of life when both therapeutic interventions are applied [23]. This type of association was observed at the beginning of the study only in the elderly population; however, at the end of the study, the relationship between the ruminative style of thinking and self-assessed quality of life was more significant in the younger respondents. A ruminative style of thinking was associated with poorer quality of life, but this relationship depended on the age of the respondent and the duration of the study [24]. The role of the ruminative style of thinking in the occurrence of psychological distress in patients with chronic pain has been proven in previous research [25].

This study showed that impaired quality of life was not significantly associated with MOH or previous headache, although the impairment of the PCS was significantly more pronounced in MOH patients who used antidepressant therapy for secondary prevention of early chronic headache. The results indicate that the occurrence of psychological distress is more often a risk factor for the transformation of migraine into MOH (present even before its transformation into MOH) than a subsequent (comorbid) occurrence after the onset of MOH [26].

The results of this study indicate that depression itself is a risk factor for all aspects of quality of life in patients with MOH, with female sex being an associated risk factor for PCS in patients with MOH. On the other hand, the degree of depression is a key risk factor for all aspects of quality of life and, in healthy individuals, smoking and smoking duration are associated risk factors for MCS, and age is an associated risk factor for TS in healthy individuals. The results of this study did not reveal a predictive role of anxiety, stress, or ruminative style on the quality of life of people with MOH or healthy individuals.

The limitations of the study stem from the nature of the study. We believe that these methodological requirements reduce the shortcomings of this study. The advantages of this study include the clinical implications of the findings, which can be useful for both primary and secondary prevention of MOH and for improving the quality of life of selected patients.

Assessment of the degree of depression in MOH patients and treatment could be useful for improving the quality of life of MOH patients. Psychological strategies aimed at evaluating and treating depression could be useful in primary and secondary prevention of MOH and its devastating effects on patients' quality of life. Additional studies are needed.

Acknowledgments

The authors gratefully thank all patients for their participation in this study.



