

Original article

Serum Pepsinogen I (PGI) and gastrin levels in children with gastritis

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SUMMARY

Background: Studies on the relationship of childhood gastritis with serum PGI and gastrin are few. This prospective study aimed to evaluate their use in the differential diagnosis and assessment of the severity of childhood gastritis. **Materials and Methods:** Serum PGI and gastrin G-17 (fast-postprandial) were estimated by RIA in 101 symptomatic children, aged 4-16 years (mean 10±2.7 y) who underwent endoscopy. PGI and gastrin were reevaluated in 14 patients after *H. pylori* eradication. **Results:** A) 45 children had *H. pylori* gastritis, B) 35 non *H. pylori* gastritis and C) 21 had non *H. pylori* normal gastric mucosa. A significant increase of PGI levels (70.9 ± 27.1 ng/ml) was found only in group A, compared to groups B (46.4±12.9 ng/ml) and C (46.38 ±11.18 ng/ml p<0.001). There was no correlation between serum PGI levels and the severity of gastritis or the bacterial load. PGI returned to normal (p=0.02) after eradication. No difference in gastrin concentrations among the 3 groups was found. However, a positive correlation of postprandial gastrin with the severity of gastritis was noticed only in the *H. pylori* gastritis group (p<0.02). Serum fasting and postprandial gastrin levels were significantly reduced after *H. pylori* eradication (p<0.008 and p<0.03 respectively). **Conclusions:** Elevated serum PGI is associated with *H. pylori* gastritis in children, while raised postprandial gastrin reflects only its severity.

Key words: Children, Gastrin, Gastritis, *H. pylori*, Pepsinogen I

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INTRODUCTION

A strong association has been recognized between the presence of *H. pylori* in gastric mucosa and histologically confirmed gastritis accompanied or not by peptic ulcer.^{1,2} Besides *H. pylori*, other aggressive factors such as acid and pepsin are necessary for this lesion. Therefore measurement of serum pepsinogen and gastrin concentrations could be a diagnostic tool for indirect assessment of gastritis. Raised serum PGI concentrations have been found in about two thirds of adults with peptic ulcer disease and were thought to be a useful marker of genetic predisposition to ulceration.^{3,4} A later study however, proved that the elevated PGI levels are more likely due to *Helicobacter pylori* infection than to a genetic predisposition.⁵ Studies concerning children are seldom⁶⁻¹⁰ and seem to have a positive correlation of serum PGI with the presence of *H. pylori*, but with conflicting data on gastrin. The aim of the present study was to evaluate serum PGI and gastrin G-17 (fasting and postprandial) concentrations in children with *H. pylori* gastritis and to compare them with those of children with non *H. pylori* gastritis, as well as with those of children with normal gastric mucosa without *H. pylori*.

METHODS

One hundred and one (49 male) symptomatic children aged 4 to 16 years (mean 10 years ±2.7 SD), who underwent upper gastrointestinal endoscopy (those with peptic ulcer excluded), were recruited consecutively in this prospective study. Patients with other diseases such as IBD, coeliac, collagen disease were excluded. None of the children had received any medication which might have affected gastric acidity before medication. They were classified into 3 groups according to histology: **A.** with *H. pylori* gastritis, **B.** with non *H. pylori* gastritis and **C.** those with nor-

mal gastric mucosa without *H. pylori* infection. Specimens were fixed in 10% buffered formalin and histology was performed by the same histopathologist. A signed parental consent was obtained before endoscopy. Upper endoscopy was performed using an Olympus XP20 gastroscope under IV sedation with midazolam or general anaesthesia. The endoscope and biopsy forceps were disinfected in 2% glutaraldehyde after each use. Three antral biopsies were taken for histology, rapid urease test (CLO test) and culture. Histological analysis for *H. pylori*, activity, chronic inflammation, atrophy, and intestinal metaplasia were noted and graded according to the updated Sydney system, using Haematoxylin-Eosin and modified Giemsa stains.

After an overnight fast, blood was drawn and serum PGI levels were determined by radioimmunoassay, using a commercial kit (Pepsik, Sorin Biomedica, Saluggia, Italy). Results were given as nanograms per milliliter (mean \pm SD).

Serum gastrin (G-17) levels were determined by radioimmunoassay using a commercial kit (Diagnostic Products Corporation, Los Angeles). Blood was drawn after overnight fasting and one hour after breakfast for basal and postprandial gastrin determination respectively.

For statistical analysis the parametric Analysis of Variance (ANOVA), the corresponding non parametric Kruskal-Wallis test, the paired samples t-test and the corresponding non parametric Wilcoxon matched paired Signed Ranks test were used.

RESULTS

Patients were divided into 3 groups according to mucosal histology: **A.** 45 children aged 10.2 ± 2.8 years with *H. pylori* chronic active gastritis, **B.** 35 children (10.5 ± 2.5 years) with non *H. pylori* gastritis and **C.** 21 children (9.5 ± 2.8 years) with normal gastric mucosa and without *H. pylori* infection. No atrophy or intestinal metaplasia was found.

