

Helicobacter pylori Treatment Failure: The Rationale for Alternative Antibiotics

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Successful and complete eradication of *Helicobacter pylori* has become a challenge in recent years [1]. Treatment failure represents a significant healthcare burden, given the complications of *H. pylori* infection, namely peptic ulcers, gastric cancer and mucosa-associated lymphoid tissue lymphoma. The major factors that impact treatment success are poor patient compliance and antibiotic resistance [2, 3]. Primary resistance rates to clarithromycin, metronidazole and levofloxacin in Europe are high at 17.5, 34.9 and 14.1%, respectively [4]. Although primary amoxicillin resistance rates are low by comparison (<1% in Europe [4]), amoxicillin is not suitable for penicillin-allergic patients. Clearly there is a pressing need for alternative antibiotic therapies to combat *H. pylori* in both primary infections and for rescue therapy following initial treatment failure.

In this issue of *Digestion*, Prof. Yaron Niv presents interesting findings from a systematic review and meta-analysis comparing eradication rates of *H. pylori* treatment regimens with and without doxycycline (manuscript number: 201509004). Both tetracycline and doxycycline have a therapeutic range similar to penicillin, implying that they represent suitable alternatives to amoxicillin in *H. pylori* treatment regimens. (manuscript number: 201509004). Although both tetracycline

and doxycycline target the 30 S ribosomal subunit, which prevents bacterial protein synthesis, doxycycline is advantageous in terms of a longer half-life. Using a fixed analysis model, Niv's data show that the OR for eradication success favours treatment regimens that include doxycycline. Although no significant difference in eradication rates was found when treatment regimens with doxycycline were compared only to those with tetracycline, the OR was even higher in favour of doxycycline in treatment regimens that included doxycycline compared with those without tetracycline (manuscript number: 201509004). When compared to tetracycline, doxycycline requires administration less frequently (twice daily), increasing the likelihood of patient compliance [5]. Moreover, another study has found no secondary resistance to doxycycline in *H. pylori* isolates from patients who had failed one or more eradication therapies [6]. Taken together, these findings provide a rationale for further investigations into the use of doxycycline as an alternative to amoxicillin in cases of peni-

In this issue of *Digestion*, Prof. Yaron Niv (manuscript number: 201509004) presents the case for considering doxycycline in *H. pylori* treatment regimens.

cillin allergy or as a component of rescue treatment regimens.

Another often overlooked antibiotic for *H. pylori* treatment is furazolidone. Rescue regimens that include furazolidone achieve high eradication rates following failure of standard first-line, second-line and rifabutin-based therapies [7]. In addition, substituting metronidazole with furazolidone in bismuth quadruple therapy has proven to be effective for *H. pylori* eradication in China [8]. Emerging data also support further evaluation of the newer generation quinolones, such as sitafloxacin, moxifloxacin or gemifloxacin. The newer generation quinolones inhibit the growth of *H. pylori* at lower concentrations than levofloxacin and may be more successful against levofloxacin-resistant strains [9–11]. Moxifloxacin-containing triple therapy has demonstrated superiority to standard first-line triple therapy in Italy [12]. In addition, moxifloxacin-containing therapies are also

showing promise in rescue treatment regimens for *H. pylori* infection [13, 14].

The commercial availability of antibiotics in many countries may limit their wider application in *H. pylori* eradication regimens. Moreover, although alternative antibiotics may provide increased eradication rates in the short term, the likelihood that resistance to these antimicrobials may emerge over time is high. The Maastricht IV/Florence consensus report has highlighted that vaccination would be the ideal option for eliminating *H. pylori* infection [15]. However, despite early signs of promise in animal models, efficient preventative or therapeutic vaccination for *H. pylori* has not been achieved in humans to date [16]. In the meantime, local antibiotic resistance surveillance [17] will play a key role in determining the appropriate treatment regimen in a given population and also provide the opportunity for tailoring therapy in individual patients.

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