



## The Effect Of Vitamin D Levels On Eradication Of Helicobacter Pylori Infection

Helicobacter Pylori Eradikasyonunda D Vitamini Düzeylerinin Etkisi

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## The Effect Of Vitamin D Levels On Eradication Of Helicobacter Pylori Infection

### Abstract

**Objective:** Many factors are known to play a role in the eradication of Helicobacter pylori (Hp). The aim of this study is to investigate the effect of 25(OH) vitamin D levels on the success of H. pylori eradication.

**Material and Method:** This retrospective study included 237 patients, aged 18-85 years, who presented at the Gastroenterology Polyclinic with dyspeptic complaints which had been ongoing for at least 6 months. Patients were divided into two groups according to their 25(OH) vitamin D level as  $>20\text{ng/ml}$  and  $<20\text{ng/ml}$ . For Hp eradication, the patients were administered treatment of 1x1 320 mg gemifloxacin, 2x1 1 gr amoxicillin, and 1 x1 40 mg rabeprazole. After 1 month of treatment, faecal examination was made to determine whether or not Hp was eradicated. The eradication rates were compared between the groups with high and low level 25(OH) vitamin D.

**Results:** The patients comprised 139 (58.6%) females and 98 (41.4%) males with a mean age of  $40.9 \pm 14.1$  years (range, 18-72 years). The 25(OH) vitamin D level was determined as mean  $16.3 \pm 8.4 \text{ ng/mL}$  (range, 3-42) in the whole sample, with an insufficient level seen in 211(89.0%) patients. In the comparison of 25(OH) vitamin D levels between the groups, the 25(OH) vitamin D level was determined to be  $16.8 \pm 8.5$  in the group with Hp eradication and  $12.7 \pm 6.5$  in the group without Hp eradication. The difference between the two groups was found to be statistically significant ( $p=0.018$ ).

**Conclusion:** Before H pylori eradication treatment, it is important to maintain optimal levels of 25(OH) vitamin D, which has an effect on the effectiveness of eradication.

**Keywords:** Eradication, helicobacter pylori, 25(OH) vitamin D.

### Özet

**Amaç:** H. pylori eradikasyonunda birçok faktörün rol oynadığı bilinmektedir. Bu çalışmanın amacı H. pylori'nin eradikasyon başarısına 25(OH) D vitamininin etkisini araştırmaktır.

**Gereç ve Yöntem:** Bu retrospektif çalışmaya Gastroenteroloji Polikliniğine en az 6 aydır devam eden dispeptik yakınmalarla başvuran 18-85 yaş arası 237 hasta dahil edildi. Hastalar 25(OH) vitamin D düzeyine göre  $>20\text{ng/ml}$  ve  $<20\text{ng/ml}$  olmak üzere iki gruptan ayrıldı. Hp eradikasyonu için hastalara gemifloksasin 320 mg 1x1, amoksisilin 1 gr 2x1 ve rabeprazol 40 mg 1x1 tedavileri verildi. Tedaviden 1 ay sonra Hp'nin eradike edilip edilmediğinin tespiti için dışkı incelemesi yapıldı. D vitamini seviyesi yüksek ve düşük olan gruplar arasında eradikasyon oranları karşılaştırıldı.

**Bulgular:** Hastaların 139'u (%58,6) kadın, 98'i (%41,4) erkekti ve ortalama yaşları  $40,9 \pm 14,1$  (18-72 yaş arası) idi. D vitamini düzeyi ortalama  $16,3 \pm 8,4$  (3-42) olarak saptandı. 211 (%89,0) hastada yetersiz düzeyde görülmüştür. Gruplar arası D vitamini düzeyleri karşılaştırıldığında, Hp eradikasyonu yapılan grupta D vitamini düzeyi  $16,8 \pm 8,5$ , Hp eradikasyonu yapılmayan grupta ise  $12,7 \pm 6,5$  olarak belirlendi. İki grup arasındaki fark istatistiki olarak anlamlı bulundu ( $p=0,018$ ).

**Sonuç:** Hp eradikasyon tedavisi öncesinde, eradikasyonun etkinliğini etkileyen D vitamini düzeylerinin optimum düzeyde tutulması önemlidir.

**Anahtar Sözcükler:** D vitamini, eradikasyon, helicobakter pilori.

## Introduction

*Helicobacter pylori* (Hp) is a microaerophilic gram-negative pathogen, which infects approximately half of the global population (1, 2). In the literature; diseases associated with Hp infection are gastritis, peptic ulcer, lymphoma and stomach cancer. (3).

In a previous study, it was determined that upper gastrointestinal bleeding due to peptic ulcer was less common in summer and autumn (4). In Hp eradication, the desired eradication rates cannot usually be reached due to both bacteria and host-related factors (5). Virulence factors affecting eradication; while the cytotoxin-related gene A product, vacuolating cytotoxin A, duodenal ulcer-promoting gene A product, external inflammatory protein A and blood group antigen-binding adhesion, the host factors are smoking, diet, treatment compliance, cytochrome P2C19 (CYP2C19) and interleukin-1 (IL-1) (6).

