THE EFFECT OF HELICOBACTER PYLORI ERADICATION ON PARAOXONASE ENZYME ACTIVITY

HELİKOBAKTER PILORİ ERADİKASYONUNUN SERUM PARAOXONAZ ENZİM AKTİVİTESİNE ETKİSİ

Muhammed SAÇIKARA¹, Oktay BULUR¹, Mehmet POLAT¹, Yaşar NAZLIGÜL¹

ABSTRACT

AIM: Helicobacter pylori (H. pylori) infection is associated with gastrointestinal and extra-gastrointestinal diseases either directly via its special virulence factors or indirectly by increasing inflammation and oxidation. Paraoxonase-1 (PON-1) enzyme that is related to High-Density Lipoprotein (HDL) cholesterol is responsible for the antioxidant and antiatherogenic effects of HDL cholesterol. PON–1 level is related to the risk of cardiovascular disease. We aimed to investigate the relation between H. pylori infection and PON-1 activity.

MATERIAL AND METHOD: The study was performed prospectively in 126 H.pylori positive adult patients. After performing eradication therapy and checking the treatment success, 38 H. pylori-positive (17 male, 21 female) and 88 H. pylori-negative (43 male, 45 female) patients were included in this study. These groups were compared in terms of serum PON-1 levels.

RESULTS: PON–1 enzyme levels were found to be 165.69 U/L in H. pylori-negative and 131.68 U/L in H. pylori-positive groups after H. pylori eradication therapy. After treatment, the difference in PON–1 enzyme levels was statistically significant (p=0.02).

CONCLUSION: Increased PON–1 enzyme levels after H. pylori eradication therapy might play a role in the antiatherosclerotic effect by reducing LDL oxidation.

Key Words: Helicobacter pylori, Paraoxonase, Atherosclerosis

ÖZET


BULGULAR: H. pylori eradiyasyon tedavisi sonrası PON-1 enzim seviyeleri; H. pylori pozitif grubu 165,69 U/L ve H. pylori pozitif grubu 131,68 U/L olarak bulundu. Tedaviden sonra gruplar arasında PON–1 enzim seviyeleri açısından istatistiksel olarak anlamlı fark saptandı (p=0,02).

SONUÇ: H. pylori eradiyasyon tedavisi sonrası PON-1 enzim seviyelerinde artış, low density lipoprotein (LDL) oksidasyonunda azalmaya ve buna sekonder antiaterosklerotik etkije neden olmaktadır.

Anahtar Kelimeler: Helikobakter pilori, Paraoksonaz, Ateroskleroz

¹Keçiören Teaching and Research Hospital, Department of Internal Medicine, Ankara, Turkey.

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INTRODUCTION
Helicobacter pylori (H. pylori) is a gram-negative bacillus which is the most common chronic bacterial infection worldwide (1,2). H. pylori infection is associated with gastrointestinal and extra-gastrointestinal diseases such as coronary artery disease, rosacea, diabetes mellitus, lymphoma, choleodocholithiasis and growth retardation in children (3-6). Paraoxonase-1 (PON-1) enzyme that is related to HDL cholesterol is responsible for the antioxidant and antiatherogenic effects of HDL cholesterol. Diet, lifestyle and environmental factors affect the level of PON-1. PON-1 levels are decreased in diabetes mellitus, chronic renal failure, coronary artery disease, systemic infection and inflammatory states (7-9). In addition, smoking and fatty foods reduce the level of PON-1 (10, 11). Decreased PON–1 activity is related to an increased risk of cardiovascular disease (12, 13). PON-1 shows its antiatherogenic effects by protecting LDL cholesterol from oxidation (14, 15). Besides, PON-1 preserves the reverse cholesterol transporting function of HDL by protecting HDL oxidation. These effects retard atherosclerosis pathogenesis (16-18).

In this study, we aimed to evaluate the effect of H. pylori eradication therapy on PON-1 enzyme levels.

MATERIAL AND METHOD
The study was performed prospectively in 126 H. pylori positive adult patients. Patients diagnosed with H. pylori were treated with eradication therapy (esomeprazole 20 mg 2x1, bismuth substitrat 300 mg 2x2, metronidazole 500 mg 3x1, tetracyclin 500 mg 4x1). Treatment success was checked 6 weeks after the end of the medications, primarily with the C14 urea–breath test and by histological method or H. pylori stool antigen test in cases where the urea–breath test was contraindicated.

After performing eradication therapy and checking the treatment success, 38 H. pylori-positive (17 male, 21 female) and 88 H. pylori-negative (43 male, 45 female) patients were included in this study. These groups were compared in terms of serum PON-1 levels.

