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• *BRIEF REPORTS* •

Influence of various proton pump inhibitors on intestinal metaplasia in noneradicated *Helicobacter pylori* patients

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Abstract

AIM: Intestinal metaplasia (IM) is more often found in patients with *Helicobacter pylori* (*H pylori*) infection, while eradication of *H pylori* results in significant reduction in the severity and activity of chronic gastritis. We aimed to determine in patients with unsuccessful eradication of *H pylori* the role of various proton pump inhibitors (PPIs) having different mechanisms in the resolution of IM.

METHODS: We confirmed endoscopically and pathohistologically (Sydney classification) the IM in 335 patients with gastritis before and after medication for eradication of *H pylori* (Maastricht Protocol 2002). *H pylori* infection was determined by using histology, urease test and culture. Control endoscopy and histology were done after 30 d and thereafter (within 1 year). Unsuccessful eradication was considered if only one of the three tests (histology, urease and culture) was negative after therapy protocol. We used omeprazole, pantoprazole, lansoprazole in therapy protocols (in combination with two antibiotics).

RESULTS: We found no significant difference in resolution of IM by using different PPI between the groups of eradicated and noneradicated patients ($P<0.4821$ and $P<0.4388$, respectively).

CONCLUSION: There is no significant difference in resolution of intestinal metaplasia by different proton pump inhibitors.

Key words: *H pylori*, Intestinal metaplasia

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INTRODUCTION

Patients with *Helicobacter pylori* (*H pylori*) infection have been found more frequently with intestinal metaplasia (IM) and atrophic gastritis[1]. Several authors (Asaka *et al* Ohkusa *et al,* and Kokkola *et al,*) have found that eradication of *H pylori* results in significant reduction in the severity and activity of chronic gastritis[2].

We know about different mechanisms of proton pump inhibitors (PPIs). Omeprazole and lansoprazole have effects on Cys 813, and pantoprazole additionally on Cys 822 which is important for irreversible acid blockade. The influence on gastric acid secretion is dose dependent, which means that a higher PPI dose has a stronger acid inhibition[3]. *H pylori* eradication was associated with a histologic improvement of gastric mucosa but in uninfected patients no significant change in inflammation or proliferation occurred during treatment with lansoprazole[4].

The aim of this study was to determine in patients with unsuccessful eradication of *H pylori* the role of various PPIs having different mechanisms in the resolution of IM.

MATERIALS AND METHODS

Patients

We followed up 335 patients with gastritis (142 males and 193 females, mean age 51.3 years, between 18 and 83 years). All patients underwent upper gastrointestinal endoscopy with pathohistologic examination. We used Olympus Q20 and Pentax video endoscopy systems.

Methods

Diagnostic procedures We confirmed endoscopically and pathohistologically (Sydney classification)[5] the IM in patients with gastritis before and after medication for eradication of *H pylori* (Maastricht Protocol 2002)[6]. *H pylori* infection was determined by using histology, urease test and culture in addition to E-test[7-9]. Control endoscopy and histology were done after 30 d and thereafter (within 1 year). Unsuccessful eradication was considered if only one of the three tests (histology, urease and culture) was positive after therapy protocol.

Therapy We used omeprazole 20 mg bid, pantoprazole 40 mg bid, and lansoprazole 30 mg bid in eradication therapy

Table 1 **Influence of various PPIs on intestinal metaplasia in the noneradicated *Helicobacter pylori* infection patients**

Intestinal metaplasia	Omeprazole (*n*)	Pantoprazole (*n*)	Lansoprazole (*n*)
Negative	20	26	14
Positive	16	22	10

$\chi^2 = 2.462$, $\gamma = 3$, $P = 0.4821$.

protocols during 7 d in combination with two antibiotics (amoxicilin 1 g bid and clarithromycin 500 mg bid), and thereafter at the same dose but once a day during the next 4 wk[6]. We included 108 patients on omeprazole protocol, 137 patients on pantoprazole protocol and 90 patients on lansoprazole protocol.

