

The role of *Helicobacter pylori* infection in functional dyspepsia

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Title: *Helicobacter pylori* eradication in functional dyspepsia

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Summary

Eradication of *Helicobacter pylori* (*H. pylori*) in patients with functional dyspepsia (FD) continues to be a matter of debate. A recent study [1] examined *Helicobacter pylori* eradication effects on symptoms and quality of life (QoL) of primary care patients. *H. pylori*-positive adult patients with FD who met the Rome III International Consensus criteria, were randomly assigned to receive omeprazole, amoxicillin trihydrate, and clarithromycin, or omeprazole plus placebo for 10 days. Endoscopy and *H. pylori* tests were performed at screening and at 12 months. Outcome measures were at least 50% symptomatic improvement at 12 months, using a validated disease-specific questionnaire (primary endpoint), patient global assessment of symptoms and QoL. 404 patients (78.7% women; mean age, 46.1 years) were randomly assigned; 201 were assigned to be treated with antibiotics (antibiotics group) and 203 to a control group. A total of 389 patients (96.3%) completed the study. The proportion of patients who achieved the primary outcome was 49.0% (94 of 192) in the antibiotics group and 36.5% (72 of 197) in the control group [$p=0.01$; number needed to treat (NNT), 8]. In the overall symptoms patient assessment, 78.1% in the antibiotics group (157/201) answered that they were better symptomatically, and 67.5% in the control group (137/203) said that they were better ($P=0.02$). The antibiotics group had a significantly larger increase in mean (SD) outcomes of the 36-item SFHSPC (Short Form Health Survey Physical Component) summary scores than the control group (4.15 [8.5] vs. 2.2 [8.1]; $p=0.02$). The conclusion of the study was

that *H. pylori* eradication provided significant benefits to primary care patients with FD.

Opinion

Dyspepsia affects up to 40% of adults in the Western world and accounts for around 8.3% of visits to primary care physicians. The majority of patients have FD (i.e. there are no apparent structural or biochemical abnormalities to explain their symptoms); the underlying pathophysiology of this is complex and various pathophysiological mechanisms, such as gastroduodenal dyskinesia [2], visceral paresthesia [3], vagal dysfunction [4], *H. pylori* infection [5], and psychosocial factors [6], have been proposed to promote the development of FD. Without a clear understanding of its pathogenesis, it is not surprising that standard and effective strategies for treatment of this disease are still unavailable. Consequently, patients with FD now receive symptomatic treatment with prokinetics, antacids, and digestive enzymes empirically, which are prone to unfavorable responses and an extremely high risk of relapse. A systematic review suggests that prokinetic therapy may have some benefit, but this is driven by small positive studies with the larger studies being negative, and any effect seen in the meta-analysis may be due to publication bias [7]. Acid suppression with proton pump inhibitor therapy has modest efficacy in FD and this may be due to the treatment of atypical gastroesophageal reflux disease [8]. Given the paucity of effective therapies, it is important to establish whether eradicating *H. pylori* in those infected will have any benefit in FD. Previous studies looking at the effects of *H. pylori* eradication in patients with FD have yielded conflicting results and in addition consensus statements also give conflicting recommendations [9-11]. Due to this uncertainty, very recently Mazzoleni et al [1] conducted the HERODS (Helicobacter Eradication Relief Of Dyspeptic Symptoms) study, a randomized, double-blind assessment of the effects of *H. pylori* eradication on the symp-

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Conflict of Interest: None

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tomatic responses and QoL of community and primary care patients with FD. The authors note that to their knowledge, this is the first large clinical trial on this topic that has focused on primary care patients. Most of the previous studies have included secondary and tertiary care patients who were likely to have more resistant symptoms, and who were not representative of the majority of patients with FD. They acknowledge its limitations, including its conduct in a single center (which may limit external validity), and that a minimum symptomatic score could have been used. They conclude that their findings support the concept of *H. pylori* eradication in primary care patients with FD and suggest their data should be considered by investigators performing cost-utility studies in this area. The importance of this well-conducted randomized control trial (RCT), from South America lies in the fact that it sheds light on the need for *H. pylori* eradication in FD, which has been a matter of controversy to date and it is expected that it may influence the treatment of primary care patients with FD. The data of this study are consistent with those from a previous Cochrane systematic review [12] that included 17 RCTs involving 3,566 patients with FD and reported that *H. pylori* eradication had a statistically significant effect compared with placebo. In the latest Maastricht IV consensus the recommendation is that *H. pylori* eradication produces long-term relief of symptoms in 1 of 12 FD patients with *H. pylori* and this is superior to any other treatment (Grade of Recommendation: A, Grade of scientific evidence supporting the recommendation: 1a) [personal communication].

Considering the above-mentioned data, it appears that *H. pylori* eradication indeed provides significant benefits to primary care patients with FD. However, the cost-effectiveness of *H. pylori* eradication in FD varies geographically. It seems that the overall response is much better in regions where *H. pylori* is highly prevalent and this is where it may be most cost-effective. Thus, patients with FD in Asia would benefit from treatment for *H. pylori* infection with an increased chance of symptom resolution of as much as 3.6- to 13-fold following its eradication [13,14]. However, since there are regional differences in the prevalence of various dyspeptic symptoms in patients with FD, global multicenter studies regarding the symptom-based benefit of *H. pylori* eradication treatment are needed for further evaluation of this regimen.

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