

Helicobacter pylori infection and gastric emptying of solids in humans

S. H. CALDWELL, G. VALENZEULA, B. J. MARSHALL, K. R. DYE, S. R. HOFFMAN, M. W. PLANKEY & R. W. McCALLUM

Department of Medicine, Division of Gastroenterology, University Medical Center, University of Virginia, Charlottesville, VA 22908, USA

Abstract *Helicobacter pylori* has been implicated in a number of upper gastrointestinal illnesses. In a controlled study, we have investigated the relationship between *H. pylori* infection and gastric emptying of solids in two groups of patients with chronic symptoms of dyspepsia. In the first group, 19 patients with non-ulcer dyspepsia and *H. pylori* infection underwent a standard test of gastric emptying after ingestion of 500 μ Ci of Tc-labelled chicken liver. The results were compared to a control group of 16 uninfected volunteers. We also studied a second group of 20 patients with previously diagnosed idiopathic gastroparesis for the prevalence of *H. pylori* infection and its relationship to symptom severity and rates of gastric emptying.

In the first group of patients, the half-time of gastric emptying was significantly less among the infected patients compared to the uninfected volunteers (108 ± 9 vs. 142 ± 14 min, $P < 0.05$). In the second group of patients with gastroparesis, the prevalence of *H. pylori* was not significantly different among these patients than among 21 age and sex matched controls (20% vs. 38%, $P = 0.32$). Gastric emptying was markedly slow in all 20 patients in the second group but less so among the four with *H. pylori* infection. Symptom scores were no different between infected and uninfected patients.

We conclude that *H. pylori* infection is not associated with abnormally slow gastric emptying. On the contrary, gastric *H. pylori* infection appears to be associated with mildly accelerated emptying of solids compared to normal controls. Idiopathic gastroparesis and dyspepsia related *H. pylori* infection are separate but sometimes overlapping disorders.

Keywords dyspepsia, gastric emptying, gastritis, *Helicobacter pylori*.

INTRODUCTION

Helicobacter pylori (formerly *Campylobacter pylori*) is a common human infection that has been implicated in a number of upper gastrointestinal illnesses. Infection with *H. pylori* is strongly associated with histological antral gastritis.^{1,2} Among patients with non-ulcer dyspepsia and *H. pylori* infection, an association between *H. pylori* and delayed emptying of radiolabelled solids has been reported.³ Abnormal gastric motility is common among patients with dyspepsia⁴ and delayed gastric emptying has been implicated as a cause of upper abdominal pain.⁵ However, other investigators have failed to demonstrate an increased prevalence of *H. pylori* in patients with symptomatic gastroparesis.⁶ To determine whether or not *H. pylori* is associated with abnormal gastric motor function, we have studied gastric motility and *H. pylori* infection in two groups of patients—one with non-ulcer dyspepsia and *H. pylori* infection and another group of patients with previously diagnosed idiopathic gastroparesis.

METHODS

Nineteen consecutive patients with symptoms of dyspepsia of at least four months' duration and *H. pylori* infection proven by Giemsa staining of gastric antral biopsies were evaluated. This method has been previously demonstrated to be very sensitive and specific (90%) for *H. pylori* and has been shown to be equivalent to other methods of detection as described below.^{7–9} None of the patients had active ulcer disease at endoscopy. Two had a prior history of gastric ulcer and one had prior duodenal ulcer. There were 7 males and 12 females. The mean age was 38 ± 9 SD, range of 24–55

Address for correspondence

S. H. Caldwell, Division of Gastroenterology, University of Virginia, Salem VAMC 111-G, Salem, VA 24153, USA.

Received: 12 July 1991

Accepted for publication: 7 January 1992

years. None was using prokinetic agents but most were using acid-suppressing medications. Histological scores were not assessed as part of this study.

Sixteen paid volunteers who were recruited from the university and the community served as controls for this group of 19 patients. All denied symptoms of dyspepsia and none had a history of previous gastro-duodenal disease. All were proven negative for *H. pylori* infection by the C₁₄ urea breath test which has a sensitivity and specificity of over 90%.^{7,8} The C₁₄ urea breath test was administered to this group in a standard fashion. After an 8-h fast, the patient ingested 5 μ Ci of C₁₄-labelled urea. Breath samples were obtained at 20 min and counted for radioactivity. Counts less than 932 c.p.m. were considered negative. There were 11 females and 5 males. The mean age was 24 ± 4 with a range of 20–40 years. The control group was significantly younger than the patient group ($P = 0.001$).

