Impact of *Helicobacter pylori* infection on serum gastrin in haemodialysis patients

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Abstract

**Background.** *Helicobacter pylori* infection is associated with increased gastrin release in patients with normal renal function. Hypergastrinaemia is a common finding in haemodialysis patients and, in many cases, may be linked to *H. pylori* infection. The aim of this study was to examine the effect of *H. pylori* infection, and its eradication, on elevated gastrin levels in haemodialysis patients.

**Methods.** Eighty-nine dyspeptic patients were included in the study. While 44 patients had normal renal function, the remaining 45 were end-stage renal failure patients. Patients were assigned to one of four groups according to their *H. pylori* and renal function status. Infected patients were re-evaluated after 2 months following eradication treatment. Serum gastrin levels were measured in these groups both before and after eradication treatment.

**Results.** Haemodialysis patients with *H. pylori* infection had higher serum gastrin levels than did *H. pylori* negative haemodialysis patients (321 ± 131 pg/ml vs 154 ± 25 pg/ml) (*P* < 0.05). Mean serum gastrin concentration was 152 ± 21 pg/ml in the non-uraemic *H. pylori*-positive group. This value was 58 ± 17 pg/ml in the non-uraemic *H. pylori*-negative group (*P* < 0.05). There were significant decreases in serum gastrin levels from pre- to post-eradication of *H. pylori* in the infected haemodialysis and non-uraemic patient groups (312 ± 131 pg/ml to 179 ± 85 pg/ml and 152 ± 21 pg/ml to 72 ± 2.4 pg/ml respectively, *P* < 0.05). Four patients in group Ib and 5 patients in group IIb who had persistent infection did not have a decrease in serum gastrin level. All patients with successful eradication had a decrease in serum gastrin concentration.

**Conclusion.** Our findings suggest that *H. pylori* infection contributes to hypergastrinaemia in haemodialysis patients. More research is needed regarding the clinical consequences of hypergastrinaemia in these individuals.

**Key words:** gastrin; haemodialysis; helicobacter pylori

Introduction

*Helicobacter pylori* infection is the major cause of chronic active gastritis and plays an important role in the pathogenesis of peptic ulcer disease. Individuals infected with this bacteria have elevated basal and postprandial serum gastrin concentrations [1,2] and *H. pylori* is known to alter acid secretory physiology in chronically infected patients. Hypergastrinaemia and subsequent acid hypersecretion that occurs are thought to be key factors in the pathophysiology of duodenal ulcer disease.

It has been shown that patients with chronic renal failure have an elevated fasting serum gastrin level [3,4] and that the level remains high while patients are on regular dialysis treatment [5]. Factors such as gastric acid suppression, decreased renal clearance of gastrin, and elevated serum gastrin-releasing peptide concentrations can contribute to the high serum gastrin concentrations seen in haemodialysis (HD) patients [6,7]. *Helicobacter pylori* infection may also contribute to the above-normal serum gastrin observed in these individuals. In this study we aimed to clarify the impact of *H. pylori* infection, and eradication, on serum gastrin levels in HD patients.

Subjects and methods

The study included 89 patients, 44 with normal renal function and 45 with end-stage renal disease who were on HD treatment.

**Inclusion criteria**

All patients had dyspeptic symptoms of at least 6 months duration. None of the patients had undergone antibiotic and/or antacid therapy within 4 months of the study and all had been on HD treatment for at least 6 months. Those with
gastric and/or duodenal ulcers as confirmed by upper gastrointestinal endoscopy were excluded from the study. None of the patients included had a history of gastric surgery, or any evidence of atrophic gastritis on upper gastrointestinal endoscopy and histopathology. In all groups, none of the patients were smokers or alcohol abusers.

All patients gave their informed consent prior to the study.

**Haemodialysis treatment schedule**

The end-stage renal disease patients were on a thrice-weekly haemodialysis programme in Başkent University Ankara Hemodialysis Center. The dialysis prescription included 4–5 h of bicarbonate haemodialysis with standard cuprophane membranes (hollow fibre 1–1.2 m² surface area, Gambro, Sweden) with average blood flow rate of 300 ml/min, and the machines used were AK90 and AK95 (Gambro, Sweden). The maintained mean Kt/V of the patients was 1.2.

**Upper endoscopy**

Upper gastrointestinal endoscopy was performed using an Olympus GIF-Q 230 videoendoscope. All patients were under conscious sedation during the procedure.

**Helicobacter pylori detection**

We obtained four gastric biopsies from the pre-pyloric region of the lesser and greater curvatures. The same pathologist evaluated two biopsy samples for the presence of *H. pylori* and the other two specimens were sent to the laboratory for urease testing. *Helicobacter pylori* positivity was defined as the presence histologically proven micro-organism and/or positive urease test. Infected patients were re-evaluated 2 months after eradication therapy with upper gastrointestinal endoscopy, histopathology, and urease testing.

