H pylori: Treatment for the patient only or the whole family?

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AIM: To compare the effects of treatment of H pylori-infected individuals with the effects of treatment of individuals as well as all H pylori-infected family members.

METHODS: H pylori-positive patients with similar demographic specifications were prospectively randomized with respect to treatment, with a triple regimen of either patients and all H pylori-positive family members living together (group I) or patients only (group II). Nine months after treatment, all patients were assessed for H pylori positivity.

RESULTS: There were 70 H pylori-positive patients in each group; patients in groups I and II lived with 175 and 190 H pylori-positive relatives, respectively. Age, sex and H pylori positivity rate were similar in both groups of relatives. Nine months after 14 d standard triple therapy, H pylori positivity was 7.1% in group I patients and 38.6% in group II patients [P < 0.01, OR = 8.61 95% confidence interval (CI): 2.91-22.84].

CONCLUSION: The present results indicate bad environmental hygienic conditions and close intra-familial relationships are important in H pylori contamination. These findings indicate all family members of H pylori-positive individuals should be assessed for H pylori positivity, particularly in developing countries where H pylori prevalence is high; they also suggest patients, their spouses and all H pylori-positive family members of H pylori-positive individuals should be treated for H pylori infection.

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INTRODUCTION

Almost half of the world’s population is infected with H pylori[1-3]. The incidence of infection has been reported to be as high as 80% in less developed countries and as low as 20% in Western countries[5]. H pylori is involved in the etiology of gastric mucosa-associated lymphoid tissue (MALT)[6] lymphoma and gastric adenocarcinoma, leading the World Health Organization to declare H pylori a first degree carcinogen[7-9]. Less invasive diagnostic methods have enabled easier and earlier diagnosis and more widespread use of treatments.

Although H pylori infection is thought to occur in childhood, its method of transmission is not known[10-13]. Research in highly infected populations has shown the importance of intra-familial infections, bad hygiene and lower socio-economical status in the spread of H pylori[5,12,14]. However, these routes suggest infection is preventable.

The total time to exposure to H pylori has been found to correlate with the development of gastric adenocarcinoma[15-19], making diagnosis and eradication of the bacteria crucial. Furthermore, re-infection with H pylori may occur after eradication, owing to exposure to untreated individuals, indicating treatment focused on the patient alone will not result in total eradication. We sought to determine whether treatment of H pylori should be extended to H pylori-positive family members dwelling with the patient, or whether treatment of the patient alone would be sufficient. Treatment extended to the family would theoretically decrease the risk of re-infection.

MATERIALS AND METHODS

A two-armed prospective, randomized study group was composed of H pylori-positive patients in our gastroscopy unit with similar socio-economic status and family backgrounds. The sampling number was calculated based on a 20% statistically significant difference (lower limit
8%) with type I error = 0.05, type II error = 0.02 and power 0.80. The minimum sample size was 67 subjects. Due to possible dropouts, 70 H pylori-positive subjects who lived with family members were included in each arm of the study. All patients and family members provided written informed consent. Using a random number table subjects were divided into two equal groups. All family members dwelling with each subject (namely, spouses, children, brothers, sisters, fathers and mothers) were screened for H pylori positivity. H pylori antigen testing of stools was used to screen children under the age of 14 years and endoscopic biopsy and/or stool test was used to screen all other subjects. In both groups, the ages of the patients as well as their family, sex, relationship to the patient, endoscopic findings, type of H pylori screening and positivity were recorded.

Patients randomized to Group I and all H pylori-positive family members were treated for H pylori infection; patients randomized to Group II only were treated, but their family members were not. Patients and their adult relatives received standard triple therapy of clarithromycin, amoxicillin and proton pump inhibitors. Treatment of children and infants was individually handled by pediatric gastroenterologists. Nine months after treatment, all patients in both groups and treated family members in group I were assessed for H pylori-positivity using stool antigen tests.

Statistical analysis
A Student’s t was used for continuous and normative variables, the \( \chi^2 \) test was used for categorical variables and the McNemar test was used to assess before and after H pylori positivity rates. Statistical significance was defined as \( P < 0.05 \), both directions.

RESULTS
Each group consisted of 70 patients, and there were no drop-outs. The two groups were similar in age and sex ratio (\( P = 0.86, \chi^2 = 0.02 \)). The 70 patients in Group I lived with 175 relatives, whereas the 70 patients in Group II lived with 190 relatives, all of whom were screened for H pylori (Table 1). The number of family members, relationship to each patient, age and sex distribution did not differ significantly between the two groups (\( P > 0.05 \)).

