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Original Article

Effects of *Helicobacter Pylori* Eradication on Chronic Idiopathic Urticaria

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Abstract

Background: Chronic idiopathic urticaria is defined as urticaria, which lasts for more than 8 weeks and has no apparent etiology. The aim of this study was to examine the causal role of *Helicobacter pylori* infection in chronic idiopathic urticaria.

Methods: Fifty-six patients with chronic idiopathic urticaria and a negative response to skin prick test for common aeroallergens were selected. They were examined for *H pylori* infection using a serologic test and urea breath test, and were divided into three groups. The first group included *H pylori*-positive patients (n=23), who did receive eradication regimen for two weeks. The second group comprised of *H pylori*-positive patients (n=15), who did not have the indications for anti *H pylori* treatment, and were not treated. The third group included *H pylori*-negative patients (n=18), who received no treatment. The patients were studied for signs and severity of urticaria.

Results: In the first group, urticaria improved partially and completely in 74% (n=17) of cases. In the second group, urticaria did not improve in 60% (n=9), and improved partially in 40% (n= 6) of cases. In the third group, urticaria did not improve in 61% (n=11), and improved partially in 39% (n=7) of cases. Patients, who had a higher titer of urea breath test and longer period of symptomatic urticaria, had better response than the others.

Conclusion: The findings suggest that anti-*H Pylori* treatment is significantly effective in the treatment of chronic idiopathic urticaria. *H Pylori* eradication can be suggested as a method for treating urticaria, if the urea breath test is positive.
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Keywords ● Urticaria ● Helicobacter pylori ● breath test

Introduction

Urticaria is an itching disease consisting of vascular dilations and edema. It is classified as acute and chronic forms. Acute urticaria is a very common disease inflicting 10-20% of general population at least once in their lives.[1] Chronic urticaria usually lasts eight weeks or more, and its signs and symptoms persist every day or at least twice a week.[1] Some drugs such as penicillins, sulfonamides, radiocontrast media, nonsteroidal anti-inflammatory drugs (NSAIDs) as well as foods and food additives such as artificial colors commonly produce acute urticaria, but occasionally lead to chronic urticaria as well.[2] Other diseases responsible for chronic urticaria include collagen-vascular diseases such as systemic lupus

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erythematosus (SLE), Sjögren syndrome, and rheumatoid arthritis (RA),[3,4] infections of unspecific origin, infective hepatitis, and infectious mononucleosis.[5-7]

In most of cases (70-80%) with chronic urticaria, the exact etiology can not be found; therefore, it is called chronic idiopathic urticaria. In patients with chronic idiopathic urticaria serum levels of immunoglobulin E (IgE), and erythrocyte sedimentation rate (ESR), as well as indices of complete blood count (CBC), are within normal ranges.[8] However, it has been suggested that *Helicobacter pylori* (*H pylori*) might be one of the etiologies for chronic idiopathic urticaria,[9-11] because the treatment of *H pylori* infection was associated with an improvement in the symptoms of urticaria.[12]

Helicobacter pylori is a gram-negative aerophilic organism with a slow growth. The dominant biochemical activity of *H pylori* is the production of significant amount of urea. Therefore, one of the methods for the diagnosis of *H pylori* infection is urea breathing test (UBT) in which the patients breathe radiolabeled (with C^{13} and C^{14}) urea.[13] Urease produced by *H pylori* hydrolyzes radiolabeled urea and produces radiolabeled bicarbonate, which is transferred from the blood circulation to the lung and can be detected in expiratory air as radiolabeled carbon dioxide.[13,14]

The objective of this study was to examine the effects of the *H Pylori* treatment in patients with chronic idiopathic urticaria to find out whether *H Pylori* infection had a casual role in chronic idiopathic urticaria.

Patients and Methods

Patients

The study included 56 patients with chronic idiopathic urticaria who referred to the Allergy Clinic affiliated to Mashhad University of Medical Sciences, Mashhad, Iran from October 2002 to December 2003. The study was approved by the ethics committee of Mashhad University of Medical Sciences. Patients with chronic urticaria, negative skin prick test for common allergens, and a negative history for physical urticaria were included. Those patients who had allergy to any drugs were excluded. All participants were informed of the protocol of the study, and informed consents were obtained.

Methods

The patients underwent serologic and UBTs to diagnose *H pylori* infection, and were then divided into three groups. The first group (n=23) was *H pylori* positive patients, who were assigned to receive amoxicillin, metronidazole, omeprazole, and bismuth for two weeks. The second group (n=15) was *H pylori* positive patients without gastrointestinal symptoms and indications for eradication treatment. The third group (n=18) were *H pylori* negative patients. The patients in the second and third groups were not treated for *H pylori* infection. In the first group, a UBT was performed one month after the end of the treatment. Those who had treatment failure, and were positive in the UBT test did receive a second round of treatment using amoxicillin, furazolidone, omeprazole, and bismuth for two weeks. Urea breath test was repeated for these patients once more. Antihistamine drugs were given to all patients in the three groups. A 12-month follow up was performed for all patients.

A self-designed scoring system (table 1) was used to assess the changes in urticaria including number of lesions, size, as well as frequency and duration of itching in each episode. The scoring system ranged from zero for a patient without urticaria to 100 for a patient with aggravation in all aspects. Accordingly, a complete response was defined as a score of more than 90, a partial response was defined as score of 50-90, and no response was considered as a score of less than 50.