25(OH) vitamin D regulates calcium and phosphorus metabolism, which are essential for bone formation, and the effect of 25(OH) vitamin D on H. pylori infection and eradication rates has recently been widely studied(7,8). It is now increasingly recognized that VitD 3 is not only involved in diseases of the skeletal system, but also in many other physiological processes in the human body.(9)25(OH) vitamin D deficiency has been recognized as one of the potential risk factors for H. pylori treatment failure, and studies recommend adding 25(OH) vitamin D as an adjuvant to standard medications(10). Additionally, H. pylori positivity rates appear to be higher among populations with low serum 25(OH) vitamin D levels.(8,11)

The purpose of this study was to investigate the effect on the success of Hp eradication of 25(OH) vitamin D level, which was considered to be another factor, in a patient group where eradication was attempted with gemifloxacin, amoxicillin, and rabeprazole.

## Material and Method

### Study Design

This retrospective study included 237 patients, aged 18-85 years, who presented at the Gastroenterology Polyclinic between April 2021 and November 2021 with dyspeptic complaints which had been ongoing for at least 6 months. Informed consent was provided by all the patients. Study exclusion criteria include; chronic disease (liver, renal), organ transplantation(bone marrow, kidney, liver), had received antibiotic treatment within the last year, GİS surgery and pregnant.

Before starting the Hp eradication treatment, the serum 25(OH) vitamin D level was measured with the ELISA method. Patients were divided into two groups according to their 25(OH) vitamin D level as >20ng/ml and <20ng/ml. For Hp eradication,

the patients were administered treatment of 1 x1 320mg gemifloxacin, 2 x 1 1gr amoxicillin, and 1 x1 40mg rabeprazole. After 1 month of treatment, faecal examination was made to determine whether or not Hp was eradicated. The eradication rates were compared between the groups with high and low level 25(OH) vitamin D.

### Endoscopic evaluation

Endoscopic and histopathological findings of the patients were documented. Endoscopy was performed on all patients with the Fujinon EG530WR endoscopy device in our endoscopy unit. The endoscopy procedure was performed after an 8-hour fast and the application of local pharyngeal xylocaine anesthesia. The stomach and duodenum were detailed analysis during the endoscopy and biopsies were taken in respect of Hp infection.

### Histopathological evaluation

During the endoscopy examination, biopsy was taken from the antrum by biopsy forceps. Paraffin blocks of the taken biopsy materials are cut to the suitable thickness and was painted with Giemsa. This preparations have been examined by three different pathologists blinded to the clinical of patients.

### 25(OH) vitamin D measurement

Serum 25(OH) vitamin D concentration was measured by Abbott Architect I4000 SR immunoassay analyzer. The results of serum 25(OH) vitamin D measurements were expressed as ng/mL.

### Ethical statement

Approval was obtained from the ethics committee of our hospital for this study. (Approval no:2022/23-01). Procedures were carried out in accordance with the Declaration of Helsinki and ethical standards. Written informed consent form was obtained from all participants.

### Statistics

Data obtained in the study SPSS vn. 19.0 software. Data were expressed as mean  $\pm$  standard deviation (SD) values, categorical data as numbers (n) and percentage (%). Parametric data were compared between groups with Student's t-test and Chi-square test was applied to categorical data. ( $p < 0.05$ ) value was considered statistically significant.

## Results

Endoscopically and histopathologically diagnosed and treated 237 patients with Hp infection were evaluated. The patients comprised 139 (58.6%) females and 98 (41.4%) males with a mean age of  $40.9 \pm 14.1$  years (range, 18-72 years). In the evaluations made after treatment, Hp eradication was obtained in 211 (89.0%) patients and not in 26

(11.0%). The 25(OH) vitamin D level was determined as mean  $16.3 \pm 8.4$  (range, 3-42) in the whole sample, with an insufficient level seen in 211 (89.0%) patients. In the comparisons between the groups with and without Hp eradication, no significant difference was determined between the groups in respect of age, height, weight, smoking status, alcohol consumption, and comorbid diseases ( $p > 0.05$ ) (Table I). In the comparison of 25(OH) vitamin D levels between the groups, the 25(OH) vitamin D level was determined to be  $16.8 \pm 8.5$  in the group with Hp eradication and  $12.7 \pm 6.5$  in the group without Hp eradication. The difference between the groups was statistically significant ( $p = 0.018$ ) 25(OH) vitamin D was seen to be at a sufficient level in 78 (37.0%) patients in the group with Hp eradication, and in 4 (15.4%) patients in the group where Hp eradication was not obtained, and the difference was statistically significant ( $p = 0.029$ ) (Table I).

