Effects of Chronic Migraine on Male Sexual Health

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ABSTRACT

Objective: To investigate the clinical implication of the sexual functions of male patients diagnosed with chronic migraine (CM) compared with the healthy population.

Study Design: Observational study.

Place and Duration of Study: Departments of Urology and Neurology, Hitit University Hospital, Turkey, from August 2019 to August 2020.

Methodology: A total of 179 patients (92 subjects diagnosed with CM and 87 control healthy volunteers) were included in this study. Demographic descriptive data including age, height, weight, and body mass index (BMI) of all patients were recorded. A 5-question version of the international index of erectile function questionnaire (IIEF-5) was applied to evaluate their sexual functions. Furthermore, a migraine identification test was performed for CM patients for the diagnosis of migraine in accordance with the International Headache Society's (IHS) definition of chronic migraine. Visual analog scale (VAS) scores between 0-10 points were recorded for the qualitative assessment of migraine pain.

Results: The IIEF-5 scores of CM patients [16 (11 – 21)] were lower compared to the control patients [21 (19 – 23), p <0.001)]. A negative correlation was found between the VAS scores and IIEF-5 scores of CM patients (rho -0.582, p <0.001). In the regression analysis, it was found that a 1-unit increase in the VAS score led to a 1.5 point decrease in the IIEF-5 score (p <0.001).

Conclusion: Migraine pain in male patients with CM adversely affected erectile functions. A more detailed investigation of the pathophysiological mechanisms may be helpful in the treatment of ED.

Key Words: Erectile dysfunction, Chronic migraine, IIEF-5, Erectile functions.

INTRODUCTION

Chronic migraine (CM), which affects approximately 5-12% of the male population, is the most common known cause of headaches.[1,2] Adverse effects on social life, which are observed in almost all chronic diseases, are also expected in CM. In migraine with chronic pain attacks, it is expected to adversely affect sexual functions. Nowadays, the search for treatment for sexual dysfunction, and consequently the rates of diagnosis, are increasing. Erectile dysfunction (ED) is the most commonly observed sexual dysfunction.[3] Many risk factors have been identified for ED. It was also demonstrated that international index of erectile function questionnaire (IIEF-5) scores, which are used to evaluate the sexual functions of chronic migraine patients, were lower compared to control patients.[4,5] Although the correlation between chronic migraine and ED risk was demonstrated, its clinical implication was not studied.

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The objective of this study was to investigate the effects of the pain scores perceived by the chronic migraine patients on erectile functions and its clinical implication. The results to be obtained are likely to be a guide in the clinical differential diagnosis and treatment of erectile dysfunction.

METHODOLOGY

This prospective observational study was reviewed and approved by the Institutional Review Board of Hitit University Ethical Committee for Clinical Investigations (Approval No. 2019-38). Informed consent was obtained from all subjects when they were enrolled. STROBE (Strengthening the reporting of observational studies in epidemiology) principles (www. strobe-statement.org/) were followed. The minimum number of participants in each group was determined as 90 with a 95% confidence level and 80% power.

Out of 137 patients between the ages of 18-65, 92 who were followed up in the Neurology Outpatient Clinic with a diagnosis of CM between the dates of August 1st, 2019 and August 1st, 2020, in accordance with the definitions of the HIS[CM implies headaches occurring ≥15 days per month for at least 3 months with migraine features on ≥8 days every month, headache without excessive use of drugs and not attributed to any other cause],[6] were included in the study. Erectile functions of the patients were evaluated in the Urology Outpatient Clinic.

Table I: Demographic and clinical characteristics of the patients.

		Group-1 n=92	Group-2 n=87	p-value
Age (years, mean ± SD)		37.64±10.54	40.45±11.15	0.085
BMI (kg/m^2) Median (25 – 75 percentile)		26.78 (23.46 – 31.80)	24.89 (23.67 – 29.70)	0.208
Diabetes mellitus	Yes n (%)	17 (18.5)	12 (13.8)	0.395
	No n (%)	75 (81.5)	75 (86.2)	
Hypertension	Yes n (%)	12 (13.0)	9 (10.3)	0.575
	No n (%)	80 (87.0)	78 (89.7)	
Other comorbidities (asthma, rheumatological diseases etc.)	Yes n (%)	7 (7.6)	5 (5.7)	0.619
	No n (%)	85 (92.4)	82 (94.3)	
Smoking	Yes n (%)	38 (41.3)	31 (35.6)	0.436
	No n (%)	54 (58.7)	56 (64.4)	

BMI: Body mass ındex, SD: Standard deviation.

Table II: Responses of the groups to the IIEF-5 questions.

