

Subjects with Compromised Stomach Health Need Special Attention: Serological Biomarker Panel (GastroPanel®) for Monitoring and Slow-Release L-Cysteine (Acetium® Capsule) for Protection of the Stomach

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Abstract

Objective: The two main causes of atrophic gastritis (AG) are *Helicobacter pylori* (HP) infection and autoimmune disease. Autoimmune AG (AAG) and pernicious anemia (PA) are common autoimmune disorders, present in up to 2% of the general population, whereas in patients with autoimmune thyroid disease (AITD) and type 1 diabetes mellitus (DM1), the prevalence of AAG is 3- to 5-fold. Both AG and AAG are associated with severe clinical sequels, including malabsorption of vitamin-B12, calcium, iron, magnesium, and zinc, with potential to develop irreversible neurological complications. HP-infection is the other causative agent of AG, and together, HP and AG/AAG are the two main risk factors of gastric cancer (GC).

It is currently possible to diagnose HP-infection and AG/AAG reliably by using serological testing with a panel of biomarkers (GastroPanel®, Biohit Oyj, Finland): pepsinogen I (PGI), pepsinogen II (PGII), gastrin-17 (G-17) and HP-antibodies. Severe AG/AAG leads to acid-free stomach colonized by HP and other bacteria, producing acetaldehyde (Group I human carcinogen; IARC). Together with other conditions leading to a) acid-free stomach (e.g. chronic users of PPI medication) or b) those exposing the subjects to increased concentrations of acetaldehyde (e.g. cigarette smokers, alcohol intake, ALDH2 enzyme mutations), these subjects are at high-risk for GC and esophageal cancer.

This communication introduces the dual concept how to i) monitor these high-risk patients with the non-invasive GastroPanel® test to disclose an early risk of GC, and how to ii) protect the stomach mucosa of these high-risk subjects by a novel formulation (Acetium® Capsule, Biohit Oyj) based on slow-release L-Cysteine, effectively eliminating carcinogenic acetaldehyde.

The results of GastroPanel® test are interpreted by a special software (GastroSoft®) identifying eight diagnostic marker profiles, recently described in this journal. During the past 10 years, GastroPanel® has gained increasing popularity and validated in both clinical and screening settings. Its excellent clinical performance was confirmed in two recent meta-analysis, and this test also has excellent longitudinal predictive values (NPV and PPV) for incident GC, as documented in two recent cohort studies.

Acetium® Capsule is a novel formulation of slow-release L-Cysteine, being a unique medical device designed to elimination of carcinogenic acetaldehyde in the stomach by forming a stable inactive compound: 2-methylthiazolidine carboxylic acid (MTCA). Regular use of Acetium® Capsule is indicated for all those who have acid-free stomach, irrespective of its cause. The efficacy of Acetium® Capsule in acetaldehyde elimination has been confirmed in placebo-controlled clinical trials where slow-release L-Cysteine effectively (by 60 - 80%) eliminated acetaldehyde in patients with acid-free stomach due to AG or PPI treatment, similarly in subjects with active or deficient ALDH2 enzyme. This capacity of slow-release L-Cysteine to eliminate acetaldehyde persisted for up to three hours after ingestion of two Acetium® Capsules.

With a rational use of these two medical devices, one can diagnose the gastric high-risk conditions and subsequently protect the stomach against exposure to carcinogenic acetaldehyde.

