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Original Article

The Effect of *Helicobacter pylori* on Vitamin B_{12} Blood Levels in Chronic Renal Failure Patients: A Single Blind Control Trial

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ABSTRACT. *Helicobacter pylori* (HP) is a common infection worldwide and has been associated with severe morbidity. The level of vitamin B_{12} in HP-infected chronic kidney disease (CKD) patients is reported to be lower than in the general population. The present study has been designed to evaluate the vitamin B_{12} level in HP-infected CKD patients. We assessed the serum levels of vitamin B_{12} in 50 CKD patients with positive HP serology, one and three months after the eradication of HP infection. There were significant differences between the serum levels of vitamin B_{12} in the study patients before (806.98 ± 466.82) and after (760.36 ± 433.93) eradication treatment (P <0.001). We conclude that our study suggests the correlation between vitamin B_{12} deficiency in CKD patients and the HP infection status.

Introduction

Helicobacter pylori (HP) is known as one of the most common gastric infections and involves more than half of the people in the world.[1,2] In some studies, HP infection is known as the causative factor of vitamin B_{12} deficiency.[3,4] According to previous reports, about 21% of the patients with pernicious anemia are infected with HP.[5-7]

There are several controversial studies about upper gastrointestinal diseases in chronic renal disease (CKD) patients.[8-10] Doherty et al reported that all of the CKD patients (pre-dialysis or in dialysis stages) developed upper gastrointestinal complications.[9] In contrast, a recent endoscopic study in CKD patients revealed that only 2% of them had gastrointestinal diseases, and this rate was not significantly different from that in the general population.[10]

Converting urea to ammonia by an urease enzyme is the mechanism of protection of HP against gastric acidity.[11] The gastric environment in uremic patients facilitates HP colonization and gastric mucosal damages.[12] In non-CKD patients, HP infection is associated with symptoms of peptic ulcer disease (PUD), but this association is controversial in CKD patients. Some studies showed that dyspeptic symptoms were more prevalent in CKD pa-

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tients, in contrast to others that did not show such association.[13,14]

Low levels of vitamin B_{12} were found in HP-infected CKD patients.[15] The aim of our study was to determine the vitamin B_{12} levels in HP-infected CKD patients and to evaluate the impact of eradication of HP on these levels.

Materials and Methods

We studied 86 chronic hemodialysis patients from the dialysis center of Baqiyatallah Hospital between January and December 2008. Patients who did not tolerate hemodialysis and patients who used antibiotics except our eradication regimen were excluded from the study. Four patients were excluded from the study due to decline to participation to the study. Finally, we performed the study and statistical analysis on 82 patients. We controlled cofounding variables and matched usage of medication that could interact with the vitamin B_{12} absorption or the vitamin B_{12} levels. Demographic data and renal failure class and dialysis duration were recorded. Hong Kong Dyspepsia Index was used for assessment of dyspepsia symptoms in the studied patients.[16] In this index, the dyspepsia symptoms scale ranges between zero and 100 and, accordingly, the patients could be classified into four groups: No symptoms, mild symptoms, moderate symptoms and severe symptoms groups. This study was approved by the ethical committee of the Baqiyatallah University of Medical Sciences and Health Services and all the study patients consented for participation in this study.

Peripheral blood samples were obtained for diagnosis of HP infection via serologic test (IgG antibody of HP). Upper gastro-intestinal endoscopy was performed for patients with positive serologic HP tests and the infection was confirmed with gastric biopsies and urease tests. Patients received a treatment regimen consisting of three antibiotics including amoxicillin 750 mg daily, clarithromycin 500 mg daily and omeperazol 60 mg daily. We measured the levels of serum vitamin B_{12} in all the patients before and one and three months after treatment of HP infection. We assessed HP infection eradication with respiratory urease test in the included patients during one and three months after treatment of HP infection.

Statistical Analysis

Data of the included patients were analyzed with SPSS 16 software. We compared serum vitamin B_{12} levels before and after HP infection treatment with paired sample t-test. All *P*-values less than 0.05 were considered as significant.

Results

We found that 50 (61%) of the screened 82 CKD patients had HP infection. Dyspepsia symptoms were present in 30 (60%) patients. Mild dyspepsia symptoms were found in 20 (40%) patients and the rest complained of moderate and severe symptoms. There was no significant association between eradication status in our patients and the dyspepsia symptoms.

The mean of serum vitamin B_{12} levels in our patients before HP treatment was 807 ± 466 pg/mL. The mean of vitamin B_{12} levels in the male patients (850 ± 542 pg/mL) was not considerably higher than that in the female patients (747 ± 340 pg/mL) ($P = 0.45$). The patients without past history of PUD did not have significantly higher levels of vitamin B_{12} than patients with this past history (822 ± 476 vs 696 ± 415 pg/mL; $P = 0.54$). The patients with mild symptoms of PUD (947 ± 609 pg/mL) had

Table 1. Frequency and mean of study variables before *H. pylori* treatment

Age	57.1 ± 10.6
Vitamin B_{12} (before treatment)	807 ± 467
Vitamin B_{12} (after treatment)	760 ± 434
Sex (male)	29 (58%)
Family history of peptic ulcer disease	6 (12%)
Dyspepsia symptoms	
No	20 (40%)
Mild	20 (40%)
Moderate	8 (16%)
Severe	2 (4%)
H. pylori infection	50/82 (60.98%)

Table 2. Evaluation of eradication status in our patients according to their dyspepsia symptoms.

