

ORIGINAL ARTICLE

PREVALENCE AND PREDICTORS OF FATIGUE IN PATIENTS WITH EPISODIC MIGRAINE

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Mykhaylo Delva, Iryna Delva, Victoria Pinchuk, Angelina Kryvchun, Tetyana Purdenko

POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: We studied prevalence, intensity and predictors of fatigue in patient with episodic migraine (EM).

Materials and methods: We enrolled in the study 85 patients with EM and 88 healthy subjects. Fatigue was identified according to Fatigue Severity Scale. We recorded socio-demographic factors: gender, age, marital status, formal education level, employment status, smoking. Anxiety and depression symptoms were assessed by Hospital Anxiety and Depression Scale, daytime sleepiness was measured by Epworth scale. The co-morbidities included history of low back pain during last year, arterial hypertension, diabetes mellitus and abdominal obesity. It was analyzed usage of non-steroidal anti-inflammatory drugs, combined analgesics, triptans for abortive migraine treatment.

Results: Fatigue prevalence in patients with EM was 41,2%, which was significantly higher than in healthy controls (11,4%). Fatigue intensity in episodic migraineurs was 5,7 (4,9-6,8) and did not differ significantly from fatigue intensity in healthy individuals – 4,9 (4,5-5,8). In multivariate logistic regression analysis independent predictors of fatigue were only migraine-related factors (number of migraine headache days per month, headache severity and migraine prodrome presence). There was weak direct correlation between the number of headache migraine days per month and fatigue intensity.

Conclusions: 1. Fatigue prevalence in patients with EM is significantly higher than in healthy controls. 2. In patients with EM fatigue has migraine-related predictors.

KEY WORDS: migraine, fatigue, peculiarities, intensity, risk factors

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INTRODUCTION

Migraine is the third most common disease worldwide, with a global prevalence estimated at 14,7% in the Global Burden of Disease Survey [1]. Although not a fatal disease, migraine ranks as the sixth highest cause of disability as measured by years lived with disability worldwide [2, 3]. In addition to the actual episodes of headache, migraine also has a variety of other negative consequences. An analysis of clinical trials and observational studies catalogued 34 psychosocial variations in patients with migraine including also such phenomenon as fatigue [4]. In general, the perception of fatigue is subjective and includes rapid inanition, persisting lack of energy, exhaustion, physical and mental tiredness [5]. As known, fatigue is a common symptom with reported prevalence in the general population ranging from 7% to 45% [6]. In healthy population of working age fatigue has variable as direct as well as hidden negative consequences since it interferes with activities of daily living and the quality of life [6]. Fatigue can be associated with a variety of pathologies and vary significantly, depending on the underlying disease. In particular, we have demonstrated that post-stroke fatigue has specific qualitative and quantitative characteristics and specific predictors even depending on the timing after stroke [7-9]. In recent years, evidence has emerged that fatigue in migraine patients is different from fatigue in healthy people [10-16]. Moreover, fatigue prevalence and fatigue intensity in episodic migraine (EM) patients were significantly

higher compared to patients with chronic migraine [15]. As known, EM represents an absolute majority (more than 92%) of the total migraine population [17]. Thus it's advisable to study fatigue prevalence and fatigue characteristic in patients with EM.

THE AIM

To study fatigue prevalence, fatigue intensity and fatigue predictors in patient with EM.

MATERIALS AND METHODS

We enrolled in the study 85 patients with EM (who have less than 15 migraine headache days per month). All patients were consulted in educational, diagnostic and treatment center for patients with primary headache at department of neurological diseases with neurosurgery and medical genetics of Ukrainian medical stomatological academy. The EM diagnoses were established according to The International classification of headache disorder 3rd edition [18].

Patients were included in the study if they agreed to participate and were able to provide informed consent. Exclusion criteria were major medical illness that could cause secondary fatigue (oncological, hematological diseases, cardiac, liver, kidney and respiratory insufficiency, alcohol abuse).

As controls for fatigue prevalence and fatigue intensity we selected 88 healthy subjects (age and gender matched).

