Non-invasive assessment of gastric secretory function in centenarians

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Abstract

Gastric acid secretion is believed to decrease in the aging stomach, but the number of elderly patients on proton pump inhibitor (PPI) therapy is increasing.

The aim was to assess gastric function by means of serology (PGI, PGII, G17 and IgG antibodies against *Helicobacter pylori*) in centenarians.

Twenty-five centenarians (2 males, 23 females, mean age 101.3 years, range 100-106 years) underwent to serological gastric markers assessment by means of Gastropanel®. Patients with laboratory signs of severe oxyntic gastric atrophy (OGA) underwent gastroscopy with biopsy samples.

Twelve patients (48.0%) had serological values according to normal gastric secretion; 3 patients (12%) had serological values according to severe OGA, confirmed by histology; 21 patients (84.0%) had serological values according to *H. pylori* infection.

Acid secretion seems to be preserved in a large part of centenarians. Serological markers may be helpful to identify patients affected by OGA, in whom the administration of PPI is inappropriate.

Introduction

Ageing is a dynamic process and population ageing is a major global demographic trend, which will intensify during the twenty first century. In the world, the number of centenarians is growing even faster: Japan, Germany and Italy are the countries with the highest median ages in the world.[1]

Gastric acid secretion is claimed to decrease lasting the years.[2] Up to now, the physiological stomach function in subjects overcome 100 years old is unknown. Studies specifically examining the effect of age upon the stomach are limited and frequently uncontrolled for the high prevalence of *Helicobacter pylori* (*H. pylori*) in this age group. This due to the significant role of *H. pylori* infection in the pathogenesis of oxyntic gastric atrophy (OGA), that is also frequently characterized by hypergastrinemia because of the interruption of the normal feedback for the release of gastrin.[3]

In the third millennium, characterized by a strong decrease of peptic ulcer, the interest toward the knowledge of gastric secretory pattern in elder population is related with the fact that an increasing number of very old people is currently taking proton-pump-inhibitors (PPIs) as a consequence of an important comorbidity and the need to *gastroprotect* gastric mucosa from non-steroidal-anti-inflammatory drugs (NSAIDs) and other potentially dangerous drugs administered daily. Awareness of evidence-based guidelines and targeted medicine reconciliation strategies are essential for cost-effective and safe use of these medications.[4]

The gold standard to measure acid secretion is represented by titration of acid pH after collection of gastric juice by a nasogastric tube and stimulation by pentagastrin, resulting in the determination of two parameters, named B.A.O. (basal acid output) and M.A.O. (maximal acid output).[5] Currently, this diagnostic method is restricted to research setting, so in clinical practice in the past 15 years other surrogate tools were proposed. Although endoscopic findings may be predictive of gastric acid secretion status, non-invasive tool as the determination of serological levels of pepsinogens and gastrin 17 maybe more useful.[6] Gastropanel® (BIOHIT Oyj, Helsinki, Finland), a combination of G-17 (gastrin-17), PG-I (pepsinogen-I), PG-II (pepsinogen-II) and *Helicobacter pylori* antibodies of IgG class, has been proposed as a simple non-invasive serological test to select patients with a high risk of harboring AG, who deserve endoscopic examination.[7] This method can effectively describe MAO, since has been already shown that PGI levels significantly correlate with MAO.[8]

Current literature data on gastric acid secretion in centenarian subjects are lacking. Our aim was to assess gastric secretory function by means of Gastropanel® in order to both assess gastric secretory function as non-invasive tool and the appropriateness of PPI treatment in a cohort of over 100 years old subjects.

Materials and Methods

We prospectively enrolled 25 asymptomatic patients over 100 years old, living in different retirement homes located in North Italy, from 1st September to 31st December 2015. In all of them, autoimmune atrophic gastritis was previously excluded by means of APCA (anti-parietal cells antibodies) assessment.

PPIs, NSAIDs, aspirin, clopidogrel, and warfarin use, as well as previous GI bleeding, were recorded. When PPI therapy was

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ongoing, it was stopped 15 days before blood collection for gastric function and temporary substituted with magaldrate.

All patients underwent Gastropanel® blood collection after an overnight fasting. Normal values for each parameter assessed were the follows: PGI: 30-65 µg/L; PGII: 3-15 µg/L; PGI-PGI: 3-20; G-17 <10 pmol/L; IgG against *H. pylori* <30 EIU.

PGI <30 µg/L, PGII <3 µg/L, PGI/PGII<3, and G17 >30 pmol/L were considered suggestive of moderate to severe OGA: detection of this result represented an indication to perform an upper digestive endoscopy in people otherwise asymptomatic for gastric discomfort. Upper GI endoscopy was also performed in any case suspected for gastric pathology.

Gastric biopsy samples (two in the fundus, two in the antrum and one at the angular incisure) were taken, and histopathology was graduated according to OLGA classification.[8]

All patients or their tutorial gave written informed consent to take part to this study.

Results

Table 1 describes the clinical and the biochemical characteristic of the enrolled population.

