FONKSİYONEL DİSPEPSİLİ HASTALARDA HELİKOBAKTER PİLORİ ERADİKASYONUNUN SERUM OKSİDE LDL DÜZEYLERİ ÜZERİNE ETKİLERİ

The Influence of Helicobacter Pylori Eradication on Serum Oxidized Low Density Lipoprotein in Patients With Functional Dyspepsia

Muammer BİLİCİ[1] (0000-0002-8678-460), Yasin ÖZTÜRK[1] (0000-0003-2634-2677), Başak DELİKANLI ÇORAKCI[1] (0000-0001-7197-5209), İshak Özel TEKİN[2] (0000-0002-9969-4254), Selim AYDEMİR[3] (0000-0002-7298-7559)

[1]Zonguldak Bülent Ecevit Üniversitesi, İç hastalıkları Anabilim dalı , Zonguldak

[2]Zonguldak Bülent Ecevit Üniversitesi, İmmünoloji Anabilim dalı , Zonguldak

[3]Zonguldak Bülent Ecevit Üniversitesi, Gastroenteroloji Bilim dalı, Zonguldak

Muammer BİLİCİ, Dr. Öğr. Üyesi
Yasin ÖZTÜRK, Dr. Öğr. Üyesi
Başak DELİKANLI ÇORAKCI, Dr. Öğr. Üyesi
İshak Özel TEKİN, Doç. Dr.
Selim AYDEMİR, Prof. Dr.

İletişim:
Dr. Öğr. Üyesi Muammer BİLİCİ
Zonguldak Bülent Ecevit Üniversitesi, Tıp Faktültesi, İç hastalıkları Anabilim Dalı, Esenköy, Kozlu, 67600 Zonguldak, Türkiye
Tel: 05387220925
e-mail:
drmbilici@hotmail.com

Geliş tarihi/Received: : 16.08.2018
Kabul tarihi/Accepted: 25.09.2018
DOI: 10.16919/bozoktip.454052

Bozok Tıp Derg 2019;9(1):106-110
Bozok Med J 2019;9(1):106-110

ÖZET

Amaç: Helicobacter pylori (H. pylori), ilk keşfinden itibaren sindirim sistemi ve diğer sistemlerle ilgili bir çok hastalığın patogenezinde yer almakla suçlanmıştır. İlginç olarak, sindirim sistemi dışı hastalıklarla ilgili literatürün çoğunluğu, özellikle iskemik kalp hastalığına odaklanmıştır. Aterosklerozun ilerlemesinde oksitlenmiş düşük yoğunluklu lipoprotein (ox-LDL) önemli bir rol oynamaktadır. Bu çalışmada, H. pylori eradikasyonunun serum ox-LDL düzeyleri üzerine etkisini değerlendirmek amaçlanmıştır.

Yöntem: Çalışmaya H. pylori ile ilişkili dispepsisi olan 73 hasta ve 23 sağlıklı gönüllü kontrol grubu olarak dahil edildi. Hastalara bizmut içeren dörtlü tedavi 14 gün süreyle verildi. Serum ox-LDL, LDL ve yüksek yoğunluklu lipoprotein (HDL) düzeyleri tedaviden önce ve 8 hafta sonra olmak üzere ölçüldü. H. pylori eradikasyonu 14C-üre nefes testi ile doğrulandı.

Bulgular: Hasta ve kontrol grubu arasında yaş ve cinsiyet açısından anlamlı fark bulunmadı (sırasıyla p = 0,066 ve p = 0,475). H. pylori eradikasyonu öncesi hastalarda serum ox-LDL ve LDL düzeyleri sağlıklı kontrollere göre anlamlı olarak yüksek bulundu (sırasıyla p = 0,04 ve p = 0,046). Düzeltilebilir kardiyovasküler hastalık risk faktörü taşımayanlarda eradikasyon başarısı sonrası ox-LDL düzeylerinde anlamlı azalma saptandı (p = 0.047). Ancak, diğer hastalar arasında tedavi öncesi ve sonrası serum ox-LDL düzeylerinde istatistiksel olarak anlamlı bir fark yoktu (p> 0.05).

Sonuç: H. pylori ilişkili dispepsi hastalarında eradikasyon tedavisinin ateroskleroz progresyonuna sınırlıda olsa yararlı etkisi olduğu kanaatindeyiz.

Anahtar Sözcükler: *Helicobacter pylori; Ateroskleroz; oksitlenmiş LDL*

ABSTRACT

Objectives: Since the discovery, Helicobacter pylori (H. pylori) it have been implicated in the pathogenesis of several diseases located both in the digestive and extradigestive systems. Interestingly, the majority of the literature on extradigestive-related disease mainly focuses on ischemic heart diseases. Oxidized low-density lipoprotein (ox-LDL) is an important key point in the progression of atherogenesis. The aim of the present study was to investigate whether the eradication of H. pylori infection affects serum ox-LDL levels.