**Patient groups**

We divided patients into four groups according to their *H. pylori* and renal function status:

- **Group Ia**: Normal renal function, *H. pylori* negative (20 patients);
- **Group Ib**: Normal renal function, *H. pylori* positive (24 patients);
- **Group IIa**: Haemodialysis, *H. pylori* negative (20 patients);
- **Group IIb**: Haemodialysis, *H. pylori* positive (25 patients).

**Serum gastrin measurement**

The fasting venous blood samples were immediately centrifuged and stored at –20°C. Serum gastrin determination was performed by RIA method (Gastrin 125 RIA, Instar Corp, Minnesota USA).

**Helicobacter pylori eradication**

We treated *H. pylori*-positive patients with famotidine 40 mg once daily, 500 mg clarithromycin b.i.d., and 500 mg metronidazole b.i.d. for 15 days. The metronidazole dosage was halved for HD patients.

**Statistics**

Statistical analysis was carried using the program SPSS for Windows. To compare the groups, we used Student’s *t*-test, Mann-Whitney *U* test, and Wilcoxon test. *P* values <0.05 were considered as significant and our confidence interval was 95%.

**Results**

The number of patients per group, their mean ages and HD duration are shown in Table 1. There were no significant differences between the study groups with regard to mean ages and HD duration (*P* > 0.05). The upper gastrointestinal endoscopy findings listed in Table 2 show that the prevalence of antral gastritis and bulbitis are significantly higher in *H. pylori*-infected patients (group Ib and group IIb) than in the other groups. Results of upper endoscopy findings in infected patients performed after the completion of eradication therapy are shown in Table 3. *Helicobacter pylori* eradication treatment was successful in 20 (83%) and 20 (80%) of group Ib and IIb patients respectively. Successful eradication therapy resulted in improvement of upper endoscopy findings in significant numbers of patients in both non-uraemic and haemodialysis groups, reflecting the importance of *H. pylori* infection (Table 3). Average serum gastrin level was 152.9 ± 21.7 pg/ml in group Ib, which was significantly higher than the group Ia level of 58.6 ± 17.1 pg/ml (*P* < 0.05). The average serum gastrin concentrations in the HD patients (groups Ia and IIb) were

**Table 1. Number, gender, mean age, and haemodialysis duration of patient groups**

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>M</th>
<th>F</th>
<th>Mean age* (years)</th>
<th>Haemodialysis duration** (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Ia</td>
<td>20</td>
<td>11</td>
<td>9</td>
<td>29.90 ± 4.90</td>
</tr>
<tr>
<td>Group Ib</td>
<td>24</td>
<td>13</td>
<td>11</td>
<td>33.80 ± 6.70</td>
</tr>
<tr>
<td>Group IIa</td>
<td>20</td>
<td>12</td>
<td>8</td>
<td>32.50 ± 5.30</td>
</tr>
<tr>
<td>Group IIb</td>
<td>25</td>
<td>14</td>
<td>11</td>
<td>35.10 ± 4.20</td>
</tr>
</tbody>
</table>

Group Ia, Normal renal function, *H. pylori* negative; Group Ib, Normal renal function, *H. pylori* positive; Group IIa, Haemodialysis, *H. pylori* negative; Group IIb, Haemodialysis, *H. pylori* positive.

*P > 0.05; **P > 0.05.

**Table 2. Upper endoscopy findings of patient groups before eradication therapy**

<table>
<thead>
<tr>
<th>Oesophagitis</th>
<th>Hiatus hernia</th>
<th>Antral gastritis</th>
<th>Erosive gastritis</th>
<th>Bulbitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Ia</td>
<td>Group Ib</td>
<td>Group Ia</td>
<td>Group Ib</td>
<td>Group Ia</td>
</tr>
<tr>
<td>Oesophagitis</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Hiatus hernia</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Antral gastritis</td>
<td>5</td>
<td>25</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Erosive gastritis</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Bulbitis</td>
<td>1</td>
<td>14</td>
<td>2</td>
<td>16</td>
</tr>
</tbody>
</table>

See Table 1 footnote for groupings.
H. pylori infection who develop duodenal ulceration have two disturbances of gastric function: increased release of gastrin by the antral mucosa and an exaggerated acid response to stimulation by gastrin [10]. Dyspeptic symptoms are quite common in chronic HD patients, a considerable number of whom are infected with H. pylori. Therefore, detection and treatment of gastroduodenal lesions are very important in this group, especially in terms of preventing complications after renal transplantation.

It is well known that serum gastrin level is elevated in most HD patients, but the role of H. pylori in hypergastrinaemia is unclear. Luzza et al. [11] found that level of gastrinaemia in HD patients who were seropositive for H. pylori exceeded that of seronegative HD patients.