The mean serum PGI levels were significantly increased ($f=14.15$, $p < 0.001$) only in the *H. pylori* positive group compared to the other 2 groups, while no significant difference among the 3 groups of children was noticed in both fasting and postprandial gastrin levels, ($p=0.97$ and $p=0.21$ respectively, Table 1) with similar results in mean and median values.

No significant correlation was found between serum PGI levels and the severity of gastritis in both *H. pylori* positive and negative patients with gastritis ($f=1.84$, $p=0.23$ and $f=0.190$, $p=0.67$ respectively, Table 2). No significant correlation of the serum basal and postprandial gastrin levels with the severity of gastritis in the *H. pylori* negative group ($p=0.4$ and $p=0.12$ respectively) was found (Table 2). On the contrary, a significant positive correlation of postprandial gastrin levels with the severity of gastritis was noticed in the *H. pylori* positive children ($p < 0.02$). No statistical correlation of serum PGI ($f=0.092$, $p=0.9$) or serum G-17 fasting levels and G-17 postprandial levels ($p=0.42$ and $p=0.63$ respectively) was found with the bacterial load of the gastric mucosa (Table

Table 1. Serum PGI and gastrin levels in the different groups of children

| Group | n | Age (years) | | PGI (ng/m) | | GASTRIN (ng/ml) | | |
|-------|----|----------------|--------|---------------------|-------------------|--------------------|----------------|--|
| | | Mean \pm 2SD | Range | Mean \pm 2 SD | Basal | | Postpradial | |
| | | | | | Mean \pm 2SD | Mean \pm 2SD | Mean \pm 2SD | |
| A | 45 | 10.2 \pm 2.8 | 4-16 | * 70.91 \pm 27.16 | 46.35 \pm 43.34 | 104.79 \pm 95.44 | | |
| B | 35 | 10.5 \pm 2.5 | 6-16 | 46.42 \pm 12.97 | 43.53 \pm 63.47 | 86.18 \pm 108.66 | | |
| C | 21 | 9.5 \pm 2.8 | 4.5-13 | 46.38 \pm 11.18 | 25.38 \pm 16.52 | 61.06 \pm 57.72 | | |

Anova: (group A to groups B,C $p < 0.001$) Anova $p=0.97$ $p=0.21$
(groups B to C $p= n.s$) Kruskal Wallis $p=0.39$ $p=0.08$

Table 2. Correlation of PGI and gastrin levels with the severity of gastritis

| severity | n | H. PYLORI +ve | | | | H. PYLORI -ve | | | |
|----------|--------------------|-------------------|-------------------|---------------------|-------------------|------------------|-------------------|---------------------|--|
| | | PGI (ng/ml) | | GASTRIN (ng/ml) | | PGI (ng/ml) | | GASTRIN (ng/ml) | |
| | | Fast | | Postprandial | | Fast | | postprandial | |
| | | mean \pm 2SD | mean \pm 2SD | mean \pm 2SD | mean \pm 2SD | mean \pm 2SD | mean \pm 2SD | mean \pm 2SD | |
| mild | 20 | 77.01 \pm 30.43 | 35.84 \pm 30.97 | 65.84 \pm 49.58 | 20 | 45.84 \pm 9.29 | 44.59 \pm 66.33 | 77.45 \pm 87.38 | |
| mod/ sev | 25 | 67.15 \pm 23.8 | 54.04 \pm 49.69 | 113.23 \pm 110.75 | 15 | 45.59 \pm 21.3 | 74.67 \pm 85.14 | 163.17 \pm 198.39 | |
| | (20 mod. 5 sev) | ($p=0.23$) | ($p=0.17$) | ($p < 0.02$) | (12 mod 3 sev) | ($p=0.67$) | ($p=0.4$) | ($p=0.12$) | |

Anova

3). A significant reduction of serum PGI ($t=2.62$, $p=0.02$), and gastrin levels (basal and postprandial), ($p=0.008$ and $p=0.03$ respectively) was found after *H. pylori* eradication (Table 4).

DISCUSSION

Several studies prove a positive correlation of serum pepsinogen levels with the *H. pylori* status of the gastric mucosa.⁶⁻⁹ Asaka et al¹⁰ in a seroepidemiological study in different age groups, from childhood to adulthood, found serum pepsinogens I and II significantly higher in *H. pylori* infected persons than in uninfected persons. Biasco et al¹¹ found significantly higher pepsinogen I and II concentrations in the *H. pylori* dyspeptic patients and they propose that this could be used as a predictor of *H. pylori* infection. Oderda et al^{7,8} also found a significant rise of serum pepsinogen in children with *H. pylori* gastritis compared to those without *H. pylori* infection.