Table I. Social and demographic characteristics of patients with EM depending on presence/absence of fatigue

Factor	Fatigue		p	
	yes	no		
gender	male, n (%)	11 (38%)	18 (62%)	0,82
	female, n (%)	24 (43%)	32 (57%)	
age (years), Me (Q1-Q3)	34 (24-41)	27 (25-37)	0,87	
familyless, n (%)	9 (26%)	11 (22%)	0,80	
higher education, n (%)	18 (51%)	19 (38%)	0,27	
employment, n (%)	25 (71%)	41 (82%)	0,30	
smokers, n (%)	6 (17%)	13 (26%)	0,43	

Table II. Comorbid characteristics of patients with EM depending on presence/absence of fatigue, n (%)

Factor	Fatigue		p
	yes	no	
anxious signs (on HADS)	10 (29%)	19 (38%)	0,49
depressive signs (on HADS)	6 (17%)	7 (14%)	0,76
excessive daytime sleepiness (on Epworth scale)	6 (17%)	6 (12%)	0,54
low back pain	11 (31%)	12 (24%)	0,47
arterial hypertension	4 (11%)	4 (8%)	0,71
diabetes mellitus	5 (14%)	5 (10%)	0,73
abdominal obesity	5 (14%)	11 (22%)	0,43

Table III. Clinical characteristics of EM depending on presence/absence of fatigue

Characteristic	Fatigue		p
	yes	no	
disease duration (years), Me (Q1-Q3)	6 (4-9)	7 (5-10)	0,27
headache days (per month), Me (Q1-Q3)	8 (5-9)	5 (4-7)	0,03
duration of headache attacks (hours), Me (Q1-Q3)	12 (8-18)	12 (8-18)	0,64
headache intensity (on VAS), Me (Q1-Q3)	7 (6-8)	6 (5-7)	0,01
migraine prodrome, n (%)	29 (83%)	28 (56%)	0,01
migraine aura, n (%)	9 (26%)	8 (16%)	0,26
photo-, phonophobia, n (%)	12 (34%)	22 (44%)	0,50

Fatigue was identified according to Fatigue Severity Scale (FSS) at a mean score ≥ 4 [19]. We recorded socio-demographic factors such as gender, age, marital status (married/single), formal education level (higher/non-higher), employment status (employed/unemployed). Patients' tobacco smoking status was classified as "non-smoker" (who didn't smoke at least 1 year before consultation) or "current smoker" (who smoked regularly for the last 1 year before stroke). Anxiety and depression symptoms were assessed by Hospital Anxiety and Depression Scale (anxiety and depression sub-scales using a cut-off of 8) [20]. Daytime sleepiness was measured using Epworth scale (scores ≥ 10 indicate excessive daytime sleepiness) [21]. The co-morbidities included history of low back pain during last year, presence of arterial hypertension and diabetes mellitus. For abdominal obesity diagnosis were used waist circumference (cut-off 102 cm for males and 88 cm for females) [22].

Migraine characteristics included disease duration (years), average headache days (per month), average duration of headache attacks (hours), average headache intensity (using visual analogue scale (VAS)), presence of migraine prodrome, presence of migraine aura, presence of photo- and (or) phonophobia during migraine attacks.

None of the patients received prophylactic migraine therapy. Thus we analyzed usage of drug groups for abortive migraine treatment: non-steroidal anti-inflammatory drugs, combined analgesics, triptans, usage of two or more drugs groups.

Quantitative values were presented as mediana (Me) and interquartile (25% -75%) range (Q1-Q3). Significant differences between quantitative values was performed using the Mann-Whitney paired U-test. Univariate logistic regression analysis was performed to analyze the odds ratio (OR) with 95% confidence intervals (CI) of factors associated with fatigue. Variables having a p value less than

Table IV. Abortive pharmacotherapy of migraine in patient with EM depending on presence/absence of fatigue

Drugs group	Fatigue		p
	yes	no	
non-steroidal anti-inflammatory drugs	4 (11%)	8 (16%)	0,75
combined analgesics	8 (23%)	14 (28%)	0,63
triptans	6 (17%)	10 (20%)	0,79
two or more drug groups	17 (49%)	18 (36%)	0,27

Table V. Correlations between clinical characteristics of EM and fatigue intensity (on FSS)

EM characteristic	Kendall's rank correlation
disease duration (years)	$\tau = -0,18$ ($p = 0,14$)
headache days (per month)	$\tau = 0,30$ ($p = 0,02$)
duration of headache attacks (hours)	$\tau = -0,13$ ($p = 0,31$)
headache intensity (on VAS)	$\tau = -0,09$ ($p = 0,43$)
migraine prodrome	$\tau = -0,01$ ($p = 0,97$)
migraine aura	$\tau = 0,06$ ($p = 0,66$)
photo-, phonophobia	$\tau = -0,06$ ($p = 0,59$)

0,05 in the univariate analysis were selected and evaluated by multivariate logistic regression models. Correlations were estimated using the τ Kendall rank correlation coefficient. Categorical data were represented by number (n) and percentage. Differences in categorical variables were compared using Fisher's exact test. P values less than 0,05 were considered significant.