The most common endoscopic findings in both groups of patients were pan-gastritis and antral gastritis. Diagnostic variables did not differ significantly between the two groups (\( P > 0.05 \)).

Ninety-five family members underwent gastroscopy and biopsy, whereas the remaining family members were assayed for H pylori by the stool H pylori antigen test. Family members in the two groups who underwent gastroscopy did not differ in number, relationship to patient, gender, age and pathological findings (\( P > 0.05 \)). Of the 95 family members who underwent endoscopy, 75 (78.9%) were spouses. Sixty-three (66.3%) family members presented with various pathologies on gastroscopy, the most common pathologies being antral gastritis (40.9%), pan-gastritis (26.4%) and hiatal hernia (17.7%). The remaining 32 family members had normal gastroscopic findings.

The highest prevalence of H pylori positivity was among the spouses of H pylori-positive individuals, followed by parents and siblings. Children and grandparents were among the least likely to be infected. Pretreatment H pylori positivity was statistically similar in both groups (\( P > 0.05 \), Table 2).

All H pylori-positive patients in both groups, and H pylori-positive family members in Group I, were treated with standard triple therapy for 14 d. Nine months later, 7.1% of Group I patients were H pylori-positive, compared with 38.6% of Group II patients (\( P < 0.001 \), OR = 8.61, confidence interval (CI): 2.91-22.84; Table 3).

Table 1  Relationship of family members to patients

| Sex       | Group 1 | Group 2 | \( P \) value |
|-----------|---------|---------|--------------|
|           | \( n (%) \) | \( n (%) \) |              |
| Spouse    | Male    | Female  | Male         | Female      |             |
|           | 31 (51.7) | 29 (48.3) | 31 (51.7) | 30 (49.2) | 0.92\* |
| 1. Child  | Male    | Female  | Male         | Female      |             |
|           | 20 (42.2) | 27 (57.5) | 26 (45.6) | 33 (54.4) | 0.87\* |
| 2. Child  | Male    | Female  | Male         | Female      |             |
|           | 18 (66.7) | 9 (33.3) | 13 (50.0) | 13 (50.0) | 0.29\* |
| Mother    | Male    | Female  | Male         | Female      |             |
|           | 16 (59.3) | 3 (50.0)  | 18 (60.0) | 4 (12.9)  | 0.99\* |
| Father    | Male    | Female  | Male         | Female      |             |
|           | 11 (40.8) | 5 (40.0)  | 12 (40.0) | 4 (12.9)  | 0.99\* |
| Siblings  | Male    | Female  | Male         | Female      |             |
|           | 3 (50.0)  | 3 (50.0)  | 4 (12.9)  | 4 (12.9)  | 0.99\* |
| Grandchild| Male    | Female  | Male         | Female      |             |
|           | 3 (60.0)  | 5 (40.0)  | 3 (60.0)  | 4 (12.9)  | 0.99\* |

\*Fisher’s absolute \( \chi^2 \); \#Yates corrected \( \chi^2 \).

Table 2  Pre-treatment H pylori positivity rates in relatives of both groups

|                | Group 1 | Group 2 | \( P \) value |
|----------------|---------|---------|--------------|
|                | \( n (%) \) | \( n (%) \) |              |
| Spouse         | Positive | Negative | Positive | Negative | 0.82\* |
|                | 46 (76.7) | 14 (23.3) | 48 (78.7) | 13 (21.3) |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 60 (100) | 30 (100) | 61 (100) | 30 (100) |            |
| 1. Child       | Positive | Negative | Positive | Negative | 0.99\* |
|                | 23 (48.9) | 24 (51.1) | 28 (47.5) | 31 (52.5) |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 47 (100) | 47 (100) | 59 (100) | 59 (100) |            |
| 2. Child       | Positive | Negative | Positive | Negative | 0.99\* |
|                | 12 (44.4) | 15 (55.6) | 11 (42.3) | 15 (57.7) |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 27 (100) | 27 (100) | 26 (100) | 26 (100) |            |
| Mother         | Positive | Negative | Positive | Negative | 0.99\* |
|                | 12 (75.0) | 4 (25.0)  | 14 (77.8) | 4 (22.2)  |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 16 (100) | 6 (100)  | 18 (100) | 7 (100)  |            |
| Father         | Positive | Negative | Positive | Negative | 0.99\* |
|                | 8 (72.7)  | 3 (27.3)  | 9 (75.0)  | 3 (25.0)  |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 11 (100) | 3 (100)  | 12 (100) | 3 (100)  |            |
| Grandchild     | Positive | Negative | Positive | Negative | 0.99\* |
|                | 2 (25.0)  | 6 (75.0)  | 2 (28.6)  | 5 (71.4)  |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 8 (100)  | 8 (100)  | 7 (100)  | 7 (100)  |            |
| Siblings       | Positive | Negative | Positive | Negative | 0.99\* |
|                | 3 (50.0)  | 3 (50.0)  | 4 (57.1)  | 3 (42.9)  |            |
|                | Total    | Total    | Total    | Total    |            |
|                | 6 (100)  | 6 (100)  | 7 (100)  | 7 (100)  |            |