In the present study serum PGI, which was compared not only with non *H. pylori* gastritis but also with non *H. pylori* normal gastric mucosa, was significantly raised only in the *H. pylori* positive group and returned to normal values after eradication. Similarly, in a previous study, Oderda et al⁸ found a significant increase of serum PGI in 44 children with *H. pylori* associated gastritis, which returned to normal after eradication, compared to the values of 27 *H. pylori* negative children. In their study the concentrations of serum pepsinogen I correlated with the inflammation score, but this was not the case in our study. In a recent study of 92 dyspeptic children, Lopez et al¹² found

that PG I and PG II levels were significantly higher in the *H. pylori* positive subjects, which was associated significantly with higher antrum inflammation scores but only PG I levels were independently associated with antrum inflammation. Despite the fact that both reflect antrum inflammation, they are not an effective screening test for *H. pylori* associated gastritis in children. In the present study inflammation was similar in antrum and corpus and metaplasia or atrophy was not found. Oksanen et al¹³ evaluated blood tests (antibodies for *H. pylori* and PG I) in 207 consecutive patients aged 19 to 83 years, who underwent endoscopy. They found that 98% of patients with normal gastric histology had both negative *H. pylori* serology and normal pepsinogen levels and interestingly these tests detected 89% of the patients with abnormal mucosa. Information for cut off values of serum PGI and Gastrin in normal children are limited. Oderda et al. found serum pepsinogen values in asymptomatic children similar with those of group C in the present study. PGI and gastrin levels in children with normal mucosa and negative for *H. pylori*, as in our study, could be used as cut off values.

While all studies in children and adults agree on the positive correlation of serum PGI levels and the presence of *H. pylori* in gastric mucosa, in children the results concerning the relationship of *H. Pylori* gastritis and hypergastrinemia are controversial.^{8,9,12,14-17} In the present study no statistical difference in serum gastrin (basal and postprandial) was found among the three groups of symptomatic children, while a significant reduction of basal and postprandial serum gastrin was noticed after *H. pylori* eradication. Similarly, Kalash et al⁹ found no difference in basal

Table 3. Correlation of PGI and gastrin levels with the bacterial load

| Bacterial load | n | PGI (ng/ml) mean ± 2SD | Gastrin (pg/ml) | |
|----------------|----|---------------------------|--------------------|----------------------------|
| | | | Fast mean ± 2SD | Postprandial mean ± 2SD |
| mild | 12 | 74.28 ± 18.57 | 36 ± 35.22 | 74.45 ± 59.81 |
| moderate | 23 | 70.11 ± 29.19 | 51.82 ± 45.17 | 117 ± 108 |
| High | 10 | 71.85 ± 33.84 | 48.7 ± 49.62 | 114 ± 98 |

$F=0.092$, $p=0.9$ (Anova) $p=0.42$ $p=0.63$ (Kruskal-Wallis test)

Table 4. PGI and gastrin levels before and after eradication of *H. Pylori*

| Groups | n | PGI (ng/ml) mean ± 2SD | Gastrin (pg/ml) | |
|--------------------|----|---------------------------|--------------------|----------------------------|
| | | | Fast mean ± 2SD | Postprandial mean ± 2SD |
| Before eradication | 14 | 74.12 ± 42.95 | 57.78 ± 53.71 | 142.42 ± 120.90 |
| After eradication | 14 | 51.49 ± 20.35 | 23.92 ± 13.88 | 65.64 ± 61.79 |

$t=2.692$, $p=0.02$ $p=0.008$ $p=0.03$
(Paired Samples *t*-test) (Wilcoxon Matched-pairs)

gastrin levels in children with *H. pylori* positive gastritis. In a similar study Oderda et al measured only basal gastrin levels and had the same findings,⁸ but they did not find a correlation of gastrin levels with the severity of gastritis in the *H. pylori* group, as we found in the present study with the postprandial gastrin levels. This could be due to the higher sensitivity and specificity of postprandial gastrin as compared to basal fasting gastrin.^{18,19} Haruma et al¹⁴ found that mean gastritis scores and fasting serum gastrin levels were significantly higher in teenage subjects with *H. pylori* positive duodenal ulcer or gastritis than in those with *H. pylori* negative gastritis or normal mucosa. On the contrary, Lopes et al¹² found that gastrin levels were significantly higher in *H. pylori* negative children.

In the present study the significant increase of PG I levels, which return to normal after *H. pylori* eradication, was found only in the *H. pylori* positive group. This could be a non invasive indicator of inflammation of gastric mucosa. In addition, the correlation of postprandial gastrin with the severity of gastritis as well as the statistically significant reduction after eradication enhances our knowledge gained from studies in adults. It seems therefore that even in children *H. pylori* plays a central role in the pathogenicity of hyperacidity. Some new approaches such as, PGI, PGII, Gastrin -17 and *H. pylori* antibodies have been developed and have currently been proposed in adults as non endoscopic tools for screening and diagnosis of chronic atrophic gastritis.^{18,19} In children this has not yet been investigated. Of course atrophic gastritis is not common in children,²⁰ but possibly the combination of anti-*H.pylori* antibodies, serum PGI, and postprandial gastrin levels could become a non invasive tool to identify the presence as well as the severity of *H. pylori* gastritis.

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