**Table I.** Relationships between 25(OH) vitamin D level and Hp eradication

| Variables                              | Patients with Hp eradication<br>N:211 (89%) | Patients without Hp eradication<br>N:26 (11%) | Total<br>N:237  | P value      |
|----------------------------------------|---------------------------------------------|-----------------------------------------------|-----------------|--------------|
| Age (years)                            | 41.1 $\pm$ 13.6                             | 39.3 $\pm$ 18.2                               | 40.9 $\pm$ 14.1 | 0.535        |
| Gender (female)                        | 120 (56.9%)                                 | 19 (73.1%)                                    | 139 (58.6%)     | 0.113        |
| Height (cm)                            | 166.9 $\pm$ 8.7                             | 165.1 $\pm$ 7.3                               | 166.7 $\pm$ 8.5 | 0.291        |
| Weight (kg)                            | 70.7 $\pm$ 13.1                             | 73.7 $\pm$ 13.8                               | 71.0 $\pm$ 13.2 | 0.276        |
| BMI                                    | 25.3 $\pm$ 4.3                              | 27.1 $\pm$ 4.2                                | 25.5 $\pm$ 4.2  | <b>0.043</b> |
| Smoking status                         |                                             |                                               |                 | 0.316        |
| -smoker                                | 61 (28.9%)                                  | 10 (38.5%)                                    | 71 (30.0%)      |              |
| -non-smoker                            | 150 (71.1%)                                 | 16 (61.5%)                                    | 166 (70.0%)     |              |
| Alcohol consumption                    |                                             |                                               |                 | -            |
| -yes                                   | 0 (0%)                                      | 0 (0%)                                        | 0 (0%)          |              |
| -no                                    | 211 (100%)                                  | 26 (100%)                                     | 237 (100%)      |              |
| Comorbid disease                       |                                             |                                               |                 | 0.554        |
| -present                               | 46 (21.8%)                                  | 7 (26.9%)                                     | 53 (22.4%)      |              |
| -absent                                | 165 (78.2%)                                 | 19 (73.1%)                                    | 184 (77.6%)     |              |
| 25(OH) vitamin D level                 |                                             |                                               |                 | <b>0.029</b> |
| -insufficient                          | 133 (63.0%)                                 | 22 (84.6%)                                    | 211 (65.4%)     |              |
| -sufficient                            | 78 (37.0%)                                  | 4 (15.4%)                                     | 26 (34.6%)      |              |
| 25(OH) vitamin D level (mean $\pm$ SD) | 16.8 $\pm$ 8.5                              | 12.7 $\pm$ 6.5                                | 16.3 $\pm$ 8.4  | <b>0.018</b> |

## Discussion

In recent years, it has been observed that eradication of Hp has become more difficult due to the increase in antibiotic resistance. This condition is caused by both environmental factors and host-related factors. The data obtained from this study showed that insufficient 25(OH) vitamin D level was a factor in failure of eradication of Hp (12).

Diverse different effects have been observed in previous studies of the effect of 25(OH) vitamin D. Guo et al. showed that the antimicrobial effect of 25(OH) vitamin D against Hp plays an important role in the homeostasis of gastric mucosa and in the protection of the host against Hp (13). In a rat model study by Zhang et al., intragastric administered 25(OH) vitamin D was shown to reduce Hp colonisation without changing serum calcium and phosphorus levels (14). Izquierdo et al. reported that in addition to the effect on bone metabolism, 25(OH) vitamin D could decrease inflammatory makers such as IL-6, CRP, IL-18, TNF- $\alpha$ , and increase the level of IL-10 (15). After artificial infection of the stomach with *H. pylori* in mice, oral administration of 25(OH) vitamin D3 has been shown to increase anti-Hp activity via VDR-Cathelicidin antimicrobial peptide (CAMP) as well as a significant reduction in colonization rates. (16,17)

In a study of 27,077 patients, Shafrir et al. observed that the 25(OH) vitamin D level was significantly higher in the Hp-negative patient group. It was shown that for every 1ng/mL increase in serum 25(OH) vitamin D, the probability of Hp infection decreased by 1.5%. In addition, in our study, it was observed that the 25(OH) vitamin D level in patients with successful Hp eradication was significantly higher than in patients with unsuccessful Hp eradication (18). In the previous study, the effect of 25(OH) vitamin D level on both Hp colonization and Hp eradication was clearly shown. It was also similarly shown that the rate of successful Hp eradication was higher in the patient group with a high level of 25(OH) vitamin D. Similarly, in a metanalysis evaluating the impact of 25(OH) vitamin D levels on *H. pylori* infection, they concluded that low 25(OH) vitamin D levels may be responsible for the higher prevalence of *H. pylori* infection and may adversely affect bacterial eradication (19). Shahawy et al. showed that 25(OH) vitamin D supplementation to the classical triple therapy given for Hp treatment significantly increased the eradication rate (20).

The limitations of this study are the retrospective, single-centre design and the limited number of patients in the group without Hp eradication. The strength of the study is that it was done with a treatment regimen not previously used in the treatment of Hp.

## Conclusion

Our study demonstrated that a high 25(OH) vitamin D level increased the success of Hp eradication. It is clear that the eradication of Hp has been made more difficult by antibiotic resistance and some other environmental factors. Therefore, it is important that before eradication treatment, 25(OH) vitamin D levels, which affect the efficacy of eradication, are kept at the optimum level. More prospective studies are needed to clarify the association of 25(OH) vitamin D replacement with Hp eradication and to evaluate its efficacy in treatment.

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