Do we need to eradicate *Helicobacter pylori* in patients with GORD?

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Abstract

Eradication of *Helicobacter pylori* should not be avoided because of complicated reflux symptoms. Previously, although *H. pylori* eradication in patients with GORD was considered to induce unfavourable effects that worsen reflux symptoms, recent reports indicate that it can have favourable consequences by reducing symptoms and therefore improving quality of life, especially in GORD patients without severe corpus atrophy or severe hiatal herniation.

Keywords

GORD, heartburn, *Helicobacter pylori*, reflux oesophagitis, symptom

Gastro-oesophageal reflux disease (GORD) is characterized by typical symptoms, such as heartburn with or without mucosal damage caused by the reflux of gastric contents into the oesophagus. Not only causing benign disease, the GORD–Barrett–adenocarcinoma sequence is assumed to be the common pathway to oesophageal adenocarcinoma. The worldwide rising prevalence of GORD is problematic.

The discovery of *Helicobacter pylori* has dramatically changed the therapeutic and preventive options of upper gastrointestinal disease, such as peptic ulcer disease, chronic gastritis, gastric MALT lymphoma, and gastric cancer.^{1–3} Moreover, *H. pylori* infection causes extra-digestive diseases like idiopathic thrombocytopenic purpura.^{4–6} Most patients with *H. pylori* infection are cured by antibiotic eradication therapy. *H. pylori* always causes macroscopic gastritis and affects gastric acid secretion. Therefore, a relationship between *H. pylori* infection and GORD has been discussed in the last decade.

Does *H. pylori* eradication develop new GORD?

In 1997, Labenz et al.⁷ reported the risk of development of reflux oesophagitis by *H. pylori* eradication in patients with duodenal ulcer. The estimated development of reflux oesophagitis within 3 years was 25.8% after cure of *H. pylori* infection and 12.9% when eradication was unsuccessful.⁷ However, many of

subsequent papers reported inconsistent results. A post-hoc analysis of eight double-blind prospective trials of *H. pylori* eradication in 1165 patients⁸ did not confirm the risk of development of GORD by *H. pylori* eradication. In this analysis, the development of erosive oesophagitis was comparable in successfully vs. unsuccessfully eradicated patients (4 vs. 3%) and the development of new GORD symptoms was also comparable in successfully vs. unsuccessfully eradicated patients.⁸ According to these reports, successful eradication does not seem to develop new GORD.

A report from Japan⁹ reported a risk of development of new GORD after eradication. The estimated prevalence of reflux oesophagitis within 3 years was 18% after eradication therapy and 0.3% without therapy. Patients who developed reflux oesophagitis after therapy had a greater prevalence of both hiatal hernia and more severe corpus gastritis before therapy. However, the newly developed reflux oesophagitis was classified as mild (Los Angeles (LA) grade A or B) in 97% of patients who developed reflux oesophagitis after eradication therapy.⁹ We should take the initial pattern of

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gastritis into account when discussing about the effect of *H. pylori* eradication on acid secretion. Patients with an antral-predominant gastritis have high stimulated acid production due to low somatostatin production in the antrum and accompanied higher gastrin levels. Clinically, patients with duodenal ulcer are common in this group. In contrast, people with corpus-predominant atrophic gastritis have low acid production due to loss of acid-secreting parietal cells.^{10,11} In the clinical setting, patients with gastric ulcer or gastric cancer are common in this group.¹¹ In Asia including Japan, CagA- VacA-positive virulent strains are common.^{12,13} Such preponderance of CagA- and VacA-positive strains and proinflammatory interleukin-1 beta polymorphism are supposed to increase the risk of hypochlohydria and protects against the development of GORD in the Asian population.¹⁴ In case of patients with corpus dominant gastritis, we should be wary of the development of new GORD; however, when it does develop, it is not so severe.

Does *H. pylori* eradication in patients with GORD worsen symptoms or gastric atrophy?