Methods: A total of 73 patients with H. Pylori–associated dyspepsia and 23 controls were included in this study. Bismuth quadruple therapy was given for 14 days. Serum levels of ox-LDL, LDL and high-density lipoprotein (HDL) were measured at baseline and 8 weeks after therapy. Successful eradication was proven with the 14C-urea breath test.

Results: There were no significant differences in terms of age and gender between the patients and controls (p=0.066 and p = 0.475, respectively). Comparing H. Pylori patients to healthy controls with respect to serum ox-LDL and LDL levels were significantly higher in the patient group (p=0.04 and p=0.046 respectively). It was noticed that oxLDL levels were lower in eradicated patients with no correctable risk factors for cardiovascular disease after therapy (p=0.047). However, there was no statistically significant difference in serum ox-LDL levels between baseline and after therapy among the other patients (p>0.05).

Conclusion: The findings of our study might indicate that H. pylori eradication influences the oxidation of LDL. However, the role of H. pylori infection on atherosclerosis progression is a controversial issue.

Keywords: Helicobacter pylori; Atherosclerosis; Oxidized LDL

INTRODUCTION

The oxidized form of low density lipoprotein (ox-LDL) has a crucial role in promoting atherosclerosis and circulating ox-LDL can also be used as a marker of cardiovascular disease (CVD) (1). There is an increasing amount of data showing elevated levels of serum LDL cholesterol in patients with Helicobacter pylori (H. pylori) infection (2-5). Many studies claim that H. pylori infection might have a role in promoting atherosclerosis by modifying serum lipids (6-9). Therefore, several studies were conducted on this topic to assess the possible effects of eradication therapy on serum lipid profile in atherosclerotic patients with H. pylori infection (4, 10-13). These studies have produced contradictory results. Indeed, the role of H. pylori infection in atherosclerosis still remains unclear. Based on these previous studies, we conducted the present study to determine the changes in ox-LDL related to the presence or absence of a correctable risk factor for atherosclerosis after eradication therapy among patients with H. pylori–associated dyspepsia.

MATERIALS AND METHODS

Study Population

One hundred and four consecutive patients with H. Pylori–associated dyspepsia and 23 healthy volunteers from the Gastroenterology Department were enrolled in the study from November 2017 to May 2018. We excluded patients with gastrointestinal system and other organ malignancies, acute or chronic infectious diseases, prior gastric surgery, ischemic heart disease, antihyperlipidemic drug users and also those who had used eradication therapy for H. pylori or anti-ulcer drugs within the last 1 month. This study was approved by the local ethics committee of Bulent Ecevit University Hospital (Ethical Application Ref: 2017-48-19/04). All individuals were fully informed about the objective of the study and agreed to participate. The state of H. Pylori infection was diagnosed with the 14C-urea breath test. Eradication therapy (LTMB), consisting of lansoprazole 30 mg (2x1/day), tetracycline 500 mg (2x1/day), metronidazole 500 mg (2x1/day) and bismuth salts 262 mg (4x1/day) taken for 2 weeks, was used in all participants. All drugs were supplied free of charge. Patients who reported that they took less than 80% of the tablets were considered violators and excluded from the study. Among patients, eradication was verified by means of the 14C-urea breath test 2 months after H. Pylori eradication treatment. A negative 14C-urea breath test result was described as successful eradication. The eradicated patients were divided into two groups according to the presence or absence of correctable cardiovascular risk factors including hypertension, diabetes, obesity and smoking.
Assessment of correctable cardiovascular risk factors

Answers to questions on history of hypertension, diabetes and smoking habits were carefully noted for each patient. Blood pressure was measured in the morning with the patient in supine position. Height and weight of all patients were measured and Body Mass Index (BMI) was calculated for each patient. The calculation was made using the formula of BMI = [weight (kg)/ height (m) ^{2}].
Laboratory Analysis

Fasting blood samples of the subjects were drawn for analysis before and 2 months after H. Pylori eradication treatment. Serum lipid levels of low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol were determined using xylidine blue with an end-point colorimetric method (Roche Diagnostics GmbH; Mannheim, Germany). Serum ox-LDL levels were measured with a commercially available kit (Immundiagnostik AG, Bensheim, Germany) based on the enzyme-linked immunosorbent assay (ELISA) method.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Version 13.0). Results are expressed as mean±standard deviation. In the comparison between groups, statistically significant differences were assessed with the Wilcoxon signed ranks test or Mann Whitney U test. $p<0.05$ was considered statistically significant.

