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The effect of *Helicobacter pylori* eradication on Severity and Frequency of Migrain's attacks

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KEYWORDS

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A B S T R A C T

Migraine is a disease characterized by throbbing and periodic headache. Clinicaly there are different types of migraine that is included migraine with or without aura. The most common type of migraine was migraine without aura. The underlying exacerbate mechanisms of migraine symptoms are still not well known. Recently, *Helicobacter pylori* infection is associated with several extra intestinal disorders such as migraine. The aim of this study was to determine the effect treatment of *Helicobacter pylori* infection on the frequency and severity of migraine attacks. In a cross-sectional study that performed in the Department of Neurology and Neuroscience Research Center of Tabriz University of Medical Sciences on patients with migraine, The effect of *Helicobacter pylori* infection treatment on the number and severity of migraine attacks were evaluated. In this study, 83 patients with migraine were evaluated that 15 patients (1/18%) of them were male and 68 patiets (9/81%) of them were female. The mean age of the male patients was 38.00±6.25 and in female patients was 34.33±6.79 year(P=0.059). At the beginning of the study, the severity of headache in 2 patients was mild, in 20 patients was moderate and in 61 patients was severe. A month later, the severity of headache in 14 patients was mild, in 38 patients was moderate and in 31 patients was severe. Two months later, the severity of headache in 18 patients was mild, in 45 patients was moderate and was severe in 20 patients was severe. Three months later, the severity of headache in 25 patients was mild, in 46 patients was moderate and in 12 patients was severe. In our study, eradication theraoy of *Helicobacter pylori* infection leads to a reduction in the severity and frequency of migraine attacks in the studied patients.

Introduction

Headache is among the most common complaints of patients who visit neurology clinics and migraine headache is one of the most common forms of headache (1).

Different factors such as rugs, specific food items, sleep disorders, stress, environmental factors (e.g. light, moisture), and menstruation cycles are also known as factors associated with migraine (2-3).

Recently, infection factors have been studied as risk factors of migraine. An example of such infections is HP infection.

HP is a gram negative organism which is known as the cause of chronic active inflammation of stomach and is highly prevalent. Its prevalence in the developed countries and developing countries is 40-50% and 80%, respectively. Considering the role of this organism in the secretion of serotonin from plackets platelets, the relationship between this infection and migraine is under study and discussion. Results of some studies introduce this infection as a factor increasing the intensity and frequency of migraine attacks. The researchers state that eradication of this infection can contribute to the decrease in the intensity and frequency of migraine attacks (4-5).

Some other researchers stated that simultaneous occurrence of migraine and HP infection is accidental and these two conditions are not significantly related.

Hence, considering the remaining ambiguities the present study aimed to study the effect of eradication of HP on the reduction in intensity and frequency of headaches in patients with migraine. Migraine is one of the most common points of complaints by patients visiting neurology clinics. Hence, if the effect of treatment of HP on the reduction in the intensity and frequency of migraine attacks is proved, it will be possible to eliminate the need for the prophylaxis treatment of migraine and administration of pain relievers for many patients. As a result, expenses imposed on patients and society by such treatments as well as by the absence of patients from work will decline (5-6).

The objective of this study was to investigate the effect of treatment of HP infection on the number and intensity of migraine attacks.

Materials and Methods

In a descriptive analytical study that was carried out in the Department of Neurology and Neuroscience Research Center of Tabriz University of Medical Sciences on patients with migraine, the effect of treatment of HP infection on the frequency and intensity of migraine attacks was examined.

The study population included patients with migraine. The sample included 83 patients who were suffering from migraine and HP infection at the same time. Participants were selected randomly from patients visiting the public and private neurology clinics of Tabriz City.

The inclusion criterion was presence of migraine proved using IHC criteria.

The exclusion criteria included the following:

- Aged below 20 years
- Presence of secondary causes of headache
- History of treatment of HP infection
- Smoking
- Suffering from auto-immune diseases

- Pregnancy
- Consumption of OCP

Stool antigen tests were carried out to diagnose the patients with HP infection. All of the tests were conducted in a laboratory. When the result of tests was positive the patients received quadruple medical treatment with Clarithromycin (500 mg/BID), Amoxicillin (1000 mg/BID), Bismuth (240 mg/BID) and Omeprazole (20 mg/BID) for two weeks. One month after the treatment course the eradication of infection was verified by stool antigen tests. Patients experiencing treatment side effects were referred to a gastroenterologist. In cases where the eradication of the infection was proved in a 3-month period (at the end of each month and a total of 3 times) the patients were followed and tests were examined to assess the intensity, length and frequency of attacks.

In order to measure the intensity of migraine the functional grading method was used.

