Letters to the Editor

Serum Levels of Pepsinogen I, Pepsinogen II, and Gastrin-17 in the Course of Helicobacter pylori Gastritis in Pediatrics

To the Editors: as a comment to the editorial of Oderda et al: In an interesting editorial in this issue of the journal, Oderda et al. (1) review which tests may be used to diagnose Helicobacter pylori (H. pylori) in children. Some are invasive (i.e., upper gastro-intestinal endoscopy and multiple gastric biopsies), and some are non invasive (i.e., serology, 13C-urea breath test and stool antigen determination). All exhibit various advantages or disadvantages, and for that purpose, their respective place in the diagnosis decision tree differ. In symptomatic children, as clearly stated by the position papers of both the European Task Force for H. pylori infection in children (2) and NASPGAN (3), upper gastrointestinal endoscopy with gastric biopsies remains the gold standard method for the diagnosis of H. pylori gastritis in children. Non-invasive tests are not longer recommended to screen children with abdominal pain. Some new approaches may currently be suggested. Recently, a new EIA blood panel test (Biohit®, Helsinki, Finland), has been developed, associating group-I pepsinogens (PGI), group-II pepsinogens (PGII), gastrin-17 (G-17), and H. pylori antibodies, and proposed as a non endoscopic tool for diagnosis and screening of chronic and atrophic gastritis in adults (4–6). In children, such an alternative procedure has not yet been investigated.

PGI are synthesized solely in the oxyntic glands and mucus neck cells of the gastric corpus, whereas, PGII are uniformly found in the antrum, the most important one being G-17. In case of atrophic antral gastritis and loss of antral G cells, serum G-17 remains low although the stomach is achlorhydric or hypochlorhydric (4).

In this new EIA blood panel test, panels include assays of postprandial (after stimulation with protein-rich drink) serum gastrin (G-17prand) which seems to be much more accurate with a higher sensitivity and specificity as compared to basal fasting serum gastrin (G-17fast) (5,6). Using an algorithm, this blood test panel is able to establish with high sensitivity and specificity whether the patient has gastritis, whether this gastritis is atrophic or not and in which part of the stomach the atrophic changes are located. The algorithm (decision tree) is used for classification of patients into different categories of atrophic gastritis by the H. pylori antibody titers, upon the cut-off levels of PGI and G-17prand. The absence of evidence of H. pylori infection is considered to indicate an autoimmune origin of gastritis (4). Finally, H. pylori gastritis, without gastric atrophy, tends to raise the serum levels of G-17 and PGI. A low intra-gastric acidity increases the serum levels of G-17 and vice versa. Permanent, long-lasting hypo- or achlorhydria results in extremely high levels of circulating G-17, possibly due to antral G-cells hyperplasia (6).

The aim of our study was a preliminary assessment of this new non endoscopic blood panel test in the course of H. pylori related gastritis in pediatrics.

An observational retrospective study was performed in 100 children, mean age 10 years (1–18), 52 females and 48 males, who underwent diagnostic upper-gastrointestinal endoscopy for various dyspeptic symptoms, recurrent abdominal pain and vomiting. Gastric biopsies were taken in antrum and corpus, at least 2 from each site, for histologic and bacterial culture assessment. Histological analysis, H. pylori, chronic inflammation, activity, atrophy, and intestinal metaplasia were noted and graded according to the updated Sydney System. H. pylori infection was considered for gastric biopsies with positive histology and/or culture. Within the same day, fasting serum samples were also analysed using the EIA blood panel tests for H. pylori antibodies (cut-off levels >38 EU), PGI, PGII and G-17fast (Biohit®, Helsinki, Finland). Non parametric Mann-Whitney U test was used in the calculation of the significance between groups, the StastView Software (Abacus®, CA, USA) values were considered significant when \( P < 0.05 \). The sensitivity, specificity, positive and negative predictive values and test accuracy of the H. pylori antibodies were calculated and compared to the results of gastric biopsies. Finally, written parental consent was obtained from all.

