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TOPIC HIGHLIGHT

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Helicobacter pylori infection in older people

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Abstract

Since the discovery of *Helicobacter pylori* (*H. pylori*) infection as the major cause of gastroduodenal disorders three decades ago, *H. pylori* has been the focus of active research and debate in the scientific community. Its linkage to several diseases, such as peptic ulcer disease, gastritis and gastric malignancy is incontestable. In particular, it has been noticed that, as the aged population is increasing worldwide, older people are at increased risk of developing several gastroduodenal diseases and related complications. At the same time, gastric cancer is definitely more frequent in elderly than in adult and young people. In addition, it has been showed that peptic ulcer and related complications occur much more commonly in aged individuals than in young people, resulting in a significantly higher mortality. Although this infection plays a crucial role in gastrointestinal disorders affecting all age groups and in particular older people, only a few studies have been published regarding the latter. This article presents an overview of the epidemiology, diagnosis, clinical manifestations and therapy of *H. pylori* infection in elderly people.

Key words: Elderly; *Helicobacter pylori*; Diagnosis; Clinical features; Treatment

Core tip: Gastritis, peptic ulcer and related complications occur more commonly in elderly people. *Helicobacter pylori* (*H. pylori*) testing and treatment should be regarded as an important goal in clinical practice in elderly people, but only a few studies have been published to date. This article presents an overview of the epidemiology, diagnosis, clinical manifestations and therapy of *H. pylori* infection with a focus on elderly people, based on a multidimensional approach and the clinical practice modifications (or not) aroused during the past three decades.

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INTRODUCTION

In 1983, *Helicobacter pylori* (*H. pylori*), a Gram-negative bacterial pathogen that selectively colonizes the gastric epithelium, was isolated by culture from gastric biopsy specimens by Warren and Marshall[1], who were then awarded the Nobel Prize in Physiology or Medicine for their imperative discovery. Their work started a new interest in the previously neglected field of gastric microbiology, and in 1994 the National Institutes of Health consensus conference in the United States declared an association between *H. pylori* and peptic ulcer disease[2,3]. In the same year, *H. pylori* was identified as a carcinogen associated with gastric adenocarcinoma[4] and gastric non-Hodgkin's lymphoma[5,6]. Thus, only a decade after its first isolation, *H. pylori* became the most important microbiological agent in human upper gastrointestinal tract disorders and it was classified as a type I carcinogen group by the World

Health Organization and the International Agency for Research on Cancer (IARC)[4].

Although *H. pylori* infection is important in gastrointestinal diseases affecting all age groups, only a few studies have been published regarding elderly people. In this review, papers published in English were searched in PubMed using the key words "*H. pylori*", "-elderly", "-geriatrics", "-diagnosis" and "-treatment", focusing on recent information and studies. The review sought to re-examine the role of *H. pylori* infection in peptic ulcer, gastric cancer (GC) and extra-digestive diseases, addressing also its diagnosis and options for treating the infection in elderly people.

EPIDEMIOLOGY

Approximately 50% of the global population worldwide is thought to be colonized with *H. pylori*, which is typically acquired within the first 5 years of life[7]. The prevalence of the infection varies according to different ages, socioeconomic strata and geographical regions. In developing countries the prevalence of *H. pylori* is higher in children, likely due to lower socioeconomic status, poor hygiene, overpopulation and lack of safe drinking water[8], whereas in developed countries the prevalence increases with age, probably as a cohort effect of an earlier generation exposed to poor sanitation. Prevalence of infection varies between 7% and 87% and was lower in European countries[9].

About 10 years ago, most of the studies reported a worldwide increasing prevalence of *H. pylori* infection with age, reaching 40%-60% in asymptomatic elderly individuals and > 70% in elderly patients with gastroduodenal diseases[10]. Studies conducted in the past decade have reported a high prevalence of *H. pylori* infection within the oldest population, especially in institutionalized old people, with a prevalence ranging from 70% to 85%[11,12]. However, a marked reduction in the prevalence of infection is noticed in elderly people (> 85 years)[9,13,14]. Chronic atrophic gastritis and the extensive use of current or previous treatment with antibiotics and antisecretory drugs may explain this observation[14]. However, it has been shown that the prevalence of the infection has decreased in adults and children in many countries almost 25 years after the discovery of *H. pylori*[15,16]. Indeed, the infection persists throughout life, unless treated. This finding suggests that attention should be paid to diagnosis in order to treat *H. pylori* infection in older people.