RESULTS

The successful eradication of *H pylori led* to the disappearance of IM in gastric mucosa (208 patients with negative IM *vs* 19 patients with positive IM) ($\chi^2 = 157.36$, $\gamma = 1$, $P<0.001$). The unsuccessful eradication of *H pylori* also led to the disappearance of IM but it was not statistically significant (48 with positive IM *vs* 60 with negative IM; $\chi^2 = 1.33$, $\gamma = 1$, $P<0.1$).

We found no significant difference in resolution of IM by using different PPI in the group of noneradicated patients ($P<0.4821$), as well as in the group of eradicated patients ($P<0.4388$) (Tables 1 and 2).

DISCUSSION

The occurrence of IM was influenced by the presence of *H pylori* infection[1,2].

H pylori modified cellular processes of the host and led to inflammation[1,2]. *H pylori* infection stimulated the infiltration of neutrophils, lymphocytes, plasma cells and macrophages in gastric mucosa[10]. There are several mechanisms by which *H pylori* infection triggers a host response (major histocompatibility complex II, translocation of *H pylori* CagA protein into human gastric epithelial cells using type IV secretion which is ATP-ase dependent)[10]. PPI could influence ATP-ase and glycoprotein[11]. *H pylori* could also influence lamina propria and activate underlying cells[10]. They could influence host response to their presence by regulating prostaglandin production over cyclo-oxgenase-2-expression, activating neutrophils and oxidative stress and mucosal products, and all these processes could result in apoptosis and cell proliferation suppression[10]. Specific gene products synthesized by bacteria or host have been implicated in the inflammatory and IM process (role of cag potency in IM and gastric cancer development)[10].

The gastritis score increased in patients who had no or only mild corpus gastritis before treatment and significantly decreased in those who had moderate or severe gastritis before treatment[12]. We could find similar results in the study of Berstad *et al*[4], with lansoprazole.

Acid secretion decreased dose-dependently in PPI users[13,14]. Reports on endocrine cell changes in the antral mucosa under chronic PPI therapy are controversial and lack clinical relevance[14,15]. Data on the progression of oxintic gastritis under chronic PPI treatment in comparison to untreated controls could not be confirmed in more recent studies including a well-matched control population[14]. The mechanism of PPI action on acid suppression is different. All PPIs bind to and act on Cys 813, which is placed near the curve where TM6 enters the membrane domain. Lansoprazole binds to Cys 321 on ectoplasmatic end TM3, but pantoprazole binds to Cys 822 which is placed deeper in the membrane domain TM6[16]. This can be an explanation for different and irreversible suppressions of Cys 822 by pantoprazole. The recovery of proton pump was measured in rat stomach, and complete recovery of ATP-aze was detected after medication with omeprazole, esomeprazole and rabeprazole but 70% recovery was detected. After medication with pantoprazole no recovery of proton pump was detected after lansoprazole[16]. We wanted to evaluate the influence of PPI on IM in patients with similar conditions (inflammation caused by *H pylori*). Eradication of *H pylori* had no difference on IM disappearance by PPI. We concluded that there was no difference in PPIs between such groups of patients. In the group of patients with unsuccessful eradication of *H pylori*, presence of *H pylori* was constant, and PPI could influence IM, but our results were negative. The explanation can be that *H pylori* disturbs the effect of PPI on IM disappearance in a different way from the mechanism by which it acts on PPI in gastric cells. But it is interesting that in the eradicated group (effect of *H pylori* on gastric cells excluded) the result was the same. Further investigations are needed.

Table 2 **Influence of various PPIs on intestinal metaplasia in the eradicated *Helicobacter pylori* infection patients**

Intestinal metaplasia	Omeprazole (*n*)	Pantoprazole (*n*)	Lansoprazole (*n*)
Negative	64	81	63
Positive	8	8	3

$\chi^2 = 2.702$, $\gamma = 3$, $P = 0.4388$.

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