We also studied a group of 20 consecutive female patients with proven idiopathic gastroparesis (half-time of gastric emptying greater than our normal control mean plus two standard deviations and no evidence of diabetes mellitus or collagen vascular disease). All had symptoms of dyspepsia and recurrent vomiting. These patients were prospectively evaluated for the presence of *H. pylori* by a rapid urease slide test (CLO Test, TriMed, St. Louis, MO., 89% sensitive and 90% specific) performed on an antral biopsy specimen taken at the time of endoscopy.^{7,9} None had active ulcer disease. A total symptom score was compiled for each patient on the basis of complaints of nausea, anorexia, vomiting, early satiety, bloating, abdominal pain, and heartburn. The mean age was 43 ± 10 years with a range of 26–74 years.

Solid-phase gastric emptying tests were performed in a standard fashion.¹⁰ After an overnight fast, the patient ingested a meal of 500 μ Ci ^{99m}Tc-labelled chicken liver in beef stew consisting of a total of 500 kilocalories as 20% protein, 50% carbohydrate, and 30% fat. The patient was then monitored by continuous anterior imaging with a gamma camera for 2 h. With correction for depth and geometric variables, the percentage of retained radiolabel was determined at one-half-hour intervals and the half-time of gastric emptying was then extrapolated from a linear regression equation. This method allows an assessment of interval phases of gastric emptying (early and late post-prandial phases) and an overall determination of the rate of emptying (the half-time of emptying).

Statistical analysis was performed using the CLINFO computer based statistical program (CLINFO is a database and statistical program run on the University VAX mainframe computer). The normality of the data was

evaluated using the Wilk-Shapiro method. The Student's *t*-test (for normally distributed values) and the Wilcoxon rank-sum test (for non-parametric values) were then used to compare continuous variables. Fisher's exact test was used to determine differences in proportions. Results are given as mean \pm one standard error of the mean unless otherwise indicated. This study was approved by the University of Virginia Human Investigation Committee.

RESULTS

Among the first group of 19 patients with dyspepsia and *H. pylori* infection, the percentage of retained radio-labelled test meal was significantly less than that of the uninfected volunteers at 30 and 60 min after the meal ($P < 0.05$) (Fig. 1). Late phase emptying (at 90 and 120 min) was not significantly different. The half-time of gastric

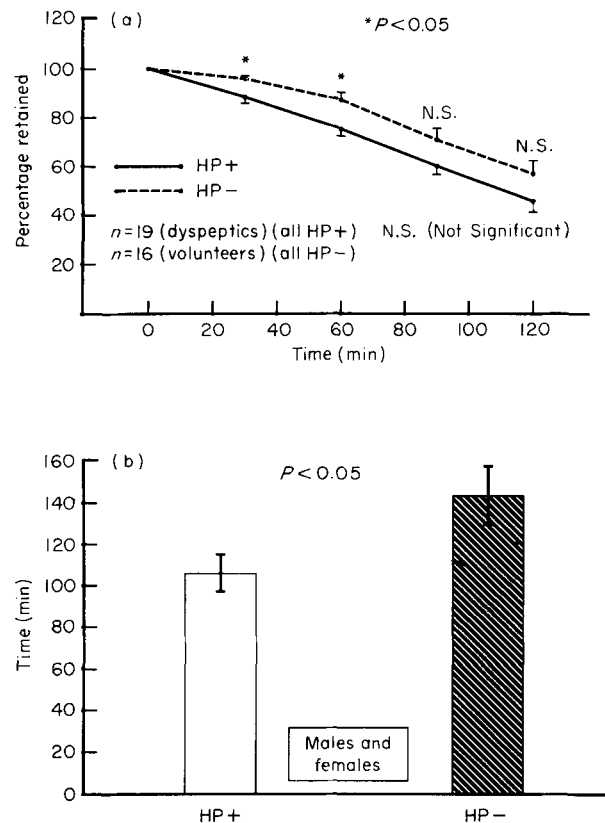


Figure 1 The percentage of retained ^{99m}Tc-labelled chicken liver at 30, 60, 90 and 120 min (\pm SE) in 19 dyspeptic patients with *H. pylori* infection vs. 16 uninfected, asymptomatic volunteers (males and females). Gastric emptying in the infected group was significantly faster at 30 and 60 min ($P < 0.05$, Wilcoxon rank sum test) and not different at 90 and 120 min ($P > 0.1$). HP+ and HP- indicate the presence or absence of *H. pylori*.

emptying was significantly less (108 ± 9 vs. 142 ± 14 min, $P < 0.05$) in the infected patients compared to the non-infected volunteers. The results were not different when the three patients with a prior history of peptic ulcer were excluded from the analysis.

