

Variables affecting factors associated with primary headache

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Abstract

Primary headache syndromes' development is associated with biological, psychological and social parameters. Factors such as daily habits, behavioral characteristics and sleep disorders also play an important role. We aim to identify the variables which affect the above factors. The study included 111 patients affected by primary headache. The patients were stratified into subgroups according to gender, age, occupation and headache type. Women attained higher scores than men in three of the evaluation rating scales and lower scores in the severity of dependence scale. Occupation was associated with SF36 and Hamilton anxiety scale. Unemployed had higher scores in Hamilton anxiety. Migraineurs and occupied individuals have lower SF36 scores. Women are associated with depression, anxiety and higher disability derived from headache. Men are more prone to dependence on opioids. Unemployment was linked with anxiety and well-being. The migraineurs presented a decreased level of quality of life.

Introduction

Primary headache syndromes' development is associated with biological, psychological and social factors. Besides the hereditary factors, daily habits, behavioral

characteristics, cognitive and sleep disorders play an important role in explaining the occurrence of pain.¹

This paper aspires to explore the variables which affect aspects of quality of life such as sleep, disability, depression, anxiety and addiction to opioids of patients who suffer from primary headache. The investigated control variables regarded gender, age, occupation and types of headache.

Materials and Methods

Subjects

The present study, conducted between January 2013 and December 2014, enrolled 111 consecutively recruited patients affected by a primary headache syndrome diagnosed at the outpatient clinic of the Neurology Department of the Evangelismos General Hospital of Athens. The gold standard of headache diagnosis according to ICDH 3 beta criteria was used.

The mean age of participants was 39.26 years (range: 16-76 years). The patients were stratified into subgroups according to the gender, their age and the occupation (Table 1). With regard to the type of headache, out of the 111 patients, episodic tension type headache (TTH) accounted for 57 (51.35%), episodic migraine for 42 (37.83%) and cluster headache for 2 (1.8%) respectively. Four patients suffered from either a combination of tension-type and migraine headaches or other types of primary headaches. No diagnosis was available for the remaining 6 participants. Migraine and tension type headache are the prevalent types of headache. Hence, we focused on migraineurs and TTH individuals. The study was approved by the Scientific Committee of the Evangelismos Hospital. Written informed consent was obtained from all participants.

Scales

The assessment of headache related disability of migraineurs was obtained with the Migraine Disability Assessment test (MIDAS).² Sleep disorders were evaluated with the Epworth and the Athens Insomnia Scale (AIS).^{3,4} For the measurement of anxiety and depression the Hamilton scales were used.^{5,6} Severity of Dependence Scale (SDS) was also included for the evaluation of addiction and dependence on opioids.⁷ Additionally, the quality of life of the participants was assessed with the SF-36.⁸ Finally, a semi-structured questionnaire

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including personal data, detailed characteristics of headache, daily habits and information about possible headache risk factors was obtained.

Statistics

Initially, we used descriptive statistical methods. Due to the lack of normality for the data in all seven scales, multiple regression and Analysis of Variance methods were inappropriate to use; for this reason, non-parametric tests (Mann-Whitney and Kruskal-Wallis) were performed in order to investigate differences between the levels of the control variables with regard to the scores in the above mentioned scales. Moreover, we used multivariate logistic regression analysis to identify significant independent factors for the scores. In order to find the optimal cutoff point for two of the scales in the logistic regression models we have used ROC curve analysis.

Unless otherwise stated, the level of significance in all tests was 0.05. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) 22.0 (IBM, USA) software.

Results

Descriptive statistics

Analysis by gender

As regards gender, females demonstrated increased mean values in Hamilton Anxiety, Hamilton Depression, MIDAS and SF36. Interestingly, the score of the severity of dependence was doubled among men compared with women (Table 2).

Analysis by age

When the patients were stratified with regard to age, the mean values of scales evaluating anxiety, depression, insomnia and dependence were increased in the group of 36-55 years. The quality of life is somewhat less affected in the patients younger than 35.