RESULTS

Of the 104 patients enrolled in the trial, 31 patients were excluded from the study (7 did not visit our clinic after treatment, 15 used antihyperlipidemic drugs, 4 had coronary artery disease (CAD), and 5 violated

protocol). The eradication of H. pylori was achieved in 62 of the 73 patients who returned for follow-up. Demographic and clinical characteristics of patients with H. Pylori–associated dyspepsia and controls are given in Table 1. The mean age of patients and controls were 47.73±12.86 and 42.08±12.22 years, respectively (p=0.066). A total of 35 (47.9%) patients and 13 (56.5%) controls were female (p = 0.475). Serum levels of ox-LDL, LDL and HDL in patients and controls were found as 177.38±66.33 ng/mL and 157.78±92.86 ng/mL; 128.78±27.26 mg/dL and 117.13±36.13 mg/dL; 43.45±9.50 mg/dL and 40.91±9.88 mg/dL, respectively (p=0.04, p=0.046 and p=0.385, respectively).

OxLDL was found to be lower in the group of eradicated patients with no correctable risk factors for CVD after treatment. However no significant differences with regard to pre and post-treatment serum ox-LDL, LDL and HDL levels were found among the other groups with or without eradication of H. pylori (p>0.05). The characteristic features of the patients are shown in Table 2.

Table 1: Demographic and clinical characteristics in patients with H. Pylori–associated dyspepsia and healthy control subjects

	Patients (n=73)	Controls (n=23)	P value
Age (years)	47.73±12.86	42.08±12.22	0.066
Sex (male/female)	38/35	10/13	0.475
Hypertension (n)	19	-	
Diabetes type 2 (n)	12	-	
Smoker (n)	26	-	
SBP (mmHg)	131.35±16.17	126.21±9.51	0.248
DBP (mmHg)	77.43±11.20	77.26±6.60	0.853
BMI (kg/m2)	24.58±2.91	24.14±2.57	0.652
Ox-LDL(ng/mL)	177.38±66.33	157.78±92.86	0.040
LDL (mg/dl)	128.78±27.26	117.13±36.13	0.046
HDL (mg/dl)	43.45±9.50	40.91±9.88	0.385

SBP; Sistolic blood pressure, DBP; Diastolic blood pressure, BMI; Body mass index, oxLDL; Oxidized low-density lipoprotein, LDL; low-density lipoprotein, HDL; High-density lipoprotein

Table 2: Comparison of the pretreatment and posttreatment ox-LDL, LDL and HDL levels among patients with H. Pylori–associated dyspepsia

Group	Ox-LDL Pretreatment (ng/mL)	Ox-LDL Posttreatment (ng/mL)	p	LDL Pretreatment (mg/dl)	LDL Postreatment (mg/dl)	p	HDL Pretreatment (mg/dl)	HDL Postreatment (mg/dl)	p
A (n=62)	179.04±66.18	174.55±66.01	0.164	128.64±27.18	125.16±26.12	0.125	43.09±9.11	45.56±.10.47	0.062
B (n=11)	168.01±69.58	169.20±71.63	0.790	129.54±29.04	128.18±23.73	0.504	45.45±11.77	48.63±8.67	0.398
C (n=35)	192.49±69.72	185.83±68.20	0.295	134.80±26.21	128.68±26.73	0.093	39.48±7.78	40.65±8.91	0.543
D (n=27)	161.60±57.97	159.93±61.19	0.047	120.66±26.80	120.59±25.06	0.648	47.77±8.69	51.92±8.90	0.058

Group A; H. pylori eradicated, Group B; H. pylori non-eradicated, Group C; H. pylori eradicated with risk faktör, Group D; H. pylori eradicated with no risk factor, oxLDL; Oxidized low-density lipoprotein, LDL; low-density lipoprotein, HDL; High-density lipoprotein

DISCUSSION

In this study, we assessed the effects of H. pylori eradication on lipid profile including ox-LDL as a marker of CVD in patients with H. pylori–associated dyspepsia. Our findings revealed that successful eradication therapy could lead to a slight but noticeable decrease in the amount of ox-LDL among patients with H. pylori infection. However, this effect was not observed in those with at least one of the correctable risk factors for CVD. Considering the alleged role of H. pylori infection in the development of atherosclerosis over chronic inflammation and oxidative damage, correctable risk factors for atherosclerosis seem to have a more crucial role in lipid oxidation compared to H. pylori infection (7, 14-16).

Recently, a large cross-sectional study showed a relation between H. pylori infection and dyslipidemia (6). Furthermore, Satoh et al. demonstrated that H. pylori infection is associated with high serum LDL and low serum HDL levels, supporting the hypothesis that H. pylori might play a role in promoting atherosclerosis by modifying lipid metabolism (2). On the other hand, H. pylori eradication has not yielded great results in terms of serum lipid profile among patients with atherosclerosis. Park et al. reported that H. pylori eradication has no effect on lipid profiles (13). Another study evaluating the effect of H. pylori eradication on coronary risk factors in 48 patients, also showed that there were no significant alterations related to the plasma TC, LDL, HDL and TG levels following H. pylori eradication (12).

