

Helicobacter pylori Antibiotic Resistance: What is the Future of Treatment?

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Dear Editor,

In a recent issue of Iranian journal of Pediatrics, we read with great interest the study by Maleknejad et al. in which they determined the susceptibility of *Helicobacter pylori* strains isolated from infected children in north Iran, to some antibiotics, such as clarithromycin, amoxicillin, and tetracycline (1).

Although the sensitivity of *H. pylori* to many antibiotics has been confirmed in vitro, its eradication is not easy in vivo. The standard triple therapy consists of a proton pump inhibitor (PPI) and two antibiotics, such as clarithromycin, metronidazole, and/or amoxicillin, for 7 - 14 days. However, the rate of eradication is lower than 80% (2). The main cause of the eradication failure is related to *H. pylori* resistance to the antibiotics. Also, surveys indicate that the prevalence of antibiotic resistance is variable among countries, and this can change within the same country (3). Results showed that the resistance to clarithromycin can occur through repeated use of this drug for respiratory infections and point mutations in the 23S rRNA gene of *H. pylori*. Also, resistance to metronidazole is probably related to inactivation of *rdxA* (which encodes an oxygen-insensitive NADPH nitroreductase), *fdxB* (ferrodoxin-like protein), and *frxA* (NADPH flavin oxidoreductase) genes (4). Additionally, *H. pylori* resistance to amoxicillin can be explained by alternations in penicillin-binding proteins (5).

Recent studies have investigated new alternatives to existing treatment approaches. For example, quadruple regimens containing a PPI plus clarithromycin, amoxicillin, and metronidazole have been shown to be more effective than standard triple therapy (6). Also, bismuth quadruple therapy has been reported to be more successful in areas with rates of clarithromycin resistance above 15 - 20%, and if not accessible, non-bismuth quadruple, both sequentially and concomitantly, can be used (7). Fur-

thermore, it has been suggested that azithromycin can be used instead of clarithromycin to treat children in standard triple therapy within a shorter period (8). This substitution can also decrease concerns about resistance to clarithromycin as a result of its widespread use. In addition, some studies have stated that specific probiotics, such as *Streptococcus boulardii* and *Lactobacilli johnsonii*, can reduce the load of *H. pylori* and increase its eradication rate, especially among children (9). Moreover, different experimental studies reveal that several bioactive compounds from medicinal plants (e.g., flavonoids, saponins, and quinones) have gastroprotective and anti-*H. pylori* activity (10). This demonstrates that herbal medicine can potentially provide a source of therapeutic agents against *H. pylori* infection.

Although classic triple therapy is still the preferred first line regimen for eradication of *H. pylori* infection, its efficacy has been seriously challenged. In addition, it seems that patterns of antimicrobial resistance are diverse in different regions. On the other hand, not enough studies have confirmed alternative strategies to current treatment methods, particularly for children. Therefore, it is necessary for more research be conducted to find new and suitable therapy regimens with high efficacy and fewer side effects for the eradication of *H. pylori* infection, considering the geographic patterns of antibiotic resistance. Greater recognition of genotypic resistance patterns of *H. pylori* to antibiotics will also help us in this regard.

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