Additional information

GastroPanel® and Acetium® inventions: The GastroPanel® blood examination reveals, e.g., atrophic gastritis (anacidic stomach) with related risks, such as risk of stomach and oesophageal cancer. Acetium® capsules, that binds the carcinogenic acetaldehyde to a harmless compound in the stomach, may decrease i.e. the risk of these serious cancers.

The GastroPanel® and Acetium® innovations are together a unique combination that can help to prevent gastric and oesophageal cancers. GastroPanel® detects atrophic gastritis and the related gastric and oesophageal cancer risks while the conditions are still treatable. Atrophic gastritis of the corpus, which is usually irreversible, leads to permanent achlorhydria. In an achlorhydric stomach (also caused by a long term PPI-treatment), microbes from the mouth can survive and produce acetaldehyde from sugars and alcohol present in food. In the new cancer classification issued by WHO in October 2009, acetaldehyde present in alcoholic beverages and formed from ethanol endogenously is in Group 1, together with carcinogens such as asbestos, tobacco and benzene. Globally, acetaldehyde exposure mediated by gastrointestinal tract microbes or tobacco smoke is associated with approximately four million new cases of cancer each year, nearly 40 per cent of all cancers. These include upper aerodigestive tract, colon and pulmonary cancers. Biohit has developed Acetium® products and a method to reduce physical and nutritional exposure to acetaldehyde (www.biohithealthcare.com/scientific/study-protocols).

In 2012, the European Commission's appointed group of scientific experts gave a unanimous recommendation stating that cosmetic products may contain at most 5 mg/l of acetaldehyde while no acetaldehyde may be added to mouth wash. Many alcoholic beverages and foodstuffs sold in Finland exceed the maximum permitted amount for cosmetic products multiple times (http://www.biohithealthcare.com-/laboratory-services).

Acetium® capsules bind the carcinogenic acetaldehyde in the stomach with individuals suffering from an anacidic stomach for the following reasons: 1) an atrophic gastritis, 2) PPI medication or 3) a stomach surgery, as well as individuals with 4) gene mutation affecting acetaldehyde metabolism or 5) chronic helicobacter infection that produces acetaldehyde. Acetium may cure atrophic gastritis and prevent migraine and cluster headache (study ongoing). Acetium® lozenges effectively bind acetaldehyde from saliva and form a harmless compound and may also help quit smoking (study ongoing).

Acetium® lozenge binds acetaldehyde into harmless compound in saliva in the mouth, which forms as a result of smoking and alcohol consumption and might facilitate smoking quit (study ongoing). Acetium lozenge removes 87% of the immediate effects of acetaldehyde in saliva from alcoholic beverages containing high levels of acetaldehyde and over 90% of acetaldehyde dissolved in saliva during smoking.

The state-of-the-art, safe and economic GastroPanel® examination for the diagnosis of *Helicobacter pylori* (*H.pylori*) infection and atrophic gastritis with all its sequels does not have any of the following serious medical problems:

The ^{13}C urea breath test (UBT), stool antigen test and antibody tests for *H. pylori* infection do not detect atrophic gastritis which is caused by *H. pylori* infection or an autoimmune disease. The early and reliable diagnosis of atrophic gastritis is important and often life-saving because of its several risks, including, e.g., unnecessary deaths due to stomach and oesophageal cancer.

Additional information

In addition to the risks of gastric and oesophageal cancer, atrophic gastritis may cause malabsorption of vitamin B12, iron, magnesium, calcium and some drugs. Calcium deficiency causes osteoporosis, and vitamin B12 deficiency can cause Alzheimer's disease, dementia, depression and polyneuropathy, as well as high homocysteine content in the body, which in turn is thought to be an independent risk factor for atherosclerosis, heart attacks and strokes. The absorption of dipyridamole, some iron products and antifungals (fluconazole, itraconazole), thyroxine and atazanavir is considerably impaired in an anacidic stomach.

Atrophic gastritis in the gastric corpus and PPI therapy cause anacidity (aclorhydria) of the stomach. The risk of pneumonias and, in senior citizens, even the risk of fatal intestinal infections (such as giardiasis, malaria, *Clostridium difficile* and *E. coli* EHEC) may increase significantly in an anacidic stomach.

H. pylori gastritis may also develop into antral atrophic gastritis, which increases the risk of peptic ulcer disease and gastric cancer. If both antrum and corpus mucosa are atrophic, this condition is the highest risk for gastric cancer known to date.

