GERD IN THE ELDERLY: AN ENDOSCOPIC EXPERIENCE

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[Titolo in italiano]

ABSTRACT

Introduction*: in elderly Gastro-Esophageal Reflux Disease (GERD) is very common among gastrointestinal diseases, unusually more severe than young patients frameworks, and frequently under-diagnosed. Here we conducted a retrospective study of our endoscopic series in order to assess the prevalence and clinical characteristics of GERD in the elderly.*

Materials and methods*: we retrospectively studied patients underwent esophagogastroduodenoscopy (EGD) with symptoms referred to the upper gastrointestinal tract (heartburn, chest pain, dysphagia, regurgitation, and dyspepsia) and/or anemia of unknown origin.*

Results*: 3663 patients with GERD-related symptoms/signs underwent EGD, 2594 aged <65 years old (GROUP A), with male/female (M/F) ratio 1.73 (1645 males vs. 949 females), and 1069 aged ≥ 65 years old (GROUP B), with M/F ratio 1.34 (613 males vs. 456 females). Esophagitis diagnosis was made on 2549 patients, 1815 were aged <65 years old and 734 aged ≥ 65 years old. Elderly showed more frequently severe esophagitis (6% vs. 11%), association with hiatal hernia (45% vs. 74%) and duodenal ulcer (4% vs. 20%), dysphagia (2% vs. 6%), dyspepsia (7% vs. 14%) and anemia (1% vs. 6%) compared to GROUP A, while among the younger patients regurgitation (33% vs. 24%) and chest pain (16% vs. 11%) were more frequent compared to GROUP B. Heartburn had a frequency similar between the two groups (39% vs. 40%). As regards the effectiveness of acute therapy and long-term treatment, PPIs showed the highest rates of healing and remission of symptoms, respectively, without differences between elderly and younger patients.*

Discussion*: our results confirmed literature data, and underlined the importance to consider this disease in these patients, at high risk because of comorbidities and polypharmacy. After EGD, severe esophagitis was found more frequently in elderly, as well as the association with other diseases, such as hiatal hernia or duodenal ulcer.*

Key words: *Gastro-esophageal reflux disease, Proton-pump inhibitors, Elderly.*

Received *January 20, 2013;* ***Accepted*** *January 25, 2013*

Introduction

Aging of population is an important social, economic and political issue. It has been estimated that in 2030, approximately 21% of the population will be aged over 65 years; thus will further increase the number of geriatric patients and health demand[1].

In elderly, Gastro-Esophageal Reflux Disease (GERD) is very common among gastrointestinal diseases, unusually more severe than young patients frameworks, and frequently under-diagnosed because of the chronic PPI therapy prescribed as protection for iatrogenic drug damages, such as antiplatelet and NSAIDs[2,3].

GERD is a consequence of pathological reflux of gastric and/or duodenal contents in the esophagus, which can induce a spectrum of clinical conditions, ranging from simple symptomatic reflux to esophageal mucosal injury (esophagitis) and even complications, such as stenosis and Barrett's esophagus[4-6].

The study of the different GERD framework in elderly is complicated by several factors. Esophageal sensitivity seems to decrease with aging and elderly patients usually underestimate and tolerate symptoms that the younger ones do not. The coexistence of other diseases, such as chronic obstructive pulmonary disease and coronary heart disease, may be confused or exacerbated by GERD[7].

Furthermore, a long-term therapy with drugs, such as calcium-antagonists and nitrates, facilitates the GERD onset, reducing lower esophageal sphincter (LES) muscle tone and consequently determining incontinence. Cholecystectomy is another possible risk factor for a constant duodenal-gastric reflux, which can easily spread to the esophagus. Generally, in elderly, most common symptoms are regurgitation, dysphagia, chest pain and respiratory symptoms rather than heartburn[8].

Here we reported a retrospective study of our endoscopic series in order to assess the prevalence and clinical characteristics of GERD in the elderly.