Alcohol ingestion, smoking, intravenous drug use, pregnancy, fish oil consumption, use of gastric acid secretion inhibitor in the last 4 weeks, total bilirubin level >2 mg/dl, cryoglobulinemia, HIV infection, active infection (except H. pylori infection), hypertension, diabetes mellitus, hyperlipidemia, chronic respiratory failure, rheumatoid arthritis, cirrhosis, renal failure, coronary artery disease, cerebrovascular disease and malignancy were exclusion criteria. PON–1 enzyme levels were measured with the spectrophotometric method using the Abbott Aeroset autoanalyzer (USA) and Rel Assay Paraoxonase Kit (Rel Assay Diagnostics, Gaziantep).

The normality of distribution of continuous variables was tested by Shapiro Wilk test. Mann Whitney U test and Chi-square test were used to compare two independent groups for continuous and categorical variables, respectively. Statistical analysis was performed with SPSS for Windows version 16.0 and a p-value <0.05 was accepted as statistically significant.

This research conducted was compatible with the Declaration of Helsinki and was approved by the local ethics committee of Keçiören Training and Research Hospital (no:2009/04/30). Detailed information about research was given to all patients and consent form was signed.

RESULTS
One hundred twenty six patients were included in the study. 66 were female and 60 were male. After eradication therapy, H. pylori was found to be positive in 38 patients (17 male, 21 female) and negative in 88 patients (43 male, 45 female). Mean age was 44 years in H. pylori negative patients and 45 years in H. pylori positive patients.

Demographic features and PON–1 enzyme levels of groups are shown in Table 1. The groups were similar in terms of gender and age. PON-1 enzyme levels were found to be 165.69 U/L in H. pylori-negative and 131.68 U/L in H. pylori-positive groups (p=0.02) after H. pylori eradication therapy.

<table>
<thead>
<tr>
<th>Table 1 Demographic data and the paraoxonase 1 levels in Helicobacter pylori positive and Helicobacter pylori negative patients after eradication therapy</th>
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<tbody>
<tr>
<td>Patients (n)</td>
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<tr>
<td>Female/Male</td>
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<tr>
<td>38</td>
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<td>21/17</td>
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<tr>
<td>Age (year)</td>
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<td>44.21 ± 8.04</td>
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<tr>
<td>Paraoxonase-1 (U/L)</td>
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<td>131.68</td>
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DISCUSSION
Our study is one of the first studies that evaluate the PON-1 activity in patients treated with H. pylori eradication therapy. We found that PON-1 levels were higher in patients with eliminated H. pylori infection compared to those who had continued to have infection after eradication therapy. This suggested that one of the modifiable risk factors of atherosclerosis could be eliminated by H. pylori eradication. The relationship between infection, inflammation and atherosclerosis has been investigated in many studies (19). In the literature, there are studies investigating the association of atherosclerosis with H. pylori, Chlamydia and Mycoplasma pneumonia (20-24). The relation between H. pylori and coronary artery disease was investigated firstly by Mendall et al. in 1994 (20). Gunn et al. found a significant relationship between atherosclerosis process and H. pylori infection (25). Besides infection, an increase in total and LDL cholesterol levels and a decrease in HDL levels are known as the major risk factors for...
coronary artery disease. Especially, oxidation of LDL is an important step in early phases of atherosclerosis development (26).

PON-1 is responsible for the antioxidant effect of HDL; it protects LDL cholesterol from oxidation, and makes an important contribution to the antiatherogenic effects of HDL (27,28).

There are a vast number of research about the relation between PON-1 and coronary artery disease. Serdar et al. reported that the patients with coronary artery disease had significantly lower PON-1 levels (29). However, Azarsız and colleagues showed lower PON-1 levels in coronary artery disease patients, but this difference was not statistically significant (30). In a meta-analysis, Knutson et al. concluded that there is an inverse association between PON-1 activity and CVD risk (31).

In our study, serum PON-1 levels were higher in patients with eliminated H. pylori infection compared to those who had continued to have infection after eradication therapy. This suggested that one of the modifiable risk factors of atherosclerosis could be eliminated by H. pylori eradication.

This study has several limitations. Firstly, the patient number included in our study was low. Secondly, H. pylori eradication success was lower than expected (69.84%). We consider that the low rate of eradication success may be due to non-compliance to treatment or possible metronidazole resistance in patients included in our study. In addition, the presence of Cag-A and Vac-A virulence factors and the effect of Cag-A or Vac-A positivity on PON-1 levels have not been evaluated.

CONCLUSION

Increment in PON-1 level after H. pylori eradication might show antithrombotic effect by a possible decrease in LDL oxidation.

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