Furthermore, none of the aforementioned three *H. pylori* tests (^{13}C urea breath test, stool antigen test and antibody test) provides any information on excessive gastric acid secretion (high acid output), which is diagnosed by GastroPanel, and which in patients with gastro-oesophageal reflux disease may cause complications of this disease in esophagus. Such complications are often asymptomatic and include ulcerative oesophagitis and Barrett's oesophagus, which may lead to oesophageal cancer if left untreated. In addition, the ^{13}C urea breath test and stool antigen test may give up to 50 % false negative results if the patient has a) atrophic gastritis b) MALT lymphoma or c) bleeding peptic ulcer disease or d) if the patient is currently receiving antibiotics or PPIs.

Diagnosis of upper abdominal complaints (dyspepsia) and *H. pylori* infection is still biased by the above described medical problems that may lead to delayed diagnosis and disease progression beyond curative treatment.

Before the entry of GastroPanel test in the market for more than ten years ago, atrophic gastritis and *Helicobacter pylori* infection, were found by chance during endoscopy (gastroscopy). Thus, acid-free stomach (AG of the corpus) which is usually asymptomatic has remained undetected in many people. These undetected lesions might have progressed to gastric or oesophageal cancer (possible in several hundred subjects every year) or resulted in B-12 vitamin deficiency with all associated sequels that are no longer curable. There are only estimates of the number of such events during the past ten years, when most of the people with dyspepsia (20-40% of the population) or *H. pylori* infection (20 to 70% of the population, pending on age) have been examined only with the ^{13}C-urea breath test (UBT). Even today, most doctors, not to mention the patients with dyspeptic disorders, are not being adequately aware of the fact that the UBT and the stool HP-antigen test may give false negative results, and about the fact that these tests will not detect atrophic gastritis and the risks associated with it e.g. the risk of gastric cancer.

Additional information

The GastroPanel® examination arguments for general practitioners – for huge unmet need (indications)

- GastroPanel® should be the first-line diagnostic test for the diagnosis of *H. pylori* infection (5-80% of the world population) and in examination of all patients with dyspepsia (20-40% of the western population).
- GastroPanel® should be used to rule out or confirm the high acid output of reflux patients instead of the trial and error use of PPIs. The long term use of PPIs may increase the risk of stomach and oesophageal cancer.
- GastroPanel® markers Pepsinogen I, PGI, Pepsinogen II, PGII, Gastrin-17, G-17 and *H.pylori* antibodies reveal:
    - Subjects at increased risk for stomach- and oesophageal cancer, i.e. those with atrophic gastritis as well as those with a low risk of cancer; *H.pylori* infection with no atrophic gastritis in the antrum or corpus.
    - Early and reliable diagnosis of *H.pylori* infection and atrophic gastritis (AG) save costs and prevent many unnecessary diseases and deaths due to stomach and oesophageal cancer.
- GastroPanel® is also indicated for special target patients, especially patients with autoimmune diseases (usually more than one at the same time), including, e.g.:
    - patients with autoimmune thyroiditis who may have autoimmune atrophic gastritis (AAG, 18% of thyroiditis patients) in the corpus with related risks,
    - patients with type 1 diabetes who may have AAG and, e.g., also deficiency of B-12 vitamin (12% of diabetes patients) with related risks, patients with celiac disease who may have AAG with related risks, and
    - patients with rheumatoid arthritis who may have AAG with related risks.
- In patients with AG or AAG, absorption of vitamin B12 is reduced.
    - Due to vitamin B12 deficiency, there is an increased risk of depression, Alzheimer's disease, dementia and polyneuropathy. Consequently, all patients with depression, Alzheimer's disease, dementia and polyneuropathy should be examined by GastroPanel® to rule out or confirm those with AG or AAG in the corpus.
    - Due to vitamin B12 deficiency, increased homocysteine levels in the body may be related to:
        - Atherosclerosis – these patients should be examined by GastroPanel® to rule out or confirm AG or AAG with related risks
        - Heart attacks – these patients should be examined by GastroPanel® to rule out or confirm AG or AAG with related risks
        - Strokes – these patients should be examined by Gastro Panel® to rule out or confirm AG or AAG with related risks.
- Furthermore, in patients with AG or AAG of the corpus, absorption of Ca, Fe, Mg and Zn is reduced. Low Ca is associated with osteoporosis, while low serum Fe results in anemia.
- All patients with osteoporosis (or otherwise prone to bone fractures) and anemia patients should be examined by GastroPanel® to rule out or confirm AG or AAG.
- The risk of pneumonia and in senior citizens also the risk of fatal intestinal infections (such as giardiasis, malaria, *Clostridium difficile* and *E. coli* EHEC) may increase significantly due to an anacidic stomach caused by AG, AAG or PPI's. All patients with such infections should be examined by GastroPanel® for detection of AG and AAG.
- All subjects diagnosed with AG and AAG in GastroPanel® need gastroscopy in order to confirm diagnosis and treatment.

