Helicobacter pylori reinfection with identical organisms: transmission by the patients’ spouses

K Schütze, E Hentschel, B Dragosics, A M Hirschl

Abstract
Reinfection with Helicobacter pylori after eradication is responsible for the recurrence of duodenal ulcer disease. The mode of transmission has not yet been established. In this study, 15 patients with chronic duodenal ulcers in whom H pylori had been eradicated with amoxicillin and metronidazole were entered into a prospective follow up study. Control endoscopies were performed 4, 8, 14, 27, and 43 months after starting treatment and the results of direct tests were compared with the kinetics of H pylori specific IgG titres. After eradication there was a noticeable and consistent fall in anti- H pylori IgG, while reinfections were characterised by a significant increase in specific titres. Reinfection was detected in two patients after 14 and 43 months, respectively. The H pylori strains responsible for these reinfections, the corresponding pretreatment isolates, and the strains isolated from the spouses of these patients were examined by polymerase chain reaction based DNA fingerprinting. Analysis showed that reinfection had been caused by the same H pylori strain and identified the spouses of these patients as carriers of the identical strain. Considering the genomic diversity and the interpatient heterogeneity of H pylori these results suggest a person to person transmission of H pylori reinfection. By the end of the observation period reflux oesophagitis had developed in 10 of the 16 patients who had not been reinfected. This surprising finding may be explained by the changed eating habits of patients after healing of duodenal ulcer disease.

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Keywords: Helicobacter pylori, chronic duodenal ulcer disease, reinfection.

Duodenal ulcer disease can be cured by eradication of Helicobacter pylori, but reinfection may occur and ulcer relapse rates of up to 11·7% have been reported. To determine the possible mode of reinfection, we followed patients with eradicated H pylori for 43 months after eradication. The objective of this prospective follow up was to investigate the frequency and the source of reinfection. A second objective was to evaluate the correlation between serology and invasive tests in detecting H pylori reinfections as varying reinfection rates have been described with different types of detection. While low rates have been reported with uninvasive methods, higher rates have been observed with direct tests.

Patients and methods
H pylori eradication in subjects with a history of at least two symptomatic recurrences and an endoscopically confirmed, active duodenal ulcer was achieved with a 12 day regimen of amoxicillin (750 mg three times daily) plus metronidazole (500 mg three times daily), already described elsewhere. Additional ranitidine was given for six (or 10) weeks. After ulcer healing and H pylori eradication, control endoscopies were performed on months 4, 8, 14±1, 27±2, and 43±4 after starting treatment or whenever symptoms occurred. If reinfection was detected, the spouse of the reinfected patient was also asked to undergo endoscopy.

H pylori status
At each endoscopy five biopsy specimens were collected from the antral mucosa. H pylori was identified by the rapid urease test, histological examination, and culture, as already described previously. The organism was considered present, if all three tests were positive. It was considered to have been eradicated, if negative results were obtained in all of the three tests. (In our investigations, diverging results for the three tests were never seen.)

SEROLOGY
Sera were stored at −20°C until use. The specific IgG titres were determined by a fluorescence enzyme immune assay (Helori-test IgG, Eurospital, Italy). The amount of specific antibodies in each sample was expressed as an index % obtained by comparing the patient’s value with that of the positive control according to the following formula:

\[
\text{INDEX }\% = \frac{\text{fluorescence units sample}}{\text{fluorescence units positive control}} \times 100
\]

All sera from each individual patient were tested in duplicate at the same time.

H pylori typing
H pylori strains were stored at −70°C in 0·5 ml horse serum +17% glycerol. If a reinfection occurred, the newly detected strains were compared to the corresponding pretreatment isolates. In addition, the isolates of the reinfected patient’s spouse were obtained at the end of the follow up period. Typing was
Ethidium bromide staining of AP-polymerase chain reaction products of several H pylori strains separated by 4-20% polyacrylamide electrophoresis. Lane 1=molecular weight marker (bp); 2=patient L before onset of treatment; 3=patient L at month 14 (reinfection); 4=patient L at month 27; 5=patient L at month 43; 6=spouse of patient L; 7=patient K before onset of treatment; 8=patient K at month 43 (reinfection); 9=spouse of patient K.

performed using polymerase chain reaction (PCR) based DNA fingerprinting. Arbitrary primer (AP) PCR was used to detect any DNA sequence diversity among the H pylori isolates. The H pylori DNA was prepared by repeated freezing and thawing of a suspension of H pylori in phosphate buffered saline. Phenol/chloroform extraction, precipitation of DNA and PCR were performed as described by Akopyanz et al. For PCR a 10nt-primer 5'-CCGCAGCCAA-3' was used.

Results
Eighteen patients (14 men and four women with a mean age of 50 years) with healed duodenal ulcers and eradicated H pylori were entered into the follow up study.

SEROLOGY AND DIRECT TESTS
The median pretreatment IgG index was 89-9%. The specific IgG titres showed a continual decrease with a median IgG index reduction of 66% up to month 14, thereafter the titres of the patients who had not been reinfected remained at a low level until the end of the follow up period. In these patients, urease tests, histological examinations, and bacteriological cultures yielded negative results at each of the controls. In patient L reinfection was detected at the 14 month check. All direct tests had become positive again and the IgG index approached the pretreatment level, falling short of this value by only 0-2%. The reinfection of patient K was diagnosed at month 43. All invasive tests yielded positive results, while the IgG index actually exceeded the pretreatment value by 17-3%.

Discussion
Since H pylori shows a high degree of genomic diversity most patients carry an individual strain with a unique pattern. As shown by Bamford et al, different family members may be infected with the same strain, but usually typable strains differ significantly from patient to patient. For cases where strains with an identical DNA pattern can be detected before eradication and after H pylori reinfection, two principal explanations may be suggested as follows:

(i) A relapse – that is the organism was not completely eradicated, but only transiently suppressed. This is highly unlikely in our two cases, because H pylori was only redetected at 14 and 43 months respectively after the onset of treatment.

(ii) Reinfection with the same strain; this would be possible by transmission from family members or spouses infected with the identical strain.

The data available on the person to person spread of these bacterial organisms are rather inconsistent. Malaty et al report a high incidence of H pylori infections in spouses of H pylori positive patients and intrafamilial clustering of H pylori infections has been described by Drumm et al. In obvious
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With this organism. In the case of positive results anti-\textit{H pylori} treatment of both patient and spouse is well worth considering.

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