

Helicobacter pylori eradication for the treatment of dyspeptic symptoms in chronic renal failure

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Patients with chronic renal failure (CRF) suffer from dyspeptic symptoms and have an increased incidence of gastritis, peptic ulceration and upper gastrointestinal hemorrhage.¹ *Helicobacter pylori* has been implicated in the development of gastrointestinal lesions in CRF. There are great variations in reported prevalences (17% to 63.5%) of *H. pylori* infection in uremic patients.^{2,3} It seems that the eradication of *H. pylori* in these patients would produce the same benefits as in the general population (gastritis and ulcer healing, reduction in ulcer relapse rate, and decrease in dyspeptic symptoms).⁴ However, indications for eradication therapy and the best therapeutic approach in CRF patients are still controversial.

Methods

To determine the prevalence of *H. pylori* infection in patients with CRF and to assess the efficacy of two therapeutic regimens, 169 patients were included in this prospective study: 55 patients on chronic haemodialysis (group I), 51 patients with chronic renal failure ($10 < \text{Cl}_{\text{cr}} < 30$ ml/min; group II), and 63 dyspeptic patients with normal renal function (group III). The groups were comparable, as observed differences between them were minimal (Table 1). Patients who had taken antibiotics during the previous 3 months, who were treated with antiulcer or antirheumatic drugs, or who had other severe disease, were excluded from the study.

At the beginning of the study, interviews, clinical examinations, and gastroduodenoscopies were performed, gastric biopsies were obtained for the rapid urease test (RUT), histology and culture, and serum *H. pylori*-specific IgG was measured by the ELISA test. The Glasgow Dyspepsia Severity Score (GDSS)⁵ was used for judging the severity of dyspepsia. The questionnaire was designed for main dyspeptic symptoms (pain, nausea, heartburn, fullness), scoring each one according to its frequency and intensity from 0 to 5. Columbia agar with 5% sheep blood was used as the base medium for cultivation, and the E-test strips were used for MIC value determination.⁶ Stomach biopsy specimens, two from the antrum and two from the body were histologically examined and graded according to the Sydney system.⁷

In ²³/₅₅ patients (41.8%) in group I, ²⁴/₅₁ (47.1%) in group II, and ³⁷/₆₃ (58.7%) in group III, *H. pylori* was demonstrated by either histology or culture (comparison of both uremic groups with control group, $P=0.056$). Forty-seven CRF patients infected with *H. pylori* received pantoprazole 40 mg twice daily and amoxicillin 1000 mg twice daily for 7 days, and were randomly assigned to either metronidazole 500 mg twice daily for 7 days (treatment group A, $n=23$) or azithromycin 1000 mg once daily for 3 days (treatment group B, $n=24$). Since these drugs are largely metabolized in the liver, dosage reductions for one week of therapy were unnecessary.

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Table 1. Demographic data.

	Group I	Group II	Group III	P
Number of examinees	55	51	63	
Age (yrs)				
Mean±SD	52.2±14.8	56.6±14.0	54.6±14.1	0.29
Range	19-77	21-78	23-79	
Sex (M/F)	30/25	28/23	31/32	0.79
Smoker	20	21	28	0.76
Alcohol use	16	17	23	0.43

Four weeks after the intervention, endoscopy, histology, RUT, dyspeptic symptoms questionnaire, and GDSS were repeated. Results were expressed as mean±SD. Comparisons between the groups were done with the Student's t test, chi-square test, and analysis of variance, depending on the nature of the data. A level of $P<0.05$ was considered significant.

Results

A high incidence and intensity of dyspepsia in CRF patients was observed. The GDSS was elevated in both CRF groups (8.4±3.4 for group I and 8.5±3.3 for group II), and was comparable to the control group (10.2±2.9). There were significant differences between CRF patients with (n=47) and without *H. pylori* infection (n=59). Infected patients had a higher prevalence of gastric ulcers (10 vs. 4; $P=0.028$) and a higher GDSS (9.2±3.7 vs. 7.8±2.9; $P=0.0039$). The presence of *H. pylori* was associated with acute ($P=0.043$) and chronic inflammation ($P=0.024$) of the gastric mucosa in CRF patients, according to the Sydney score.