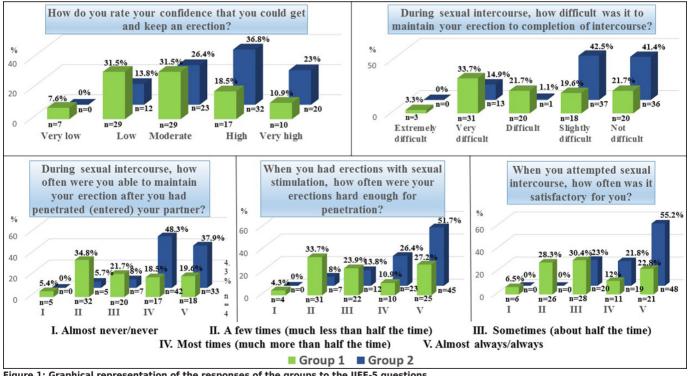|	Group-1 (n=92) Median (25th-75th percentile)	Group-2 (n=87) Median (25th-75th percentile)	p-value
How do you rate your confidence that you could get and keep an erection?	3 (2 – 4)	4 (3 – 4)	<0.001
When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	3 (2 – 5)	5 (4 – 5)	<0.001
During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	3 (2 – 4)	4 (4 – 5)	<0.001
During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	3 (2 – 4)	4 (4 – 5)	<0.001
When you attempted sexual intercourse, how often was it satisfactory for you?	3 (2 – 4)	5 (4 – 5)	<0.001

Figure 1: Graphical representation of the responses of the groups to the IIEF-5 questions.

The exclusion criteria of the study were determined as the presence of hypogonadism (Testosterone level <12 nmol/L (3.5 ng/ml)); use of antidepressants and phosphodiesterase 5 inhibitors (PDH-5); having previous prostate surgery or pelvic surgery; severe lower urinary tract symptoms (LUTS); benign prostatic hyperplasia (BPH) symptoms; presence of bladder pain syndrome; or interstitial cystitis. Patients using drugs known to cause ED for the treatment of CM were excluded from the study. Patients who were treated with botulinum toxin-A or used calcium channel blockers due to

chronic migraine were included in the study. Including 87 control patients, a total of 179 patients were included in the study.

The study questionnaire filled out by the doctor who informed the patients about the study; was created by the study team. The study questionnaire consisted of 3 parts: (1) Demographic descriptive part including age, height, weight and BMI of the participants; (2) The part consisting of the migraine identification test for the diagnosis of migraine and the VAS scored between 0 and 10 points for the qualitative evaluation of migraine pain in accordance with the definitions of the HIS;[6] (3) The part that evaluates the sexual activity of patients. This part was evaluated using the Turkish validated form IIEF-5.[7] This questionnaire consists of four questions about sexual function and one question about sexual satisfaction. Each question is scored between 1-5 points (total score was in the range of 5-25 points, minimum and maximum respectively).

The SPSS version 22 programme was used for statistical analysis. Normal distribution of the data was tested by visual (histogram) and analytical methods (Kolmogorov-Smirnov tests). Number, percentage, mean, standard deviation, median (25th percentile-75th percentile) expressions were used for descriptive statistics. Student t-test and Mann-Whitney U-test were used for comparisons between two independent groups. Chi-square test was used for the comparison of categorised data. The correlations between the IIEF-5 score and different parameters were analysed using the Spearman correlation tests. The independent effects of different predictors on IIEF-5 score were examined, using a multivariate linear regression model. Model fit was examined using the required residual and fit statistics. The results with $p < 0.05$ were considered statistically significant.

RESULTS

A total of 179 patients, including 92 patients diagnosed with CM (Group-1) and 87 patients constituting the control group (Group-2), were included. The mean age of the patients was 37.64 ± 10.54 years for Group-1 and 40.45 ± 11.15 years for Group-2. The median body mass index (BMI) was 26.78 Kg/m^2 (23.46 – 31.80 Kg/m^2) for Group-1 and 24.89 Kg/m^2 (23.67 – 29.70 Kg/m^2) for Group-2. There was no statistically significant difference between the groups in terms of age and BMI distribution ($p = 0.085$ and $p = 0.208$, respectively). The characteristics in terms of smoking, diabetes mellitus, hypertension and other comorbidities (asthma, rheumatological diseases, etc.) between the groups are presented in Table I. No statistical difference was found between the groups in terms of smoking and comorbidity characteristics.

When the erectile capacities of the patients were evaluated, IIEF-5 total scores [16 (11– 21)] of Group-1 were statistically significantly lower compared to Group-2 [21 (19 – 23), p <0.001]. When the responses of the groups to the IIEF-5

questions scored between 1-5 points were examined, Group-1 had lower scores in all questions compared to Group-2. The responses of the groups to the IIEF-5 questions scored between 1-5 points are presented in Table II and Figure 1.

