Annals of Gastroenterology (2015) **28,** 415-416

Recent advances in *Helicobacter pylori* eradication

Yaron Niv[a], Theodore Rokkas[b]

Rabin Medical Center, Tel Aviv University, Israel; Henry Dunant Hospital, Athens, Greece

The most popular regimen for eradication of *Helicobacter pylori (H. pylori)* infection is triple therapy, composed of a potent proton pump inhibitor (PPI), amoxicillin (AMOX), and clarithromycin (CLA). Emerging resistance to CLA changed this strategy, and according to Maastricht IV recommendation, this regimen can be used only in countries with low (<20%) CLA resistance [1]. A regimen for the treatment of *H. pylori* is now acceptable if it is associated with at least 90% success [2].

In addition to CLA resistance several other factors may influence the success or failure of *H. pylori* eradication: duration of therapy and dosage, PPI effect on gastric acid secretion, other drugs' resistance, and patients' compliance. Regardless of the antibiotic used, prolonging treatment duration from 7 to 14 days significantly improved eradication rates [3]. PPI is an important part of the treatment protocol, since a gastric higher pH is essential for antibiotics function. Esomeprazole is more effective in acid inhibition and *H. pylori* eradication than other PPIs such as omeprazole, lansoprazole and pantoprazole, especially in patients with polymorphisms in S-mephenytoin 4'-hydroxylase (CYP2C19) associated with extensive PPI metabolism [4]. Several single nucleotide polymorphisms in the *CYP2C19* gene, which affect gene function, lead to rapid or slow PPI metabolism. In extensive metabolizers *H. pylori* eradication rate may be improved by increasing PPI dosage or by reducing the intervals between the doses [5]. Treatment may be individualized by testing susceptibility to antibiotics. Four single nucleotide polymorphisms are responsible for most resistance to CLA and may be tested in gastric or stool samples [6]. Culture-guided therapy yields superior eradication rates [7].

Lactobacillus, *Bifidobacterium* and *Saccharomyces boulardii*-containing probiotic compounds given together with antibiotics, increased the eradication rate and reduced treatment-associated side effects, particularly diarrhea [8,9].

To overcome the limitations of triple therapy, several first-line regimens are available such as quadruple therapy with nitroimidazole or bismuth, sequential therapy [AMOX-PPI for 5-7 days, followed by CLA-metronidazole (MET)-PPI for 5-7 days], concomitant therapy (AMOX-CLA-MET-PPI taken together for 10-14 days), hybrid therapy (AMOX-PPI for the entire duration of treatment, while adding CLA-MET for the second half alone) [10]. Although fluoroquinolones are usually reserved for salvage therapy, they are also effective as first-line therapy. In 9 randomized controlled trials levofloxacin-based therapy was superior to regular triple therapy, regardless of treatment duration [11]. Clinicians must consider antibiotic resistance patterns in their population before choosing a particular regimen.

Dual therapy with a PPI and AMOX was one of the first regimens used for *H. pylori* eradication [12]. The success rate was very poor, thus neglected till today, when high-dose dual therapy (HDDT) was described with a significant success. Since *H. pylori* resistance to AMOX in both treatment-naïve and experienced patients is very rare, the only obstacle for the antibiotics is the gastric pH. Higher dose and longer duration, at least theoretically, make HDDT very effective. In Asia HDDT achieved 95.3% eradication compared to 85.3% with sequential therapy [12,13]. Since many factors are responsible for the success of *H. pylori* eradication, the results of HDDT may differ between populations. Trials that examine this issue are therefore required. Towards this end, in this issue of *Annals of Gastroenterology,* an Italian group performed a prospective, multicenter trial, studying the concept of HDDT in Europe [14]. They concluded that the 10-day high-dose dual therapy with esomeprazole plus AMOX might be an effective and safe first-line regimen. However, as the authors themselves point out, adequate randomized controlled trials evaluating this regimen are warranted.