Success in *H. pylori* eradication was evaluated in 44 patients (three patients did not attend control examination) and was achieved in 16/21 (76.2%) patients from the treatment group A, and in 19/23 (82.6%) patients from treatment group B (per protocol analysis, $P=0.59$; ITT analysis $P=0.45$). Eradication of *H. pylori* significantly improved both ulcer-like and

oesophagitis-like dyspeptic symptoms in both groups (Table 2; $P<0.05$ for each symptom within-group). The average GDSS was significantly decreased in both treated groups: from 9.22±3.59 to 5.14±2.57 in group A, and from 9.25±3.94 to 5.96±2.55 in group B, respectively. There were no significant differences between the two regimens in attenuation of dyspeptic symptoms. Eradication led also to a gradual improvement in gastric mucosa, independent of therapy combination, showing a reduction of acute and chronic inflammation ($P<0.0001$). Minor side effects including diarrhea and nausea were reported by 5/44 (11%) patients, with no significant differences between two regimens.

Discussion

The lower prevalence of *H. pylori* infection in our CRF patients compared with patients with dyspepsia and normal renal function, which is congruent with most previously published studies,^{1,2,3} can be explained by frequent use of antibiotics. We found a strong relationship between dyspeptic symptoms intensity in CRF patients and the presence of *H. pylori* infection: GDSS was 9.2±3.7 in *H. pylori* positive patients and 7.8±2.9 in *H. pylori* negative patients ($P=0.0039$). Aguilere and coworkers⁸ showed that *H. pylori* infection in CRF patients induces anorexia and malnutrition, but also a decrement in serum albumin, transferrin, and lymphocyte number. All of those parameters improved after *H. pylori* eradication. Successful *H. pylori* eradication does not always lead to improvement of dyspepsia in CRF patients because of other well known reasons for dyspeptic symptoms in CRF: acidosis, electrolyte disturbances, drugs (taken either because of different underlying diseases, or for routine CRF treatment), gastrin level, stress, immunosuppressive therapy, and finally infections.⁹

One-week triple therapy is widely accepted as a first-line therapy for eradication of *H. pylori* in the general population, providing satisfactory efficacy,

Table 2. Effect of eradication therapy on dyspeptic symptoms in CRF patients.

Symptoms	Group A (n=21)			Group B (n=23)			Between-groups comparison
	Improvement	No change	Worsening	Improvement	No change	Worsening	
Pain	8	12	1*	11	10	2*	NS
Nausea	9	12	0*	10	10	3*	NS
Heartburn	10	10	1*	8	15	0*	NS
Fullness	16	4	1*	12	10	1*	NS

* $P<0.05$ (within-group comparison); NS=not significant

safety, compliance, and preventing antibiotic resistance. There is no firm consensus about the best strategy in infected CRF patients.¹⁰ The results of our study show that metronidazole- and azithromycin-based standard triple therapy can be successfully used in those patients. Azithromycin is an acid-stable macrolide that achieves remarkably high concentrations in gastric tissue after a single 500 mg oral dose.¹¹ The treatment with only one antibiotic (amoxicillin) was successfully tried because CRF patients usually take a large number of drugs.¹² Azithromycin therapy is simple (once daily for only three days) and achieves good compliance even in those patients. Recent results, which show excellent effects of single-day quadruple therapy compared with the usual one-week triple therapy, are most promising.¹³ Of course,

further studies are needed. Eradication therapy can be improved by isolating and microbiologically testing *H. pylori*, by taking a history of previous antibiotics usage, and by random testing of the efficacy of the chosen therapy protocol. It is possible that in the near future microbiological testing will be necessary before each *H. pylori* eradication!¹⁴

In conclusion, the prevalence of *H. pylori* infection in patients with CRF is lower than in dyspeptic patients with normal kidney function. Both triple therapies showed comparable efficacy, safety and tolerability, with the azithromycin regimen allowing a much easier (once daily) and shorter (3 days) course. The treatment of *H. pylori* should be carefully chosen with consideration of antibiotic resistance and compliance in CRF patients.

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