In 1996, Kuipers et al.¹⁵ reported an increased risk of the development of gastric atrophy by the combination of acid suppression and *H. pylori* infection. Among patients with reflux oesophagitis treated with omeprazole, although none of whom had atrophic gastritis at base line, atrophic gastritis developed in 30.5% of *H. pylori*-positive patients and 4.3% of *H. pylori*-negative patients. This article suggested the increased risk of atrophic gastritis in patients with reflux oesophagitis and *H. pylori* infection treated with proton pump inhibitors (PPI).¹⁵ However, Kuipers himself revised his result later in subsequent study.¹⁶ In PPI-treated patients with *H. pylori* infection, there was no change in antral and corpus gastritis activity or atrophy. Moreover, *H. pylori* eradication did not alter the dose of required PPI or reflux symptoms.¹⁶ Recently, meta-analyses about development of GORD after *H. pylori* eradication have been reported. A meta-analysis of 10 randomized controlled trials comparing *H. pylori* eradication with no treatment on symptomatic GORD patients found no statistically significant effect of eradication on symptomatic GORD (OR 0.81, 95% CI 0.56–1.17; $p=0.27$) or endoscopic evidence of reflux oesophagitis (OR 1.13, 95% CI 0.72–1.78; $p=0.59$).¹⁷ A subgroup analysis revealed improvement of GORD symptoms by successful eradication.¹⁷ We also recently investigated the influence of *H. pylori* eradication on the risk of GORD by focusing on the quality of life (QOL) and evaluating reflux symptoms.¹⁸ At 3 months and 1 year after the *H. pylori* eradication therapy, surveys were conducted to determine the health-related

QOL by QOL in Reflux and Dyspepsia – Japanese version (QOLRAD-J) and the severity of GORD symptoms by Carlsson-Dent questionnaire (CDQ). Although no significant changes of QOLRAD-J and CDQ were apparent 3 months after *H. pylori* eradication, these scores were significantly improved after 1 year. The degree of improvement was even more marked in cases with severe reflux symptoms.¹⁸

In this issue of *UEG Journal*, Schwizer et al.¹⁹ report the results of a randomized, double-blind, multicentre trial performed in patients presenting with reflux symptoms.¹⁹ They aimed to resolve these controversies regarding the effects of *H. pylori* eradication in GORD. A total of 198 *H. pylori*-positive patients were randomized to receive either antibiotics or placebo for 7 days, and 113 *H. pylori*-negative patients served as controls and received placebo. All received esomeprazole 20 mg b.d. for 7 days, followed by 40 mg o.d. to complete an 8-week course, and were followed up for 32 weeks by telephone. In the study, baseline endoscopy revealed oesophagitis LA grade 0A (63%) and grade BCD (37%) with no difference between patient groups. Symptom improvement on esomeprazole was seen in 89%. *H. pylori* eradication had no effect on symptomatic relapse. Overall, *H. pylori*-positive patients had a lower probability of relapse compared to *H. pylori*-negative controls and this effect was significant for patients randomized to either placebo or antibiotics compared to non-randomized *H. pylori* negative controls. For *H. pylori*-positive patients, relapse hazard was modulated also by oesophagitis grade. Increased time to relapse in non-eradicated *H. pylori*-positive patients compared to *H. pylori*-negative controls was observed for those with LA 0A, but not patients with LA BCD. Authors concluded that relapse of GORD symptoms after a course of high-dose acid suppression took longer for *H. pylori*-positive patients than *H. pylori*-negative controls although *H. pylori* eradication had no effect on the risk of relapse. This study has some attractive findings. First, short- to mid-term management of GORD was focused on symptom control, independent of the decision to investigate and treat *H. pylori* infection. Second, withdrawal of PPI therapy was less likely to cause a relapse of reflux symptoms in patients with GORD with a history (past or present) of *H. pylori* infection.

Conclusion

The Maastricht IV/Florence Consensus Report¹⁹ mentioned that *H. pylori* status has no effect on symptom severity, symptom recurrence, and treatment efficacy in GORD. Moreover, the Report mentioned that *H. pylori* eradication does not exacerbate pre-existing GORD or affect treatment efficacy.²⁰ Previously,

although *H. pylori* eradication in patients with GORD was considered to induce unfavourable effects that worsen the symptoms of GORD, recent reports indicate that it can have favourable consequences by reducing symptoms and therefore improving QOL. *H. pylori* eradication can be recommended when we find *H. pylori* in GORD patients at least without severe corpus atrophy or severe hiatal herniation.

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