DIAGNOSIS OF *H. PYLORI* INFECTION

Diagnosis of *H. pylori* can be achieved with invasive or noninvasive techniques. Invasive tests (histology, culture, and rapid urease test) need upper gastrointestinal endoscopy and biopsy material for tests, whereas the noninvasive techniques [C-urea breath test (UBT), stool antigen test, and serological blood test] use other methods. Each test has advantages, disadvantages and limitations.

INVASIVE TESTS

Histology

Histological evaluation has traditionally been the gold standard method for diagnosing *H. pylori* infection. The disadvantage of this technique is the need for endoscopy to obtain tissue specimens. However, upper gastrointestinal endoscopy is always indicated for elderly people with different abdominal symptoms because of the high prevalence of severe gastric diseases in this age group[17]. Histology has the benefit of evaluating the morphological parameters of the gastric mucosa in order to identify the presence and severity of histological gastritis[18]. Recently, an international group of gastroenterologists and pathologists Operative Link on Gastritis Assessment (OLGA) has developed a new system of histologically reporting gastritis[19]. The assessment/description of the elementary lesions (in each of the biopsy samples considered) represents the core element in the histology report. A semiquantitative score of some of the elementary lesions should be provided, that is: (1) lymphoid-monocytic inflammation; (2) polymorphs (*i.e.* activity); (3) atrophy (distinguished as metaplastic and nonmetaplastic); and (4) *H. pylori* status (positive *vs* negative). This system places the histological phenotype of gastritis on a scale of progressively increasing risk of GC, from the lowest (stage 0) to the highest (stage Ⅳ) stage.

In order to provide a proper evaluation of the presence of *H. pylori* in elderly patients, it is necessary to go through a bioptic sampling with two antral and two body gastric biopsies. The high level of atrophic gastritis in elderly people can, in fact, reduce the sensitivity of the test itself.

Rapid urease test

The rapid urease test [CLO (Campylobacter-like organism) test] can detect the presence of *H. pylori* within 1 h with satisfactory accuracy (90%)[20]. However, as for the histology, the rapid urease test performed on antral biopsies has a lower sensitivity in 60-year-old (and older) compared to younger patients (57% *vs* 75%)[21]. Moreover, false-negative results can occur in patients taking antisecretory drugs.

Bacterial culture

H. pylori is difficult to grow on culture media, thus, the role of culture in diagnosis of infection is limited mostly to research and epidemiological considerations. Its interest mainly lies in the possibility of performing antimicrobial susceptibility testing. The rationale relates to the fact that in the case of clarithromycin resistance, the rate of success of clarithromycin-containing triple therapy is low, ranging between 10% and 30%[22]. After a second failure, it should be performed in all cases as recommended at the Maastricht Ⅲ Conference[23].

These findings suggest that in elderly people it is advisable to obtain gastric biopsies at least from both the antrum and corpus of the stomach, and to perform a

second test for *H. pylori* if a urease-based or histological test is negative, and it is mandatory to suspend antisecretory drugs at least 10 d prior to the tests.

NONINVASIVE TESTS

UBT

The C-UBT is a noninvasive test that relies on bacterial urease activity. The main principle involved is the conversion of urea into NH_3 and CO_2 by urease. Urea marked by ^{13}C and ^{14}C is hydrolyzed by *H. pylori* into NH_3 and CO_2 in the stomach and then labeled isotopes of carbon in the CO_2 exhaled by the lungs are measured. The greatest advantage of the C-UBT is that it samples the whole stomach, avoiding obstacles normally linked to invasive tests such as biopsy, which can hardly detect the bacteria if it is patchily distributed on the stomach mucosa.

