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Research Article

THE EFFECT OF HELICOBACTER PYLORI ERADICATION ON MIGRAINE WITHOUT AURA

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ABSTRACT

Helicobacter pylori is a gram-negative bacterium that is present in almost half of the population. Recent studies have shown a positive correlation between H. pylori infection and migraine headache. The aim of this study was to asses the impact of H. pylori eradication on migraine headache. This randomized clinical trial study carried out on 108 patients with migraine without aura, who were admitted in neurology clinics in a university affiliated hospital. Patients randomly were divided into two groups. The first group underwent eradication of H .pylori infection with a three drug regimens. H.pylori infection confirmed by Urease Breathing Test. Patients in the second group received only migraine treatment. One month after completion of therapy was repeated to assess eradication of infection. The number and severity of attacks in both groups before treatment, second and fourth months after eradication was measured. Eradication of H. pylori was successful in 47 patients. In treatment group score of attacks during 2th ($p<0.001$) and 4th months after eradication were significantly decreased ($p<0.001$). Also, such decrease was observed in the control group ($n=61$). Migraine score change in the two groups after 2 months of eradication was significantly different ($p= 0.049$). But 4 months after eradication, there was no significant difference between the two groups ($p = 0.082$). According to our study, clinical manifestation of migraine improves two months after H. pylori eradication but four months after eradication. Eradication of this infection can be effective in decreasing severity of the migraine attacks.

INTRODUCTION

Migraine is a common, episodic neurological disorder characterized by severe, usually unilateral and often pulsatile headaches. It is accompanied with autonomic and neurological symptoms (Weir and Cader, 2011). There are two common type of this headache, migraine with aura (20%) and migraine without aura (80%). Migraine without aura is characterized by an unheralded onset of hemi cranial headache or by generalized headache with or without nausea and vomiting, which then follows the same temporal pattern as the migraine with aura (Bigal and Lipton, 2009).

Migraine has complex and multi-factorial pathophysiology and so far it has not been possible to determine a unifying theory for pathogenesis of this disease. Migraine without aura seems to be caused by a combination of genetic and environmental factors. Migraine is a major cause of non-fatal disease-related disability, which affects11%ofworld's population (14% of women and 6% of men). The investigation about prevention and treatment of this common disease is crucial (Semenov, 2015).

Recently the role of infectious diseases, the immune responses, and also the impact of digestive system disorders on migraine headaches have been noted (Lipton *et al* 2007, May and Schulte 2016).

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Helicobacter pylori (*H. pylori*) is a gram-negative bacterium that causes gastric inflammation and peptic ulcer. It is common and present in approximately one-half of the world's population. Besides gastrointestinal problems, *H. pylori* has been associated with a number of extraintestinal diseases such as renal failure, type 2 diabetes, skin diseases, respiratory problems, Alzheimer's disease and ischemic heart disease (Gasbarrini *et al* 2010, Krueger *et al* 2011, Malfertheiner *et al* 2011, Ruggiero 2010, Sugimoto and Yamaoka 2011, Suzuki *et al* 2011).[6-11]

Recently a relation between H. pylori chronic infection and migraine has been proposed in literatures. This theory has been studied by researchers but the results are controversial. Some studies have suggested an positive association between H. pylori infection and migraine headache (Yiannopoulou *et al* 2007, Su *et al* 2014, Hong *et al* 2007, Faraji *et al* 2015, Bakhshipour *et al* 2012).[12-16] On the other hand some studies not confirmed this association (Ciancarelli *et al* 2002, Pinessi *et al* 2000).[17,18] Some of this studies used serology for detection of H. pylori infection that has low sensitivity and specificity and cannot use for follow up of treatment (Faraji *et al* 2015, Hosseinzadeh *et al* 2011).[15, 19] The aim of this study was to evaluate the effect of eradication of H. pylori on patients' symptoms that had migraine without aura.

