Serological Assessment of Samples from Patients Complaining of ‘Dyspepsia’

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Abstract

Background: Many people consult their GP for upper gastrointestinal (GI) symptoms, which are often associated with pain or burning and discomfort in the abdomen and range from heartburn and acid regurgitation to nausea and vomiting. Historically, all of these symptoms have been grouped together under the single term ‘dyspepsia’, defined as having one or more symptoms of epigastric pain, burning, postprandial fullness, or early satiation. While gastric or oesophageal cancer is an unusual finding in patients with dyspepsia, excluding malignancy is a common reason for performing endoscopy.

Methods: Quest Diagnostics has been offering the GastroPanel® assays for those patients who have been referred to the walk-in clinic complaining of ‘dyspepsia’. This is a set of three assays (Pepsinogen I, Gastrin 17 and Helicobacter pylori) and the results use an algorithm which can provide information about the stomach health and about the function of the stomach mucosa.

Results: Of all the samples tested 63.5% showed no abnormalities and were reported as ‘normal function of gastric mucosa.’ These patients would be classed as having functional dyspepsia. Thirty-six samples (19.9%) were positive for Helicobacter pylori and the remaining samples had a variety of abnormal results.

Conclusion: Dyspepsia is a common problem seen both by primary care physicians and gastroenterologists. Using the results from the serological analysis of the patients’ serum the clinician can delineate between gastric atrophy and a normal health stomach usually without the need to refer the patient for endoscopy.

Keywords: Dyspepsia; Helicobacter pylori; Gastric atrophy

Aim

To evaluate the utility of a serological panel combining pepsinogen I, gastrin-17, and anti-Helicobacter pylori antibodies (Gastropanel®) as a screening method for patients attending a walk in clinic complaining of dyspepsia.

Introduction

Many people consult their GP for upper gastrointestinal (GI) symptoms, which are often associated with pain or burning and discomfort in the abdomen and range from heartburn and acid regurgitation to nausea and vomiting [1-3]. These symptoms can cause problems with a person’s physical and social activities and are generally related to the consumption of food and drink. Historically, all of these symptoms have been grouped together under the single term ‘dyspepsia’ or poor digestion [4,5]. Dyspepsia is defined as having one or more symptoms of epigastric pain, burning, postprandial fullness, or early satiation [6].

One common cause of serious stomach complaints is infection with Helicobacter pylori (H. pylori) which can be acquired at a young age and colonize the stomach mucosa permanently in the absence of treatment [7,8]. In nearly half of the H. pylori infected cases gastritis develops over the years into atrophic gastritis (loss of glands and function of the stomach mucosa), which is most common in people aged over 50 years (Figure 1).

H. pylori infection and atrophic gastritis often cause no symptoms. Atrophic gastritis (AG) may be present in the upper stomach (corpus), in the lower stomach (antrum), or both (Figure 2). Corpus AG is linked with an increased risk of gastric cancer and of the deficiencies of vitamin B12, iron and calcium, all associated with low acidity (hypochlorhydria) caused by corpus AG. Antrum AG is connected with an increased risk of gastric cancer and peptic ulcer diseases. The risk for gastric cancer increases up to 90-fold, if severe or moderate atrophy exists in both antrum and corpus [9-11]. Normally, if these patients had a long history of symptoms they might require empirical treatment, endoscopy, testing for Helicobacter pylori or a combination of these approaches [12-14].

Quest Diagnostics (UK) has been offering the GastroPanel® assays from Biohit Oyj (Laippatie 1, 08800, Helsinki, Finland) for those patients who have been referred to the walk-in clinic at the Upper Wimpole Street Laboratory complaining of ‘dyspepsia’.

The commercial kit GastroPanel® served to determine serological levels of PGI, G17 and H. pylori IgG antibodies. Specific enzyme

Figure 1a: Severe gastritis caused by Helicobacter pylori.

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Results

In order to assess the effectiveness of the GastroPanel® test, Quest Diagnostics laboratory at Heston UK, evaluated 181 patients (age range 19-75 years, median 41 years). Of these 105 (60.7%) could be characterized as Japanese (including 23 couples [husband and wife]), 53 (30.6%) as European and the remainder 15 (8.7%) an assortment of nationalities, and eight (4.4%) were of unknown nationality.

Of the 181 samples tested, 115 (63.5%) showed no abnormalities in the samples and were reported as ‘normal function of gastric mucosa.’ Thirty-six samples (19.9%) were positive for Helicobacter pylori only and a report was issued with a recommendation to return to their GP and start an appropriate course of antibiotics to eradicate the infection. The remaining 30 samples had a variety of abnormal results (Table 1) and a report was issued with an appropriate comment and a recommendation to seek further advice from a gastroenterologist.

There were only 27 (14.9%) patients over 50 years of age, and of these 18 were reported as normal, four were positive for H. pylori only, four showed increased Pepsinogen I levels and the final sample was positive for both (51 years old Japanese woman) H. pylori and Pepsinogen I.

