Research Article

The Health Related Quality Of Life among Patients with Medication Overuse Headache: One Year University Headache Center Experience

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Abstract:

Background: The negative impact of medication overuse headache (MOH) on the quality of life (QoL) of the patient is undoubted.

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

Patients and Methods: 183 patients (111 men and 72 women) firstly diagnosed as having MOH and 81 healthy subjects (22 men and 59 women) in control group (CG) were enrloed in this study. The age of the study subjects range from 18 to 71 years. HRQoL was assessed using a Short Form - 36 questionnaire (SF-36), measuring its Physical Composite Score (PCS), Mental Composite Score (MCS) and Total score (TS).

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

Conclusions: Screening for depression among MOH patients and its treatment could be useful for improving their HRQoL

Introduction

Medication overuse headache (MOH) is a secondary headache caused by excessive use of therapy to stop an acute headache attack (International Headache Society, 2018). It is estimated that about 80 million people worldwide have MOH (Steiner, 2014) in different population. Also in relation to place of residences, socio economic staus, employment and level of education.

MOH is more prevalent in urban areas (14.5% vs. 2.1%) (Mbewe et al., 2015). Some studies have shown a higher prevalence of MOH among people with lower socioeconomic status (Hagen et al., 2012). Some data showed the highest prevalence of MOH among those patients using social assistance (11%), in newly retired (7.5%) and in patients on extended sick leave (6%) (Westergaard et al., 2014b). A higher prevalence of MOH is observed in migrants (Westergaard et al., 2014a). There is no clear evidence of a link between this parametes ans and the development of MOH (Hagen et al., 2012; Westergaard et al., 2016).

The negative impact of MOH on the quality of life of the patient is undoubted. The economic costs of national and health funds related to MOH have been assessed as very significant (D'Amico et al, 2017; Raggi et al, 2020). Low quality of life, high degree of disability, sleep problems, insufficiently functional mechanisms/coping strategies have already been previously recognized as important parameters for the occurrence of chronic headache (Boardman et al., 2005). On the other hand, it has been shown that patients with chronic headaches generally have a reduced quality of life and an increased degree of disability. There are results that indicate that patients with chronic migraine and MOH have a higher degree of functional disability compared to patients with chronic migraine without MOH (Bendsten et al., 2014). There is insufficient research on the relationship between the quality of life among patients with MOH and other their characteristics, comorbidities and habits.

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 data base of headsche patient consists of more thaa 400 patients. For this research we include only those with voluntary written informed consent to participate in the study. From these patients , were completed the socio-demographic and medical questionnaire including demographics, educational level, marital, family, and work status, number of family members, residence, personal history, existence of other illnesses, existence of previous (primary and / or secondary) headaches (type, characteristics, duration, frequency, and 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 about 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 valid 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.). In all patients, the diagnosis of MOH was made by the same doctor, 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.

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, occipital), lateralization (unilateral, diffuse) , character of pain (muffled, pulsating pain), intensity of pain (using numerical scale for pain assessment), existence of related symptoms and signs (nausea / vomiting, photophobia, phonophobia, diplopia, neck and shoulder stiffness, blurred vision, tinnitus, hypoxia), the type of analgesic therapy used, the use of preventive therapy, the 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 (Ljubisavljevic et al, 2020).

Control group

The control group (CG) was selected from the group of companions (relatives, friends) of all patients who were examined in the Headache Center during the period of this study, after their voluntary consent to participate in the study. These individuals were included consecutively (in order) up to the predicted number (according to the number of patients in the MOH group). The precondition for their inclusion was 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 a Short Form (SF) - 36 questionnaire. The SF-36 questionnaire has previously been approved for use in Serbian language and showed good internal consistency (internal consistency ranging from .80 to .90) (https://eprovide.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. Physical Composite Score (PCS) represents the mean value of scores of the first four domains, and the Mental Composite Score (MCS) represents the mean value of scores of the last four domains. The Total score (TS) is calculated as mean of the Physical Composite Score (PCS) and the 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. Data are presented as mean±standard deviation, or as counts and percentages. Unpaired Student's t test or Mann-Whitney test was used to compare continuous data, as appropriate. Analysis of variance (ANOVA) or Kruskal-Wallis test was performed for continouous data among three or more groups, as appropriate. Chi-squared test or Fisher`s test was used in analysis of categorical data. An exploratory logistic regression analysis (enter method) was 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 regression were performed, The Hosmer-Lemeshow test was performed for estimating calibration ability in the models. A complete case analysis was performed. A p-value was set at $p<0.05$. All statistical analyses were performed using R software, version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The study covered 164 subjects (33 men and 131 women), 83 patients (11 men and 72 women) in MOH and 81 subject (22 men and 59 women) in CG. The average age of the study

subjects was 40.2 ± 11.9 years (min 18, max 71 years). Data in details are described in our previous published paper (Ljubisavljevic et al, 2020). All SF-36 scores (PCS, MCS, TS) were statistically significantly lower in MOH compared to the CG (p <0.001). The strong correlations were observed between parameters of quality of life and psychological distress parameters as well as the ruminative through style (Ljubisavljevic et al, 2020) (p<0.05) (Table 1).