Table1: Scoring system for urticaria changes

Urticaria characteristics	Change rate	Score
Number	No change or increased	0
	Decreased (0-50%)	10
	Decreased (50-100%)	20
Size	Reduction less than 1 cm or increased	0
	Reduction 1-5 cm	5
	Reduction 5-10 cm	10
	Reduction more than 10	20
Frequency (Times/week)	More than 2	0
	2	5
	1	10
	less than 1	20
Itching	No change or increased	0
	Decreased	10
	Significant reduction	20
Duration	No change or increased	0
	Decreased	10
	Significant reduction	20

Statistical Analysis

The urticaria responses from the 3 groups were compared with Chi-Squared test and one way analysis of variance followed by Duancan's Multiple Range test using SPSS software. A P value of ≤ 0.05 was considered statistically significant.

Results

The ratio of female to male cases was 2.5 (71.4% *vs* 28.6%). There was no significant relation between *H pylori* infection and sex

(table 2). Moreover, there was no significant difference between the ages of the patients in the groups positive or negative for *H pylori*.

Table 2: General description of the patients

Group	First group	Second group	Third group
Mean age	32± 14	35±14	29±11
Female/male ratio	17/6	10/5	13/5
Mean urticaria duration (months)	42±10	40±11	28±18

In the first group, urticaria did not improve in 26% (n=6), improved partially in 21% (n=5), and improved completely in 53% (n=12) of the cases. In the second group, urticaria did not improve in 60% (n=9), and improved partially in 40% (n= 6) of cases. In the third group, urticaria did not improve in 61% (n=11), and improved partially in 39% (n=7) of cases. There was a significant difference between the percentage of patients whose urticaria improved in group 1 (53%) and group 2 (0%). However, there was no significant difference between group 2 and 3 in terms of response to treatment.

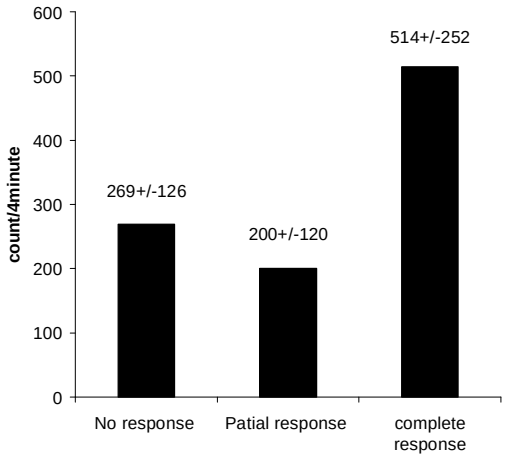

Fig 1: The levels of UBT test before treatment in responders, partial responders, and non responders based on urticarial response

The failure rate to anti *H pylori* treatment in the first group as evaluated by UBT done at the end of the treatment was 43% (n=10). The UBT was negative for such patients after the second round of treatment. Urticaria did not improve in 40% of cases who received two treatment cycles. Thirty percent of these patients had complete response and the remainders (30%) had partial response.

At the beginning of the study 12 cases (52%) of the first group had gastrointestinal symptoms such as abdominal pain and pyrosis; however, only one case (4%) had these symptoms after the treatment.

The average titer of UBT (count/4minute) before treatment in patients who improved completely, partially and did not improve were 514±252, 200±120, or 269±126, respectively (figure). There was no relation between the UBT titers and improvement in urticaria.

Discussion

The female to male ratio in the present study (2.5) was similar to previously-reported values (2 to 2.5).[15,16]

In spite of its uncertain etiology, chronic idiopathic urticaria is mostly self-limiting, and improves as the patient's age increases. Generally, improvement of chronic idiopathic urticaria is mostly seen more in men rather than women. Moreover, younger patients respond better to treatments.[15,17]

In a study in Portugal, better treatment results were seen with a higher UBT titration and shorter duration of skin signs.[18] Although in the present study the most complete improvement was seen in patients with a higher UBT titration, it did not reach statistical significance. The findings of the present study and those of others,[18] emphasize the role of *H pylori* colonization rate in the pathogenesis of chronic urticaria.

In the first group, urticaria did not improve in 26% (n=6), showed partial response in 21% (n=5), and had complete response in 53% (n=12). The comparison of the results between the first and second group shows that anti *H pylori* treatment plays a significant role in the improvement of urticaria. Similar beneficial effects of *H pylori* eradication on chronic idiopathic urticaria were reported in previous studies. In one study,[19] 42 cases with chronic idiopathic urticaria were treated for *H pylori* infection. Twenty three cases were infected and received eradication regimen. In 88% of cases urticaria improved either completely or partially as a result of anti *H pylori* treatment. The remaining 19 cases were not infected with *H pylori*, and their urticaria did not improve[19] In another study 67% of patients with urticaria (n=18) were infected with *H pylori*. Infected cases were treated by anti *H pylori* medications, which resulted in complete improvement (50%), partial improvement (33%), and no improvement (17%).[20] However, some studies did not show beneficial effects of *H pylori* treatment on chronic idiopathic urticaria.[11,21]

In our study a significant number of patients did not respond to treatment. Ten cases (43%) in the first group had treatment failure. Therefore, it is necessary to perform a control UBT, and a second course of treatment should be considered in case of positive UBT. Failure in the eradication of *H pylori* is reported,[22] and adverse treatment outcome is associated with

advanced age, smoking, high intragastric bacterial load before treatment, bacterial genotype, and host genetic polymorphisms of the cytochrome-P450 isoenzymes.[22]

In conclusion, the findings of the present study indicate that in all cases of chronic idiopathic urticaria serologic and UBT for the diagnosis of *H pylori* might be considered, and if positive, appropriate treatment for eradication of *H pylori* should be instituted.

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