RESULTS

Throughout patients with EM fatigue was diagnosed in 35 cases (41,2%) whereas throughout healthy subjects fatigue prevalence was 10 cases (11,4%). According to Fisher's exact test, fatigue prevalence in patients with EM was significantly higher ($p < 0,05$) compared to fatigue prevalence in healthy people.

Fatigue intensity in episodic migraineurs, by FSS, was 5,7 (4,9-6,8) and according to Mann-Whitney test did not differ significantly ($p = 0,29$) from fatigue intensity in healthy individuals - 4,9 (4,5-5,8).

As shown in Table I, none of the studied socio-demographic factors was associated with fatigue in patients with EM.

As can be seen from Table II, in patients with EM none of the studied comorbid factor was associated with fatigue.

As Table III demonstrates, fatigue presence in episodic migraineurs was associated with higher number of headache days per month, with more severe headache episodes, as well as with more frequent occurrence of migraine prodromal phenomena. In univariate logistic regression analysis, predictors of fatigue were number of headache days per month (OR, 1,26; 95% CI, 1,05-1,51; $p = 0,01$), headache severity on VAS (OR 1,58; 95% CI, 1,12-2,23; $p = 0,01$) and migraine prodrome (OR 1,80; 95% CI, 1,34-10,76; $p = 0,01$). Moreover, in multivariate logistic regression analysis all above mentioned factors were independent predictors of

fatigue - number of headache days per month (OR, 1,33; 95% CI, 1,08-1,63; $p = 0,01$), headache severity on VAS (OR 1,59; 95% CI, 1,08-2,35; $p = 0,02$) and migraine prodrome (OR 4,46; 95% CI, 1,44-13,83; $p = 0,01$).

It can be concluded from Table IV that usage of none studied drugs group for abortive treatment of migraine was associated with fatigue in patients with EM.

Due to Table V, it has been found weak direct correlation between the number of headache days per month and the intensity of fatigue in patients with EM.

DISCUSSION

In our study fatigue prevalence in patients with EM was 41,2%. In the similar study by using FSS fatigue rate in migraineurs was 58,8% [16]. This difference in results can be explained by less strict inclusion criteria in the latter study that included also chronic migraine (in chronic migraineurs fatigue prevalence according to FSS is much higher - 84,1% [11]).

We revealed that fatigue intensity in episodic migraineurs did not differ significantly from fatigue intensity in healthy individuals. Whereas in other similar studies levels of fatigue (including measured by FSS) were significantly higher in EM patients compared to healthy subjects [12, 14]. Perhaps this difference is the result of social, demographic, comorbid and other characteristics of patients.

In our study none of the socio-demographic factors influenced the characteristics of fatigue in patients with EM. However, there is report that the predictor of fatigue in migraineurs was age [16]. We used strict exclusion criteria so there was not enough variability of patients ages for revealing such association.

We found that independent predictors of fatigue in episodic migraineurs are number of headache days

per month, headache severity on VAS and migraine prodrome. However, in the similar study only migraine headache intensity (on VAS) was revealed as fatigue predictor [16].

We found weak direct correlation between the number of headache days per month and the intensity of fatigue in patients with EM. The same results were also obtained by Lucchesi C. and coauth. using FSS [15]. In another similar study the FSS score was significantly associated with patients' age, age of migraine onset, headache severity on VAS, photophobia and phonophobia [16].

Thus, in patients with EM, fatigue is a common phenomenon that has migraine-related predictors. So, it's very likely that proper migraine treatment may also indirectly affect fatigue characteristics and improve patients' social well-being. In the future, it is necessary to study the effects of adequate abortive and (or) prophylactic migraine therapy on fatigue prevalence and severity.

CONCLUSIONS

1. Fatigue prevalence in patients with EM is 41,2%, which is significantly higher than in healthy controls (11,4%).
2. In patients with EM independent predictors of fatigue are migraine-related factors (number of migraine headache days per month, headache severity on VAS, migraine prodrome).
3. In patients with EM there is weak direct correlation between the number of headache migraine days per month and fatigue intensity by FSS.

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ORCID and contributionship:

Mykhaylo Delva: 0000-0001-5648-7506 ^{A-F}

Iryna Delva: 0000-0002-2795-4897 ^{B-D}

Victoria Pinchuk: 0000-0003-0622-0322 ^{B,C}

Angelina Kryvchun: 0000-0003-0987-6503 ^{B,C}

Tetyana Purdenko: 0000-0002-3561-4331 ^{B,C}

Conflict of interest:

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CORRESPONDING AUTHOR

Mykhaylo Delva

Poltava state medical university

23 Shevchenko st., 36000 Poltava, Ukraine

e-mail: mdelwa@gmail.com

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