Table 1. Study patient's data

	CG		MOH		p-values
	N	%	N	%	
Gender					
Male	22	27.2	11	13.3	**0.043[1]**
Female	59	72.8	72	86.7	
Age†	39.94±12.36	20-65	40.54±11.58	18-71	0.747[2]
Values of measured outcomes of quality of life					
SF 36 - PCS†	67.22±10.60	40.0-91.25	37.32±20.18	5.0-82.5	**<0.001[3]**
SF 36 - MCS†	69.53±11.80	41.75-93.75	44.58±15.46	10.0-78.25	**<0.001[3]**
SF 36 - Total score†	68.38±16.22	45.63-88.25	40.95±16.22	8.75-79.63	**<0.001[3]**
HIT-6 (for MOH) †	-	-	65.39±5.45	49-77	-

† Mean±Standard deviation, [1] The chi-squared test, [2] The t-test, [3] Mann-Whitney test

CG-control group, MOH-medication overuse headache, SF-36- Short Form - 36 questionnaire, PCS - physical composite score, MCS – mental composite score, TS-total score, HIT-6- headache impact test

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 / non-smoker) 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 CG, a statistically significant impairment of the PCS was observed in those older than 40 years (p=0.004), and in persons with a lower level of education (p=0.004). In the MOH group, a statistically significant impairment of the PCS was observed in women (p = 0.002) (Table 2).

Table 2. Physical composite score of health related quality of life among MOH patients and healthy control subjects (regarding sociodmographic and other clinical data)

Parameters	PCS				
		CG		MOH	
	N	X̄±SD	N	X̄±SD	p-value[1]
Age (years)					
<40	45	70.36±8.21	44	40.40±17.99	**<0.001**
≥40	36	63.31±11.98	39	33.85±22.13	**<0.001**
p-value[1]		**0.004**		0.100	
Gender					
Male	22	68.57±9.25	11	56.07±19.15	0.076
Female	59	66.72±10.10	72	34.45±18.87	**<0.001**
p-value[1]		0.489		**0.002**	
Residence					
City	68	67.96±10.26	65	38.76±20.88	**<0.001**
Village	13	63.36±11.93	18	32.14±16.95	**<0.001**
p-value[1]		0.154		0.230	

Education					
Elementary school			6	27.58±13.22	
High school	27	62.13±1091	44	35.08±22.06	**<0.001**
College	54	69.77±9.56	33	42.08±17.75	**<0.001**
p-value[2]		**0.004**		0.108	
Marriage status					
Married	33	66.17±10.43	57	37.04±20.22	**<0.001**
Divorced	13	62.02±15.22	7	33.75±31.36	0.056
Widower	5	70.00±6.79	1	7.50	0.333
Unmarried	30	70.17±8.01	18	41.6±14.06	**<0.001**
p-value[2]		0.193		0.231	
Working status					
Work	56	67.52±11.36	55	39.94±20.84	**<0.001**
Doesn't work	24	66.93±8.84	25	32.72±16.80	**<0.001**
Retired	1	57.50	3	27.58±31.59	1.000
p-value[3]		0.642		0.269	
Comorbidities					
Yes			36	36.17±21.50	
No			47	38.20±19.31	
p-value[1]				0.594	
Type of comorbidities					
Cardiovascular			10	21.42±6.77	
Pulmological			7	16.75±6.33	
Rheumatological			9	20.21±6.74	
Endocrinological			7	44.07±24.80	
Neurological+ Psychiatric			3	24.58±20.62	
p-value[2]				0.232	
Smoking					
Yes	30	65.73±11.24	34	34.19±19.13	**<0.001**
No	51	68.11±10.22	49	39.50±20.80	**<0.001**
p-value[1]		0.337		0.319	
Alcohol use					
Yes*	12	66.00±4.65	4	53.50±20.79	**<0.001**
No	69	67.44±11.33	79	36.50±19.94	0.170
p-value[1]		0.338		0.116	
Caffeine use					
Yes*	70	67.12±10.71	74	37.46±20.96	**<0.001**
No	11	67.89±10.38	9	36.17±12.82	**<0.001**
p-value[1]		0.825		0.994	
Physical activity					
Yes*	27	69.15±8.06	8	33.94±14.84	**<0.001**
No	54	66.26±11.62	75	37.68±20.72	**<0.001**
p-value[1]		0.318		0.758	