Additional information

Please note that the urea breath test (UBT), stool antigen test or *H.pylori* antibody test alone do not reveal AG or AAG. Furthermore, UBT and stool antigen test give 50% of false negative results in *H. pylori* patients, particularly if the patient has AG due to *H. pylori* infection or AAG, bleeding peptic ulcer, chronic use of PPIs, antibiotic treatment or MALT lymphoma due to *H. pylori* infection. GastroPanel® is also suitable for screening of healthy (asymptomatic) people, because *H. pylori* infection, AG or AAG with related risks are often asymptomatic.

Biohit emphasizes that the GastroPanel blood test is not a test for stomach cancer, but instead a test that detects the subjects at risk for gastric cancer. GastroPanel test finds with high precision, asymptomatic and *H. pylori* infection and gastric mucosal atrophy (atrophic gastritis), at an early stage when still amenable to curative treatment.

In 2012, group of 16 of the leading gastroenterologist from 12 different countries released a joint statement that the atrophic gastritis screening and detection by GastroPanel is a clearly justified (1). The same conclusion was reached by the widespread Maastrich IV recommendation, according to which the biomarker tests are recommended as part of the diagnosis and management strategy of *Helicobacter pylori* infection and atrophic gastritis (2).

In addition, a recent international conference held in Kyoto published recommendations that the use biomarkers included in GastroPanel is a very suitable method to replace the often unnecessary endoscopies for the diagnosis and screening of stomach diseases (3). Furthermore in 2012, 63 experts from 24 countries found that gastric mucosal atrophy (atrophic gastritis) may result in, among other things, gastric cancer, and therefore should be monitored at regular intervals (4). Finding atrophic gastritis requires gastric endoscopy and regular monitoring. Early detection and treatment of stomach cancer significantly improves the patient's prognosis. In current practice, gastric cancers are almost always diagnosed too late, because the current practice used in the diagnosis of *Helicobacter pylori* infection (^{13}C-urea breath test and stool antigen test) do not reliably find *Helicobacter pylori* infection.

GastroPanel blood test has been shown to be highly cost-effective. According to cost-efficiency model developed by Nordic Healthcare Group, organized GastroPanel screening of one single age group (50-year-old) for the risk of gastric cancer potentially saves more than EUR 60 million in the national healthcare costs in Finland. Worldwide, already millions of people have been tested with this test.

H. pylori infection or autoimmune atrophic gastritis (AG), with associated risk of gastric cancer and other sequels, or the level of acid output in the stomach, cannot be accurately diagnosed by the conventional tests used for diagnosis of dyspepsia and H. pylori infection, e.g. 13C-urea breath test (UBT) stool antigen test or -antibody test. In subject with AG, MALT-lymphoma or bleeding peptic ulcer, and in those on PPI medication or antibiotics, UBT or stool antigen test frequently give false negative results, and H. pylori infection (with all its risks) remains undetected (5 - 9).

GastroPanel is capable of diagnosing atrophic gastritis affecting either the corpus or antrum or both. As compared with gastroscopy, accurate diagnosis of atrophic gastritis is not always possible in a few small biopsy specimens representing only a minimal sample of the adult gastric mucosal area. In addition, the mucosal atrophy (mild atrophy in particular) is a subjective diagnosis, with substantial inter-observer variation among pathologists. Similarly, the accuracy of gastroscopy is dependent on the experience and competence of the gastroscopist. GastroPanel is devoid of these shortcomings, because it is an automated ELISA-based laboratory assay. In fact, endoscopic biopsy histology is not a reliable gold standard (10), albeit currently used as such. As compared with serum biomarkers, its limitations in diagnostic accuracy should be kept in mind (11, 12).

