Helicobacter pylori Eradication With Levofloxacin or Clarithromycin in Dialysis versus Nonuremic Patients

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Introduction. Various medication regimens have been used to eradicate *Helicobacter pylori* in dialysis patients; however, optimal response to treatment is still a challenge. This study aimed to compare response to *H pylori* eradication in dialysis and nonuremic patients.

Materials and Methods. In a randomized controlled trial, dialysis patients with dyspepsia and confirmed positive endoscopic biopsy for *H pylori* were compared to nonuremic patients. Participants were randomly assigned to receive clarithromycin or levofloxacin. *H pylori* eradication was assessed using stool antigen test 4 weeks later.

Results. Forty-four dialysis and 44 nonuremic patients participated in the study. Four dialysis patients and 2 nonuremic patients did not respond to levofloxacin (P = .35). Six dialysis patients and 4 nonuremic patients did not respond to clarithromycin (P = .47).

Conclusions. Response rate to *H pylori* eradication by clarithromycin and levofloxacin was slightly lower in dialysis patients compare to nonuremic patients. In dialysis patients, response rate to levofloxacin was slightly higher than clarithromycin, but the results were not significantly different.

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INTRODUCTION

Helicobacter pylori is the most common chronic gastrointestinal infection in the population. Research has established that a number of diseases of the gastrointestinal system are linked with *H pylori* infection. Specifically, this condition is known to play an important role in the pathogenesis of peptic ulcer disease, and is also associated with gastric cancer.[1] About 36% to 47% of gastric cancers are induced by *H pylori* infections.[2] Detection of *H pylori* is performed by the urease breathing test, serology, stool antigen test, and endoscopy (rapid urease test and biopsy).

Dialysis patients have lower *H pylori* infection rates than the general population, but *H pylori* eradication is more difficult due to resistant drug therapy.[3] *Helicobacter pylori* eradication in dialysis patients is of paramount importance due to the risk of peptic ulcers and gastric cancer. Peptic ulcer incidence is more common in dialysis patients compared to otherwise healthy population.[4] Several drug regimens have proposed for *H pylori* eradication; however, none has proven acceptable efficacy. Antibiotic therapies remain the mainstay for *H pylori* eradication; however, this strategy is hampered by the emergence and spread of *H pylori* antibiotic resistance species. The prevalence of bacterial antibiotic resistance is regionally variable and appears to be markedly increased in many countries.

The epidemiological data concerning *H pylori* infection in end-stage renal disease (ESRD) patients

are insufficient.[5] Most studies of the epidemiological features of *H pylori* infection have revealed similar findings in ESRD and nonuremic patients.[6] Patients contracting concomitant diseases including ESRD have an increased risk of developing ulcer disease through pathogenic mechanisms that lead to a more resistant pattern.[7]

Triple therapy is accepted as the treatment of choice for *H pylori* eradication, but there is no consensus on what therapy should be recommended in hemodialysis patients.[8] Recently, clarithromycin-resistant *H pylori* strains represent the main cause of treatment failure, with rates as high as approximately 30%.[9] This study aimed to determine the prevalence and pattern of *H pylori* resistance to clarithromycin and levofloxacin in dialysis patients. The objective was set to compare response of dialysis and nondialysis patients to *H pylori* eradication by levofloxacin and clarithromycin.

MATERIALS AND METHODS

Ethics Considerations

The study protocol was reviewed and approved by the University of Medical Sciences Ethics Committee. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee. Information about the study was given comprehensively both orally and in written form to all patients or their accompanying adult. They gave their informed written consents prior to their inclusion in the study.

Participants and Intervention

In a double-blinded randomized controlled trial, 88 patients, including 44 dialysis and 44 nonuremic patients, all with *H pylori* infection were included. The infection was confirmed by a history of dyspepsia, *H pylori* using the rapid urease test, endoscopic biopsy from stomach, and then *H pylori* culture and a positive pathologic examination result. In each group, the patients were randomly divided into 22 patients to receive either levofloxacin or clarithromycin, in addition to amoxicillin and omeprazole. Patients and the doctors involved in this study were both blinded to the allocations. The exclusion criteria were if the patient had history of proton pump inhibitors use in the previous 2 weeks, history of previous *H pylori* eradication, and history of steroid or immunosuppressive use.

The participants received one of the treatment regimens for 2 weeks. By the completion of the 2-weeks treatment, they were requested to have a follow-up visit 4 weeks later. Then, *H pylori* antigen stool exam was performed to confirm eradication.

Sample Size and Statistical Analysis

The sample size was estimated using a sample size calculator software with 95% confidence interval, an alpha of 0.05, and a power of 80%. Statistical calculations were conducted using the SPSS software (Statistical Package for the Social Sciences, version 22.0, IBM Corp, New York, NY, USA). The parametric variables were presented as mean ± standard deviation and were analyzed using the *t* test or the Mann-Whitney test, and nonparametric variables were analyzed using the chi-square test or the Fisher exact test. A *P* less than .05 was considered significant.

RESULTS

A total number of 88 patients were enrolled in the study, of whom 44 were dialysis patients and 44 were nonuremic patients. In each group, the patients were randomly divided into 22 patients in the levofloxacin and clarithromycin subgroups.