METHODS

This randomized, double blind clinical trial conducted during the period from 2012 until 2014 in a university affiliated hospital in Semnan. Iran. New cases with diagnosis of migraine (n=186) aged 20 to 40 who were visited in neurology were included. Diagnosis of migraine was according to International Headache Society criteria (Headache Classification 2013).[20] Demographic data including age and gender of the patients were recorded. Included patients were selected from individuals that have had migraine without aura and with two or more attack each month.

Exclusion criteria included other causes of headache except migraine, prior H. pylori treatment in recent month, smoking, metabolic disorders, autoimmune diseases, pregnancy, steroid treatment and use of immunosuppressive drugs.

The study was approved by the Research and Ethics Committee of the Semnan University of Medical Science. Written consent was obtained from all participants.

All patients were tested for H. pylori Urease Breathing Test (UBT). From these patients 125 had positive UBT. Seventeen patients refused to participate. Finally 108 patients were randomized into two groups. The block randomization procedure was used to allocate the patients into the two groups. Patients in the first group received an H. pylori eradication regimen in addition to migraine treatment. The eradication treatment protocol consisted of Metronidazol (500 mg BID) for one week, Azithromycin (250 mg BID) for one week and Omeprazole(20 mg BID) for two weeks. All patients received migraine prophylaxis with propranolol 20^{mg} two times a day.
Patients in the second group received only migraine treatment. In the first group, eradication of H. pylori was successful in 47 patients (treatment group). Seven patients of the first group and 54 patients in second group considered as control group (n=61)(Figure 1).

Number and severity of attacks during previous month and second and fourth months after eradication were registered. The reason for evaluation of patients during second and fourth was that the eradication remains at least for 6 month after treatment (Longo *et al* 2012).[21]

Patients were taught to register the number and severity of attack in a diurnal sheet during the study. Severity of headache scored as mild=1, moderate=2 and sever=3. Total migraine score was calculated by multiplying number of attack and severity score. For example if patient has had four severe attacks and five moderate attacks, the final score for the patient was 22. To confirm H. pylori eradication and treatment efficacy, the patients again underwent second UBT one month after the end of treatment.

Data analyzing was done by Chi-Square, t-student, Wilcoxon, Mann-Whitney and Friedman tests using SPSS software version 16.0. A p-value less than 0.05 were considered statistically significant.

RESULTS

The UBT was positive in 67.2% patients affected by migraine without aura. The mean (±SD) age of treatment group was 32.5±5.8 years and for control group was 30.9±5.8 years, that showed no significant difference (p = 0.185).

For gender distribution, 21.3% of cases and 23% of control group were male. The two groups were matched based on gender (p = 0.836).

Number of migraine attacks in the two groups before the eradication, during second and fourth months after H. Pylori eradication was not significantly difference (p> 0.05)(Table 1).

Table 1 Mean and Standard Error (SE) of number migraine attacks before, second and fourth months after eradication in two study groups

Group	N	Number of migraine attacks		
		Before HP Eradication	During second month	During fourth month
HP eradicated	47	14.2±2.1	7.9±1.1	6.4±1.1
Control	61	12.3±1.1	±1.0 8.1	7.5±0.9
p-value		0.782	0.968	0.212

Table 2 Mean and Standard Error (SE) of severity of migraine before, second and fourth months after eradication in two study groups

Group	n	Severity of migraine		
		Before HP Eradication	During second month	During fourth month
HP eradicated	47	2.60±0.07	2.22±0.11	2.20±0.11
Control	61	2.59±0.06	±0.11 2.17	2.21±0.11
p-value		0.818	0.820	0.575

Table 2 shows Mean and Standard Error (SE) of severity of migraine before the eradication, during second and fourth months after that showed no significant difference (p> 0.05). Mean score of migraine before the eradication, during second and fourth months after eradication in two study groups are showed in (Table 3).