Analysis by occupation

With the exception of the SDS scale, in all other cases patients who are employed have lower scores than unemployed persons. The group whose occupation is marked as *other* exhibits a somewhat unusual behavior, which can be attributed to the heterogeneity of this group (4 retired persons, 5 students and 3 patients whose occupation status is missing). With the exception of the MIDAS and Epworth scales, this group has lower scores compared with the other two groups.

Analysis by type of headache

The quality of life is more affected in the migraneurs. Anxiety and depression are increased in TTH patients (Table 2).

Table 2 shows that the majority of the patients with primary headache are occupied individuals and belong to female gender. Tension type headache is prevalent in the younger and older subgroups of patients

and in individuals, which are occupied. Migraine accounted equally for the ages 36-55 years. None of the older patients had migraine.

The distribution of the scores

Several statistical tests depend on the crucial assumption of a normal distribution for the data. Here, we tested the assumption of normality via the Shapiro-Wilk test for the scores in the 7 scales. In all cases, a clear departure from normality was demonstrated (all P-values <0.01), with the scores exhibiting in general a moderate to strong positive skewness. Regression and ANOVA methods are therefore inappropriate, and we used nonparametric tests to examine which groups differ for each of the seven scales.

Nonparametric tests

For each of the four control variables, and each of the 7 scales, we have performed a Kruskal-Wallis test, which is the nonparametric analogue of ANOVA, in order to detect, which group differences account for significant changes in the scores.

At a 5% level of significance, gender is

an important factor for 5 out of the 7 scales, and it is the only significant factor in 3 of them (SDS, Hamilton anxiety, MIDAS). Age is marginally insignificant for the Epworth scale, while it seems to have no effect on the other scales. Occupation status is significant only for the Epworth scale, while the type of headache seems to be marginally important and very important for the Hamilton Depression and the SF36 scales respectively. It is worth noting that none of the four control variables has a significant impact on the Athens Insomnia scale.

Multivariate logistic regression

Finally, we conducted multivariate logistic regression for the scores in the seven scales, with a further view to investigate which factors affect significantly the probability that a person is beyond a certain threshold. Compared with ANOVA, logistic regression has the advantage that it does not rely on the distribution of the data, as the dependent variable is binary. We set the threshold (cutoff point) for the Epworth scale to be 9 and for the Hamilton Depression and Anxiety scales to be 7 and 5 respectively and for the AIS to be 5. For the

Table 1. Overview of study population and clinical characteristics of patients with TTH and migraine.

	TTH	Migraine	N
Gender			
Female	46	35	81 (79.3%)
Male	13	8	21 (20.7%)
Age			
16-35	28	22	50 (49.1%)
36-55	18	21	39 (38.2%)
56-76	13	0	13 (12.7%)
Occupation			
Yes	29	30	59 (55.9%)
No	24	10	34 (33.3%)
Other/Missing	5	2	7 (10.8%)

Table 2. The descriptive statistics for the scores in the 7 different scales (in each case, mean value±S.D. is given).

	Anxiety Hamilton	Depression Hamilton	MIDAS	SDS	Epworth	AIS	SF-36 Total
Gender							
Male	7.83±7.79	5.65±6.49	9.16±16.62	3.55±3.33	5.91±3.12	5.45±5.50	36.76±12.78
Female	11.63±9.61	9.01±8.73	25.87±39.07	1.96±3.28	6.77±3.89	5.87±4.88	44.07±12.76
Age							
16-35	9.25±8.47	7.17±7.82	21.93±29.37	1.98±2.96	7.06±3.40	5.27±4.59	43.09±14.00
36-55	13.50±10.97	10.07±9.89	22.43±42.00	3±4.04	5.51±3.95	6.97±5.94	41.81±13.65
56-76	8.53±4.61	7.13±3.99	23.36±42.66	1.38±1.71	7.86±3.63	4.79±3.42	42.87±14.61
Type of headache							
TTH	11.93±9.64	9.83±9.03	26.22±44.35	2.13±3.18	6.71±3.73	6.16±5.38	44.94±13.65
Migraine	9±8.95	6.72±7.79	17.97±24.81	2.51±3.66	6.41±3.90	5.44±4.69	39.56±13.77
Occupation							
Yes	9.40±8.02	6.84±6.75	18.11±25.675	2.38±3.35	6.02±3.34	5.75±4.80	40.55±12.62
No	13.43±10.67	11.27±10.33	28.08±49.08	2.33±3.57	6.79±3.91	6.52±5.62	47.11±14.80
Other/Missing	6.67±7.14	4.78±5.60	28.13±48.29	1.43±1.61	10.38±3.46	3.13±2.59	35.64±14.42