The ^{13}C-UBT is an accurate, practical and easily available test[24]. The diagnostic accuracy of the ^{13}C-UBT was 95% in several studies[25]. In elderly people, the ^{13}C-UBT has demonstrated significantly higher sensitivity (100%), specificity (95.7%) and diagnostic accuracy (98%) compared to serology (IgG *H. pylori* antibodies)[26]. Furthermore, the ^{13}C-UBT has shown to be unaffected by potential co-variables, such as cognitive function, disability, comorbidity and co-treatments[27].

Recently, a study performed in 100 patients aged > 65 years, using ^{14}C-UBT, demonstrated a sensitivity of 91.4% and specificity of 93.8%[28].

Serological IgG test

After *H. pylori* infection is acquired, the immune system typically reacts by producing IgG against organism-specific antigens. These antibodies can be detected in serum or whole-blood samples. The presence of IgG antibodies against *H. pylori* can be detected through a biochemical assay and several different ones are available. The sensitivity, specificity and diagnostic accuracy of serology in a study of elderly patients were 74.4%, 59% and 67%, respectively[29]. It is important to remember that it does not effectively tell apart current from past infections. This method is not a useful means to confirm the eradication of *H. pylori*, but it may be used in the monitoring phases after eradication; indeed, it could be useful to observe and verify the former presence of *H. pylori* in patients with atrophic gastritis.

H. pylori stool antigen testing

H. pylori stool antigen (HpSA) testing involves an enzyme immunoassay to detect the presence of *H. pylori* antigen in stool specimens. The monoclonal HpSA test is an accurate noninvasive method for both the initial diagnosis of *H. pylori* infection and confirmation of its eradication after treatment[30]. The sensitivity and specificity of the HpSA test compared with two tests (histology and UBT) were respectively 76% and 95% in 122 elderly hospitalized patients[31]. Similar results were found in a study involving 85 hospitalized frail elderly people[32]. According to the Maastricht Ⅳ Conference, the diagnostic accuracy of the HpSA test is equivalent to the UBT if a validated laboratory-based monoclonal test is used with an evidence level "1a" and grade of recommendation "A"[33]. In older people, however, some limitations of the HpSA test could be due to constipation, a frequent disorder in elderly people. Indeed, as previously suggested, the prolonged gastrointestinal transit time could slow down the passage of the bacteria into the colon, leading to degradation of *H. pylori* antigens and compromising their detection[14].

Other noninvasive tests (GastroPanel blood)

GastroPanel is determined by four parameters measured in blood samples: serum pepsinogen (s-PG) Ⅰ and s-PG Ⅱ, gastrin-17 and anti-*H. pylori* IgG. Levels of s-PGI and s-PGII are known to increase in cases of *H. pylori*-related nonatrophic gastritis. s-PG Ⅱ levels are higher in patients with peptic ulcer and are correlated with the severity of inflammation[34]. *H. pylori* eradication induces improvement of histological gastritis activity. A study performed in elderly patients demonstrated that s-PG Ⅱ levels decreased significantly in the case of successful eradication of *H. pylori*[35]. Therefore, s-PG Ⅰ /PGII ratio could be a useful marker for monitoring the outcome of *H. pylori* treatment[29,36]. Moreover, the measurements of s-PGI or the ratio of s-PG Ⅰ /s-PG Ⅱ may be useful to identify atrophic gastritis of the gastric corpus, and assays for gastrin (particularly gastrin-17) could be an indicator of the morphological status of the antral mucosa[37]. Further studies are needed to evaluate the clinical usefulness of the GastroPanel test in clinical practice, especially in older people.

CLINICAL FEATURES

Epidemiological and clinical studies suggest that with advancing age there is an increase in both the prevalence and severity of upper gastrointestinal diseases[38]. As reported above, *H. pylori* infection is the major risk factor for developing chronic gastritis and peptic ulcer, and it is also related to gastric mucosa-associated lymphoid tissue lymphoma and GC[2-4]. Moreover, interesting data suggest a clinical association between *H. pylori* infection and extra-digestive disorders, including some that are particularly frequent in older people.