Materials and methods

We conducted a retrospective study of patients (both outpatient and inpatients), who underwent EGD, from January 2001 to December 2010, at our Gastroenterology and Digestive Endoscopy Service, inside the Department of Geriatrics of University Hospital of Palermo.

The study population was divided into two groups, respectively aged <65 years old (GROUP A) and ≥ 65 years old (GROUP B), who complained about symptoms referable to the upper gastrointestinal tract (heartburn, chest pain, dysphagia, regurgitation, and dyspepsia) and/or anemia of unknown origin. The endoscopic diagnosis of esophagitis was made according to Los Angeles classification. It was also evaluated the pharmacological therapy assigned to included patients, both in acute and maintenance phase: antacids were excluded from the evaluation, as often self-prescribed and not objectively quantifiable.

The study was conducted in accordance with the principles of the Declaration of Helsinki (World Medical Association Declaration of Helsinki 1989) and Good Clinical Practice (European Agency for the Evaluation of Medicinal Products 2002). The Ethics Committee of the University Hospital of Palermo approved the study and all patients gave their informed consent to participate.

Results

In the study period, 11.758 outpatient and inpatient visits were carried out, followed by 9457 EGDs. Considering exclusively the subjects who underwent EGD, the patients (M/F) ratio was 1.7 (5968 males vs. 3489 females), aged between 12 and 94 years old (mean age 50.8 ± 16.4 years old). Of these patients, 6308 were aged <65 years old with M/F ratio 2.66 (4583 males vs. 1725 females) and 3149 were aged ≥ 65 years old with M/F ratio 2.67 (2292 males vs. 857 females).

The number of patients subjected to EGD with GERD-related symptoms and/or signs were 3663 (almost one third of the total), of whom 2594 aged <65 years old (GROUP A), with M/F ratio 1.73 (1645 males vs. 949 females), and 1069 aged ≥ 65 years old (GROUP B), with M/F ratio 1.34 (613 males vs. 456 females).

Esophagitis diagnosis was made on 2549 patients, while 1114 did not have esophageal injury, only reporting symptoms. Among the patients with esophagitis, 1815 were aged <65 years old with M/F ratio 1.55 (1103 males vs. 712 females) and 734 aged ≥ 65 years old M/F ratio 1.58 (450 males vs. 284 females).

Figure 1 shows the frequency of esophagitis and its different degrees in the 3663 patients underwent EGD with GERD-related symptoms/sings. In GROUP A, GERD symptoms/signs in absence of injury were found more frequently (41% vs. 29%), while esophagitis severe grade (III-V) were rarely observed (6% vs. 11%), compared to the GROUP B.

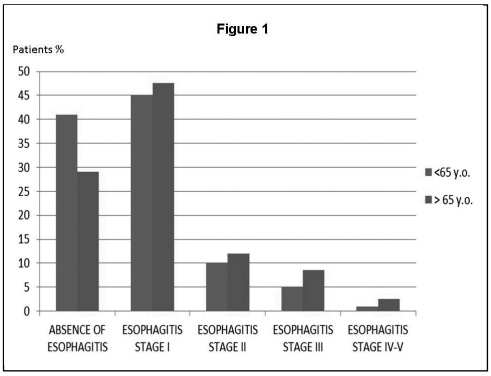

Figure 1: esophagitis frequency.

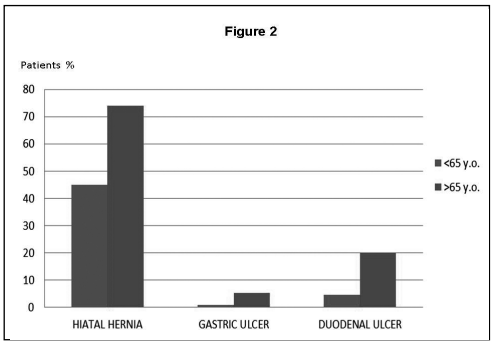

Figure 2: association of esophagitis with hiatal hernia, gastric ulcer and duodenal ulcer.