When only male patients ($n = 7$) were compared to normal male volunteers ($n = 5$), gastric emptying was faster at 30, 60, 90 and 120 min but none reached statistical significance. However, when taken together the interval differences were sufficient to cause the half-time of gastric emptying to be significantly less in the infected patients (92 ± 13.8 vs. 124 ± 9.9 , $P < 0.05$).

Among the 20 patients presenting with idiopathic gastroparesis, all had markedly delayed gastric emptying of solids. Four (20%) were found to be infected with *H. pylori*. The overall scores on symptom questionnaires were not different between infected and uninfected gastroparetic patients (39 ± 4 vs. 31 ± 3 , $P > 0.05$). The percentages of retained solids at 30, 60, 90 and 120 min were less among the four patients with *H. pylori* infection but this reached statistical significance only at the 90 minute level (Fig. 2). The half-time of gastric

emptying was not significantly different. The prevalence of *H. pylori* in this group of patients was not different from a group of age and sex matched consecutive non-ulcer dyspepsia patients referred for routine upper endoscopy at our institution (20% vs. 38%, $P = 0.32$).

DISCUSSION

The ^{99m}Tc -sulfur-colloid labelled chicken liver meal is a commonly available and reliable means of assessing post-prandial gastric dysfunction.¹⁰⁻¹² As utilized in our institution, there is only a 10-15% range of variability between tests performed on the same patients on different days (R. W. McCallum, unpublished data).

A large number of factors have been variably reported in the literature to influence the results of gastric emptying tests. Using techniques similar to our own, Horowitz *et al.* reported a statistically significant (but clinically insignificant) delay in solid-phase gastric emptying in elderly volunteers.¹³ All of our patients (except one individual in the second group with idiopathic gastroparesis) were young to middle-aged adults and thus aging was unlikely to have significantly influenced these results. In fact, our infected group of 19 patients were significantly older than our group of 16 controls. Thus the slower emptying noted in the uninfected (and younger) group is unlikely to represent an age-related effect.

The luteal phase of the menstrual cycle has also been reported to delay gastric emptying of ^{99m}Tc -labelled chicken liver.¹⁴ Therefore, we conducted a separate analysis of the data using only infected male patients and uninfected male volunteers (Fig. 3). After exclusion of females, the half-time of gastric emptying remained significantly shorter in the infected group although the number of individuals used in this comparison was small.

Medication use is another potential confounding factor in the interpretation of gastric emptying data. The majority of patients in the first group were using H_2 -receptor blocking drugs (oral ranitidine in most) on a regular basis. Oral ranitidine may delay solid-phase gastric emptying of radiolabelled eggs.¹⁵ However, no medications were given on the morning of the studies and any potential effects of these medications would likely have favoured a delay in gastric emptying in the infected group rather than the observed increase. Long-term effects of these medications on gastric motility have not to our knowledge been documented.

Helicobacter pylori was found in a minority of our patients with idiopathic gastroparesis (20%). We specifically studied this group of patients to investigate more

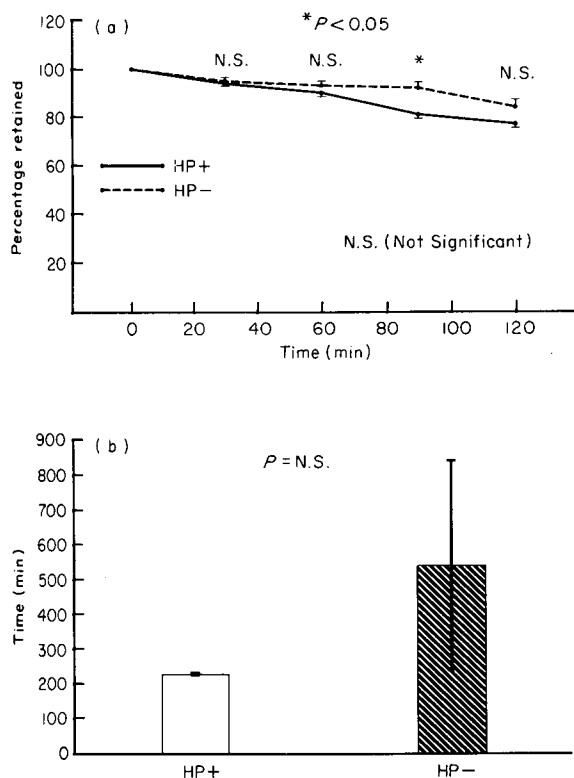


Figure 2 The percentage of retained isotope at 30, 60 and 120 min among infected ($n = 4$) vs. uninfected ($n = 16$) consecutive gastroparetics was not significantly different ($P > 0.05$, Student's *t*-test). At 90 min, the infected patients retained less isotope ($P < 0.05$, Student's *t*-test).