CHRONIC ATROPHIC GASTRITIS

Although previous studies have reported that advancing age is independently related to chronic atrophic gastritis and a functional status of hypo/achlorhydria, more recent data suggest that atrophic changes of the gastric mucosa are associated with *H. pylori* infection rather than with aging[4]. Eradication of *H. pylori* infection in elderly patients can lead to a significant decrease in gastritis activity as compared with no change in histology in patients with continuing chronic infection[39]. Eradication of *H. pylori* infection in elderly patients with advanced atrophic

gastritis may also lead to significant improvement in the mean histological scores of inflammation, atrophy and intestinal metaplasia, after a mean follow-up of 2.5 years[40] after eradication therapy. In a recent study performed in 84 elderly patients, the authors confirmed that eradication of *H. pylori* infection improved gastric atrophy and prevented the progression of intestinal metaplasia during long-term follow-up[41]. Lastly, in patients with corpus atrophic gastritis, there is long-term improvement of physiological gastric function after *H. pylori* eradication, as suggested by the significant and continuous increment of s-PGI levels over a 4-year period[42].

GASTROESOPHAGEAL REFLUX DISEASE

Gastroesophageal reflux disease (GERD) is a multifactorial disorder characterized by reflux of acidic gastric contents into the esophagus, leading to tissue damage and symptoms. Gastric acid secretion does not decrease with age, although factors leading to atrophic gastritis, such as *H. pylori* infection, reduce gastric acid secretion[43].

Although it has been previously suggested that *H. pylori* eradication may cause both reflux symptoms and erosive esophagitis, the relationship between *H. pylori* infection and GERD has not been clarified yet, particularly in elderly people.

Epidemiological data do not seem to support a role for *H. pylori* in the pathogenesis of reflux disease, and suggest a negative association with the increasing incidence of esophageal diseases[44,45]. A recent meta-analysis of 10 trials in which data of patients treated for *H. pylori* infection were compared to those receiving placebo concluded that the post-treatment incidence of reflux symptoms (17% *vs* 22.6%) and erosive esophagitis (5% *vs* 5.1%) were similar between both groups[46]. However *H. pylori* testing should be considered in older patients affected by GERD and receiving long-term maintenance treatment with proton pump inhibitors (PPIs)[39].

PEPTIC ULCER DISEASE

The correlation between *H. pylori* infection and peptic ulcer and peptic bleeding diseases has been widely studied. A meta-analysis reported that the prevalence of peptic ulcer disease ranged worldwide between 0.1% and 4.7%, with an annual incidence ranging from 0.19% to 0.3%[47]. Epidemiological studies have indicated that the prevalence and incidence of peptic ulcer show a constant decline in the general population, but current studies report an increased rate of peptic ulcer disease, its complications and mortality in older patients[48,49]. Two major factors that might explain the observed increasing incidence of peptic ulcer in elderly patients are the high prevalence of *H. pylori* infection and the large use of nonsteroidal anti-inflammatory drugs (NSAIDs) and/or aspirin. An endoscopic study carried out in 520 peptic ulcer patients aged > 65 years (mean age: 81 years) reported that 67% of gastric ulcers and 69% of duodenal ulcers were *H. pylori* positive; moreover, NSAID or aspirin use, alone or in combination with *H. pylori* infection, were reported by 39% of gastric ulcer and 25% of duodenal ulcer patients[50].

NSAID use and *H. pylori* infection are independent risk factors for peptic ulcer and gastroduodenal bleeding in elderly patients. In *H. pylori*-positive older patients who are starting long-term treatment with NSAIDs, the treatment of *H. pylori* infection significantly reduces the 6-mo risk of peptic ulcer[51]. In elderly high-risk patients, however, the use of PPIs concomitantly with NSAIDs reduces the occurrence of NSAID-related gastroduodenal damage more effectively than the eradication of *H. pylori* infection[52].