Table 3 Mean and Standard Error (SE) of scores of migraine before, second and fourth months after eradication in two study groups

Group	n	Scores of migraine		
		Before HP Eradication	During second month	During fourth month
HP eradicated	47	35.8±4.9	17.2±2.5	15.0±2.6
Control	61	32.5±3.2	±2.6 19.6	19.1±2.6
p-value		0.735	0.818	0.179

The treatment group mean score during second months after eradication showed 18.5 reductions when compared with the before treatment. This reduction for control group was 12.9. Changes of scores were significantly different between the two groups (p= 0.049). But changes of scores in treatment and control group, during fourth months after treatment was not significantly different (p = 0.082) (Table 4).

Table 4 Mean and Standard Error (SE) changes of migraine scores during second and fourth months after eradication respect to month before HP eradication in two study groups

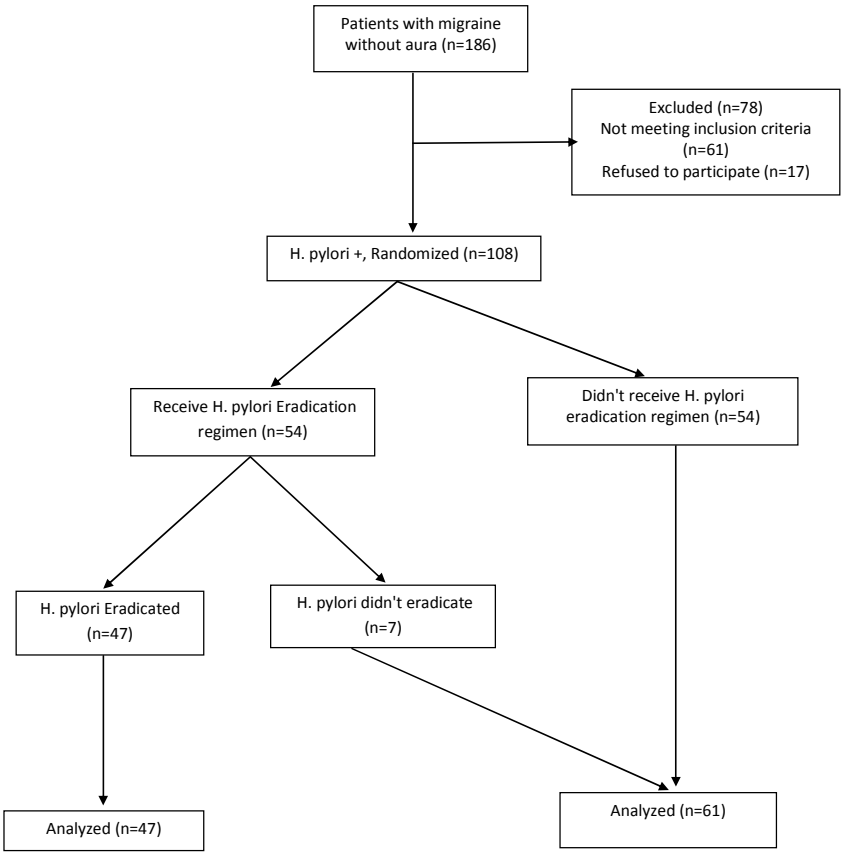
Group	n	Changes of migraine scores	
		During second month	During fourth month
HP eradicated	47	18.5±4.8	20.7±4.7
Control	61	12.9±3.0	13.4±3.1
p-value		0.049	0.082

Migraine score significantly reduced during second and fourth month (p<0.001) after eradication when compared with pre-treatment month. Similar changes were seen in control group. When comparing score changes during second and fourth months there was significant in treatment group (p=0.003) but not in control group (0.903).

