Indications for HP eradication : gastro-esophageal reflux disease

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Abstract

HP infection of the stomach is not a risk factor for reflux oesophagitis, and may even protect against reflux oesophagitis. HP eradication may lead to an accelerated development of GERD in duodenal ulcer disease patients. It is unknown whether this is also true for HP positive patients who do not suffer from duodenal ulcer disease. HP eradication may decrease the effcacy of acid secretion lowering drugs such as Proton Pump Inhibitors and H2-Receptor Antagonists. It is unclear whether this has any practical consequences, but it cannot be excluded that some patient may need an increased dose of acid secretion lowering drugs after HP eradication for control of symptoms and lesions of GERD.

There are conflicting data on the possibility that long-term proton pump inhibitor treatment may accelerate the development of atrophic gastritis in Helicobacter pylori positive patients. The possible acceleration of atrophic gastritis development in HP positive patients using strong acid secretion inhibitors is the strongest argument in favour of eradicating HP in patients receiving long term potent acid inhibition, especially GERD patients. In view of the uncertainty concerning these data, both eradicating and non eradicating HP in patients with GERD can be defended. (Acta gastroenterol. belg., **1998**, 61, **313-315**).

1. Introduction

The past two years have shown a marked interest in the interaction between H. pylori and gastro-oesophageal reflux disease (GERD). It appears that infection with this organism may interfere with the aetiology and management of GERD : H. pylori may become important in the management of GERD, whereas GERD may complicate the management of H. pylori.

2. H. pylori and the development of GERD

Several studies in the past had shown that the prevalence of H. Pylori is not higher in patients with reflux oesophagitis than in control subjects (1-8). Two large recent studies reported a significantly lower H. pylori prevalence in GERD patients compared to controls. In a Japanese study (9), 26 (37%) of 70 GERD patients were H. pylori infected compared to 47 (67%) of 70 matched controls. GERD patients had a lower gastritis and atrophy score than controls. Similar results were obtained by Werdmuller (10), who assessed the prevalence of Helicobacter pylori (using histology, culture, quick urease test, and serology) in 1527 consecutive patients. As a reference group patients presenting with a normal esophagus, stomach, and duodenum were taken. Reflux esophagitis was diagnosed in 118 patients, hiatal hernia without esophageal inflammation in 109, and Barrett's esophagus in 13. Helicobacter pylori was present in 74/240 (30%) of these patients and in 204/399 (51%) of the reference group. The prevalence of H. pylori was significantly lower among each of these three GERD subgroups than among the controls. There was no difference when patients with esophagitis, Barrett's esophagus, or hiatal hernia were compared. The authors concluded that H. pylori infection has no role in the pathogenesis of reflux oesophagitis. However, in the perspective of other recent data, another plausible explanation for the data is that H. pylori infection actually protects against the development of GERD.

3. HP eradication and GERD symptoms

Some studies show that the incidence of heartburn decreases after HP eradication. In a study on 42 patients with chronic duodenal ulcer disease, Phull *et al.* (11) report a decrease of heartburn from 28.7% prior to HP eradication, to 7.1% 12 months after HP eradication. Labenz *et al.* (12) report that after HP eradication in duodenal ulcer patients, the prevalence of heartburn diminishes from 30% before HP eradication to 25% up to 3 years after HP eradication.

4. HP eradication and GERD lesions

Duodenal ulcer patients who were successfully treated with H. pylori eradication therapy, may be at increased risk to develop GERD lesions. Hirschl *et al.* (13) reported the development of endoscopically verified reflux oesophagitis in 10/16 duodenal ulcer patients who during a mean follow-up of 43 months were persistently H. pylori negative after successful eradication therapy. Sacca *et al.* (14) found that 24/169 (14%) patients with peptic ulcer disease without oesophagitis had developed mild (stage 1) reflux oesophagitis 6 months after HP eradication.

The largest study, with the longest follow-up, and the only one with a control group, is Labenz's *et al.* (12). They found that within 3 years after H. pylori eradication an endoscopically proven reflux oesophagitis developed in 25.8% of 244 patients with endoscopically proven relapsing duodenal ulcer disease and

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without endoscopic signs of reflux oesophagitis at the time of H. pylori eradication, whereas in 216 patients who remained HP positive, 12.9% developed oesophagitis. The life-table analysis suggested that cure of the infection was associated with an increased risk of reflux oesophagitis during the first year after treatment, whereas later the incidence of reflux oesophagitis was similar in both groups. Patients who developed reflux oesophagitis after the cure had a more severe body gastritis before cure, gained weight more frequently after cure, and were predominantly men.

