Rational Use of BIOHIT tests in Diagnosis of Abdominal Symptoms — The GI-Panel
Gastrointestinal disorders are among the most common complaints encountered by the primary care physicians and currently comprise an increasing healthcare and health economic burden.

Despite their increasing significance in the global healthcare, the causes of these gastrointestinal tract diseases are still incompletely understood, and their treatment options are far from optimal. This leaves many patients dissatisfied with their current treatment which far too often is based on outdated guidelines and/or tests that give false positive or false negative results [1-6,14,19,20].

Specific diagnosis cannot be reached on the basis of clinical symptoms

Dyspeptic symptoms include constant or intermittent upper abdominal pain, bloating, hearth burn, belching and nausea, and dyspepsia (20-40% lifetime frequency) belongs among the most frequent clinical symptoms complained by the patients within the primary healthcare.

On the basis of the non-specific symptoms alone, functional dyspepsia cannot be distinguished from often asymptomatic Helicobacter pylori (HP)-infection and atrophic gastritis (AG) with related risks, such as gastric cancer (GC)[4,19]. In addition, similar symptoms can be caused by a number of clinically important diseases of extra-gastric origin, such as lactose intolerance (LI) (the average at 65% of the global population), celiac disease (CD)[1-2%], inflammatory bowel disease (IBD)<1%, irritable bowel syndrome (IBS)[10-15%], and colorectal neoplasia (CRC) suggested by fecal occult blood (FOB)[11,12]. Far too often in the current clinical practice, the patients are offered invasive endoscopy as the first-line examination.

GastroPanel® - The first-line diagnostic examination

Replacing gastroscopy by the unique plasma biomarker panel (GastroPanel®) as the first-line diagnostic examination for dyspepsia and HP, it is possible to stratify the patients into three categories at different risk for GC, in addition to reaching the specific diagnosis of gastric functional disorders (Figure 1)[4,14].

GastroPanel profile implicating a dysfunction in the acid output [high or low], can be affirmed by a simple clinical procedure. In case of high acid output (G-17b low), a 2-week test treatment with PPI-medication should normalize the profile. When low acid output (G-17b high) is ascribed to PPI-medication itself [with no implications of AG], interrupting the PPI-treatment for two weeks should restore acid output to normal level (8,9).

GastroPanel is a sensitive and comprehensive test for Helicobacter pylori (HP) infection with related risks [3]. When HP-infection is detected [with no accompanying AG], the logical next step is eradication of the bacteria by any of the standard therapies [1]. Following the international recommendations, eradication should always be controlled. Biohit offers several optional tests for that: GastroPanel, HPQT and UFT300 tests. If the symptoms continue after HP-eradication, a feasible option is to make gastroscopy that enables i) direct visualization of HP as well as ii) testing the biopsy with HP Quick tests. Whenever gastroscopy is performed, testing for LI can be conveniently done using LIQT.

The patients at high risk for subsequent GC include all those with GastroPanel® implicating AG (atrophic gastritis). In this high-risk category, one cannot avoid performing gastroscopy to confirm the AG diagnosis, its severity and topography in the stomach, i.e. antrum, corpus or both (2,6,9,10). Additional information can be obtained by complementing the targeted biopsies with the laboratory tests for HP, LI, CD and vitamin B12 deficiency (15), not infrequently accompanying atrophic corpus gastritis, particularly of the autoimmune type [22].

Summary

Replacing gastroscopy by GastroPanel® as the first-line diagnostic test in patients with dyspeptic complaints allows a rational diagnostic algorithm whereby carefully selected BIOHIT non-invasive tests are applied to screen for specific clinical conditions that all share in common the non-specific abdominal symptoms. Substantial savings in healthcare costs can be achieved while avoiding up to 80% of unnecessary gastroscopies by screening the dyspeptic patients at first by GastroPanel®, and targeting the other tests using a rational diagnostic algorithm (Figure 1; Table 1).

However, if GastroPanel® detects i) symptomatic H.pylori (HP)-infection after eradication, ii) atrophic gastritis (AG) or iii) symptomatic high acid output, these are indications for gastroscopy and biopsy examination (4).
Figure 1. Diagnostic algorithm for symptomatic (dyspeptic) patients

- **Abdominal complaints**
  - Biohit GastroPanel
    - **Normal**
      - Follow-up
        - Celiac disease test, CDQT
          - Normal
            - Confirmation by clinical means
            - Colonoscopy
          - Positive
            - Biopsies
              - H. pylori test, UFT300, HPQT
              - Lactose intolerance test, LIQT
        - Symptomatic
          - ColonView FIT test
            - Calprotectin test
              - High acid output
                - Control by GastroPanel
                  - Biopsies
                    - H. pylori test, UFT300, HPQT
                    - Lactose intolerance test, LIQT
              - Low acid output
                - Colonoscopy
                - Biopsies
                  - H. pylori test, UFT300, HPQT
                  - Lactose intolerance test, LIQT
      - Symptoms
        - H. pylori antibodies
          - Eradication
            - Follow-up
              - Other tests
              - Gastroscopy
                - Other tests
          - Control by GastroPanel
            - Biopsies
              - H. pylori test, UFT300, HPQT
              - Lactose intolerance test, LIQT
      - Dysfunction
        - Calprotectin test
          - Negative
            - Normal
            - Abnormal
            - Celiac disease test, CDQT
          - Positive
            - Re-eradication or new control
            - Celiac disease test, CDQT
          - Follow-up
            - Colonoscopy
              - Biopsies
                - H. pylori test, UFT300, HPQT
                - Lactose intolerance test, LIQT