[1] Mann-Whitney test, [2] Kruskal Wallis test, * daily or often (several times during the week)

CG-control group, MOH-medication overuse headache, PCS - physical composite score

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 / non-smoker) 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 CG, a statistically significant impairment of the MCS was observed in those older than 40 years (p = 0.010) and in physically less active persons (p = 0.044) (Table 3).

Table 3. Mental composite score of health related quality of life among MOH patients and healthy control subjects (regarding sociodmographic and other clinical data)

Parameters	MCS				
	CG		MOH		
	N	$\bar{X}\pm SD$	N	$\bar{X}\pm SD$	p-value[1]
Age (years)					
<40	45	72.69±8.69	44	46.73±15.28	**<0.001**
≥40	36	65.58±13.96	39	42.15±15.50	**<0.001**
p-value[1]		**0.010**		0.183	
Gender					
Male	22	70.93±10.29	11	47.20±13.31	**<0.001**
Female	59	69.00±12.37	72	44.18±15.80	**<0.001**
p-value[1]		0.517		0.549	
Residence					
City	68	70.24±10.90	65	44.80±15.8	**<0.001**
Village	13	65.81±15.77	18	43.80±14.53	**0.001**
p-value[1]		0.343		0.765	
Education					
Elementary school			6	44.17±13.82	
High school	27	67.12±12.75	44	43.94±16.15	**<0.001**
College	54	70.73±11.24	33	45.51±15.19	**<0.001**
p-value[2]		0.204		0.881	
Marriage status					
Married	33	67.28±13.40	57	44.72±15.51	**<0.001**
Divorced	13	64.35±13.72	7	47.28±23.68	0.115
Widower	5	73.45±8.98	1	21.00	0.333
Unmarried	30	73.59±7.75	18	44.40±11.25	**<0.001**
p-value[2]		0.089		0.514	
Working status					
Work	56	68.69±12.18	55	47.22±15.39	**<0.001**
Doesn't work	24	72.45±9.75	25	39.38±13.41	**<0.001**
Retired	1	45.75	3	39.58±26.16	1.000
p-value[3]		0.130		0.082	
Comorbidities					
Yes			36	43.32±14.86	
No			47	46.31±15.85	
p-value[1]				0.201	
Type of comorbidities					
Cardiovascular			10	45.42±9.58	
Pulmological			7	42.18±12.92	
Rheumatological			9	37.03±16.52	
Endocrinological			7	50.54±16.26	
Neurological+ Psychiatric			3	29.00±19.65	
p-value[2]				0.321	
Smoking					
Yes	30	66.62±13.81	34	43.79±16.79	**<0.001**
No	51	71.24±10.22	49	45.13±14.62	**<0.001**

p-value[1]		0.176		0.697	
Alcohol use					
Yes*	12	70.19±6.88	4	56.56±7.21	**0.008**
No	69	69.41±12.50	79	43.97±15.54	**<0.001**
p-value[1]		0.889		0.079	
Caffeine use					
Yes*	70	69.10±11.55	74	45.05±15.54	**<0.001**
No	11	72.23±13.65	9	40.75±15.08	**0.001**
p-value[1]		0.507		0.420	
Physical activity					
Yes*	27	72.86±9.66	8	44.44±18.35	**<0.001**
No	54	67.86±12.49	75	44.59±15.26	**<0.001**
p-value[1]		**0.044**		0.945	

[1] Mann-Whitney test, [2] Kruskal Wallis test, * daily or often (several times during the week)

CG-control group, MOH-medication overuse headache, MCS - mental composite score

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 / non-smoker), 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 CG, a statistically significant impairment of the TS was observed in those older than 40 years (p=0.002) and in persons with a lower level of education (p=0.015). In the MOH group, impaired TS was observed in women (p=0.023) (Table 4).