It was also evaluated the association with hiatal hernia and gastric and/or duodenal ulcer (Figure 2). The hiatal hernia was more common in GROUP B (45% vs. 74%), as well as duodenal ulcer (4% vs. 20%).

As regards symptoms (Figure 3) elderly showed more frequently dysphagia (2% vs. 6%), dyspepsia (7% vs. 14%) and anemia (1% vs. 6%) compared to GROUP A, while among the younger patients regurgitation (33% vs. 24%) and chest pain (16% vs. 11%) were more frequent compared to GROUP B. Heartburn had a frequency similar between the two groups (39% vs. 40%).

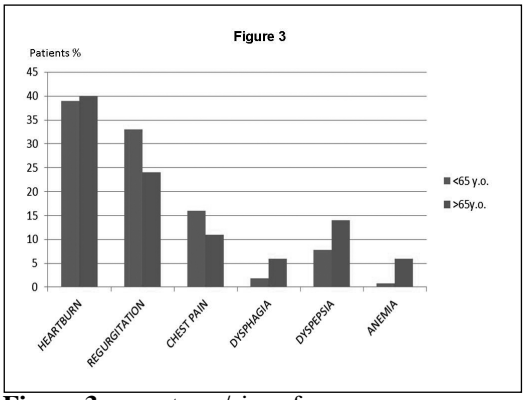

Figure 3: symptoms/signs frequency.

An acute therapy was carried out by 2439 patients (96% of the 2549 patients with esophagitis), it was differentiated in relation to the molecules used (cisapride, H2-receptor antagonists, PPIs, and drugs association) and the results were comparable to those referred in the current literature, as shown in Figure 4. The long-term treatment (3-48 months), followed by 1507 patients (59% of the 2549 patients with esophagitis) is shown in Figure 5, also comparable with the results currently available in the literature. Non significant differences where found between elderly and younger patients as regards healing and remission rates (data not shown).

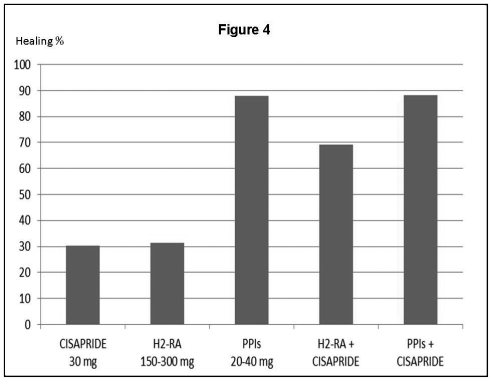

Figure 4: GERD short-term therapy expressed as healing rate.

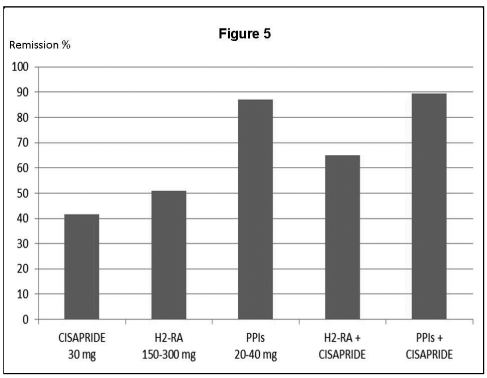

Figure 5: GERD long-term therapy expressed as remission rate.

Discussion

In our series, comparing elderly and younger patients, with GERD-related symptoms/sings, underwent EGD, severe esophagitis was found more frequently in the elderly, as well as the association with other gastroduodenal diseases, such as hiatal hernia or duodenal ulcer. Comparison of GERD-related symptoms/signs between the groups showed that dysphagia, dyspepsia and anemia were more represented in the elderly, while in the younger group regurgitation and chest pain had a higher frequency; heartburn had a similar rate in both groups. As regards the effectiveness of acute therapy and long-term treatment, PPIs showed the highest rates of healing and remission of symptoms, respectively, in both groups, without significant differences.