Discussion

When GastroPanel® examination gives a normal result for a healthy stomach mucosa, those patients suffering with stomach problems usually have ‘functional dyspepsia’, or disease outside the stomach, e.g. in the colon, and can be directed to other type of testing and treatment. About half the World’s population carries Helicobacter pylori in their stomach mucosa, and approximately half of these people will develop atrophic gastritis in their lifetime [16]. In atrophic gastritis, the cells and glands of stomach mucosa are destroyed, which causes serious structural and functional damage, and increases the risk of many stomach related diseases. Atrophic gastritis, which is most commonly asymptomatic, can progress into gastric cancer in a few percent of the sufferers. Even though the incidence of gastric cancer is on the decline, it is still relatively common in the older population as the average lifetime increases.

Another important problem resulting from atrophic gastritis is deficiency of vitamin B₁₂, and deficiencies of iron, calcium and magnesium. It has been found that nearly half the people suffering from asymptomatic atrophic gastritis have deficiency of vitamin B₁₂ in the time of atrophic gastritis diagnosis, and possibly all atrophic gastritis patients will develop the deficiency with time as stocks of vitamin B₁₂ run out. Untreated deficiency of vitamin B₁₂ may cause permanent damage to the nervous system, resulting in depression and dementia. It may also cause elevated homocysteine levels, which is an independent risk factor for atherosclerosis and stroke. Iron deficiency can cause anaemia, and calcium deficiency osteoporosis. In addition to atrophic gastritis patients, coeliac disease patients and elderly on poor diet may also suffer from these deficiencies.

The ability to differentiate between patients with healthy or diseased stomach mucosa is useful in the diagnosis of atrophic gastritis. Currently there are two options; the first is gastroscopy and microscopic examination of endoscopic biopsy from the gastric antrum and corpus. More recently there have been advances in the use of a less invasive option, the examination of gastric markers from serum or plasma [17-20]. A recent study concluded that use of the biomarkers of the modern GastroPanel® test for safe and cost-efficient primary diagnosis and screening of Helicobacter pylori infection and atrophic gastritis in patients with stomach discomfort and in asymptomatic patients,
as it is neither safe nor cost-efficient to use the 13C urea breath test for this purpose. In addition, the authors of the publication state that acetaldehyde generated in an achlorhydric stomach (a consequence of atrophic gastritis) is a significant reason for an increased gastric and oesophageal cancer risk. Acetium capsules can reduce the amount of cancer-causing acetaldehyde generated in the stomach -and thus, very likely, they also reduce the cancer risk [21].

**Gastric Summary**

If the GastroPanel® examination gives a normal result, the diagnosis is either functional dyspepsia or another disease not involving the gastric mucosa. The examination diagnoses *H. pylori* infection, atrophic gastritis, and its location (corpus, antrum, or both). GastroSoft interpretation software shows the test results, reference ranges, and diagnosis, and when necessary gives recommendation on possible treatment or further testing. The GastroSoft report also indicates if there is an increased risk of gastrooesophageal reflux disease. Unfortunately, this study was only a snapshot with no confirmatory evidence of histopathology for the results and no follow-up with the patients. It would, therefore be difficult to verify if the results were genuine or not. In this instance, however, the majority of patients (64%) had normal results, indicating the presence of a normal stomach mucosa. This group would be less likely to benefit from gastroscopy to detect gastric cancer. Clearly, identifying such patients before

<table>
<thead>
<tr>
<th>Number of patients (% of total)</th>
<th>Results</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>115 (63.5) Normal</td>
<td>Normal Function of Gastric Mucosa</td>
<td></td>
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<tr>
<td>36 (19.9) <em>Helicobacter pylori</em> Positive</td>
<td>Non-atrophic risk of gastritis, related to <em>H. pylori</em> infection. Increased risk of peptic ulcer disease (duodenal or gastric). - Treatment of <em>H. pylori</em> infection is recommended if successful therapy has not been given to the patient earlier.</td>
<td></td>
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<tr>
<td>13 (7.2) Raised Pepsinogen</td>
<td>Pepsinogen levels in the blood reflect the structure and function of the gastric corpus mucosa. A high PGI may indicate high acid output or ongoing PPI-medication.</td>
<td></td>
</tr>
<tr>
<td>8 (4.4) All analytes raised</td>
<td>Non-atrophic risk of gastritis, related to <em>H. pylori</em> infection. Increased risk of peptic ulcer disease (duodenal or gastric). - Treatment of <em>H. pylori</em> infection is recommended if successful therapy has not been given to the patient earlier. - High PGI value may indicate high acid output and/or ongoing PPI medication.</td>
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<tr>
<td>5 (2.7) Raised Pepsinogen and Gastrin-17 (G17)</td>
<td>A high PGI may indicate high acid output or ongoing PPI-medication. The blood G17 level reflects the structure and function of the mucosa in gastric antrum. The fasting blood level of G17 falls when the acidity of the stomach increases (pH &lt;2.5). Fasting G17 level &lt;1 pmol/L indicates very high acid secretion is very high and atrophy of the antrum mucosa, with loss of antral G cells. Fasting level of G17 &gt;10 pmol/L, usually indicates a hypoacidic stomach due to PPI medication, or limited to corpus mucosa atrophy.</td>
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<tr>
<td>4 (2.2) Low Pepsinogen (&lt;30 ug/L)</td>
<td>PGIs levels &lt;30 ug/L indicate atrophy of the corpus mucosa</td>
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Table 1: GastroPanel® results and interpretive information.
gastroscopy, using a non-invasive test such as the GastroPanel®, could help to reduce unnecessary invasive procedures, prevent discomfort for the patient, and decrease healthcare costs.

Acknowledgements

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References