It should however be noted that at the start of these three studies, patients were excluded if they also presented with reflux oesophagitis. There are no data on the fate of the oesophagus after HP eradication in patients with reflux oesophagitis. The data thus strongly suggest that there is a risk for developing reflux oesophagitis after HP eradication in patients with duodenal ulcer. Although there is anecdotal evidence of oesophagitis developing after HP eradication in patients without peptic ulcer disease, it is unknown whether HP eradication in patients without duodenal ulcer also increases the risk for developing reflux oesophagitis.

5. HP eradication and efficacy of acid secretion inhibitors

It should be mentioned, as is developed in another chapter, that HP eradication may diminish the efficacy of acid-lowering drugs. Although theoretically, this may complicate the management of GERD patients, there are at this time no data in favour of this possibility, as there are no data disproving it.

6. HP eradication and accelerated development of atrophic gastritis in patients using proton pump inhibitors

Logan *et al.* (15) showed that during omeprazole treatment, there was a shift of HP from antrum to body mucosa. After four weeks of omeprazole treatment, the histological density of H. pylori in the antrum and corpus was reduced, while that in the fundus was increased. This was associated with a corresponding decrease in the activity of antral gastritis. These data were confirmed by Kuipers *et al.* (16), who showed that H. pylori-negative patients had no histological signs of active gastritis before or after 8 weeks treatment with omeprazole 40 mg/d. However, H. pylori positive patients showed predominant colonization and associated inflammation in the antrum before therapy, but after therapy, the infection predominantly affected the corpus. The inflammation and bacterial colonization in the antrum significantly decreased, leading to negative antral cultures in 61% (20 of 33 patients). In contrast, the inflammation of the corpus mucosa significantly increased despite stable bacterial counts.

This effect is not limited to omeprazole. Both Berstad *et al.* (17) and Eissele *et al.* (18) showed a similar increase in body gastritis score during long term treatment with lansoprazole in HP positive patients, whereas there was no change in the gastritis activity in HP negative patients. Since superficial corpus gastritis has a tendency to lead to atrophic gastritis (19,20), the increased body inflammation in HP positive patients observed during short term omeprazole therapy may lead to atrophic gastritis during long term omeprazole therapy. Kuipers *et al.* (21) studied patients from two separate cohorts who were being treated for reflux esophagitis ; 72 patients treated with fundoplication in Sweden and 105 treated with omeprazole (20 to 40 mg once daily) in the Netherlands. In both cohorts, the patients were followed for 3 to 8 years. H. pylori infection was not treated. After fundoplication, the patients did not receive acid-suppressive therapy. Among the patients treated with fundoplication, atrophic gastritis did not develop in any of 31 who were infected with H. pylori at base line or in 41 who were not infected ; 1 patient infected with H. pylori had atrophic gastritis before treatment that persisted after treatment. Among the patients treated with omeprazole, none of whom had atrophic gastritis at base line, atrophic gastritis developed in 18 of 59 infected with H. pylori ($P < 0.001$) and 2 of 46 who were not infected ($P = 0.62$). The authors concluded that patients with reflux esophagitis and H. pylori infection who are treated with omeprazole are at increased risk of atrophic gastritis.

The Kuipers study has been challenged by data of Lundell *et al.* (22) who show that atrophic gastritis develops almost exclusively in HP positive patients ; although they find a higher incidence of atrophic gastritis in HP positive patients treated with omeprazole (4.3% per year) than HP positive patients treated by anti-reflux surgery (2.8% per year), this difference is not statistically significant.

Although the Kuipers' study is contested, this is the strongest argument in favour of eradicating HP in patients receiving long term potent acid inhibition. However, in view of the uncertainty concerning these data, both eradicating and non eradicating HP in patients with GERD can be defended.

7. Conclusion

H. pylori is not a risk factor for GERD. In contrast, there is increasing evidence for the hypothesis that the presence of H. pylori infection may actually protect against the development of GERD. H. pylori eradication may induce reflux oesophagitis in some duodenal ulcer patients. HP also has a potential role in the management of GERD. H. pylori eradication may decrease the acid-lowering capacity of proton pump inhibitors and H2-receptor antagonists, which may interfere with treatment of reflux. To which extent these

potential problems are clinically important remains to be determined. One heavily criticised report suggests that proton pump inhibitor treatment of GERD may be associated with an accelerated development of atrophic gastritis in H. pylori positive patients ; randomized studies should indicate whether H. pylori should be eradicated in these patients. In the meantime, in view of the uncertainty concerning these data, both eradicating and non eradicating HP in patients with GERD can be defended, and treating HP in patients with GERD is a matter of personal conviction.

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