General population complains of monthly heartburn between 21% and 36%, and between 5% and 7% of daily one. In a recent study, performed on 559 elderly patients, symptoms were reported at least once a month in 54% of men and 66% of women, while 8% of males and 15% of females had symptoms suggestive of gastro-esophageal reflux at least once a week. In addition to reflux typical symptoms, chest pain, dyspepsia, and respiratory symptoms were associated too (6).

Another study showed that 32-43% of patients with GERD did not present endoscopic lesions, while 50-60% of patients with typical symptoms and 60% of patients with atypical symptoms had an endoscopic diagnosis of esophagitis. Respiratory symptoms were reported in 57% of patients with esophagitis compared with 33% of those without this last one[9].

Moreover, in elderly, is frequent the finding of hiatal hernia, a GERD closely related condition. As

well as GERD prevalence increases with age, becoming particularly high after 50 years old, so the incidence increases significantly (mean age 55 years old). Even esophagitis severity increases significantly with aging, as reported in an endoscopic study in which 75% of patients with esophagitis was represented by "sixties". In this regard, a recent US study has confirmed this trend showing an increase in hospital admissions for esophagitis, esophageal ulcer and stenosis[8].

GERD complications are more common among the elderly. In particular, esophageal stenosis and Barrett's esophagus reach their maximum frequency between 50 and 70 years old. Prevalence of esophageal stenosis in patients with esophagitis ranges between 10% and 20%, while incidence is estimated around 8%. Barrett's esophagus, characterized by the presence of columnar epithelium replacing normal squamous epithelium in the third lower esophageal, is considered a pre-neoplastic lesion, which neoplastic transformation risk is from 30 to 125 times higher than the normal epithelium; adenocarcinoma onset within a Barrett's esophagus has a prevalence ranging between 8% and 15%, with an average age around 60 years old[5,10].

However, reduction or disappearance of symptoms does not always coincide with reflux disease disappearance: patients tested 17-32 years after diagnosis, treated with medical therapy, have shown that, though 75% had symptoms improvement, about 66% showed pathological reflux signs (pH-metry positive, esophagitis, and Barrett's esophagus)[11,12]. Most of the patients with a durable remission, changed lifestyle, took antacids as needed, but most of all cycles of 4-8 weeks with anti-secretory drugs, while in others was necessary a continuous control by means of medication and in rare cases, non-responders to therapy with high proton pump inhibitors (PPIs) dose, an anti-reflux surgery[13].

In elderly patients, endoscopy must be considered a first-level exam, especially if there are alarm symptoms (e.g. weight loss, dysphagia, anemia, etc.). EGD execution is necessary because symptomatology is often poorly represented and neoplastic diseases of esophagus and/or of gastric fundus, which initially may provoke symptoms similar to those of GERD, must be excluded[14-16].

Monitoring esophageal pH can be useful for GERD diagnosis and therapy, in particular for non-esophageal manifestations and non-cardiac chest pain. Is a valid method, fairly widespread, to quantify esophageal acid exposure. Calculate the percentage of total time spent below pH values of 4.0 in 24 hours (optimal discriminant value) and the association with symptoms is essential to evaluate atypical or sporadic disorders[17,18].

Gastric scintigraphy has become the gold standard for the study of gastric emptying, however it is not quite common or standardized. The lack of standardization and the probable heterogeneity of populations studied, justify the different results reported by literature, although the majority of studies seems to show a slow emptying in the elderly[9].

Treatment goals are, in the attack phase, symptoms resolution and healing of injuries resulting from changes in lifestyle, not always effective and practicable, and from drug therapy. Another objective is to consolidate the results obtained maintaining remission of symptoms, healing of injuries, and also preventing the complications[19].

Antacids and mucous-protectors, such as sucralfate and alginic acid, are usually taken as self-medication. In literature, there are some comparative studies between alginate-antacids and placebo, which show a limited role in controlling symptoms for alginic acid[2,3,20].