Keywords: GastroPanel; Atrophic Gastritis; Autoimmune Disease; AITD; DM1; Screening; Acetaldehyde; Carcinogenic; Gastric Cancer; Slow-Release L-Cysteine; Acetium Capsule; Stomach Protection

Introduction

Atrophic gastritis (AG) in the stomach body (corpus) leads to decreased gastric acid output and eventually acid-free stomach. The age-specific prevalence of AG increases with age, reaching 8% among people over 70 years of age [1,2]. In most cases, achlorhydria had remained undiagnosed, and 13% of them used PPI medication regularly [2,3]. AG develops by two different mechanisms: 1) as a result of *Helicobacter pylori* (HP) infection, and 2) through an autoimmune mechanism [4,5]. In 1994, IARC declared HP-infection as carcinogenic to humans [6]. Indeed, the two major risk factors of gastric cancer (GC) are HP-infection and AG. The relative risk of GC increases in parallel with increasing severity and extent of AG [7-12]. In addition to increasing the risk of GC, AG is associated with a wide variety of clinical sequels, many of which causing significant comorbidity particularly among elderly people [13,14]. As the output of gastric acid is reduced, absorption of vitamin-B12, iron, calcium, zinc and some drugs is impaired [13,14]. Iron deficiency anemia and osteoporosis are the clinically most relevant consequences of iron and calcium malabsorption, respectively [13].

Autoimmune atrophic gastritis (AAG) and pernicious anemia (PA) are common autoimmune diseases with respective prevalence of 2% and 0.15 - 1% in the general population, also increasing with age [15-17]. In patients with autoimmune thyroid disease (AITD) [18,19] and those with type 1 diabetes (DM1) [20,21], the prevalence is 3- to 5-fold increased. AAG is characterized by atrophy of the corpus and fundus, and the presence of circulating autoantibodies to the parietal cell (PCA) and to their secretory product, intrinsic factor (IF) [22]. Chronic auto-aggression to the gastric proton pump, H⁺/K⁺ATPase may result in decreased gastric acid secretion and hypergastrinemia [23,24].

Similar to HP-induced AG, also in a later stage of AAG, PA may result from vitamin-B12 deficiency, which is significantly more common among AITD patients than in non-AITD patients [25], and up to 10 times more common in DM1 patients than in non-diabetic subjects [21]. Finally, in up to 10% of these patients, AAG may predispose to gastric carcinoid tumors or CG [26-32]. PA is a growing health concern worldwide, particularly in aged populations, leading to protean clinical manifestations: peripheral neuropathy, depression and dementia, sometimes very quickly. Elevated concentrations of homocysteine (Hcy) can interfere with folic acid metabolism [33,34], increasing the risk of dementia, vascular calcification and cardiovascular obstructions. Early diagnosis of AG and AAG is very important to prevent and treat iron deficiency anemia, PA, and (pre)malignant gastric lesions: intestinal metaplasia (IM), enterochromaffin-like cell (ECL) hyperplasia, and dysplasia [21]. Similarly, an early detection of vitamin-B12 deficiency is the prerequisite for effective prevention of its potentially harmful clinical sequels [13,14,33,34].

The present communication is a brief introduction to a novel concept by which both an early detection of the subjects at risk is possible by using a panel of serum biomarkers (GastroPanel®), and protection of stomach mucosa can be instituted by eliminating carcinogenic acetaldehyde with a novel slow-release L-Cysteine formulation (Acetium® Capsule) [35].

Subjects at risk for AG/AAG and its clinical sequels

As already mentioned, there are special groups of people who are at increased risk of developing AG and acid-free stomach, with all potential clinical sequels [1-15,20-34]. After a protracted clinical course, the outcome is similar in AG caused by HP-infection and in AAG; an atrophic gastric mucosa is associated with achlorhydria (acid-free stomach). Apart from the well-known conditions of malabsorption [13,14,33,34], both AG and AAG predispose the subjects to increased risk of GC [26-32]. The carcinogenic agent in common to both AG/AAG and acid-free stomach is acetaldehyde, classified as Group I human carcinogen by IARC in 2009 [35,36]. Apart from HP itself which is capable of synthesizing acetaldehyde, the other bacteria colonizing in acid-free stomach, are an abundant source of this carcinogenic substance [37,38].

