Serum pepsinogen I and gastrin concentrations in children positive for Helicobacter pylori

G Oderda, D Vaira, D Dell’Olio, J Holton, M Forni, F Altare, N Ansaldi

Abstract

Serum pepsinogen I, serum gastrin concentration, and inflammatory scores were measured in a population of 71 children undergoing upper gastrointestinal endoscopy for investigation of upper abdominal pain. Forty four were initially colonised with Helicobacter pylori. The indices were measured before treatment (in 71 children), one month (in 41 children), and six months (in 21 children) after stopping treatment. Before treatment there was a significant correlation between serum pepsinogen concentration, total inflammatory score, and H pylori state, but no correlation between serum gastrin concentrations and H pylori state. Similarly, the total inflammatory score and serum pepsinogen concentrations were significantly correlated. There was no such correlation in children negative for H pylori. After treatment the inflammatory score improved in those patients in whom H pylori had been eradicated. There was also a significant fall in serum pepsinogen I and serum gastrin concentration in those patients in whom H pylori had been eradicated. These results were similar to those found six months after treatment had been stopped.

These findings suggest that the serum pepsinogen I concentration could be considered a useful marker for gastritis and can be used as an index of severity of gastritis in H pylori positive subjects. The measurement of serum gastrin concentrations does not give useful information.

In adults a strong association is now recognised between the presence of Helicobacter pylori in gastric mucosa and histologically confirmed gastritis. H pylori has also been specifically associated with primary antral gastritis in children, and as in adults the organism is present only in the gastric mucosa with concomitant gastric inflammation. Raised serum pepsinogen I concentrations are found in about two thirds of adults with peptic ulcer disease, and are thought to be a useful subclinical marker of genetic predisposition to ulceration. Serum pepsinogen I concentrations and a high titre of antibody to H pylori have been found to be raised in children with H pylori associated gastritis. Moreover, it has been shown that the concentrations of serum pepsinogen I, gastrin, and IgG antibody to H pylori significantly decreased after a six week course of amoxicillin and tinidazole.

The concentration of serum pepsinogen I in adults has been reported to be correlated with the histological gastritis associated with the presence of H pylori and to correlate with the degree of inflammation. A significantly raised 24 hour plasma gastrin concentration, which was inappropriate for the gastric acidity, was reported in asymptomatic subjects infected with H pylori.

We report the findings of a prospective study in which we used Giemsa staining, culture, and urease testing of antral biopsy specimens obtained from children undergoing upper gastrointestinal endoscopy for investigation of upper abdominal pain. We also report the concentrations of serum pepsinogen I and gastrin compared with the degree of severity of antral inflammatory cells in children positive or negative for H pylori associated gastritis before and after antimicrobial treatment.

Methods

Over two years, antral biopsy specimens were obtained from 71 children (46 male) undergoing upper gastrointestinal endoscopy for investigation of upper abdominal pain. The mean age was 10 years (range 1–18 years). None of the children had received any medication which might have affected gastric acidity before endoscopy. Fully informed parental consent was obtained before all endoscopies and biopsies were carried out.

Oesophagogastroduodenoscopy was performed using an Olympus GIF P3 or XP20 gastroscope after oral diazepam had been given. The endoscope and biopsy forceps were disinfected in 2% glutaraldehyde after each use.

Specimens were immediately fixed in 10% buffered formalin and stained with haematoxylin and eosin to determine the presence of gastritis, as described by Whithead et al. A diffuse chronic inflammatory infiltrate of the lamina propria was regarded as a “quiescent” chronic superficial gastritis; when polymorphonuclear cells were present in the lamina propria or within the superficial or glandular epithelium, gastritis was considered to be “active”. To grade the degree of severity of antral inflammatory cells, Marshall’s criteria were adopted. We also quantified the numbers of mononuclear and polymorphonuclear cells infiltrating surface and glandular epithelium as follows:
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Mononuclear cells:
(0) No intraepithelial lymphocytes (IELs);
(1) few IELs (less than 10 per high power field) seen in some fields;
(2) less than 10 IELs per high power field seen in every field;
(3) more than 10 IELs per high power field seen in every field.

Polymorphonuclear cells:
(0) No polymorphonuclear cells invading gland necks or surface epithelium;
(1) less than five invading polymorphonuclear cells per high power field seen in some fields;
(2) less than five invading polymorphonuclear cells per high power field in every field;
(3) more than six invading polymorphonuclear cells seen in every field.