H2-antagonists in the elderly may cause various dose-dependent side effects. The most important is central nervous system involvement with a variety of symptoms, including: delirium, confusion, hallucinations, depression, decreased libido and Parkinsonism. The incidence of these effects increases particularly in patients with renal failure, so these medicaments should be abandoned[2,3].

The first PPI introduced in clinical practice was omeprazole, to which was subsequently added lansoprazole and pantoprazole, molecules with a faster activation, with a greater selectivity for the acid compartment of the gastric parietal cell and, above all, with a less interaction with the hepatic oxidative enzyme systems, connected to cytochrome P450, which make them more manageable, and secure specially in elderly patients or in those with decreased hepatic and renal function, without adjusting the dose and, above all, with a lower risk of drug interactions[21]. The last molecule of PPIs group, esomeprazole, isomeric omeprazole derivative, showed a more powerful anti-secretory action with daily doses of 40 mg, which produced a significant benefit in the treatment of erosive esophagitis and in pain chest, with healing rates slightly higher than with other PPIs[2,22].

Prokinetics most frequently used are domperidone (anti-dopaminergic action), metoclopramide

(central dopaminergic antagonist), and levosulpiride, which due to the several side effects has limited use[23].

GERD natural history shows that up to 80% of patients have a relapse after acute healing, usually within six months from treatment interruption. This determines the need for a long-term therapy[23].

Surgery is a viable option if symptomatology interferes significantly on the patient quality of life, if the latter refuses a long term medical therapy, and in case of complicated disease (severe esophagitis and/or stenosis). Nevertheless, indications for surgery are generally limited to young patients with a life expectancy of many years, in which surgical therapy may be an effective alternative to medical one. Recent introduction of laparoscopic surgery in GERD treatment expanded the number of subjects eligible for Nissen fundoplication intervention. The short-medium term clinical results are comparable to those produced by traditional surgery. A study carried out on 359 patients aged> 65 years showed, after the intervention, a similar symptoms improvement to that found among younger patients, an equivalent morbidity and length of hospitalization, emphasizing that the choice of surgical treatment is no longer limited by age. However, it must be considered that elderly patients have a higher surgical risk than younger ones[2,24].

Medical and surgical therapy are undoubtedly two cornerstones of GERD treatment, but to date endoscopy offers new possibilities[25]. Three different approaches are available today:

1) endoscopic "sewing machine", by which could be performed sutures within the cardia creating mucosal folds to contrast reflux[26];

2) Radio-Frequency (NARROW procedures), producing focal lesion in the cardia muscle layer, that hesitate in fibrosis with reflux reduction[27];

3) injection of inert substances (polymers) into the esophageal-gastric junction determining the creation of an anti-reflux barrier[28]. These procedures seem very promising but unfortunately are just in an experimental stage. Before being widely adopted will be necessary to make more accurate studies and a better standardization of procedures.

Conclusions

In conclusion, GERD is a common condition in the elderly, which often develops itself in an atypical way, with more frequent and severe complications. As regards the pathophysiological mechanisms in elderly patients compared to younger ones, it seems to have a specific role factors such as use of drugs that reduce the LES tone or have direct detrimental action on the esophageal mucosa (in this regard a special note, in women, the use of osteoporosis medications, especially bisphosphonates, for the well-known esophageal lesions that can cause), hiatal hernia, probably duodenal-gastric reflux, presence of comorbidities (overweight, being bedridden, diabetes mellitus and neurological disorders). In this context, the progressive age-related decrease of hydrochloric acid secretion does not seem to have an important protective role. Diagnostic and therapeutic approach must consider the psychological and physical changes often present in the elderly. In absolute terms, treatment effectiveness is very similar between young and elderly. PPIs in the elderly, as in the young, are considered the most effective molecules on symptoms and lesions of all grades. The choice of a specific molecule between PPIs has no influence in the young, while in the elderly is required, accounting comorbidities and polypharmacy (drug interactions). Our results confirm literature data.

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