Table 4. Total score of health related quality of life among MOH patients and healthy control subjects (regarding sociodmographic and other clinical data)

Parameters	TCS				
	CG		MOH		
	N	X̄±SD	N	X̄±SD	p-value[1]
Age (years)					
<40	45	71.52±7.22	44	43.57±15.09	**<0.001**
≥40	36	64.44±11.42	39	38.00±17.12	**<0.001**
p-value[1]		**0.002**		0.072	
Gender					
Male	22	69.75±8.26	11	51.64±14.77	**0.001**
Female	59	67.86±10.48	72	39.32±15.90	**<0.001**
p-value[1]		0.878		**0.023**	
Residence					
City	68	69.10±9.08	65	41.78±16.60	**<0.001**
Village	13	64.59±13.29	18	37.97±14.81	**<0.001**
p-value[1]		0.283		0.380	
Education					
Elementary school			6	35.88±12.14	
High school	27	64.62±10.60	44	39.51±17.52	**<0.001**
College	54	70.25±9.08	33	43.80±14.91	**<0.001**
p-value[2]		**0.015**		0.258	

Marriage status					
Married	33	66.73±10.31	57	40.88±16.24	**<0.001**
Divorced	13	63.18±13.63	7	40.52±26.04	0.056
Widower	5	71.72±7.76	1	14.25	0.333
Unmarried	30	71.88±6.24	18	42.83±10.75	**<0.001**
p-value[2]		0.137		0.406	
Working status					
Work	56	68.11±10.44	55	43.58±16.14	**<0.001**
Doesn't work	24	69.69±8.19	25	36.05±13.97	**<0.001**
Retired	1	51.62	3	33.58±28.85	1.000
p-value[3]		0.353		0.081	
Comorbidities					
Yes			36	39.25±16.92	
No			47	42.26±15.72	
p-value[1]				0.325	
Type of comorbidities					
Cardiovascular			10	45.24±13.75	
Pulmological			7	37.68±13.88	
Rheumatological			9	31.69±17.39	
Endocrinological			7	47.30±20.13	
Neurological+ Psychiatric			3	26.79±15.73	
p-value[2]				0.209	
Smoking					
Yes	30	66.18±11.01	34	38.99±15.94	**<0.001**
No	51	69.67±9.08	49	42.31±16.44	**<0.001**
p-value[1]		0.126		0.450	
Alcohol use					
Yes*	12	68.09±4.12	4	55.03±10.76	0.058
No	69	68.42±10.62	79	40.24±16.17	**<0.001**
p-value[1]		0.429		0.079	
Caffeine use					
Yes*	70	68.11±9.83	74	41.26±16.57	**<0.001**
No	11	70.06±10.77	9	38.46±13.55	**<0.001**
p-value[1]		0.424		0.593	
Physical activity					
Yes*	27	71.00±7.17	8	39.19±13.57	**<0.001**
No	54	67.06±10.86	75	41.14±16.54	**<0.001**
p-value[1]		0.186		0.758	

[1] Mann-Whitney test, [2] Kruskal Wallis test, * daily or often (several times during the week)

CG-control group, MOH-medication overuse headache, TS - total score

In relation to the clinical characteristics of MOH and previous headaches, a statistically significant impairment of 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, and 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 have been identified for MOH patients: for PCS, female gender (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); for TS, depression (B = -0.69, 95% CI -1.16—0.22, p = 0.005) (Table 5). Also, 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 have been 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. Risk factors for physical, mental and total score of health related quality of life among MOH patients and healthy control subjects   (multivariate analysis)

	PCS			MCS			TS		
	B	95%CI	p	B	95%CI	p	B	95%CI	p
MOH									
Gender (Female)	-15.47	-26.79- -4.14	**0.008**						
Depression	-0.70	-1.32- -0.08	**0.027**	-0.71	-1.14 - -0.29	**0.001**	-0.69	-1.16 - -0.22	**0.005**
CG									
Age							-0.16	-0.32 - -0.01	**0.046**
Smoking				-10.25	-19.13 - -1.38	**0.024**			
Smoking durat.				-0.52	-0.92- -0.13	**0.009**			
Depression	-1.01	-1.34- -0.69	**<0.001**	-0.96	-1.40 - -0.52	**<0.001**	-0.90	-1.23 – -0.54	**<0.001**

CG-control group, MOH-medication overuse headache, PCS - physical composite score, MCS – mental composite score, TS-total score