Statistical analysis

The collected data were analyzed by SPSS-17 statistical software. The collected data were expressed as percentage and mean ± SD. Continuous (quantitative) variables were compared by Independent samples and Paired t test. Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's exact test. P-value ≤ 0.05 was considered statistically significant.

Ethical considerations

The written consent of all of the participants was obtained after explaining the research objective and the necessary parts of the research method. No patient was forced to take part in the study. In the case of patients who were not capable of reading and signing the written consent form, after explaining the necessary considerations to the patients and their companions (who were preferably among their first-degree relatives) the forms were completed by the companions and the finger print of patients was obtained. No expense was imposed on the participants for the research. Every patient was permitted to leave the study whenever he/she pleased. The possible side effects of eradication of HP were also explained to the patients.

Results and Discussion

In this study, 83 patients with migraine were examined. Of the total participants, 15 (18.1%) were male and 68% (81.9%) were female.

The average age of male and female patients was 38.00 ± 6.25 and 34.33 ± 6.79 years ($p=0.059$). In 9 (3 male and 6 female), 46 (5 male and 41 female), and 28 (7 male and 21 female) patients the headaches relieved using nonmedical agents, medical agents, and a combination of medical and nonmedical agents, respectively ($p=0.140$).

Moreover, of the male and 29 of the female patients had a family history of migraine ($p=0.851$). The history of aura was positive in 5 male and 14 female patients ($p=0.317$).

Of the patients with aura, 6 (2 male and 4 female), 2 (all female), 3 (1 male and 2 female) and 8 (2 male and 6 female) patients suffered from blindness, vertigo, bright lights, and blurred vision, respectively.

Five male and 14 female patients had migraine with aura while 10 male and 54 female patients had migraine without aura ($p=0.317$). The history of digestive problems was positive in 17 patients. Migraine is a disease characterized by period headaches

and throbbing headaches. From the clinical point of view, there are different types of migraine including migraine with aura and migraine without aura. The most common type of migraine is the migraine without aura.

In our study, 77.1% of patients were diagnosed with migraine without aura.

Several case control studies have reported the existence of an effective relationship between HP infection, occlusive vascular diseases (AMI, Raynaud's disease, and CVA) and migraine. However, there are differences in the results of such studies (13-14).

The increased risk of HP-related extra-intestinal disorders is the result of release of substances with vascular and proinflammatory effects by this microorganism (15).

In the study by Tunca et al. on 70 migraine patients and 60 control samples, the time and intensity of migraine headaches before and after eradication of HP were studied. The researchers reported that HP was eradicated in 84.6% of patients and 75% patients used a classic treatment which led to a decrease in the signs of headache and improvement (16).

In the study by Gasbarrini et al. on 148 patients with migraine the existence of active HP infection was proved with UBT (urea breath test). The patients, therefore, received suitable antibiotic treatments and treatments for eradication of the bacteria. Next, the frequency, intensity and time of outbreak of migraine attacks were tracked in the patients for one year. In the case of patients in whom HP was eradicated a significant difference in the reduction in the frequency, intensity and duration of migraine attacks was seen as compared to patients with a history of reoccurrence of the disease (17).

In another study by Gasbarrini, 49 patients with aura and 126 patients without aura were compared to 152 similar control samples. The HP infection was equally prevalent in the groups with and without aura (18).

In this regard, some researchers studied the effect of the IgG and IgA antibodies on patients with migraine and observed no significant difference after administration of these antibodies (19).

In addition, in another research chronic HP infection was not more prevalent among the patients with migraine than the control group (20). However, the serum prevalence of the aforementioned antibodies was significantly higher in the migraine group (21). Gasbarrini et al. observed that eradication of HP reduces the number of migraine attack (22).

In the study by Jiankar Lee etl. The ELISA method was used to study the effect of the IgA and IgG antibodies on 30 migraine patients. No significant relationship was observed between the antibodies and the health condition of the patients (19).

In Italy, Pinessi et al. studied 103 patients and did not report the higher prevalence of chronic HP infection in patients with migraine as compared to the control group. According to these researchers, this infection does not contribute to the change in the clinical characteristics of patients with migraine (20).

On the other hand, Tunca et al. reported a significantly higher serum prevalence of the aforementioned antibodies in 35 patients with migraine as compared to 29 healthy participants in the control group (21).

Gasbarrini observed that eradication of HP leads to a reduction in the number of migraine attacks (22).

In 2007, Yiannopoulou studied 49 migraine patients in Greece and reported that presence of this infection in patients without hormone and genetic predisposing agents is a possible risk factor for the outbreak of migraine attacks (23).

In the study by Afra Khosravi et al. in Ilam, the titer of IgG antibody against HP was measured in 70 healthy individuals and 70 patients. The level of this titer in the control and experiment groups was 21.8% and 60%, respectively. This reflected the existence of a significant statistical difference between the results (1).

