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 gastritis. Raised serum pepsinogen I concentrations are found in about two thirds of adults with peptic ulcer disease, and are thought to be a useful sub-clinical 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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Table 1  Inflammation scores in 71 children with H pylori positive or negative gastritis

<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>Total</td>
<td>5.4 (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) *</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.

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 macroscopic 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 concen-
Table 2. Total and lamina propria inflammation scores in \( H \) pylori positive children one and six months after stopping treatment

<table>
<thead>
<tr>
<th></th>
<th>( H ) pylori positive</th>
<th>( H ) pylori negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total median (range)</td>
<td>5 (3-6-5) *</td>
<td>2-5 (0-4-5)</td>
</tr>
<tr>
<td>Lamina propria median</td>
<td>3-5 (2-5-4) *</td>
<td>1-7 (0-3)</td>
</tr>
<tr>
<td>Six months after treatment</td>
<td>4-4 (3-6) **</td>
<td>2-5 (0-5-4-5)</td>
</tr>
</tbody>
</table>

*p < 0.05.  **p < 0.001.

not correlate with any inflammation score in children positive for \( H \) pylori nor in those who were negative. Neither serum pepsinogen 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 pepsinogen 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 pepsinogen 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 pepsinogen 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 pepsinogen 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 pepsinogen 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 pepsinogen I concentrations and increasing age. Previous epidemiological studies have reported an increase of serum pepsinogen 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 pepsinogen I correlated with the inflammation score. Thus we suggest that serum pepsinogen 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 pepsinogen I concentration by 32\%. Six months after stopping treatment the serum pepsinogen 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 pepsinogen 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 pepsinogen 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...
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subjects. Serum gastrin concentrations do not give crucial information about the gastric mucosa.

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