In the univariate model of analysis of risk factors for health related quality of life in MOH patients have been identified following risk factors: **for PCS**, female gender (B = -21.61, 95% CI -33.79--9.43, p = 0.001), ruminative style of thinking (B = 0.26, 95% CI -0.43 - -0.09, p = 0.003), depression (B = -0.93, 95% CI -1.28 - -0.57, p <0.001), anxiety (B = -1.04, 95% CI -1.45—0.62, p <0.001) and stress (B = -0.86, 95% CI -1.26-0.46, p <0.001); **for MCS**, ruminative style of thinking (B = -0.22, 95% CI -0.35- -0.09, p = 0.001), depression (B = -0.95, 95% CI -1.18 - -0.72, p <0.001), anxiety (B = -0.96, 95% CI -1.25 - -0.66, p <0.001) and stress (B = -0.90, 95% CI -1.17 - - 0.62, p < 0.001); **for TS**, female gender (B = -12.32, 95% CI -22.47 - -2.16, p = 0.018), ruminative style of thinking (B = -0.24, 95% CI -0.38 - - 0.11, p = 0.001), depression (B = -0.94, 95% CI -1.19 - - 0.68, p <0.001), anxiety (B = -1.00, 95% CI -1.31 - - 0.69, p <0.001) and stress (B = -0.88, 95% CI -1.18- - 0.58, p <0.001).

In the univariate model of analysis of risk factors for health related quality of life in CG have been identified following risk factors: **for PCS**, age (B = -0.26, 95% CI -0.44 - - 0.08, p = 0.006), level of education (B = 7.64, 95% CI 2.94-12.34, p = 0.002), number of children (B = -3.25, 95% CI -6.46 - - 0.04, p = 0.047), depression (B = -1.01, 95% CI -1.34 - - 0.69, p <0.001), anxiety (B = -1.02, 95% CI -1.43 - - 0.60, p <0.001) and stress (B = -0.50, 95% CI -0.83—0.17, p = 0.003); **for MCS**, age (B = -0.27, 95% CI -0.47- - 0.06, p = 0.011), number of children (B = -4.02, 95%CI -7.58 - - 0.46, p = 0.027), smoking length (B = -0.26, 95% CI -0.48 - - 0.04, p = 0.019), ruminative style of thinking (B = -0.23, 95% CI -0.43 - - 0.03, p = 0.027), depression (B = -1.30, 95% CI - -1.64 - - 0.96, p <0.001), anxiety (B = -1.23, 95% CI -1.68—0.78, p <0.001) and stress (B = -0.72 , 95% CI -1.07- - 0.36, p <0.001); **for TS**, age (B = -0.26, 95% CI -0.43- - 0.10, p = 0.003), level of education (B = 5.62, 95% CI 1.12-10.13, p = 0.015), number of children (B = -3.63, 95% CI -6.61 - - 0.67, p = 0.017), smoking length (B = -0.19, 95% CI -3.78 - - 0.01, p = 0.043) , depression (B = -1.16, 95% CI -1.42 - - 0.89, p <0.001), anxiety (B = -1.12, 95% CI -1.48 - -0.76, p <0.001) and stress (B = -0.61, 95%) CI -0.90- -0.31, p <0.001).

Discussion

The results presented here indicate that impairments of 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 compared to healthy women and healthy subjects who do not consume alcohol. 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 depression and anxiety are of particular importance in this impairment of quality of life as frequent comorbidities of MOH (Kristoffersen et al., 2015). 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 depression and 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 (Zebenholzer et al., 2012). 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 (Benz et al., 2017).

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 (Massey et al., 2011). 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 (Bakhshani et al., 2016). There are suggestions that the application of combined models of acceptance and the type of cognitive-defusion-related process can influence the improvement of the PCS and MCS in people with chronic pain (Mc Cracken et al., 2014).

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 (Craner et al., 2016). 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 (Shabani et al., 2019). 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, the relationship between ruminative style of thinking and self - assessment of quality of life was more significant in the younger respondents. Ruminative style of thinking was associated with poorer assessment of quality of life, but this relationship depended on the age of the respondents and the duration of the study (Thomsen et al., 2004). The role of ruminative style of thinking in the occurrence of psychological distress in patients with chronic pain has been proven in previous research (Rogers et al., 2019).

This study showed that impaired quality of life was not significantly associated with the characteristics of MOH and previous headache, although the impairment of the PCS was statistically significantly more pronounced in MOH patients who used antidepressant therapy for secondary prevention of early chronic headache. There are results that indicate that the existence 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 (Radat et al., 2005).

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 gender 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 subjects, with smoking and smoking length as associated risk factors for MCS and age as an associated risk factor for TS in healthy individuals. The results of this study do not find a predictive role of anxiety, stress, and ruminative style of thinking for the quality of life of people with MOH and healthy individuals.

The limitations of the study stem from the study nature. We believe that methodological requirements reduce its shortcomings. The advantages of this study are clinically implicable conclusions that can be useful in both, primary and secondary prevention of MOH, and improving the quality of life in selected patients.

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

Author Contributions

Conflicts of Interest

Acknowledgments

Conflict of interest

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