Atrophic gastritis
- Gastroscopy
  - Biopsies
    - H. pylori test, UFT300, HPQT
    - Lactose intolerance test, LIQT
  - Active vitamin B12 test
  - Abnormal
Table 1. Rational use of BIOHIT tests at each optional step of the algorithm ('The GI-Panel')

### SYMPTOMATIC PATIENTS WITH DYSPEPTIC COMPLAINTS

<table>
<thead>
<tr>
<th>GastroPanel test</th>
<th>NORMAL</th>
<th>DYSFUNCTION</th>
<th>HP-INFECTION (No AG)</th>
<th>ATROPHIC GASTRITIS (AG)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Symptoms</td>
<td>High acid output</td>
<td>Low acid output</td>
<td>Eradication (Standard regimens)</td>
</tr>
<tr>
<td>NActs</td>
<td>CDQT</td>
<td>Colon View</td>
<td>Calprotectin</td>
<td>PPI+</td>
</tr>
<tr>
<td>T-</td>
<td>T+</td>
<td>T-</td>
<td>T+</td>
<td>T-</td>
</tr>
<tr>
<td>Normal profile</td>
<td>N-Sympt</td>
<td>Sympt</td>
<td>Re-eradication</td>
<td>ERA</td>
</tr>
<tr>
<td>NActs</td>
<td>OTests</td>
<td>Gastroscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bx</td>
<td>HPQT</td>
<td>LIQT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Explanation of the abbreviations:
- HP: *Helicobacter pylori*
- AG: Atrophic gastritis
- NActs: No specific actions needed
- N-Sympt: No symptoms
- CDQT: Celiac Disease Quick Test
- Sympt: Symptoms
- PPI+: Test PPI-treatment for 2 weeks
- PPI-: Intermittent PPI-treatment for 2 weeks
- Bx: Gastroscopic biopsies
- HPQT: *Helicobacter pylori* Quick Test
- LIQT: Lactose Intolerance Quick Test
- UFT300: *Helicobacter pylori* UFT300 Test
- B12: Active B12-vitamin test
- T-: Test-negative
- T+: Test-positive

### Biohit diagnostic tests used in the algorithm (in blue):
- GastroPanel®
- Active Vitamin-B12®
- Calprotectin®
- Lactose Intolerance Quick Test®
- *Helicobacter Pylori* UFT300 Quick Test®
- *Helicobacter Pylori* Quick Test®
- ColonView-FIT®
- Celiac Disease Quick Test®
Appendix

The GastroPanel® innovation is based on follow-up studies on gastritis patients conducted by research groups in Finland and Estonia and the discovery of the role of Helicobacter pylori in pathogenesis of gastritis and peptic ulcer disease, which led to Nobel Prize in 2005. Of crucial importance has been Biohit’s R&D and the microplate immunoassay analysers, based on the invention of the vertical light beam measurement principle, one of the inventions of Biohit’s founder, currently the worldwide global standard. Starting from the 1970’s, this invention has prompted an extensive research on and fast development of microplate immunoassay techniques, e.g., for analysis and screening of infectious diseases, including Helicobacter pylori, gastritis, atrophic gastritis and related risks, such as peptic ulcer disease and gastric cancer [1-4, www.biohithealthcare.com/About Us/History: Aggressive innovation and patenting strategy].

The unique GastroPanel® is the primary examination from a blood sample for dyspepsia (the prevalence 20-40%) to reveal H. pylori infection (5-80%) and atrophic gastritis (2-12%) with related risks, such as gastric cancer and the deficiency of vitamin B12 [2,4]. GastroPanel® increases patient safety and decreases healthcare costs. Biohit has launched the GastroPanel screening model which can be used to calculate levels of savings achievable with the use of the GastroPanel® in the screening program of the risk of gastric cancer. For example in Finland, the total lifetime savings are over € 800 million for 10 age groups [6].

Today, the ageing population has a great benefit of GastroPanel® diagnosis/screening – and needless to reiterate, GastroPanel® could be the test-of-choice for the diagnosis/screening of gastric and esophageal cancer risks. In addition to this increased cancer risk, atrophic gastritis due to H. pylori infection or autoimmune disease, may cause malabsorption of vitamin B12, iron, magnesium, zinc, calcium and some drugs.

As to the diagnosis of H. pylori infection, 13C-urea breath test (UBT) or stool H. pylori antigen test (SAT) frequently give false negative results, and H. pylori infection with all its possible consequences) remains undetected. UBT may also give false positive results in subjects with acid-free stomach colonized by urease-positive bacteria. In addition, the conventional H. pylori tests (UBT, SAT) and antibody tests do not detect atrophic gastritis with all the above mentioned risks [2-5,19,20].

Because GastroPanel® does not have the limitations of the conventional H. pylori tests [8,20], GastroPanel® is recommended for the primary diagnosis of dyspepsia and H. pylori infection. Similarly, all subjects should be tested before prescribing any PPI medication, because PPIs are contraindicated for patients with acid-free stomach due to atrophic gastritis [18].

In addition to the reliable diagnosis of H. pylori infection and atrophic gastritis, GastroPanel® also reveals high acid output of the gastric mucosa, which remains undiagnosed with the conventional H. pylori tests and which predisposes to esophageal reflux disease (GERD) with potential complications. These are ulcerative esophagitis, Barrett’s esophagus or lower esophageal cancer [2,4,14].

We hope that this information will encourage doctors and laboratories to utilize GastroPanel® in checking the stomach health and in diagnosis of symptomatic patients as well as for screening of the risk groups [4,8,21,22].

References

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