When the correlation analysis between migraine VAS scores and IIEF-5 scores of patients with chronic migraine is examined, a negative correlation was found between the IIEF-5 score and all parameters, and the strongest correlation was found with the VAS score (rho -0.582, p<0.001). The correlation between IIEF-5 score and age (rho-0.266, p = 0.010) and BMI (rho -0.313, p = 0.002) were found. In the regression analysis, it was determined that a 1-unit increase in the VAS score led to a 1.561 [%95 CI (confidence intervals), 2.092– 1.030] point decrease in the IIEF-5 score (p<0.001); and similarly, it was also determined that a 1-unit increase in BMI value led to a 0.249 (%95 CI, 0.479–0.019) point decrease in the IIEF-5 score (p = 0.034). No statistically significant correlation was found in the regression analysis between age and the IIEF-5 score (p = 0.818).

DISCUSSION

CM, which affects approximately 5-12% of the male population, is the most common known cause of headaches.[1,2] Adverse effects on social life, which are observed in almost all chronic diseases, are also expected in chronic migraine. It is known that chronic pain has adverse effects on sexual desire, arousal and sexual activity.[8-11] In migraine with chronic pain attacks, it is expected that sexual functions are adversely affected. With regard to pathophysiological mechanisms of migraine in sexual dysfunction, it was indicated that dopamine, and serotonin were reported to be responsible for it in another study.[12,13] It is known that dopamine has a role in sexual function and motivation, and it seems possible that irregularities in dopamine pathways affect sexual function negatively.[12-15] It is suggested that the increase in serotonin may lead to sexual dysfunction by having an antagonist effect on testosterone.[13-16]

Except for the specified physiological mechanisms, there are limited numbers of publications in the literature investigating the correlation between CM and sexual dysfunction. Nowadays, the search for treatment for sexual dysfunction, and consequently the rates of diagnosis, are increasing. ED is the most commonly observed sexual dysfunction, which is characterised by an inability to develop or maintain penile erection during sexual activity.[3] In epidemiological studies on ED, the main risk factors are divided into four categories: (1) Urological and andrological risk factors, (2) Cardiovascular and metabolic risk factors, (3) Psychiatric diseases, and 4-Lifestyle-related risk factors.[17] It has been stated in the literature that migraine is also a risk factor for ED. Wu et al.[18] indicated that ED was observed more frequently in patients with migraine compared to the control group and that the risk of developing ED is 1.75 (95 CI% = 1.27-2.41) times higher after

adjusting age and comorbidity compared to the control group. Similarly, Huang et al.[12] indicated that the probability of having a previous diagnosis of migraine in ED patients was 1.64 (95 CI%, 1.40-1.92) compared to the control group and 1.63 (95 CI%, 1.39-1.91) after adjusting the comorbidity. These studies report the association and risk rates of migraine and ED as a population-based cohort study or a population-based case-control study. In the studies examining the clinical relationship, Bellosta-Diago et al.[4] indicated that the IIEF scores of chronic migraine patients were lower compared to the control group. Aksoy. et al.[5] reported that the IIEF-5 scores of migraine patients were also lower compared to the control group. In the study of Aksoy et al.[5] testosterone levels were also examined between the groups, and no difference was found. It was indicated that there was only a negative correlation between age and the IIEF.[5] While this study supports the similar result between the IIEF and age, it also demonstrated that there was a negative correlation between BMI and VAS scores, as a contribution to the literature. The negative correlation between the IIEF-5 scores and VAS scores felt during CM pain, was stronger than age and BMI. It was determined that a 1-unit increase in the VAS score could cause a 1.5-point decrease in the IIEF-5 score. Since there is no study on this subject in the current literature, we consider that our results will contribute to the literature and add a different perspective. Furthermore, the responses to the IIEF-5 scores were examined for the first time in this study; and it was observed that chronic migraine patients had lower scores in all questions of the IIEF-5 questions.

There are some limitations to the generalisation of results of this study. Although the groups were similar to each other in terms of the presence of factors such as smoking, diabetes mellitus and hypertension that may cause ED, there was no information about how long the patients in both the groups had these risk factors. They are likely to affect ED in a chronic process. Another limitation of this study is that although it was not evaluated in terms of depression in both groups, CM may have increased the susceptibility to depression, and the possible effects of CM disease duration were not evaluated.

CONCLUSION

Sexual dysfunction is more commonly observed in patients with CM compared to normal healthy individuals. It may be expected that ED is more frequently observed in patients who indicate having more CM pain. The pathophysiological mechanisms, occurring in relation to pain, are likely to affect sexual function. Future studies and the reduction of pain in migraine can be a guide in the treatment of ED.

ETHICAL APPROVAL:
This prospective observational study was reviewed and approved by the Institutional Review Board of Hitit University Ethical Committee for Clinical Investigations (Approval No. 2019-38).

PATIENTS' CONSENT:
Informed consents were taken from all patients before writing the article.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
MMB: Supervised the study, literature review and manuscript writing.
AB: Concept, design, literature review, data collection, results, and finalised the study.
HYB, SE: Data collection, processing and interpretation and critical reviews.
FUT: Supervised the study, helped in manuscript writing, reference citation and proofreading of the article.

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