	Eradication situation		
	Eradicated (N, %)	**Non-eradicated (N, %)**	
No symptoms	11 (55)	9 (45)	20 (100)
Mild symptoms	16 (80)	4 (20)	20 (100)
Moderate symptoms	7 (87.5)	1 (12.5)	8 (100)
Sever symptoms	1 (50)	1 (50)	2 (100)
Total	35 (70)	15 (30)	50 (100)
P-value	0.20		

the highest and the patients with severe PUD (675 ± 237 pg/mL) had the lowest serum vitamin B_{12} levels. However, there was no correlation between the past history of PUD and serum vitamin B_{12} levels. ($P = 0.39$).

The mean of serum vitamin B_{12} level in our patients after HP treatment was 760 ± 434 pg/mL. The mean of vitamin B_{12} in male patients (776 ± 429 pg/mL) was not higher than that in female patients (739 ± 451 pg/mL) ($P = 0.77$). Patients without past history of PUDs did not have a significantly higher level of vitamin B_{12} than patients with this past history (781 ± 443 vs 611 ± 357; $P = 0.38$). Patients with mild symptoms of PUDs (873 ± 503) had the highest and patients with severe PUD (503 ± 144) had the lowest serum vitamin B_{12} levels. There is no significant association between past history of PUD and serum vitamin B_{12} level ($P = 0.25$).

After treatment of CRF patients with therapeutic regimen, the urease breathing test (UBT) was performed for HP eradication assessment. The level of serum vitamin B_{12} in patients with negative UBT (857 ± 475 pg/mL) was significantly higher than that in patients with positive UBT (535 ± 178 pg/mL) ($P = 0.02$).

Finally, there was a significant difference between serum levels of vitamin B_{12} in our patients before (807 ± 467 pg/mL) and after (760 ± 434 pg/mL) HP eradication treatment ($P = 0.00$).

Discussion

The results of our study did not show a significant association between past history of PUD in CKD patients and levels of serum vitamin B_{12}. However, the levels of serum vitamin B_{12} in CKD patients after HP eradication were significantly higher than those in the infected CKD patients. On the other hand, eradication of HP infection causes a significant increase of serum vitamin B_{12} levels in CKD patients.

Previous reports showed that HP infection was related to adult vitamin B_{12} deficiency.[3,4] Kaptan et al[17] reported that HP eradication can improve anemia and serum vitamin B_{12} levels in up to 40% of the patients and that HP plays an important role in adult vitamin B_{12} deficiency. Karnes et al[18] and Varis et al[19] reported that HP infection is involved in a process that decreases the serum levels of vitamin B_{12}. In contrast, some authors believed that improvement of vitamin B_{12} absorption after suitable antibiotic therapy might be a result of removing aerobic and anaerobic bacterial suppression.[20] Although in countries with a high prevalence of HP infection, pernicious anemia (due to decrease in vitamin B_{12}) appears to be

Table 3. Comparing mean of serum B_{12} level between four dyspepsia symptoms groups before and after eradication treatment.

Mean of serum B_{12}	**Before eradication**	**After eradication**
Dyspepsia symptoms		
No symptoms	701 ± 336	634 ± 369
Mild symptoms	947 ± 609	873 ± 503
Moderate symptoms	757 ± 317	860 ± 282
Severe symptoms	675 ± 237	503 ± 144
P-value	0.39	0.25

uncommon, in patients with pernicious anemia, based on serological and histological studies, evidence of HP infection is often less demonstrated as a cause compared with age-matched controls.[6,7]

In previous studies, the main mechanism that links HP infection to vitamin B_{12} remains undefined. HP can induce chronic antral gastritis with increasing achlorhydria and food cobalamin malabsorption.[21] However, some patients with HP infection and severe cobalamin malabsorption did not have atrophic gastritis and achlorhydria, whereas others with HP infection and hypochlorhydria maintained normal food cobalamin absorption.[20]

The pathogenesis of PUD in CKD patients remains undefined. Elevated fasting serum gastrin, which is commonly elevated in these patients, is suggested for the same.[22] Serum levels of hormones involved in the regulation of hunger and satiety, such as cholecystokinin and glucagon, and other hormone abnormalities (hypocalcemia, hypokalemia and acidosis) are raised as a result of renal failure. All these factors might play roles in motility and acid secretion abnormalities in CKD patients.[23] Luzza et al[24] and Abu Frasakh et al[25] in their studies reported that HP infection had a main role in dyspeptic symptoms in CKD patients. However, Schoonjans et al recently reported that dyspepsia and delayed gastric emptying were not related to HP infection in uremic patients.[14] Recently, Huang et al found that in CKD patients without HP infection, the prevalence of gastrointestinal discomfort was higher than that in the general population, while the prevalence of duodenal ulcer was markedly higher in HP-positive patients.[26] High concentration of urea in the gastric juice of uremic patients can affect the urease activity of HP or the modified gastric environment may favor the presence of other urease-producing organisms.[26]

In conclusion, PUD and, specially, HP infection are more prevalent in CKD patients and the infection can decrease serum levels of vitamin B_{12}. Therefore, a suitable antibiotic therapy for the treatment of this infection may result in an increase of the serum levels of vitamin B_{12} in CKD patients.

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