Moreover, after eradication of *H. pylori*, maintenance treatment with a PPI is more effective than placebo in the prevention of ulcer bleeding in elderly patients[53]. All these findings suggest that *H. pylori* eradication would surely be a useful strategy, but it is not sufficient for the prevention of severe gastroduodenal damage in elderly *H. pylori*-positive patients and NSAID and aspirin users[39,54].

Indeed, the few short- and long-term studies performed in elderly patients with *H. pylori*-positive peptic ulcer have demonstrated that treatment of *H. pylori* infection results in ulcer healing in > 95% of patients. Moreover, it significantly improved clinical outcomes, including a reduction in recurrence[55], but unfortunately the percentage of elderly patients with peptic ulcer who are treated for their *H. pylori* infection is still low[56].

All the above-mentioned considerations suggest that, along with aging of the population, the risk of developing peptic ulcer and related complications, including gastrointestinal bleeding, is more frequent in elderly patients than in younger ones[57]. Consequently, we suggest testing for and treating *H. pylori* infection in elderly people. Moreover, it has been proposed that in patients characterized by comorbidity or a history of peptic ulcer and requiring long-term NSAID or aspirin treatment, *H. pylori* infection should be eradicated before starting the above-mentioned therapy[58,59].

GC

GC is the fourth commonest cancer in the world and accounts for 8% of the total cancer cases and 10% of total cancer-related deaths worldwide, with > 70% of new cases and deaths occurring in developing countries[60]. GC is rare below the age of 30 years; thereafter, it increases rapidly and steadily to reach the highest rates in the oldest age groups, both in men and women. Although the incidence of GC has declined in the general population, the incidence in elderly people is increasing, most probably as a result of extended life expectancy.

It is now clear that *H. pylori* infection induces a cascade of events that could ultimately lead to gastric neoplasia in genetically predisposed hosts[61]. The key pathophysiological events include the onset of gastric atrophy and hypochlorhydria. The increased proliferation induced by inflammation creates a genetically unstable gastric

mucosa, which is further compromised by the presence of genotoxic substances generated by inflammatory and bacterial products[62]. The hypochlorhydria contributes to bacterial overgrowth, which further exacerbates the inflammation and leads to generation of carcinogenic nitrogenous products. Elderly people have a higher prevalence of *H. pylori* infection and those who are infected develop a gradual decline in gastric acid secretory function, which is induced by the chronic gastritis and atrophy. In the presence of other environmental factors such as poor diet and smoking, the neoplastic process is even accelerated.

Several animal studies have confirmed that gastric carcinogenesis originates from *H. pylori*[63,64]. Meta-analyses that included additional epidemiological studies have confirmed the association between the bacterium and GC[65]. To prevent the development of GC, eradication therapy should be ideally administered early, before premalignant gastric lesions (*i.e.* atrophy) develop[66,67]. In fact, a prospective observational study in 1526 Japanese patients revealed that 2.9% of the *H. pylori* infected patients developed GC after 7.8 years, whereas none of the noninfected individuals developed GC[68]. Furthermore, an interventional study in China has shown a risk reduction of 37% after 7.5 years in patients who received *H. pylori* eradication therapy. *H. pylori* eradication reduces the incidence of gastric adenocarcinoma, therefore, a deeper screening activity and calculated treatment strategy for this infection in the general population in high-risk areas are suggested.

EXTRA-DIGESTIVE DISEASES

The list of diseases associated with *H. pylori* seropositivity is long[69]. We consider only those extra-digestive diseases that can represent an interest for the treatment of elderly patients and/or that have a significant social impact.

The proinflammatory nature of *H. pylori* infection could be the common factor in the pathogenesis of those diseases in which inflammation is an important feature in the pathogenesis. Thus, it is possible that *H. pylori* infection triggers or aggravates a systemic inflammatory response that acts concurrently with the key triggering factors in many diseases. The apparent association of so many different diseases with *H. pylori* infection also suggests that a final common pathway could exist for all these conditions. The effects of this local inflammation may not be confined only to the digestive tract, but may also spread to involve extraintestinal tissues and/or organs.

