Practical Aspects in Choosing a *Helicobacter pylori* Therapy

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KEYWORDS

• *Helicobacter pylori* • Therapy • Eradication • Triple • Quadruple • Concomitant • Bismuth • Resistance

KEY POINTS

- Antibiotic resistance is the critical factor responsible for eradication treatment failure. Because of increasing clarithromycin resistance, first-line triple therapy for *Helicobacter pylori* (*H pylori*) infection is currently ineffective in most settings worldwide.
- Treatment results for infectious diseases are best (>90%–95%) when regimens are reliably used to treat patients with organisms susceptible to the antimicrobials chosen. Most eradication therapies, however, are prescribed empirically.
- The choice of therapy may depend on patient previous antibiotic treatment, local patterns of antibiotic resistance, and drug availability. Currently, the most effective first-line eradication regimens are 14-day bismuth and nonbismuth concomitant quadruple therapies.
- Fluoroquinolone-, furazolidone-, and rifabutin-containing regimens might be effective rescue treatments, as well as bismuth quadruple therapy if not used previously.
- Optimization of all eradication regimens (increased duration, adequate proton pump inhibitor, and antibiotic doses and dosing intervals) is key to maximize their efficacy.
- Besides antibiotic resistance, compliance is a major concern with increasing complex eradication therapies. Probiotics show promise as an adjuvant treatment to reduce side effects and improve adherence to therapy. Whether probiotics can also increase eradication rates should be further elucidated.
- On large variations in *H pylori* resistance patterns, the golden rule for choice of treatment is only to use what works locally (>90%–95% success) and to closely monitor its effectiveness over time.

Disclosure Statement: The authors have no conflict of interest to declare.
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Gastroenterol Clin N Am 44 (2015) 519–535
http://dx.doi.org/10.1016/j.gtc.2015.05.004 **gastro.theclinics.com**
0889-8553/15/$ – see front matter

INTRODUCTION

Thirty years after the transcendental discovery of the originally termed *Campylobacter pyloridis* as a causative agent for gastritis and peptic ulceration in 1984,[1] *Helicobacter pylori (H pylori)* remains the most common bacterial infection in humans. It is estimated that approximately 50% of the world's population is infected; this infection is currently the main cause of gastritis, gastroduodenal ulcer disease, and gastric cancer. Eradication of *H pylori* infection has dramatically changed the natural history of peptic ulcer disease.[2] Furthermore, the World Health Organization classified *H pylori* as a definite carcinogen in 1994 for its established role in the pathogenesis of gastric cancer and gastric mucosa–associated lymphoid tissue lymphoma.[3] Emphasis has been lately made on the importance of primary and secondary gastric cancer prevention, starting with *H pylori* eradication.[4] In fact, Japan has recently embarked on population-wide *H pylori* eradication coupled with surveillance targeted to those with significant remaining risk.

Standard triple therapy, consisting of a proton pump inhibitor (PPI) plus amoxicillin and either clarithromycin or metronidazole, has been (and unfortunately still remains in many settings) the gold standard eradication therapy for *H pylori* infection over the last 2 decades. However, the efficacy of triple therapy at the present time is seriously challenged in many parts of the world, where eradication rates have declined to unacceptably low levels, largely related to the development of resistance to clarithromycin.[5] Moreover, *H pylori* resistance to metronidazole is prevalent as well in certain geographic areas (ie, South America, Turkey, Iran, China) and fluoroquinolone resistance is rapidly growing worldwide due to widespread use of levofloxacin for ear, nose and throat, bronchial and urinary tract infections. Failure of *H pylori* treatment, in addition, selects antibiotic-multiresistant strains, which will be even more difficult to treat. Complicating this scenario, rescue drugs may be unavailable (eg, bismuth, tetracycline, furazolidone) or may lead to severe adverse effects (eg, rifabutin).

This article aims to revisit all practical aspects that should be taken into consideration when choosing an *H pylori* eradication regimen. Increasing antibiotic resistance coupled with a lack of new therapeutic alternatives can seriously hamper the fight against *H pylori* infection. Now more than ever, a clear understanding of the interplay between the bacteria, the individual patient, its geographic area, and the drugs selected becomes pivotal to select and optimize the best therapeutic strategy for each patient, maximizing the efficacy of eradication regimens and minimizing treatment failures, selection of resistant strains, and need for step-up antibiotic therapy.

Why Is Helicobacter pylori Difficult to Treat?

The *H pylori* infection should be treated by means of a combination of acid-suppressive agents and several antibiotics, yet it has proven challenging to cure. Several factors may account for difficulties associated with cure of the infection, including bacteria-, environmental-, host-, and drug-associated variables. All of these factor influencing eradication rates and potential solutions to overcome these obstacles are summarized in **Table 1**. By far, the most important factor is the development of *H pylori* resistance to many antimicrobial agents, especially clarithromycin, metronidazole, and fluoroquinolones. In *H pylori* infection, resistance usually develops because of the outgrowth of a small existing population of resistant organisms. Clarithromycin must bind to ribosomes in order to kill *H pylori*. Acquired resistance is associated with failure to bind to ribosomes, such that resistance cannot be overcome by increasing the dose or duration. Likewise, resistance to fluoroquinolones (eg, levofloxacin, moxifloxacin) is not responsive to changes in dose or duration. Metronidazole