In the study by Yiannopoulou, the prevalence of helicobacter pylori in patients with migraine was significantly higher than members of the control group who did not suffer from migraine (61% vs. 37%) ($p=0.016$) (2).

In Turkey, Tunca et al. compared the HP infection in 70 migraine patients and 60 participants without migraine with similar demographic properties. In this study, the prevalence of HP in the migraine and non-migraine groups was 57% and 33%, respectively ($p=0.007$).

84% of the patients with migraine and HP infection experienced a reduction in the frequency and intensity of migraine attacks after HP eradication. In two patients (18%) also the migraine attacks were fully eradicated (4).

In our study, 61 patients (73.5%) suffered from severe headache at the beginning. However, the frequency of severe headache in the first, second and third months was 31 (37.3%), 20 (24.1%), and 12 (14.4%) patients, respectively. The severity of headaches also declined in the course of study.

Gabrielli examined 148 patients with migraine using urea breath test for the existence of HP infection. Of the 148 patients, 62 (42%) patients were diagnosed with HP infection. The patients were exposed to a triple therapy by Clarithromycin, Amoxicillin and Omeprazole. Eradication of the infection was investigated 2 months after the completion of the treatment period. The infection was eradicated in 57 patients (82%). The duration, intensity and frequency of migraine attacks were also measured 2, 4, 6 and 12 months after eradication. Of the 57 patients who experienced successful eradication, 16 (28%) experienced no headache in the follow up and others mentioned a considerable decline in the intensity and frequency of attacks ($p<0.01$) (4).

In our study, the average frequency of headache in patients under study was 4.83 ± 4.07 at the beginning and it declined to 4.04 ± 2.79 in the next third months. The reduction was statistically significant ($p<0.001$).

Alireza Bakhshipour et al. examined the development of the helicobacter pylori infection in 60 patients in Zahedan. They exposed the patients with the infection (40 patients) to eradication therapy. The average frequency of migraine attacks in helicobacter pylori positive patients who were subjected to eradication therapy was 7.2 and 2.7 attacks per month before and after the therapy.

Tabel.1 Symptoms and Triggers of Patients

	Diagnosis	
	Migraine with aura	Migraine without aura
	Symptoms	
Nausea	9	43
Vomiting	7	25
Restlessness	0	2
	Triggers	
Trauma	0	1
Voice	17	54
Smell	10	35
Light	11	33
Fatigue	17	47
Starvation	15	39
Special food	5	5
Menstruation	10	27
Stress and anger	13	43

Table.2 Frequency of headache based on Migraine type of patients

	Diagnosis	
	Migraine with aura	Migraine without aura
Frequency of headache an first	3.87 ± 2.36	5.11 ± 4.43
Frequency of headache one month late	3.71 ± 2.13	4.66 ± 3.64
Frequency of headache Two months late	3.61 ± 2.09	4.42 ± 3.28
Frequency of headache Three months late	3.45 ± 1.83	4.27 ± 3.01

Table.3 Frequency of headache based on patients gender

	Gender	
	Male	Female
Frequency of headache an first	6.00 ± 5.84	4.57 ± 3.58
Frequency of headache one month late	5.47 ± 4.82	4.21 ± 2.95
Frequency of headache Two months late	5.27 ± 4.42	4.01± 2.66
Frequency of headache Three months late	5.00 ± 3.95	3.88 ± 2.47

Therefore, the reduction in the frequency of attacks was statistically significant (p=0.001). The severity of attacks on the basis of MIDAS criterion was 9 before the treatment and reached 4.5 following the eradication (p=0.02) (5).

In our study, eradication of HP led to a reduction in the intensity and frequency of migraine attacks in patients under study. In the research by Faraji, 64 patients with migraine and helicobacter pylori infection were randomly classified into two groups: one group received treatment for migraine and HP eradication while the other received migraine treatment and placebo. The MIDAS score of patients in the experiment group was higher than the participants of the control group at the beginning of treatment (p<0.05). After the treatment, no significant difference was observed between the two groups (P=0.5). However, iterations of measurements by the general linear model revealed that the reduction in MIDAS was higher in the treatment group (p=0.05) (6).

Conclusion

Most patients with migraine did not have aura. In our study, at the beginning of the study 61 participants (73.5%) were suffering from severe headache. The frequency of headache in the first, second and third month was 37.3%, 24.1% and 14.4%, respectively. The severity of headaches declined in the course of the study. In our research, 77.1% of patients under study suffered from a migraine without aura.

In our study, the average frequency of headache in patients under study was 4.83 ± 4.07 at the beginning and three months after the study it declined to 4.04 ± 2.79. The reduction was statistically significant (p<0.001). In our study, eradication of HP led to a significant decrease in the intensity and frequency of migraine attacks in patients under study.

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