MIDAS scale, we tried two cut-off points, 10 and 20 (with regard to mild and moderate disability respectively) while for the remaining two scales (SDS and SF36) we used ROC curve analysis, as there appears to be no consensus about the optimal cut-off. The factors with a p-value less than 0.10 for a particular scale have been included subsequently as potential explanatory factors in a (multivariate) logistic regression model. The results are as follows.

Hamilton depression

Three variables entered as potential explanatory factors in a multivariate logistic regression model, where depression is coded as the binary (7, and >7) dependent variable; gender was the only significant variable, with a P-value =0.012.

Hamilton anxiety

Here anxiety, measured on the Hamilton scale was the dependent variable. Both gender and occupation were significant, with P-values 0.009 and 0.043 respectively. While it is clear that women have higher anxiety levels than men (Table 3), to investigate the effect of occupation we performed post-hoc Mann-Whitney tests; it was found that people in employment have lower scores than those who are unemployed [P-value=0.037, OR= 2.796; 95% CI= (1.104, 7.086)], while the *Other* group also differs significantly (having lower anxiety levels) from the group of unemployed (P-value=0.025). There is no statistical difference between the group of employed and the *Other* group.

Epworth scale

No factor was found to be significant here.

Athens insomnia scale

There was no evidence that a factor has a significant effect on the AIS score.

MIDAS scale

Gender seems to be the overriding issue for the scores on the MIDAS scale. Using a cut-off point =10 on that scale, the P-value of gender is 0.004, while for a cut-off point =20, gender is again significant, but the P-value increases to 0.039.

SDS scale

Here we have used ROC curves to determine the *optimal cut-off*, using gender as the explanatory factor. The best fit was observed when the cut-off is equal to 3, and the corresponding P-value for gender is 0.008.

SF-36 quality of life

Using ROC curve analysis again, the

optimal fit is obtained when the cut-off point for the SF36 scale is set to 43. In that case, there are two significant factors: type of headache, with a P-value=0.039, OR=2.018; 95% CI=(1.049, 3.881) (people who suffer from TTH have higher SF36 scores than migraineurs), and occupation [OR= 3.099; 95% CI= (1.325, 7.249)], with a P-value=0.040; gender is insignificant. Performing a post-hoc Mann-Whitney test to see which levels of occupation differ significantly, we found that both the employed and the *Other* group have lower SF36 scores than those who are not in employment (P-values 0.012 and 0.010 respectively).

Discussion

It is well known that there are a number of conditions, which are influenced by headache. The most common regard well-being, welfare, anxiety, depression, sleep and dependence. To the best of our knowledge, this study is probably the first to investigate and offer new insight to the control variables, which influence this diversity of parameters. However, our results could not be generalized due to low sample size.

We have presented results of descriptive statistics, non-parametric tests and multivariate logistic regression analysis, as each of them has its own strengths and offers insight from a different perspective. While the Kruskal-Wallis and Mann-Whitney tests use the actual scores and look at potential differences between the different subgroups, logistic regression examines the influence that the factors have on the scores in the scales exceeding a certain threshold, by treating each scale as a dichotomous response variable. We observed that depression and anxiety share the factor sex. This notice is in agreement with the results of other studies which indicate that women suffered from headache had more severe depressive psychological symptoms compared with men.¹⁹ Interestingly, anxiety appears to be more strongly related to chronic pain in men than women.¹⁰ The high disability scores, nausea and the type