Elderly people

It is well known that the age-specific prevalence of AG increases with age, reaching 8% among people over 70 years [2]. To further assess the prevalence of AG and its clinical sequels in the Nordic region, we screened a cohort of 209 elderly people (mean age 82 years) by

GastroPanel® and active B12-vitamin test in Finland and Estonia [39]. The study subjects in Tampere (Finland) (n = 106) and Tartu (Estonia) (n = 103) differed in many characteristics of their medical history, including previously diagnosed B12-vitamin deficiency (p = 0.006). Also the clinical data recorded for GastroPanel® testing disclosed significantly less use of PPI medication and B12-vitamin supplementation in Tartu (p = 0.0001) [39]. GastroPanel® marker profile was significantly different (p = 0.0001), most markedly the HP-prevalence (52.4% vs 24.5%). AG in Finland (12.3%) and Estonia (15.6%) was not different (p = 0.494), but manifest B12-vitamin deficiency was more common in Tartu (23.3% vs. 3.8%) (p = 0.0001). Of all known complications of AG, only i) the diagnosed vitamin-B12 deficiency (OR = 3.5), and ii) diagnosed PA (OR = 9.4) were significantly associated with AG. These data implicate that in Estonia, the majority (92%) of B12-vitamin deficient cases remained undiagnosed as compared to Finland (23.5%) [39]. To prevent irreversible neurological complications, early diagnosis and adequate supplementation of vitamin-B12 deficiency are essential. This is best done by detecting the subjects at risk by targeted GastroPanel® screening, even years before the development of protean clinical manifestations [35,39,40-43].

Patients with autoimmune diseases (AITD, DM1)

In patients with AITD (Hashimoto thyroiditis and Grave's disease) and DM1, the prevalence of AAG/PA is increased up to 3- to 5-fold [15-23]. AAG is typically characterized by: 1) atrophy of the corpus and fundus; 2) autoantibodies to the parietal cell (PC) and to the intrinsic factor (IF); 3) achlorhydria; 4) iron deficiency anemia; 5) hypergastrinemia; 6) vitamin-B12 deficiency leading to PA; 7) in up to 10% of the patients, AAG may predispose to GC or carcinoid tumor [15-23].

The association of AITD and other autoimmune diseases was first suggested in the 1960's [19]. More recently, the association between AITD and PA has been included in type IIIb polyglandular autoimmune disease (PGA) [44]. A more systematic survey of the association of AITD with AAG was started more recently by Centanni, *et al* [18]. The authors confirmed that in the patients with AITD, one third had AAG, which was diagnosed also in young patients [18]. Subsequently, this close association has been confirmed in several large clinical studies.

Recently, Venerito, *et al*. [45] made a case-control study in AITD patients to evaluate the usefulness of serum pepsinogens in the identification of AGC, and to determine the relationship of HP with AAG, including 34 AITD patients and 30 controls. Serological AAG (defined by GastroPanel®) was present only in AITD patients (OR = 8.3, 95% CI = 1.9-36.2) [45]. The authors made several important conclusions: 1) sero-prevalence of AGC is high in patients with AITD; 2) testing of serum pepsinogens (GastroPanel®) should be included in the clinical assessment of these patients; 3) HP-infection is unlikely to be a principal factor in the pathogenesis of AAG in AITD patients; and 4) in AAG, mucosal atrophy can spread from the corpus (AGC) towards the antral mucosa (AGA) [45].

In the general population, there is an age-related increase in the prevalence of PCA, from 2.5% in the third decade to 12% in the eighth decade [15,16]. In DM1 patients, PCAs are found in 10 - 15% of the children and in 15 - 25% of the adults [18,19,46-50]. The respective prevalence of AAG and PA in the general population are 2% and 0.15 - 1% [16,17], compared with 5 - 10% and 2.6 - 4%, respectively, in DM1 patients [21]. Iron deficiency anemia is present in 20 - 40% of patients with AAG [2], whereas PA can be diagnosed in up to 15 - 25% of the patients [47]. Finally, gastric carcinoid tumors are observed in 4 - 9% of the patients with AAG/PA, which is 13 times more frequent than in controls [26]. Patients with AAG/PA also have a 3- to 6-fold increased risk of GC [26].