The findings of our study showed that successful eradication of H. pylori infection resulted in significant decrease in dyspeptic symptoms both in non-uraemic and haemodialysis groups. We also detected significant improvement in upper endoscopic findings after successful eradication in both groups, reflecting the importance of H. pylori infection in both groups.

In our study, we found that serum gastrin concentrations was significantly higher in H. pylori-positive HD patients than in HD patients who were not infected. Moreover, these high levels of serum gastrin decreased significantly after successful eradication of H. pylori.

The hypergastrinaemia associated with chronic renal failure may be due to multiple factors. Reduced excretion of gastrin by the kidneys undoubtedly plays a role [12,13]. Atrophic gastritis and inhibition of acid secretion, both of which are quite commonly observed in chronic renal failure patients may also contribute to the condition [5].

The mechanisms that lead to exaggerated gastrin secretion in chronic H. pylori infection are unclear. One theory is that ammonia generation by H. pylori urease creates an alkaline environment in the vicinity of G cells, which thus stimulates gastrin release [14]. Another possible mechanism rests on the finding that both the antral mucosal somatostatin concentration and the number of antral somatostatin-producing D cells are lower in H. pylori-infected individuals than in uninfected controls [15–17]. Since endogenous somatostatin is known to be an important inhibitor of gastrin secretion, an H. pylori-induced decrease in somatostatin concentration at the antral mucosa could result in hypergastrinaemia.

There is also evidence to suggest that gastrin release

**Table 3.** Upper endoscopy findings of infected patients in whom successful eradication was achieved

<table>
<thead>
<tr>
<th></th>
<th>Group Ib* <em>(n=20)</em></th>
<th>Group Ib** <em>(n=20)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophagitis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hiatus hernia</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Antral gastritis</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Erosive gastritis</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Bulbitis</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*Group Ib, Normal renal function and successful H. pylori eradication; **Group Ib, Haemodialysis and successful H. pylori eradication.

154.9 ± 25.6 pg/ml and 321.2 ± 131.9 pg/ml respectively (P<0.05).

After successful eradication of the infection, we detected serum gastrin levels of 72.1 ± 22.4 pg/ml and 179.3 ± 85.9 pg/ml in groups Ib and IIb respectively. All patients in both groups Ib and IIb who cleared their infection showed serum gastrin decreases. These decreased levels differed significantly from the respective pre-eradication values (P<0.05). Four patients in group Ib and five patients in group IIb who had persistent infection did not have a decrease in serum gastrin level. Group serum gastrin concentrations are summarized in Table 4.

Dyspeptic symptoms disappeared in 17 group Ib patients after successful eradication; the remaining three patients had improvement in their symptoms. Four patients with persistent infection still had dyspeptic symptoms. In group IIb, successful eradication led to the disappearance of symptoms in 15 patients, and five patients had an improvement of their symptoms. The remaining five patients with persistent infection still had similar dyspeptic symptoms.

**Discussion**

*Helicobacter pylori* infection affects mainly the gastric antrum where the gastrin-producing G cells are located. Thus, it is logical to assume that chronic infection of this type affects gastrin release and in turn gastric acid secretion. This excess secretion may contribute to the development of peptic ulcer disease.

Studies of patients with normal renal function have shown that *H. pylori* infection results in hypergastrinaemia [2,8,9]. Others have reported that patients with

**Table 4.** Serum gastrin concentrations (pg/ml) in study groups before and after *H. pylori* eradication

<table>
<thead>
<tr>
<th></th>
<th>Group Ia</th>
<th>Group Ib</th>
<th>Group IIa</th>
<th>Group IIb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eradication</td>
<td>58.6 ± 17.1</td>
<td>152.9 ± 21.7</td>
<td>154.9 ± 25.6</td>
<td>321.2 ± 131.9</td>
</tr>
<tr>
<td>Post-eradication</td>
<td>—</td>
<td>72.1 ± 2.4*</td>
<td>—</td>
<td>179.3 ± 85.9*</td>
</tr>
</tbody>
</table>

*Group Ia, Normal renal function, *H. pylori* negative; Group Ib, Normal renal function, *H. pylori* positive (after successful eradication); Group IIA, Haemodialysis, *H. pylori* negative; Group IIb, Haemodialysis, *H. pylori* positive (after successful eradication). *P<0.05.
may be affected by the presence of gastric inflammation. Gastric epithelial cells and mucosal inflammatory cells that are attracted and activated by \textit{H. pylori} release cytokines such as tumour necrosis factor, IL-8 and interferon-\gamma, all of which are capable of stimulating gastrin release by G cells [18].

In conclusion, we believe that \textit{H. pylori} infection contributes to the hypergastrinaemia observed in HD patients since eradication of the infection led to a significant decrease in plasma gastric concentration. Moreover, successful eradication may lead to decreased complication rates after renal transplantation. More studies are needed to define the clinical significance of these findings.

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\section*{References}


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