Cardiovascular and Alzheimer's diseases

Several studies have demonstrated a relationship between *H. pylori* seroprevalence and coronary artery disease[70,71]. However, it has not yet been determined if *H. pylori* infection is associated with increased risk of coronary heart disease. The few studies performed in elderly populations have failed to find any association between *H. pylori* infection and coronary heart disease[72,73] or extracardiac atherosclerosis[74].

Recent data have demonstrated that *H. pylori* chronic infection can play a role in mild cognitive impairment[75] and Alzheimer's disease[76-78], but further studies are needed to attest to the impact of *H. pylori* infection on disease course, especially on cerebrovascular lesions and neuroinflammation.

Appetite regulation

The possible role of *H. pylori* infection in appetite regulation in elderly people is an interesting new area of research. *H. pylori* has an influence on the release of gastric hormones and therefore it plays a significant role in the regulation of body weight, hunger and satiety[79,80]. The main hormones involved are leptin and ghrelin, which are multifunctional hormones that co-operate in order to balance different metabolic functions. They both act at the hypothalamic level, but with opposite effects. Ghrelin increases appetite, and decreases the waste of energy and catabolism in adipose tissue and plasma glucose, improving body weight. Leptin acts in the opposite way. *H. pylori* infection leads to a decrease of circulating ghrelin through a reduction of ghrelin-producing cells in the gastric mucosa and increases the amount of gastric leptin with no effect on circulating leptin levels[68]. One study has reported that treatment of *H. pylori* infection increases the level of plasma ghrelin, leading to a more intense appetite and weight gain[81]. Another study concerning frail elderly patients aged > 80 years has shown that the presence of *H. pylori* chronic gastritis induces a decrease in both leptin and ghrelin gastric production, probably due to the high prevalence of atrophic lesions observed in this particular population[82].

Iron-deficiency anemia

Iron-deficiency is a common cause of anemia in elderly people. Several studies have shown a relationship between *H. pylori* and iron-deficiency anemia (IDA)[83,84]. Possible pathogenetic mechanisms involved in IDA in patients with *H. pylori* infection include: occult blood loss secondary to chronic erosive gastritis; decreased iron absorption secondary to chronic gastritis of the corpus causing hypo- or achlorhydria; and increased iron uptake and use by bacteria.

Cobalamin deficiency

Cobalamin (vitamin B12) deficiency is particularly common in elderly people but is often unrecognized because its clinical manifestations are subtle and nearly undetectable[85,86]. Vitamin B12 is a water-soluble vitamin needed for DNA replication, production of S-adenosyl-L-methionine, normal nerve cell activity, and above all, it acts together with folic acid to control homocysteine levels. An excess of homocysteine is associated with an increased risk of heart disease, stroke and potentially other diseases such as osteoporosis and Alzheimer's disease[87].

Cobalamin malabsorption could be due to several

factors including pernicious anemia, gastrectomy, histamine-2 antagonists, PPIs, and *H. pylori* infection itself[88]. Food cobalamin malabsorption is caused primarily by chronic atrophic gastritis[89]. This theory has been supported by two different studies evaluating the effect of eradication treatment of *H. pylori* infection on the improvement of vitamin B12 deficiency in patient groups with atrophic[90] and non-atrophic gastric mucosa[91].

All these findings suggest that in presence of IDA and cobalamin deficiency, *H. pylori* should be sought and eradicated.

TREATMENT

The triple therapy regimens including a PPI, clarithromycin and amoxicillin or metronidazole for *H. pylori* infection have been universally accepted since they were recommended at the first Maastricht Consensus. This regimen has also been reported as effective and safe for the treatment of *H. pylori* infection in older people[92]. The most recent data, however, show that this combination has lost some efficacy and often allows the treatment of only a maximum of 70% of the patients, which is less than the initial target rate of 80% and far below what should be expected for an infectious disease. Consequently, the recommended first-line therapy regimens are dependent on the prevalence of antibiotic resistance[22]. In a recent study performed in 2204 patients in 18 European countries, the resistance rate of *H. pylori* was 17.5% for clarithromycin, 14.1% for levofloxacin and 34.9% for metronidazole, while the prevalence was ⩽ 1% for other antibiotics tested[93]. Actually, no data on antibiotic resistance in elderly patients are available.