Patients with *Helicobacter pylori* infection

Although HP itself is not directly carcinogenic, AG is the single most potent risk factor of GC [50-52]. In some 5-10% of the patients with HP infection, mucosal atrophy is moderate or severe, and the risk of GC increases in parallel with the severity of AG. Compared with healthy stomach, the risk is 2 - 5 times higher in those with only chronic HP gastritis but up to 90-fold in patients with severe AG both in the corpus and antrum (pan-gastritis; AGpan) [50-53].

The main histological type of GC (intestinal type) develops in atrophic mucosa through various degrees of dysplasia (mild, moderate, severe), which are often accompanied by intestinal metaplasia (IM). This pathogenetic chain of events is known as the "Correa cascade"

[7,50]. It is estimated that HP-infection is involved in > 90% of all GC cases that develop through the “Correa cascade”, from intermediate steps of AG, IM, and dysplasia. It is important to recall that this cascade can often (but not invariably) be interrupted by appropriate early treatment of HP infection [12,50-53]. Based on the Updated Sydney System classification (USS), AG is classified by its topographic location in the stomach (antrum, corpus, or both) as AGA, AGC or AGpan, respectively [54]. In addition to being the key risk factor of GC, HP-infection also plays a causative role in the development of peptic ulcer disease [51,52]. Similarly, both AG and HP can be responsible for the symptoms known as dyspepsia; organic or functional [55]. Debate still continues on the value of systematic HP eradication in relieving the dyspeptic symptoms [52,53,55].

Subjects at risk for increased exposure to acetaldehyde

Apart from the above described well-defined groups of patients with AG/AAG, another group of people at increased risk of GC are all those who are subjected to increased exposure to carcinogenic acetaldehyde [36-38]. These can be roughly divided into two groups: 1) those with acid-free stomach irrespective of its cause, and 2) those exposed to acetaldehyde due to specific reasons.

Accordingly, acid-free stomach due to any cause predisposes the subject to acetaldehyde exposure and thus increases the risk of developing GC and esophageal cancer [36-38]. Accordingly, AG caused by HP infection is a common cause of acid-free stomach, and as an intermediate step in “Correa cascade”, is a high-risk lesion for GC. The same applies to AAG, which is another well-known variant of AG [15,21,23]. Acetaldehyde is the major carcinogenic substance in cigarette smoke, predisposing cigarette smokers to acetaldehyde exposure in oral cavity and the upper gastrointestinal tract [36-38,56,57]. The same applies to alcohol intake, because acetaldehyde is the first metabolite of alcohol, also produced in the stomach endogenously from ethanol, e.g. by local microbial or mucosal oxidation of ethanol to acetaldehyde [36-38,58,59].

Another well-known condition that increases the risk of acetaldehyde exposure is a point mutation in ALDH2-gene resulting in deficient activity of the main acetaldehyde-metabolizing mitochondrial enzyme (ALDH2), and provides conclusive evidence for the causal relationship between local acetaldehyde exposure and upper digestive tract cancer [60,61]. When drinking alcohol, the upper digestive tract mucosa of ALDH2-deficients is exposed via saliva to about 2-times and via gastric juice, up to 5-6 times higher acetaldehyde concentrations than in persons with active ALDH2-enzyme [59-62]. Parallel to increased local acetaldehyde exposure, the risk of ALDH2-deficient alcohol drinkers for oral, pharyngeal, esophageal and gastric cancer is many-fold compared to alcohol drinking ALDH2-actives. Thus, ALDH2-deficiency provides a unique human cancer model for local acetaldehyde exposure in the upper digestive tract.