Inflammatory cells were counted by two observers (DDO and MF) who were unaware of the patient data, using the same microscope at an enlargement of 400 times on at least 10 fields on four to six haematoxylin and eosin stained sections 5 μm thick. The area covered by a high power field is 0.159 m². Only antral biopsy specimens containing muscularis mucosa were considered.

H pylori had to be seen on microscopical examination (Giemsa) for a diagnosis of H pylori associated gastritis to be made.2 10

Gastric antral biopsy specimens were examined by culture and by urease testing and serum pepsinogen I concentrations were measured.2 Serum gastrin concentrations were measured by the method of Ansaldi et al.11

Endoscopy and a fasting blood test were performed before a six week course of oral amoxycillin (50 mg/kg/day) and tinidazole (20 mg/kg/day). Four weeks after stopping treatment endoscopy and fasting blood test were repeated in 41 children. Twenty one children were reinvestigated six months after stopping treatment.

Paired and unpaired parametric data were analysed by the appropriate t test, non-parametric data by the Wilcoxon matched pairs signed rank test and Mann-Whitney U test, and correlation between inflammation scores and serum pepsinogen I concentrations, gastrin concentrations and age by Spearman’s rank test.

Results
Before treatment the macroscopic endoscopic diagnoses were normal (n = 24), antral gastritis (n = 31), oesophagitis (n = 3), duodenal ulcer (n = 6), gastric ulcer (n = 7). In 44 children histological gastritis was associated with the presence of H pylori. Culture was positive in 40 (90%) and urease testing was positive in 34 (77%). There were no false positive culture or urease tests in patients negative for H pylori on microscopical examination. The remaining 27 children, although having histological gastritis, were negative for the presence of H pylori on Giemsa staining, culture, or urease testing. H pylori positive children (n = 44) had significantly higher serum pepsinogen I concent-

Table 1

<table>
<thead>
<tr>
<th>Inflammation scores</th>
<th>H pylori positive (n = 44)</th>
<th>H pylori negative (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>Median (range)</td>
<td>Median (range)</td>
</tr>
<tr>
<td>Total</td>
<td>5.0 (3-10)</td>
<td>2.5 (1-3)</td>
</tr>
<tr>
<td>Lamina propria</td>
<td>3.5 (2-6)</td>
<td>1.5 (1-5)</td>
</tr>
<tr>
<td>Surface and glandular epithelium</td>
<td>2 (1-5-5)</td>
<td>1.1 (0-2)</td>
</tr>
<tr>
<td>Mononuclear cells</td>
<td>3 (1-5)</td>
<td>2 (1-2-5)</td>
</tr>
<tr>
<td>Polymorphonuclear cells</td>
<td>1.5 (0-4)</td>
<td>0.5 (0-2)</td>
</tr>
</tbody>
</table>

*p < 0.001.

trations than H pylori negative patients (n = 27) (72.5 (SD 22.7) ng/ml and 48.4 (8) ng/ml, respectively; p < 0.005). Moreover, H pylori positive children did not have a significantly higher serum gastrin concentration than those who were negative (40.7 (12.4) mU/ml and 35.2 (11.9) mU/ml, respectively; p = NS).

Table 1 shows the scores of antral inflammation in H pylori positive children compared with those who were negative (p < 0.001, respectively). In those H pylori positive (n = 44) there was a significant correlation between serum pepsinogen I concentrations and the total inflammation score (r = 0.821; p < 0.001) (figure). The main factor influencing the total score was the lamina propria inflammation score with which serum pepsinogen I concentration was highly correlated (r = 0.751, p < 0.001). Correlation between the other inflammation scores and pepsinogen I concentration were r = 0.542, p < 0.001 for polymorphonuclear cells; r = 0.511 for surface and glandular epithelium score; and r = 0.436, p < 0.001 for mononuclear cells. Total inflammation score was also significantly correlated with age (r = 0.417, p < 0.05). In children negative for H pylori (n = 27) the inflammation score was neither correlated with serum pepsinogen I concentration nor with age. Serum gastrin concentrations did

![Graph](graph.png)

Serum pepsinogen I (PG I) concentrations in 44 children with H pylori positive gastritis in relation to total inflammation score of antral mucosa.
not correlate with any inflammation score in children positive for *H pylori* nor in those who were negative. Neither serum peptsinogen I nor serum gastrin concentrations correlated with age in children either positive or negative for *H pylori*.