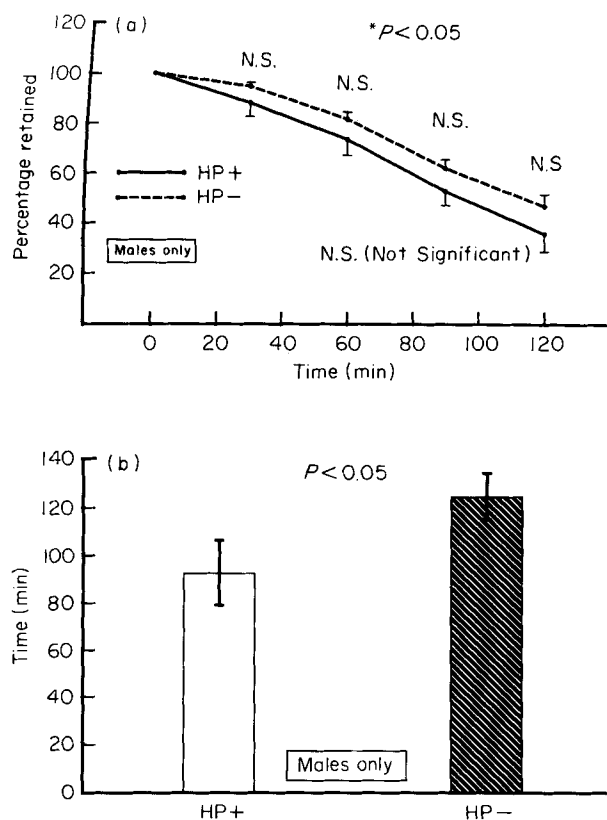


Figure 3 (a) When females were excluded from the analysis, the percentage of retained isotope in male patients ($n = 7$) compared to uninfected, asymptomatic male volunteers ($n = 5$) did not reach statistical significance in the interval analysis (Wilcoxon rank sum); (b) when the differences were analysed globally, the half-time of gastric emptying remained significantly less in the infected males ($P < 0.05$, Wilcoxon rank sum test) compared to uninfected male volunteers. HP+ and HP- indicate the presence or absence of *H. pylori*.

directly the purported role of *H. pylori* in symptomatic gastroparesis. The prevalence that we observed among these patients was no greater than that among a group of consecutive age- and sex-matched patients presenting for routine upper endoscopy for symptoms of dyspepsia. These findings are in keeping with those recently reported by Barnett *et al.* who found no increase in the prevalence of *H. pylori* among patients with gastroparesis.⁶

Wegener *et al.* have previously reported the results of a study on gastric emptying and *H. pylori* infection.¹⁶ In that study, the authors compared gastric emptying between *H. pylori* infected and uninfected dyspeptic patients and asymptomatic adults. The presence or absence of *H. pylori* was not determined in the control group. The test meal comprised a radiolabelled liquid (coffee) and unlabelled solids. Compared with the controls, both infected and uninfected patients had a pro-

longed half-time of solid-liquid emptying with no difference between the two symptomatic groups regardless of the presence or absence of *H. pylori*. Their use of a labelled liquid test meal and an unknown prevalence of *H. pylori* infection in their control group may explain our diverging results.

In another study, Barrilleaux *et al.* reported gastric emptying of radiolabelled solids in a group of 22 patients with dyspepsia and *H. pylori* infection.³ The median half-time of emptying was prolonged in this group (controls not reported). Eradication of the infection in 11 patients resulted in significantly improved emptying as compared to 11 patients without eradication. Additional control data from their study would be essential to clarify the differences between our results and theirs.

In summary, these data show that *H. pylori* gastric infection in symptomatic middle-aged adults is not associated with gastroparesis and may be associated with an increased rate of solid-phase gastric emptying. Among gastroparetic patients, infection was seen in only one-fifth and was not associated with increased or decreased symptoms. Accelerated gastric emptying in *H. pylori* infection may have important implications in the pathogenesis of gastric metaplasia of the duodenum, histological duodenitis and duodenal ulcer through increased exposure of the duodenum to gastric acid. Additional studies are needed to examine the relationships between gastric motility, *H. pylori* infection, duodenal histology and the effects of antibacterial therapy on gastric motor function.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the assistance of Sherry Boyd, Linda Mosen and Sherry Honig in the preparation of this manuscript. This work was supported, in part, by Janssen Pharmaceuticals and Proctor & Gamble and the University of Virginia Clinical Research Center Grant No. 9723.

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