DISCUSSION

This study showed that patients with migraine headache have a high rate of H. pylori infection. Other studies have provided evidence that migraine is related to *H. pylori* infection. Yiannopoulou *et al*. in a study on 49 patients with migraine without aura and 51 without migraine showed that H. pylori infection is as a possible environmental factor for migraine without aura (Yiannopoulou *et al* 2007).[12] Another study conducted on 70 patients with migraine and 70 healthy people without any history of migraine. Findings showed that there was a significant difference in mean value of both antibodies to *H. pylori* amongst the case and control groups. Authors concluded that *H. pylori* infection is strongly related to the outbreak and severity of migraine headaches (Hosseinzadeh *et al* 2011).[19] These findings suggested that chroinc inflammation caused by *H. pylori* may play an important role in the pathogenesis of migraine. The possible explanation is that inflammation caused by *H. pylori* stimulates the gastrointestinal neuroendocrine cell to secrete5-hydroxytryptamine, substance P, and vasoactive intestinal polypeptides and causes a central nervous system disorder (Mavromichalis 2003).[22]

Our findings demonstrated that H. pylori eradication significantly improved the clinical presentation of migraine. Patients evaluation two months after eradication showed that the migraine score decreased significantly in intervention than the control group (p = 0.049).



Previous studies have reported different results. For example Gasbarrini *et al* evaluated 225 patients with migraine and reported significant reduction in severity of migraine headaches during 6 month after eradication of H. pylori in comparison with controls (Gasbarrini *et al* 1998).[23] Study of Hong and colleagues on 50 patients with cirrhosis and migraine showed significant reduction in the severity and frequency of attacks in patients that H. pylori was eradicated compared with patients that successful eradication was not observed (Hong *et al* 2007).[14] In another prospective study on migraine patients, severity of headaches was improved after H. pylori eradication (Faraji *et al* 2015).[15] Similarly Bakhshipour *et al*. showed that eradication of H. pylori is effective in decreasing of the migraine attacks (Bakhshipour *et al* 2012).[16] Savi and co-worker in a review article reported that the eradication of H. pylori seems efficient at least in a subgroup of patients suffering from migraine (Savi *et al* 2013).[24] Tunca *et al*. in an observational and case-controlled study examined with migraine. They compared duration and severity of the migraine attacks before and after eradication of *H. pylori* infection. The researchers found that 84.6% of patients who have used *H. pylori* eradication pylori and 75% of patients who have taken advantage of conventional treatment got better condition and underwent lower attacks. They concluded that eradication treatment will be benefit for relief of clinical attacks (Tunca *et al* 2004).[25]

In contrast Pinessi *et al*, compared 103 migraine patients with 103 match controls. They didn't find any significant relation between H. pylori infection and migraine (Pinessi *et al* 2000).[18] In similar study, prevalence of H. pylori didn't differ between migraine with aura patients and matched controls (Gasbarrini *et al* 2004).[26] During H. pylori infection, superoxide radicals and nitrite oxide are produced. These free radicals can cause changes in regional cerebral blood flow and may have a role during a migraine attack (Gasbarrini *et al* 1998,Tunca *et al* 2007).[23,27]

Our study has several limitations. Firstly, our study sample was not large, thus limiting the possibility of stronger statistical significance. Secondly there was short-term follow-up of patients.

CONCLUSION

Our findings showed that clinical conditions of patient with migraine without aura improved two months after H. pylori eradication. But four months after eradication, the significant improvement was not observed. A study with a larger sample size and using C-urea breath test at appropriate intervals to reach more conclusive results is recommended. Eradication of this infection can be effective in decreasing severity of the migraine attacks.

References

Bakhshipour A, Momeni M, Ramroodi N (2012). Effect of Helicobacter pylori treatment on the number and intensity of migraine attacks. *Zahedan J Res Med Sci*. 14: 6-8.

Bigal ME, Lipton RB (2009). The epidemiology, burden, and comorbidities of migraine. Neurol Clin. 27:321-34.

Ciancarelli I, Di Massimo C, Tozzi-Ciancarelli MG, De Matteis G, Marini C, Carolei A (2002). Helicobacter pylori infection and migraine. Cephalalgia. 22:222-5.

Faraji F, Zarinfar N, Zanjani AT, Morteza A (2012). The effect of Helicobacter pylori eradication on migraine: a randomized, double blind, controlled trial. Pain Physician. 15:495-8.

Gasbarrini A, De Luca A, Fiore G, Gambrielli M, Franceschi F, Ojetti V, *et al* (1998). Beneficial effects of Helicobacter pylori eradication on migraine. Hepatogastroenterology. 45: 765-70.