Four weeks after stopping treatment five out of 41 (12%) children had evidence of *H pylori* on microscopic examination of biopsy specimens. Two out of these five had an active antral gastritis but in one inflammation was quiescent. In the 36 children cleared of *H pylori* there was persisting but improved antral gastritis in 29 and normal histological appearances in seven. One month after stopping treatment serum peptsinogen I concentration was significantly decreased in children negative for *H pylori* (49.5 (10.7) ng/ml) compared with 70.6 (26.5) ng/ml (*p < 0.01*) in those who were still positive. Table 2 shows the total median and the lamina propria inflammation scores in treated children negative for *H pylori* compared with treated children positive for *H pylori* (*p < 0.05*). The serum peptsinogen I concentration no longer correlated with the inflammation scores in treated *H pylori* positive children. One month after stopping treatment serum gastrin concentrations were significantly decreased in children cleared of *H pylori* (32 (5) mU/ml) (*p < 0.01*); it was unchanged in children in whom *H pylori* persisted. The serum gastrin concentrations were not correlated with the inflammation score on either positive or negative treated children.

Six months after stopping treatment seven out of 21 (33%) had relapsed with *H pylori* positive gastritis. All seven children had superficial antral gastritis; in four inflammation was unchanged, but in the other three inflammation was less severe. Six months after stopping treatment the serum peptsinogen I and gastrin concentrations were similar to those at one month. Table 2 shows the total median and the lamina propria inflammation scores after six months in children in whom *H pylori* had recurred or in whom it had been eradicated (*p < 0.001*).

**Discussion**

It has been shown that endoscopy could be completely unhelpful in adults with dyspepsia if endoscopic biopsy specimens are not taken routinely. In our series we confirmed these data in a population of children. Indeed, one third of our children with histological gastritis showed macroscopically normal endoscopic findings.

Serum peptsinogen I concentration has been reported to be predictive of the histological state of the gastric mucosa by Samloff et al. In their study 66 patients had superficial gastritis of the gastric body and in 63 of them the inflammation was also found in the antrum. In the Samloff study the concentration of serum peptsinogen I was significantly higher in the population with gastritis. Unfortunately, we do not know about the *H pylori* state in that study.

In our study we did not find any correlation between serum peptsinogen I concentrations and increasing age. Previous epidemiological studies have reported an increase of serum peptsinogen I with age. This discrepancy could have been due to a higher prevalence of *H pylori* infection at older ages or to the increasing severity of antral gastritis. The total inflammation score was indeed significantly correlated with age in our *H pylori* positive children. *H pylori* positive children have a higher prevalence of active gastritis (p < 0.01) and significantly higher numbers of polymorphonuclear cells than *H pylori* negative children. The concentrations of serum peptsinogen I correlated with the inflammation score. Thus we suggest that serum peptsinogen I could be used in *H pylori* positive children as a marker of the severity of the histological gastritis.

One month after stopping treatment the inflammation scores decreased by 55% and the serum peptsinogen I concentration by 32%. Six months after stopping treatment the serum peptsinogen I concentration decreased by an additional 12%; the inflammation scores remain unchanged.

Six months after the treatment was stopped a mild inflammatory infiltrate was still present in 78% of patients in whom *H pylori* had been eradicated: it was mild and always comprised mononuclear cells, not correlated with serum peptsinogen I concentrations. Similar data have been reported in adults: after eradication of *H pylori* has been achieved a mild mononuclear cell infiltration may persist, while a polymorphonuclear infiltrate is always absent.

Basal serum gastrin concentrations significantly decreased after eradication of *H pylori* but no difference was found between *H pylori* positive and negative children, and no correlation was found with the severity of the inflammation in the gastric mucosa. No association between the presence of *H pylori* and the level of serum gastrin concentration has been found in adults when basal gastrin concentrations were assessed, but when gastrin concentration after food was studied in patients with duodenal ulcers, higher gastrin concentrations in *H pylori* positive patients were found. These data suggest that *H pylori* in the gastric antrum may affect gastrin release, but from our data it seemed that the inflammatory infiltrate in the antral mucosa is not affected by gastrin release.

In summary, we suggest that the serum peptsinogen I concentration could be regarded as a marker of gastritis and could be used as an index of severity of gastritis in *H pylori* positive children.
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subjects. Serum gastrin concentrations do not give crucial information about the gastric mucosa.

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J Clin Pathol 1990 43: 762-765
doi: 10.1136/jcp.43.9.762