References

1. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection-the Maastricht IV/Florence Consensus Report. *Gut* 2012;**61**:646-664.
2. Graham DY, Lee Y, Wu M. Rational *Helicobacter pylori* therapy: evidence-based medicine rather than medicine-based evidence. *Clin Gastroenterol Hepatol* 2014;**12**:177-186.
3. Yuan Y, Ford AC, Khan KJ, et al. Optimum duration of regimens for *Helicobacter pylori* eradication. *Cochrane Database Syst Rev* 2013;**12**:CD008337.
4. Tang H, Li Y, Hu Y, Xie H, Zhai S. Effects of CYP2C19 loss-of-function variants on the eradication of *H. pylori* infection in patients treated with proton pump inhibitor-based triple therapy regimens: a meta-analysis of randomized clinical trials. *PLoS One* 2013;**8**:e62162.
5. Xiong LJ, Tong Y, Wang Z, Mao M. Detection of clarithromycin-resistant *Helicobacter pylori* by stool PCR in children: a comprehensive review of literature. *Helicobacter* 2013;**18**:89-101.
6. McNicholl AG, Linares PM, Nyssen OP, Calvet X, Gisbert JP. Meta-analysis: esomeprazole or rabeprazole vs. first-generation pump

Departments of Gastroenterology, [a]Rabin Medical Center, Tel Aviv University, Israel (Yaron Niv); [b]Henry Dunant Hospital, Athens, Greece (Theodore Rokkas)

Conflict of interest: None

Correspondence to: Prof. Yaron Niv, 39 Jabotinski Street, Petach Tikva, 49100, Israel, Tel.: +972 50 4065401, Fax: +972 3 9210313, e-mail: nivyaron80@gmail.com

Received 2 July 2015; accepted 4 July 2015

inhibitors in the treatment of *Helicobacter pylori* infection. *Aliment Pharmacol Ther* 2012;**36**:414-425.
7. Wenzhen Y, Yumin L, Quanlin G, et al. Is antimicrobial susceptibility testing necessary before first-line treatment for *Helicobacter pylori* infection? Meta-analysis of randomized controlled trials. *Int Med (Tokyo, Japan)* 2010;**49**:1103-1109.
8. Wang Z, Gao Q, Fang J. Meta-analysis of the efficacy and safety of *Lactobacillus*-containing and *Bifidobacterium*-containing probiotic compound preparation in *Helicobacter pylori* eradication therapy. *J Clin Gastroenterol* 2013;**47**:25-32.
9. Szajewska H, Horvath A, Piwowarczyk A. Meta-analysis: the effects of *Saccharomyces boulardii* supplementation on *Helicobacter pylori* eradication rates and side effects during treatment. *Aliment Pharmacol Ther* 2010;**32**:1069-1079.
10. Hsu P, Wu D, Wu J, Graham DY. Modified sequential *Helicobacter pylori* therapy: proton pump inhibitor and amoxicillin for 14 days with clarithromycin and metronidazole added as a quadruple (hybrid) therapy for the final 7 days. *Helicobacter* 2011;**16**:139-145.
11. Xiao S, Gu M, Zhang G. Is levofloxacin-based triple therapy an alternative for first-line eradication of *Helicobacter pylori*? A systematic review and meta-analysis. *Scand J Gastroenterol* 2014;**49**:528-538.
12. Yang J, Lin C, Wang H, et al. High-dose dual therapy is superior to standard first-line or rescue therapy for *Helicobacter pylori* infection. *Clin Gastroenterol Hepatol* 2015;**13**:895-905.
13. Attumi TA, Graham DY. High-dose extended-release lansoprazole (dexlansoprazole) and amoxicillin dual therapy for *Helicobacter pylori* infections. *Helicobacter* 2014;**19**:319-322.
14. Zullo A, Ridola L, De Francesco V, et al. High-dose esomeprazole and amoxicillin dual therapy for first-line *Helicobacter pylori* eradication: a proof of concept study. *Ann Gastroeneterol* 2015;**28**:448-451.