Another risk group are the chronic users of PPI-medication. Two recently published meta-analyses suggest that the use of acid-suppressive (PPI) drugs is associated with an increased risk of GC [63,64]. A denominator in common with AG is acetaldehyde endogenously formed from ethanol [36-38,56-59]. An acid-free stomach secondary to either AG or PPI-treatment is colonized by oral microbes, which effectively produce acetaldehyde from ingested alcohol via their ADH enzymes. This was convincingly demonstrated in recent experiments, where PPI-treatment for 7 days significantly increased gastric juice acetaldehyde levels in ALDH2-active subjects after intra-gastric infusion of alcohol. However, the highest gastric juice acetaldehyde concentrations were measured in PPI-treated, ALDH2-deficient subjects [62].

Monitoring the patients with AG/AAG and/or increased exposure to acetaldehyde

So far, it has been argued whether patients with AG/AAG and PA should be placed under a surveillance program with regular gastroscopies, including multiple gastric biopsies [21,24]. The gastric carcinoids that occur in these patients generally do not pose a major threat to life, whereas the risk of developing GC is real. Nevertheless, in many clinics, endoscopy with biopsies remains the gold standard diagnostic tool, disclosing HP-infection, AG, IM or dysplasia, and their topography [50,51]. However, this invasive method is uncomfortable, distressing and quite costly, emphasizing the need for rapid, reliable and inexpensive non-invasive tests for screening and monitoring these patients [65,66].

As a response to this unmet need, a Finnish biotechnology company Biohit Oyj (Helsinki) developed a simple blood test based on a panel of serum pepsinogen I (PGI) and II (PGII), gastrin-17 (G-17) and HP IgG antibodies (IgG-HP) using ELISA technique (GastroPanel® test), proposed as the first-line diagnostic test for dyspeptic symptoms [12,67,68]. According to a recent meta-analysis, serum PGs are not suitable for screening of GC, but extremely useful for disclosing the patients at risk for GC [69], as also recommended by an authoritative international group of experts [70].

The GastroPanel® test is based on combined analysis of PG-I, PG-II, amidated G-17 and HP-antibodies, designed to give information on both the structure and function of the stomach mucosa. Most importantly, this panel gives accurate estimates of the capacity of the corpus and antrum mucosa to secrete acid and G-17, respectively, as well as of important gastric pathologies like inflammation, grade and topography of AG [1,12,67,68,71,72]. Normal plasma levels of these biomarkers indicate that the stomach mucosa has normal structure and function, whereas the abnormal levels are signs of a non-healthy stomach, reflecting the disturbances in the feedback mechanisms between the acid output, PGs and G-17 [40-43,73].

GastroPanel® test

GastroPanel® test has been on the market for several years by now, and during that time, it has been validated in clinical studies in Finland and elsewhere [2,74-76]. Due to the inherent characteristics of the natural history of AG/AAG, the PGI values (and PGI/PGII ratio) remain within normal range as long as AG of the corpus (AGC) is graded only mild. However, mild AG/AAG is a poorly reproducible diagnostic category even among experienced pathologists, and because of this, mild AG of the corpus should never be used as the study endpoint in calculating the performance indicators of the PGI, PGI/PGII, as repeatedly emphasized [75-77]. The correct way of calculating the predictive indicators of PGI and PGI/PGII ratio for AGC is to use the combined moderate/severe AG as the study endpoint [40,78].

To provide an unbiased estimate of the accumulated evidence, two recent meta-analysis have been performed with a systematic review of all studies published on GastroPanel® test since its introduction in the early 2000's [40,78]. Both meta-analyses gave practically similar results, despite some methodological differences. In both analyses, the pooled sensitivity of GastroPanel® in detection of AG exceeded 70% and the pooled specificity was close to 95% [40,78]. Both meta-analyses concluded that GastroPanel® test appears to be a reliable tool for the diagnosis of AG, and applicable for both screening of the subjects or populations at high-risk of GC [40,78].

Interpretation of the GastroPanel® results

GastroPanel® is optimized for use in context with the USS classification of gastritis [54]. Both the USS and the GastroSoft® software use five diagnostic categories to classify the biopsies and the GastroPanel® results, respectively. These include: 1) normal mucosa, 2) superficial (HP) gastritis, 3) AGA, 4) AGC, and 5) AG in both antrum and corpus (AGpan) [54]. In addition to these five categories related to stomach morphology, three other marker profiles are produced by GastroSoft®, being specific for functional disturbances with normal morphology [40-43].

