Adverse events of HP eradication : long term negative consequences of HP eradication

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Abstract

Two problems can be identified as possible long term negative consequences of HP eradication : diminished efficacy of acid-lowering drugs, and an accelerated development of GERD.

It was shown that omeprazole produces a greater decrease in gastric acidity in subjects with H. pylori infection than in those who are H. pylori negative, and that omeprazole produces a smaller decrease in gastric acidity after cure of H. pylori. This effect persisted for at least one year after HP eradication. It is not limited to omeprazole, but can also be seen with the H2 receptor antagonist ranitidine. At least one proven mechanism involved in this phenomenon is the disappearance of the alkalinizing effect of ammonia, generated from urea by HP's urease, after eradication of the bacteria ; other mechanisms may also be involved. HP eradication may therefore potentially hamper acid inhibitory treatment. It is unknown to what extent this is clinically relevant. Although one study did not observe a relation between H. pylori status and efficacy of omeprazole maintenance therapy for GERD, it cannot be excluded that some patients may need more potent or higher doses of acid-lowering medication after HP eradication.

Three studies suggest that duodenal ulcer patients who were successfully treated with H. pylori eradication therapy, may be at increased risk to develop GERD. Labenz's study finds that the incidence of GERD may be double 3 years after eradication. 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. 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. It is unknown whether HP eradication in patients without duodenal ulcer also increases the risk for developing reflux oesophagitis. (Acta gastroenterol. belg., **1998**, 61, **350-351**).

I. Introduction

Apart from the possible induction of resistance to antibiotics in HP when eradication fails, and in other microorganisms of the host, whether eradication succeeds or not, little attention has been given in the litterature on possible unwanted consequences of HP eradication. Two important unwanted gastroenterological consequences of HP eradication have been described : a diminished efficacy of acid-lowering drugs, and the possible induction of GERD.

II. Diminished efficacy of acid lowering drugs

The seminal observation was made by Verdu *et al.* (1), who showed that omeprazole produces a greater decrease in gastric acidity in subjects with H. pylori infection than in those who are H. pylori negative. Furthermore, they showed that (2) omeprazole produces a smaller decrease in gastric acidity after cure of H. pylori. This was confirmed by Labenz *et al.* (3), who showed that in 17 duodenal ulcer patients, H. pylori eradication resulted in a marked decrease of the pH-increasing effect of omeprazole (24-hour median gastric pH, 5.5 vs. 3.0 ; $P < 0.002$) that was most pronounced during nighttime (median gastric pH, 6.4 vs. 2.1 ; $P = 0.001$). Baseline intragastric pH remained unchanged after eradication (median gastric pH, 1.0 vs. 1.1 ; $P = 0.5$). These authors showed that this effect persisted for at least one year after HP eradication (4). They showed that this effect is not limited to omeprazole, but can also be seen with the H2 receptor antagonist ranitidine (5) : cure of the HP infection did not affect the acidity during daytime (median gastric pH : 1.3 vs 1.2) and after meals (median gastric pH : 1.4 vs 1.2), while it was associated with a decreased efficacy of the drug during night-time (10:00 p.m. to 6:00 a.m.) : median gastric pH 6.8 vs 5.4. At least one proven mechanism involved in this phenomenon is the disappearance of the alkalinizing effect of ammonia, generated from urea by HP's urease, after eradication of the bacteria (6). HP eradication may therefore potentially hamper acid inhibitory treatment. It is unknown to what extent this is clinically relevant. Although one study did not observe a relation between H. pylori status and efficacy of omeprazole maintenance therapy for GERD (7), it cannot be excluded that some patients may need more potent or higher doses of acid-lowering medication after HP eradication.

III. HP eradication may induce gastro-oesophageal reflux disease

It has been reported that duodenal ulcer patients who were successfully treated with H. pylori eradication therapy, may be at increased risk to develop GERD. Hirschl *et al.* (8) reported the development of endoscopically verified reflux oesophagitis in 10/16 duodenal ulcer patients who during a mean follow-up of

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43 months were persistently H. pylori negative after successful eradication therapy. Sacca *et al.* (9) 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.* (10). 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 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. These three studies report on patients with duodenal ulcer disease ; it is unknown whether HP eradication in patients without duodenal ulcer also are at risk for developing reflux oesophagitis.

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