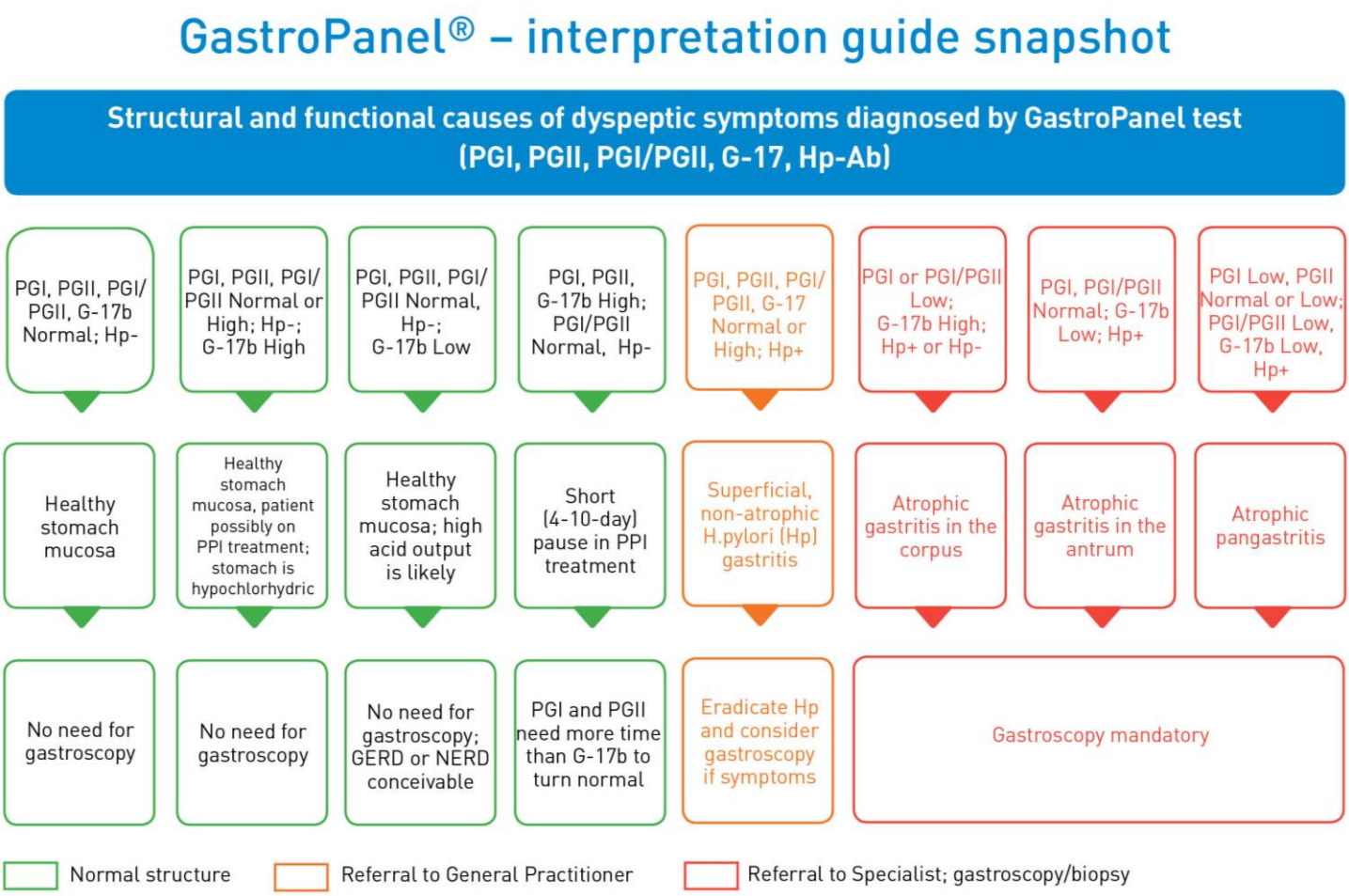
When performed by skillful gastroenterologists and pathologists, the agreement between GastroPanel and gastric biopsy histology is very good, exceeding 0.8 (the limit of almost perfect) by weighted kappa test (13).

Additional information

Importantly, the diagnosis of gastric atrophy is highly subjective without use of gastric biopsies, i.e., on the basis of gastroscopy alone (14). When GastroPanel indicates that gastric mucosa is healthy (no H. pylori infection and/or no atrophic gastritis), the clinical symptoms are often caused by functional dyspepsia or other functional disturbance without an organic disease in the gastric mucosa.

Additional information

The Gastropanel marker profiles



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