The interpretation of GastroPanel® test with GastroSoft® has been described in detail in a series of recent reports [40-43,79-81]. These reviews include detailed descriptions of the eight diagnostic marker profiles that are possible to obtain with GastroPanel® test [40-43,79-81]. It is not feasible to re-iterate this discussion in the present communication, but suffice it to list these profiles: 1) normal profile; 2) high acid output; 3) low acid output due to proton pump inhibitor (PPI) medication; 4) superficial (non-atrophic), HP-associated gastritis, with 3 options (4.1. active HP-infection; 4.2. successful HP eradication; 4.3. failed HP eradication); 5) atrophic gastritis of the corpus (AGC); 6) atrophic gastritis of the antrum (AGA); 7) atrophic gastritis of the antrum and corpus (AGpan); and 8) panel profile in context of PPI medication. For details, the reader is being referred to the recent communications [40-43,79-81].

Acetium® Capsule for protection of stomach in high-risk subjects

The carcinogenic agent in common to both HP and AG/AAG is acetaldehyde, determined as Group I human carcinogen by IARC in 2009 [36]. Apart from HP itself which is capable of synthesizing acetaldehyde, the other bacteria colonizing in acid-free stomach of patients

with AG, are an abundant source of this carcinogenic substance. Acid-free stomach due to any cause predisposes the subject to acetaldehyde exposure and thus increases the risk of developing GC and esophageal cancer [36-38]. The special groups of patients at increased risk of the carcinogenic exposure to acetaldehyde are those listed above (section 3). These high-risk subjects should be closely monitored for the eventual development of GC precursor lesions (AG, IM) by GastroPanel® and/or gastroscopy [35]. Preferably, these patients should also be instituted on regular stomach protection by Acetium® Capsules, as recently described in detail in this journal [35]. The theoretical basis and rationale for this practice are summarized here only in brief to avoid re-iterating all the details [35].

Acetium Capsule effectively eliminates acetaldehyde in the stomach

L-Cysteine is a non-essential amino acid, which was shown (in 1975) to be capable of eliminating the toxicity of acetaldehyde by reacting covalently with it to form a stable 2-methylthiazolidine-4-carboxylic acid (MTCA) [82]. This binding results in inactivation of the reactive aldehyde group. MTCA is a stable and inert compound that is eliminated from the body mainly through feces. This principle was used by Biohit in its recent innovation of Acetium® Capsule, which contains 100 mg L-Cysteine. The novelty of this new formulation of slow-release L-Cysteine is based on the local elimination of carcinogenic acetaldehyde in the stomach [35]. After the proof-of-concept experiments in the laboratory, the efficacy of this novel Acetium® formulation has been conclusively demonstrated in three carefully controlled clinical studies in Finland [59], Sweden [83], and Japan [62].

Elimination of acetaldehyde in subjects with acid-free stomach

In a placebo-controlled study, slow-release L-Cysteine capsules effectively eliminated ethanol-derived acetaldehyde in the gastric juice of patients with AGC [59]. Seven volunteers with acid-free AGC were given either slow-release L-Cysteine or placebo capsules in a double-blinded randomized trial. Five-milliliter samples of gastric contents were aspirated at 5-minute intervals [59]. During the follow-up, the mean acetaldehyde level in gastric juice was 2.6-times higher with placebo than with L-Cysteine ($p = 0.005$) [59]. These results confirm that Acetium® Capsule effectively decrease acetaldehyde concentration in an acid-free stomach during alcohol exposure.