There were 64 H. pylori positives (Hp+ve) and 36 H. pylori negatives (Hp−ve). Among them 61 Hp+ve (95.3%) and 3 Hp−ve (8.3%) had evidence of chronic superficial gastritis, mild (25), moderate (21) and severe (13). None exhibited gastric atrophy or intestinal metaplasia. Serum PGI and PGII levels showed a significant increase and the PGI/PGII ratio significantly decreased in Hp+ve children as compared to Hp−ve ones, \( P < 0.0002 \). No significant variation of G-17fast serum level occurred between Hp+ve and Hp−ve children, Table 1. Compared to gastric biopsies, H. pylori antibodies showed 3 false positive and 23 false negative results. Their

### TABLE 1. Pepsinogen I (PGI), Pepsinogen II (PGII) and Gastrin-17 (G-17) levels (mean ± SD) in 100 studied children

<table>
<thead>
<tr>
<th></th>
<th>PGI (µg/l)</th>
<th>PGII (µg/l)</th>
<th>PGI/PGII (µg/l)</th>
<th>G-17 (pmol/l)</th>
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<tbody>
<tr>
<td>Hp−ve</td>
<td></td>
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<tr>
<td>(n = 36)</td>
<td>73.6 ± 18.2</td>
<td>6.3 ± 3.4</td>
<td>12.6 ± 3.2</td>
<td>7.1 ± 25.8</td>
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<tr>
<td>Hp+ve</td>
<td>(n = 64)</td>
<td>102.7 ± 31.9</td>
<td>12.2 ± 7.5</td>
<td>9.8 ± 3.6</td>
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<td>*p &lt; 0.0001</td>
<td>&lt;0.0001</td>
<td>0.0002</td>
<td>0.2746</td>
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* Upon the Mann-Whitney test, \( P < 0.05 \).
levels for PGI and G-17 prand. In children the prevalence of gastritis based on the classification of patients into different categories of atrophic gastritis. The sensitivity and specificity of these antibodies were population might be due to the absence of histologic atrophic gastritis in as series of 404 consecutive adult outpatients undergoing diagnostic upper-gastrointestinal endoscopy, G-17 fast and prand and PGI levels decreased with increasing grade of atrophy of the antrum or corpus, respectively. G-17 prand levels were significantly lower in patients with advanced (moderate or severe) atrophic antral H. pylori gastritis than in those with non-atrophic H. pylori gastritis. Using the cut-off levels for G-17 fast and PGI with the best discrimination, the sensitivity and specificity of the blood test panel in delineation of patients with advanced atrophic gastritis (either in the antrum or the corpus or both) were 83% and 95%, respectively. The predictive values of the positive and negative test results were 75% and 97%.

In our study, H. pylori-infected children exhibited higher serum levels of PGI, PGII and a lower PGI/PGII ratio as compared to non infected ones. These results were comparable to those found in adults (4). The lack of variation of G-17 in our study, especially during histologic gastritis, a common feature of H. pylori infection in children, related or not to CagA have a high sensitivity but a low specificity. The combination of H. pylori antibodies, PGII, and G-17 may balance this issue and provide adequate screening tools, although there is a clear need for further improvement and simplification of serological testing for atrophic gastritis (7). Recently, Vaananen et al (6) determined this blood test panel, together with the assay of H. pylori antibodies, as a good non-endoscopic diagnosis and screening tool of atrophic gastritis in a series of 404 consecutive adult outpatients undergoing diagnostic upper-gastrointestinal endoscopy, G-17 fast and prand and PGI levels decreased with increasing grade of atrophy of the antrum or corpus, respectively. G-17 prand levels were significantly lower in patients with advanced (moderate or severe) atrophic antral H. pylori gastritis than in those with non-atrophic H. pylori gastritis. Using the cut-off levels for G-17 fast and PGI with the best discrimination, the sensitivity and specificity of the blood test panel in delineation of patients with advanced atrophic gastritis (either in the antrum or the corpus or both) were 83% and 95%, respectively. The predictive values of the positive and negative test results were 75% and 97%.

In conclusion, PGI, PGII serum levels and their ratio could be used as a non-endoscopic indicator of H. pylori infection in children: invasive, non-invasive or both? J Pediatr Gastroenterol Nutr 2004 (In press).

REFERENCES


To the Editor: We read with interest the manuscript written by Peña-Quintana et al. (1) and we agree that the presence of the DQ2 (DQA1* 0501/DQB1* 02) heterodimer is strongly associated with celiac disease (CD) and that typing might be...