of headache (actually migraine) were pointed out to be independent factors associated with depression in a study carried out in Brazil.¹¹ The role of marital status is debatable.¹² It has also been observed that medication overuse¹³ and obesity¹⁴ are connected with depression and anxiety in patients. Additionally to female gender, high educational level,¹² unemployment¹⁵ and older age are strongly associated with depression in population suffering from primary headaches.⁹ The longer history and the high frequency of headaches are possibly associated with depressive disorders.¹⁹ Nevertheless, chronicisation of primary headaches is not unlikely to be the consequence of psychiatric co-morbidity leading to bi-directional relationship.¹⁶ The diagnosis of migraine was significantly more prevalent among patients with anxiety rendering the type of headache a potential associated factor.¹⁷ We pointed out that unemployment is correlated with anxiety. Searching the literature no other study with similar observation came up.

The relationship between sleep and primary headaches is well known. However, in our study we failed to identify a factor connected with sleep disorders. In nearly all studies, authors correlate sleep disorders with type of headache, suggesting a bidirectional, possibly causal, association.^{18,19} Lebedeva *et al.* and Spierings *et al.* pointed out gender as an additional factor.^{20,21} Our finding that sex is the factor associated with the disability derived from headache is in accordance with the results of other studies.²² In our data, there appears to be concrete evidence that women have higher MIDAS scores than men. Other studies have demonstrated that pain intensity and headache frequency seem to be other prevalent correlated factors. Jelinski *et al.* demonstrated a link between depression and disability status among migraineurs.^{15,22} Our study identified male gender as the one and only factor responsible for individual's predispositions for dependence. Several clinical studies show co-morbidity between substance-related disorders and medication-overuse headache (MOH), suggesting the

Table 3. Odds ratios with 95% CIs for gender (female vs male).

Scale	OR	95% CI
Hamilton depression	3.599	(1.228, 10.550)
Hamilton anxiety	3.515	(1.356, 9.107)
MIDAS (cut-off=10)	5.000	(1.597, 15.657)
MIDAS (cut-off=20)	4.160	(1.593, 10.859)
SDS	0.305	(0.112, 0.831)

existence of an overlap between their pathophysiological mechanisms. These data support the proposition of separating two groups of patients; the first regards patients with severe headache-related disability and the second refers to individuals with behavioral issues such as depression and anxiety.²³ With regard to well-being, we found that employment and migraine are linked with lower level of quality of life. The literature does not confirm that employment influences the level of well-being among the patients with primary headache. Contrariwise, disability due to headache leads to missed days of work and reduced productivity.²⁴ Pain in episodic migraine is intense and obsessive resulting reduced functionality. Episodic TTH is usually infrequent and mild. However, it is chronic TTH that is likely to cause significant impairment. Apparently, the intensity of pain of episodic migraine is counterbalanced with the greater frequency of chronic TTH.²⁴ Besides the frequency and the intensity of pain, gender and psychological comorbidity were pointed out to influence quality of life in a large number of studies.^{24,25} Patients with medication overuse headache (MOH) experience decreased quality of life.¹³

Conclusions

Apparently, our results represent the Greek population of an urban centre. We focused our study on how determinate factors influence the studied parameters. In case the range of the control variables was expanded including factors such as education, daily habits (alcohol consumption, smoking), co-morbidity, further information about the recruited population would be obtained. The main weakness of this study is the number of participants. The assessment of the severity of primary headache was obtained with the MIDAS. Nevertheless, there are not further data with regard to the number and severity of attacks and their possible correlation with the studied parameters. This is an additional limitation of our study.

In conclusion, in this study we detected factors associated with daily living conditions, which are influenced by headache. Female gender is associated with depression, anxiety and higher disability derived from headache whereas; men are more prone to addiction and dependence on opioids. To be unemployed was linked with

anxiety and higher level of quality of life. However, the present study could not provide any further explanation for this. Finally, the migraneurs presented a decreased level of quality of life.

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