The recommended treatment strategy in the Maastricht Consensus Report was triple therapy with PPI, clarithromycin and metronidazole in areas with clarithromycin resistance rates < 15%-20% and metronidazole resistance rate < 40%, and triple therapy with PPI, clarithromycin and amoxicillin in areas with clarithromycin resistance rates < 15%-20% and metronidazole resistance rate > 40%. Bismuth-containing quadruple therapy (10 or 14 d) is an option for first-line treatment. It leads to satisfactory eradication rates despite the increased resistance to both clarithromycin and metronidazole.

Although it is now known that the increase in duration of triple therapy (from 7 to 14 d), as well as quadruple treatments, may be associated with more successful eradication, few studies have evaluated the clinical utility of these regimens in elderly patients. Only one study in 95 dyspeptic elderly patients (aged 65-81 years) demonstrated that the eradication rate of quadruple therapy including 20 mg esomeprazole, 500 mg tetracycline, 500 mg metronidazole and 240 mg bismuth subcitrate tablets twice daily for 10 d was 91% (intention-to-treat analysis) and 95% (per-protocol analysis); the compliance was excellent, but mild-to-moderate side effects occurred in 27 patients (28%)[94]. Prolonging the duration of treatment may increase the risk of side effects, which tend to become more marked after the first week of therapy[95].

Recently, sequential treatment consisting of 5 d of PPI plus amoxicillin followed by five additional days with PPI plus clarithromycin and tinidazole has revealed a better solution than the combination of a PPI plus amoxicillin and clarithromycin for 7 d[96,97]. In a study designed to assess the eradication rate of this 10-d sequential regimen in geriatric patients with peptic ulcer, the authors confirmed that the 10-d sequential treatment regimen achieved significantly higher eradication rates in comparison with standard triple therapy[98].

Eradication of *H. pylori* infection is more difficult when a first treatment attempt has failed[99]. The optimal strategy for retreatment after failure of eradication has not yet been established yet in elderly patients. Thus, the choice of a second-line treatment depends on which treatment was used initially. Despite retreatment ideally being guided by data on susceptibility, the updated Maastricht Consensus Report[23,33] recommends that culture and antimicrobial sensitivity testing should be routinely performed only after two treatment failures with different antibiotics.

The leading second-line therapy regimens are quadruple therapies, in which a PPI is added to a bismuth-based triple regimen. A different approach of retreatment without susceptibility testing is to prescribe a second course of PPI-based triple therapy avoiding antimicrobial agents against which prior therapy may have induced resistance, such as clarithromycin-based and/or metronidazole-based regimens. It has recently been suggested[100] that levofloxacin-based rescue therapy constitutes an encouraging second-line strategy, representing an alternative to quadruple therapy in patients with previous PPI-clarithromycin-amoxicillin failure, with the advantage of efficacy, simplicity, and safety. However the rapid acquisition of resistance may compromise its future efficacy, and levofloxacin should not be used in patients with chronic infectious bronchopneumopathy, who may have received fluoroquinolones[33].

CONCLUSION

H. pylori testing and treatment in elderly people should be regarded as an important goal in clinical practice due to its crucial role in gastrointestinal disorders in that age group. The current recommendations confirm that the standard methods for diagnosis and treatment of *H. pylori* infection could be safe and effective in elderly patients. However, because of the impact of underlying conditions, that is, multi-morbidity and functional impairments that may influence the outcome in older people[101], a multidimensional approach including the evaluation of functional, cognitive, nutritional and social conditions in addition to comorbidity and concomitant treatments is required in clinical practice and research to manage older patients better[102], in accordance with the high epidemiological and clinical impact that *H. pylori* infection has aroused during the past three decades in older people.

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