Gasbarrini A, Gabrielli M, Fiore G, Candelli M, Bartolozzi F, De Luca A, *et al* (2000). Association between Helicobacter pylori cytotoxic type I CagA-positive strains and migraine with aura. Cephalalgia. 20:561-5

Gasbarrini G, Racco S, Franceschi F, Miele L, Cammarota G, Grieco A, *et al* (2010). Helicobacter pylori infection: from gastric to systemic disease. Recenti Prog Med. 101:27-33.

Headache Classification Subcommittee of the International Headache Society (2004). The International Classification of Headache Disorders: 2nd edition. Cephalalgia. 24: 9-160.

Hong L, Zhao Y, Han Y, Guo W, Wang J, Li X, *et al* (2007). Reversal of migraine symptoms by Helicobacter pylori eradication therapy in patients with hepatitis-B-related liver cirrhosis. Helicobacter. 12:306-8.

Hosseinzadeh M, Khosravi A, Saki K, Ranjbar R (2011). Evaluation of Helicobacter pylori infection in patients with common migraine headache. Arch Med Sci. 7: 844-849

Krueger S, Roessner A, Kuester D (2011). Murine models of H. pylori-induced gastritis and gastric adenocarcinoma. Pathol Res Pract. 207:599-607.

Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF, *et al* (2007). Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 68:343-9.

Longo DL, Fauci AS, Kasper DL, Hauser SL, Jamsone JL, Loscaizo J editors (2012). Harrison's Principles of Internal Medicine. 18th edition, New York, McGraw-Hill. p 2450

Malfertheiner MV, Kandulski A, Schreiber J, Malfertheiner P (2011). Helicobacter pylori infection and the respiratory system: a systematic review of the literature. Digestion. 84: 212-20.

Mavromichalis I (2003). The role of Helicobacter pylori infection in migraine. Cephalalgia. 23: 240; author reply 240-241

May A, Schulte LH (2016). Chronic migraine: risk factors, mechanisms and treatment. Nat Rev Neurol. Jul 8.

Pinessi L, Savi L, Pellicano R, Rainero I, Valfre W, Gentile S, *et al* (2000). Chronic Helicobacter pylori infection and migraine: a case-control study. Headache. 40: 836-9.

Ruggiero P (2010). Helicobacter pylori and inflammation. Curr Pharm Des. 16:4225-36.

Savi L, Ribaldone DG, Fagoonee S, Pellicano R (2013). Is Helicobacter pylori the infectious trigger for headache?: A review. Infect Disord Drug Targets. 13(5):313-7.

Semenov IA (2015). Migraine headaches. Dis Mon. 61(6): 218-22.

Su J, Zhou XY, Zhang GX (2014). Association between Helicobacter pylori infection and migraine: ameta-analysis. *World J Gastroenterol*. 28; 20(40):14965-72.

Sugimoto M, Yamaoka Y (2011). Review of Helicobacter pylori infection and chronic renal failure. Ther Apher Dial. 15:1-9.

Suzuki H, Franceschi F, Nishizawa T, Gasbarrini A (2011). Extragastric manifestations of Helicobacter pylori infection. Helicobacter. 16 (Suppl 1): 65-9.

Tunca A, Ardiçoğlu Y, Kargili A, Adam B (2007). Migraine, Helicobacter pylori, and oxidative stress. Helicobacter. 12:59-62.

Tunca A, Türkay C, Tekin O, Kargili A, Erbayrak M (2004). Is Helicobacter pylori infection a risk factor for migraine? A case-control study. Acta Neurol Belg. 104(4):161-4.

Weir GA, Cader MZ (2011). New directions in migraine. BMC Med. 9:116.

Yiannopoulou KG, Efthymiou A, Karydakis K, Arhimandritis A, Bovaretos N, Tzivras M (2007). Helicobacter pylori infection as an environmental risk factor for migraine without aura. *J Headache Pain*; 8:329-33.

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