Gastropanel® provided the following results: i) 12 out of 25 patients (48.0%) had serological values according to normal gastric secretion: 10 patients (40%) had PGI, PGII, PGI/PGII ratio and G-17 within the range of normality; 2 patients (8%) had all parameters significantly increased (PGI >65 µg/L, PGI >15 µg/L, G-17 >3 pmol/L). These last patients were treated with PPI until 15 days before blood collection: since PPI may cause significant increase of all parameters investigated,[6,9] both of patients were considered as normal; ii) 3 patients (12%) had serological values according to severe OGA (PGI<30 µg/L, PGII<3 µg/L, PGI/PGII<3, and G17 >30 pmol/L). None of them took clopidogrel or warfarin, and underwent to upper GI endoscopy with biopsy: histopathology confirmed that all patients having serological values according to OGA had OGA (two having OLGA III and one having OLGA IV staging); iii) 10 patients had serological values according to antral gastritis, nine of them with atrophy, that do not influence gastric secretion.[6,10]

Twenty-one out of 25 patients (84.0%) had serological values according to *H. pylori* infection (IgG against *H. pylori* >30 EIU). Due to the age of our population, no further investigation on current *H. pylori*-status were performed.

Discussion

Progressive reduction in hydrogen ion output is claimed to occur with increasing age; in truth, the studies on this topic show contrasting results.

By using the gold standard method, two pivotal studies in United Kingdom[11] and Finland[12] found gastric HCl output unchanged with age in subjects with normal gastric histology. More recently, a study performed by using a mathematical model, demonstrated that age has an increasing effect on acid secretion.

About histo-pathology, studies found the number of parietal cells increasing with age and the number of mucous cells reduced in elderly subjects;[13] the existence of intact molecular biological basis for acid secretion in healthy elderly individuals;[14] a decreased gastric secretions and impairment of the mucous-bicarbonate barrier in elderly.[15]

Conflicting results arose also regarding acid secretion in elderly subjects affected by peptic ulcer. In summary, even in the elderly, secretory patterns remain well defined in gastric ulcer patients, who generally result as being acid hyposecretors with an increased susceptibility of the gastric mucosa to damage, whereas duodenal subjects result as being hypersecretors even in geriatric age.[14]

The aim to explore physiology of gastric secretion in very old subjects (over 100 years old, so called *centenarians*), up to now lacking, permits to asses a very important function of upper GI tract directly related with digestive process and indirectly with other aspects like the influence of gut microbiota. Moreover, it focuses on the large use of PPI for *gastroprotection*, being the centenarians affected by possible important comorbidities and related therapies. Recently, Kelly *et al*. underlined how inappropriate PPI therapy is still a problem in hospitals, though it appears to be at a lower level compared with previous studies.[16,17]

The present study clearly demonstrated that in over 100 years subjects the gastric acid production is preserved in 80% of the studied population. This results is quite dif-

Table 1. Clinical and biochemical features of the study group.

Characteristics	
Age, years, median (range)	101 (100-106)
Female sex	23 (92.0)
Co-morbidities	
None	4 (16.0)
Cardiovascular	9 (36.0)
Metabolic	9 (36.0)
Rheumatic	4 (16.0)
Parkinson	15 (60.0)
Therapy	
Acetil-salicylic acid	25 (100.0)
Clopidogrel	-
Warfarin	-
Previous upper gastrointestinal bleeding	-
Pepsinogen I, ng/mL	
<30	3 (12.0)
30-160	5 (20.0)
>160	17 (68.0)
Pepsinogen II, ng/mL	182 (9-749)
<3	-
3-15	1 (4.0)
>15	24 (96.0)
Pepsinogen I/Pepsinogen II	
<3	12 (48.0)
3-20	13 (52.0)
>20	-
sG-17, pmol/L	238 (1-2044)
<3	5 (20.0)
3-30	3 (12.0)
>30	17 (68.0)
Presence of *Helicobacter pylori* antibodies, >30 EIU	21 (84.0)

Values are expressed as number (percentage) of patients unless otherwise specified. EIU, enzyme immune unit.

fering from that previously thought, and why this occurs is unknown. One hypothesis is that longevity guarantees long-lasting normal gastric function, as well as guarantees long-lasting heart or lung or kidney function. In this way, Italian population may be a typical example of this population, since it represents the second older population in the world. These results suggest that use of PPI in those patients is appropriate when GERD symptoms are present or drugs potentially dangerous for the integrity of gastric mucosa are administered. On the other hand, the determination of serum levels of pepsinogens and gastrin 17 singled out also people with the lab phenotype of OGA, characterized by hypoacidity, in which PPI administration is strongly not appropriate. The determination of serum pepsinogens and gastrin 17 represents therefore an useful non-invasive tool to collect this critical information in such particular subgroup of patients, the centenarians, in whom upper GI endoscopy may be not always appropriate/feasible.

This study suffers from two main limits. First, the low sample size of patients enrolled. However, despite the well know longevity of the Italian people, is very difficult to enroll a large population of centenarians. Second, the absence of control groups. In particular, these results could suggest to use the same strategy for similar people. In this way, a prospective study comparing gastric function in several classes of elderly, *i.e.* in people over 70, over 80, and over 90 years, by using Gastropanel®, is warranted.

Conclusions

In conclusion, this study found that the physiological levels of acid secretion assessed by Gastropanel® persisted in about 50% of subjects over 100 years old. This blood test seems to be also able to identify patients affected by severe OGA characterized by low levels of acid production, in which the administration of PPI is inappropriate.

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