\*Fisher’s exact test.
Four of the 5 Group I patients (80%) and 24 of the 27 Group II patients (88.9%) who remained _H pylori_ positive 9 months after initial therapy had _H pylori_-positive spouses at follow-up. The rate of spousal infection in Group II was higher at follow-up than before treatment (78.7% vs 88.9%). The 65 initially _H pylori_-positive relatives in Group I were all _H pylori_-positive at follow-up.

A total of 15 children aged 5 years or less (8 in Group I and 7 in Group II) were included in the study. Four infants, 2 in each group (26.7%), were initially _H pylori_ positive; all in group I were _H pylori_ negative 9 months after treatment.

### DISCUSSION

Although the exact environmental factors contributing to _H pylori_ infection are unclear, bodily fluids and personal contact may be key factors in the spread of disease among family members[10-12,14,16]. Due to improved hygiene and environmental conditions, _H pylori_ prevalence has decreased significantly in Western countries, but it remains high in developing countries such as Turkey[17,18]. Lower socio-economic status resulting in more personal contact (for example, sharing sleeping facilities), crowded families and sharing of common living areas with compromised hygiene can also lead to increased dissemination of _H pylori_[2,12,19,20].

Patients who are diagnosed _H pylori_ positive should be unquestionably treated. The recommended treatment regimen for _H pylori_ eradication consists of 7 to 14 d of triple therapy with clarithromycin, amoxicillin and a proton pump inhibitor[21-24]. Theoretically, in areas and socio-economic groups where intra-familial infection is highly probable, treatment of the patient only may not prevent re-infection over the long term. The present study was designed to investigate this hypothesis.

The most important finding from this study was that statistically significant _H pylori_ eradication was achieved in patients whose _H pylori_-positive family members were also treated, compared with those whose _H pylori_-positive family members were not treated, in long-term follow-up (7.1% vs 38.6%, group I and II, respectively). The rate of resistant _H pylori_ infection (7.1%) was higher than expected, possibly due to other environmental, lifestyle and hygiene issues outside the family.

_H pylori_ is highly prevalent in the healthy partners of patients with _H pylori_ infection. To decrease long-term re-infection rates, family members of _H pylori_-positive patients should be tested and, if positive, treated for _H pylori_ infection. Since spouses had the highest _H pylori_ positivity rates, our findings suggest that at least the spouse of an _H pylori_-positive patient should be screened and treated if positive. The prevalence of _H pylori_ in children aged 5 years or less (6.7%) was also alarming, considering the long-term health problems associated with this infection.

Among the possible routes of _H pylori_ infection, the fecal-oral, oro-oral and gastro-oral routes are the most probable. _H pylori_ has been cultivated in vomit, feces and sputum[2,3,11,15,16,25]. Although intra-familial transmission is a major factor contributing to _H pylori_ infection, the relative contributions of close interpersonal contact and genetic similarity are not known[10,26-28]. Spouse-spouse transmission would appear to be an obvious source of infection in adulthood[10,29].

In areas where the risk of contamination is high, re-infection can be prevented by eradication programs[9,30]. Lifestyle changes are recommended, but they are unlikely to occur in the short term. Thus, in such areas, the re-infection rate is high due to contact with the source of _H pylori_ infections. Our findings clearly show the necessity of screening and treating all _H pylori_-positive family members to eradicate the source of infection. Larger scale studies, in Turkey and in other developing countries with high _H pylori_ infection rates, may determine the routes of infection and other possible methods of prevention.

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**Table 3**

_H pylori_ positivity rates after 9 mo in relatives of both groups

| Group 1 | | Group 2 | |
| --- | --- | --- | --- |
| | n (%) | | n (%) |
| Positive | 5 (7.2) | Positive | 27 (38.6) |
| Negative | 65 (92.8) | Negative | 43 (61.4) |
| Total | 70 (100) | Total | 70 (100) |

*P* < 0.001, OR = 8.61, 95% CI: 2.91-22.84.

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