Elimination of acetaldehyde in patients with AG

In the second study, patients with AGC received 15% ethanol (0.3 g/kg) through a nasogastric tube on two separate days, accompanied by randomized Acetium® Capsule (2 x 100 mg) or placebo [83]. After intra-gastric infusion of 15% ethanol with placebo, gastric juice acetaldehyde levels increased from zero to mean 36 μM (peak) and remained elevated up to 100 min. Slow-release L-Cysteine decreased gastric juice acetaldehyde by a mean of 68% (max. 87% at 60 min) and the decline persisted for up to two hours [83]. Furthermore, the peak gastric juice MTCA level (233 μM) was seen at 80 min and gastric juice MTCA remained elevated for up to 180 min (36 μM at 180 min). These data implicate that i) an exposure of gastric mucosa to acetaldehyde is decreased by a mean of 68% ($p < 0.0001$) with slow-release L-Cysteine capsule, and this effect continues for at least two hours; ii) MTCA remains stable in the gastric juice for up to three hours [83].

Acetaldehyde elimination, ALDH2 mutation and PPI-treatment

The third clinical trial confirmed that slow-release Acetium® Capsule (2 x 100 mg) reduced markedly the gastric juice acetaldehyde levels also in PPI-treated individuals with either active or deficient ALDH2 enzyme [62]. This study was conducted in Japan, showing that acetaldehyde eliminating capacity of slow-release L-Cysteine was effective even after a moderate dose (0.5 g/kg, 3 doses) of alcohol and persisted for 2 hours. This acetaldehyde-eliminating effect of L-Cysteine persisted almost 120 minutes. Quantitatively, L-Cysteine resulted in a mean of 67% (3-fold) decrease in gastric juice acetaldehyde ($p = 0.001$) [62].

Conclusions

GastroPanel® biomarker test for monitoring the high-risk subjects

GastroPanel® is the first non-invasive diagnostic tool based on physiology of three stomach-specific biomarkers of both health and disease. The panel also includes testing for HP-infection, the key etiological factor in pathogenesis of peptic ulcer and GC. In the current test

version (the Unified GastroPanel®), all 4 biomarkers are being processed under similar conditions. GastroPanel® will be soon available in the quick test version (GPQT) as well, particularly suitable for the POC (point-of-care) testing at doctors' offices with restricted facilities for blood sample processing. In GastroPanel®, the HP antibody measurement is complemented by the other three biomarkers (PGI, PGII, G-17) which are sensitive indicators of mucosal inflammation. This 4-marker panel makes GastroPanel® the most comprehensive HP test, devoid of the known shortcomings (false negative and false positive results) of the conventional HP tests [79-81].

The non-invasive GastroPanel® test is particularly suitable for monitoring of i) all patients at increased risk of GC, irrespective whether due to AG caused by HP-infection or autoimmune disease, as well as of ii) all those who are subjected to increased exposure to carcinogenic acetaldehyde due to specific reasons (acid-free stomach, smokers, alcohol intake, ALDH2 mutation, chronic PPI users) [35].

Acetium® Capsule for protection of the stomach against carcinogenic acetaldehyde

Acetium® Capsule is a unique medical device designed for elimination of carcinogenic acetaldehyde in the stomach. A regular use of this device is indicated for all those who have acid-free stomach, irrespective of its cause. This formulation effectively protects the stomach against the exposure to acetaldehyde, classified as Group I carcinogen by IARC [36]. The efficacy of Acetium® Capsule in acetaldehyde elimination has been documented in three placebo-controlled clinical trials [59,63,83]. In all studies, slow-release L-Cysteine effectively (by 60 - 80%) eliminated acetaldehyde in patients with acid-free stomach caused by either AG or PPI-treatment, similarly in individuals with active or deficient ALDH2 enzyme. This capacity to eliminate acetaldehyde persisted for up to three hours after ingestion of two Acetium® Capsules [59,62,83].

It is recommended that this special slow-release L-Cysteine formulation, devoid of any systemic side effects, should be used for long-term protection of the stomach mucosa against the effects of acetaldehyde by all those who are over-exposed to this carcinogenic substance because of acid-free stomach [35,36-38,59,62,83].

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