Positive Result by Serology Indicates Active *Helicobacter pylori* Infection in Patients with Atrophic Gastritis

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Patients with atrophic corpus gastritis and elevated *Helicobacter pylori* antibody titers but 13C-urea breath test (13C-UBT) and histology results negative for *H. pylori* were randomized into eradication therapy or follow-up only. Antibody levels decreased significantly in six out of seven patients in the eradication group, while in the follow-up group, the titers declined in only one out of eight patients. In patients with atrophic corpus gastritis, positive serology results may indicate an ongoing infection in spite of negative 13C-UBT and histology results.

Atrophic gastritis, a well-established risk condition for gastric cancer, is a late consequence of *Helicobacter pylori* infection in about one-third of patients (9, 14). It has not been shown whether eradication of *H. pylori* would decrease the incidence of gastric cancer in these patients. However, one report suggests that the normalization of intestinal metaplasia could occur after successful eradication therapy (13).

Numerous methods have been developed for the detection of *H. pylori* infection, but there is no single universally accepted "gold standard." It has been shown that *H. pylori* antibody levels are elevated in atrophic gastritis without histologic evidence of *H. pylori* (7, 12), suggesting that the accuracy of invasive diagnostic tests based on gastric biopsies might be restricted if *H. pylori* infection is patchy or if the number of bacteria is low.

The present study was undertaken to analyze whether the elevated *H. pylori* antibody levels in patients with atrophic gastritis would be a sign of an ongoing infection, although the 13C-urea breath test (13C-UBT) and histologic examination of gastric biopsies did not reveal *H. pylori*.

Sixteen elderly men (mean age, 69 years) with atrophic corpus gastritis and elevated *H. pylori* antibody titers in enzyme immunoassay, but negative 13C-UBT and histology results for *H. pylori* in samples taken at the same hospital visit, were included in the study. At least two biopsy specimens were taken from both the antrum and corpus and stained with hematoxylin-eosin, Alcian blue (pH 2.5)-periodic acid-Schiff stain, and modified Giemsa stain. Biopsy specimens were examined in a blinded manner by the same pathologist (P.S.) and scored in accordance with the Sydney System (11). None of the patients had been treated earlier for *H. pylori* infection.

13C-UBT was performed as described earlier (10). The results were expressed as ‰ after subtracting the baseline from the pooled sample. The result was considered positive if excess $\delta^{13}CO_2$ excretion was $>4\%e$. Serum samples collected prior to the study period and control samples drawn approximately 6 months after the therapy or the follow-up were tested for *H. pylori* antibodies of the immunoglobulin G (IgG) and IgA classes by an enzyme immunoassay method (8). The lower limits of the raised titers were 700 for IgG antibodies and 70 for IgA antibodies. Separate reference pools were used for IgG and IgA. Paired serum samples of each patient were always tested in parallel on the same microtiter plate.

Eight men were randomized (18 March 1997) into the eradication therapy group (amoxicillin at 1 g twice a day, metronidazole at 0.4 g three times a day, and lansoprazole at 30 mg twice a day), and eight men were randomized into the control group for follow-up only. The primary samples for the detection of *H. pylori* were taken approximately 5 months (range, 2 to 9 months) prior to the randomization, and the control serum samples were collected 6 months after the randomization. The study protocol was approved by the Ethical Committee of the Helsinki University Central Hospital, and all patients gave informed consent. Statistical analysis was performed with Fisher’s exact test, and $P$ values of <0.05 were considered significant.

Six patients had severe, eight had moderate, and two had mild atrophy in the mucosa of the corpus. None of the patients showed any histologic evidence of *H. pylori*, although seven patients had at least once shown helicobacters on histology in previous samples. Four such patients belonged to the control group. All 16 patients were negative in 13C-UBT but showed elevated *H. pylori* antibody titers in the enzyme immunoassay (Table 1). One patient in the eradication group died of pneumonia before control serum samples were collected. Three patients in the control group (patients 9, 11, and 15 in Table 1) were treated with antimicrobials during the study period.

In the eradication group, the *H. pylori* antibody titers dropped significantly in six of seven patients (86%). In contrast, in the control group, the antibody titers declined significantly only in one of eight patients (12%) ($P = 0.01$, Fisher’s exact test) (Table 1). In the control group, the only significant decline was observed in a patient who received antibiotics during the study period (no. 9 in Table 1).

Our results suggest that in patients with atrophic gastritis, elevated *H. pylori* antibodies indicate an ongoing *H. pylori* infection in spite of negative 13C-UBT and histologic exami-
nation of gastric biopsies. After eradication therapy, *H. pylori* antibody titers of our patients declined in a manner similar to that shown for patients with histologically verified *H. pylori* infection (8). A drop of 40 to 60% or more of initial antibody titers within 5 to 6 months indicates eradication of bacteria (5, 8). The eradication rate was 86% in the present study. This is in accordance with treatment studies published earlier by others using the same antibiotics and a proton pump inhibitor (1, 6). One of our patients had raised IgA titers only, which has been shown in about 2% of *H. pylori*-positive patients (8). Although changes in IgA titers are not always as consistent as those in IgG titers (8), our patient showed a significant drop in his IgA titer after eradication therapy. One patient in the control group showed a significant drop in his antibody titers. It is unclear whether his penicillin treatment for a dental infection caused this change or whether the antibody levels declined because of a long-standing gastric atrophy.

It has been shown earlier that *H. pylori* antibody titers might be elevated in atrophic corpus gastritis with no histologic evidence of helicobacters (7, 12). In addition, disappearance of *H. pylori* in biopsies but stability of positive serology have been demonstrated in patients developing gastric atrophy (9). It seems that as the number of helicobacters in the atrophic gastric mucosa decline, the invasive diagnostic methods first become negative. Recently, Testoni and coworkers found that 67% of patients with chronic gastritis and antral atrophy had elevated *H. pylori* IgG antibody levels in serum, suggestive of a current infection in spite of negative histology results (12). If this were the case, studies not using serologic diagnostic methods would underestimate the role of *H. pylori* infection in patients with atrophic gastritis.

Although some spontaneous regression of atrophic gastritis has been observed (3, 9), intestinal metaplasia has been regarded more or less as an irreversible state (3, 4, 15), and very little is known of the possibility of modifying the natural course of these conditions. In a few patients, regression of gastric atrophy has been demonstrated after eradication of the concomitant *H. pylori* infection (9, 13). However, in these cases, *H. pylori* infection has been verified histologically. To our knowledge, there is only one earlier report in which a patient with atrophic gastritis and positive serology as the only sign of *H. pylori* infection was treated successfully, resulting in significant decline in *H. pylori* antibody titers and regression of atrophy (2). In the present study, follow-up is under way to detect the potential beneficial effect of the *H. pylori* eradication on the atrophic mucosa.

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**REFERENCES**