References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders. 3rd edition. Cephalalgia: 2018; 38: 1-211.
2. Steiner T, Stovner L, Katsarava Z, Lainez J, Lampl C, Lantéri-Minet M, et al. The impact of headache in Europe: Principal results of the Euro light project. *J Headache Pain*. 2014; 15: 31.
3. Mbewe E, Zairethiama P, Yeh H, Paul R, Birbeck G, Steiner T. The epidemiology of primary headache disorders in Zambia: A population-based door-to-door survey. *J Headache Pain*. 2015; 16: 515.
4. Hagen K, Linde M, Steiner TJ, Stovner LJ, Zwart JA. Risk factors for medication-overuse headache: an 11-year follow-up study. *The Nord-Trøndelag Health Studies*. *Pain*. 2012; 153: 56–61.
5. Westergaard M, Hansen E, Glumer C, Olesen J, Jensen R. Definitions of medication overuse headache in population-based studies and their implications on prevalence estimates: A systematic review. *Cephalalgia*. 2014; 34: 409–425.
6. Westergaard M, Glümer C, Hansen E, Jensen R. Prevalence of chronic headache with and without medication overuse: Associations with socioeconomic position and physical and mental health status. *Pain*. 2014; 155: 2005–2013.
7. Westergaard ML, Munksgaard SB, Bendtsen L, Jensen RH. Medication-overuse headache: A perspective review. *Therapeutic Advances in Drug Safety*. 2016; 7: 147–158.
8. D'Amico D, Grazi L, Curone M, Leonardi M, Raggi A. Cost of medication overuse headache in Italian patients at the time-point of withdrawal: A retrospective study based on real data. *Neurol Sci*. 2017; 38: 3-6.
9. Raggi A, Leonardi M, Sansone E, Curone M, Grazi L, D'Amico D. The cost and the value of treatment of medication overuse headache in Italy: A longitudinal study based on patient-derived data. *Eur J Neurol*. 2020; 27: 62.
10. Boardman HF, Thomas E, Millson DS, Croft PR. Psychological, sleep, lifestyle, and comorbid associations with headache. *Headache*. 2005; 45: 657–669.
11. Bendtsen L, Munksgaard S, Tassorelli C, Nappi G, Katsarava Z, Lainez M, et al. Disability, anxiety and depression associated with medication-overuse headache can be considerably reduced by detoxification and prophylactic treatment. Results from a multicentre, multinational study (COMOESTAS project). *Cephalalgia*. 2014; 34: 426-433.
12. Ljubisavljevic M, Ignjatovic A, Djordjevic V, Hadzi Pestic M, Ljubisavljevic S. Depression, anxiety, stress and health related quality of life among patients with medication overuse headache in tertiary headache center: A Cross Sectional Study. *Journal of Neuropsychiatry and Clinical Neurosciences*. 2021; 33: 132-143.
13. ProQolid Patient-Reported Outcome and Quality of Life Instruments Database SF-36 Health Survey Serbian version.
14. SF-36 Health survey (original version) language recalls.
15. Ljubisavljevic M, Ignjatovic A, Ljubisavljevic S. The ruminative thought style with associated anxiety influences the occurrence of medication overuse headache. *Journal of Clinical Neurology*. 2021; 17: 419-427.
16. Kristoffersen ES, Straand J, Russell MB, Lundqvist C. Disability, anxiety and depression in patients with medication-overuse headache in primary care – the BIMOH study. *European Journal of Neurology*. 2015; 23: 28–35.
17. Zebenholzer K, Thamer M, Wober C. Quality of life, depression, and anxiety 6 months after inpatient withdrawal in patients with medication overuse headache an observational study. *Clin J Pain*. 2012; 28: 284–290.
18. Benz T, Nüssle A, Lehmann S, Gantenbein AR, Sándor PS, Elfering A, et al. Health and quality of life in patients with medication overuse headache syndrome after standardized inpatient rehabilitation A cross-sectional pilot study. *Medicine*. 2017; 96: 47.
19. Massey EK, Garnefski N, Gebhardt WA, van der Leeden R. A daily diary study on the independent and interactive effects of headache and self-regulatory factors on daily affect among adolescents. *British Journal of Health Psychology*. 2011; 16: 288–299.
20. Bakhshani NM, Amirani A, Amirifard H, Shahrakipoor M. The effectiveness of mindfulness-based stress reduction on perceived pain intensity and quality of life in patients with chronic headache. *Global Journal of Health Science*. 2016; 8: 142-151.
21. McCracken LM, Barker E, Chilcot J. Decentering, rumination, cognitive defusion, and psychological flexibility in people with chronic pain. *J Behav Med*. 2014; 37: 1215-1225.
22. Craner JR, Gilliam WP, Sperry JA. Rumination, magnification, and helplessness: how do different aspects of pain catastrophizing relate to pain severity and functioning? *The Clinical Journal of Pain*. 2016; 32: 1028-1035.
23. Shabani M, Nejat H, Saffarian MR. Comparison of the effectiveness of mindfulness-based cognitive therapy and a quality of life-based therapy on rumination in patients with migraine. *Int J Basic Sci Med*. 2019; 4: 61- 68.
24. Thomsen DK, Mehlsen MY, Olesen F, Hokland M, Viidik A, Avlund K, et al. Is there an association between rumination and self-reported physical health? A one-year follow-up in a young and an elderly sample. *Journal of Behavioral Medicine*. 2004; 27: 215-231.
25. Rogers AH, Bakhshaie J, Ditre JW, Manning K, Mayorga NA, Viana AG, et al. Worry and rumination: Explanatory roles in the relation between pain and anxiety and depressive symptoms among college students with pain. *Journal of American College Health*. 2019; 67: 275-282.
26. Radat F, Creac'h C, Swendsen JD, Lafittau M, Irachabal S, Dousset V, et al. Psychiatric comorbidity in the evolution from migraine to medication overuse headache. *Cephalalgia*. 2005; 25: 519–522.