Demographic variables, including age, sex, and body mass index were not significantly different between the two groups of the study (Table 1). There were no significant differences in demographic variables among the levofloxacin and clarithromycin subgroups, either (Table 2).

The number of patients who did not respond to levofloxacin was 4 in the dialysis group and 2 in the nonuremic group (*P* = .35). The number of patients who did not respond to clarithromycin was 6 in the dialysis group and 4 in the nonuremic group (*P* = .47; Table 3). Among the dialysis patients, there were 18% who did not respond to *H pylori* eradication by levofloxacin and 27% who did not respond to clarithromycin (*P* = .47). Among the

Table 1. Demographic Variables of Studied Groups

Parameter	Dialysis Group (n = 44)	Nonuremic Group (n = 44)	*P*
Age, y	45.5 ± 12.5	36.2 ± 11.3	.001
Sex			
Male	28	26	
Female	16	18	.71
Body mass index, kg/m^2	24.3 ± 4.3	23.8 ± 4.6	.38

Table 2. Demographic Variables by Treatment Group

Parameter	Levofloxacin Group (n = 22)	Clarithromycin Group (n = 22)	*P*
Dialysis Patients			
Age, y	46.3 ± 9.5	45.2 ± 10.4	.72
Sex			
Male	15	14	
Female	7	8	.30
Body mass index, kg/m^2	24.7 ± 4.8	23.3 ± 4.9	.25
Nonuremic Patients			
Age, y	36.6 ± 12.3	36.8 ± 11.8	.64
Sex			
Male	12	14	
Female	10	8	.29
Body mass index, kg/m^2	23.2 ± 3.8	23.8 ± 3.5	.45

Table 3. Number of Patients (Percentage) With *Helicobacter pylori* Not Responded to Eradication Treatment

Treatment Group	Dialysis Group	Nonuremic Group	*P*
Levofloxacin	4 (18)	2 (9)	.35
Clarithromycin	6 (27)	4 (18)	.47

nonuremic patients, 9% did not respond to *H pylori* eradication by levofloxacin and 18% did not respond to clarithromycin (P = .35).

DISCUSSION

In this study, we embarked on *H pylori* eradication in dialysis patients. These patients showed less response to *H pylori* eradication regimen compare to the nonuremic group. In addition, *H pylori* eradication in dialysis patients showed less response to clarithromycin compared to levofloxacin, but the differences did not reach a significance level.

Various studies have shown that *H pylori* subtypes could become more resistant to eradication in dialysis patients.[10] This is mainly due to environmental factors and inadequate therapies.[11] As a matter of fact, emergence of resistant types of *H pylori* in dialysis patients is due to unknown factors. Mutations of various genes in *H pylori* result in decreased membrane permeability and altered oxidation-reduction potential with more efficient efflux pump system.[12] These molecular modifications ultimately introduce resistance to clarithromycin.[13] Various subtypes of resistant *H pylori* have been detected in different populations around the world.[14] It is possible that in Iran, a type of resistant *H pylori* has been spread accordingly in dialysis patients.

In dialysis patients, an increase in blood urea is an inhibitor to *H pylori* growth; however, spread of resistant types of *H pylori* is accompanied with more incidences of intractable peptic ulcer and gastric cancers. This notion implies that *H pylori* eradication is more challenging in dialysis patients, which raises great concerns due to higher incidence of gastric cancers and peptic ulcers, which increase morbidity and mortality in uremic patients.

There is still much controversy over appropriate *H pylori* eradication regimen in dialysis patients and no consensus on superior choices of antibiotics. Our results showed that the number of dialysis patients who did not respond to *H pylori* eradication by levofloxacin (18%) were less than patients who did not respond to clarithromycin (27%). Although larger sample size is needed to affirm a significant difference, our study results confirm slightly more resistance to clarithromycin compared to levofloxacin. Eradication rate has been reported as 72.5% in other studies, which is close to our results of 73%. Aydemir and colleagues showed that 36.4% of the ESRD group strains was resistant to clarithromycin.[15] In Lim and coworkers' study, failure rates increased significantly in patients with a history of clarithromycin (odds ratio, 4.45).[16] Liou and colleagues depicted that the prevalence of clarithromycin and levofloxacin resistance was 60% and 17.6%, respectively.[17] Frequency of *H pylori* clarithromycin resistance in Iran is relatively high. Since clarithromycin is not commonly used in Iran for *H pylori* eradication, the high rate of resistance could be related to cross-reactivity between other macrolides.[18] In our study, the sample size was not sufficient enough to have a conclusive argument regarding Iranian patients.

The choice of empiric therapies should be predicated on accurate information regarding antibiotic resistance rates; such information would help in selection of appropriate empiric antibiotic therapy. Currently there is no ideal first- or second-line treatment for achieving 100% eradication. The therapeutic order should be carried out according to the initial treatment and local antimicrobial resistance studies.[19] However, the use of clarithromycin-based triple therapy is not advisable as an empiric first-line regimen for *H pylori* eradication in dialysis patients.

CONCLUSIONS

Helicobacter pylori eradication in dialysis patients is more challenging compared to nonuremic patients. A response to *H pylori* eradication by clarithromycin and levofloxacin was lower in dialysis compared to nonuremic patients. In dialysis patients, response to levofloxacin was slightly higher than clarithromycin

CONFLICT OF INTEREST

None declared.

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