In contrast, there is an increasing amount of data showing a beneficial effect on lipid metabolism of eradication treatment. Gen et al. reported changes in lipid profile including an increase in HDL levels and a fall in LDL levels with H. pylori eradication (11). Other studies have also indicated reductions in TC and LDL levels and an increase in HDL levels following H. pylori eradication (17-19).

Consistent with the previous reports, in our study we found that serum LDL and ox-LDL levels were higher in patients with H. pylori infection than healthy controls. There was also a significant reduction in ox-LDL levels in eradicated patients without correctable risk factors for CVD. However, pre and post-treatment serum LDL and ox-LDL levels exhibited no significant difference among the patients with or without eradication of H. pylori infection. Actually, it was stated that conventional risk factors for CVD are associated with disturbances of the lipid profile which can explain the atherosclerosis risk (20-22). Therefore, it may be possible that the dominant factors can mask the efficacy of eradication therapy on the lipid profile among patients with H. pylori infection.

Our patient population was relatively small, which may be a limitation related to statistical power. In the present study, we focused on the effects of H. pylori eradication on serum ox-LDL level which has great importance in the pathogenesis of atherosclerosis. The findings of our study support the hypothesis that eradication therapy for H pylori could play a role in preventing the progression of silent CVD via ox-LDL. Nevertheless, the theories explaining the role of H. pylori infection in the pathogenesis of atherosclerosis are still debated. More comprehensive studies covering larger populations and long-term follow-up are needed to elucidate such a relationship between H. pylori eradication and atherosclerosis.

CONCLUSION

We found that plasma oxLDL levels were significantly higher in patients with H. pylori infection than in control subjects. OxLDL as an indicator of oxidative stress can be influenced by many other factors. Among patients, H. pylori eradication appears not to be more effective than dominant factors. Furthermore, H. pylori eradication might contribute to preventing atherosclerosis by lowering conventional risk factors.

ACKNOWLEDGMENT

The authors would like to thank the patients who willingly participated in the study.

DISCLOSURES OF INTEREST

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Ahotupa M. Oxidized lipoprotein lipids and atherosclerosis. Free radical research. 2017;51(4):439-47.
2. Satoh H, Saijo Y, Yoshioka E, Tsutsui H. Helicobacter Pylori infection is a significant risk for modified lipid profile in Japanese male subjects. Journal of atherosclerosis and thrombosis. 2010;17(10):1041-8.
3. Kim H-L, Jeon HH, Park IY, Choi JM, Kang JS, Min K-W. Helicobacter pylori infection is associated with elevated low density lipoprotein cholesterol levels in elderly Koreans. Journal of Korean medical science. 2011;26(5):654-8.
4. Buzás GM. Metabolic consequences of Helicobacter pylori infection and eradication. World Journal of Gastroenterology: WJG. 2014;20(18):5226.
5. Nasif WA, Mukhtar MH, Eldein MMN, Ashgar SS. Oxidative DNA damage and oxidized low density lipoprotein in Type II diabetes mellitus among patients with Helicobacter pylori infection. Diabetology & metabolic syndrome. 2016;8(1):34.
6. Kim TJ, Lee H, Kang M, Kim JE, Choi Y-H, Min YW, et al. Helicobacter pylori is associated with dyslipidemia but not with other risk factors of cardiovascular disease. Scientific Reports. 2016;6.
7. Vijayvergiya R, Vadivelu R. Role of Helicobacter pylori infection in pathogenesis of atherosclerosis. World journal of cardiology. 2015;7(3):134.
8. Huang B, Chen Y, Xie Q, Lin G, Wu Y, Feng Y, et al. CagA-positive Helicobacter pylori strains enhanced coronary atherosclerosis by increasing serum OxLDL and HsCRP in patients with coronary heart disease. Digestive diseases and sciences. 2011;56(1):109-14.
9. Ibrahim HA, Mohammed MO, Dhahir HA, Mahmood KA, Nuradeen BE. Impact of Helicobacter pylori infection on serum lipid profile and atherosclerosis of carotid artery. International Journal of Clinical Medicine. 2014;5(15):933.
10. Pellicano R, Oliaro E, Fagoonee S, Astegiano M, Berrutti M, Saracco G, et al. Clinical and biochemical parameters related to cardiovascular disease after Helicobacter pylori eradication. International Angiology. 2009;28(6):469.
11. Gen R, Demir M, Ataseven H. Effect of Helicobacter pylori eradication on insulin resistance, serum lipids and low-grade inflammation. Southern medical journal. 2010;103(3):190-6.
12. Lu Y-H, Yen H-W, Lin T-H, Huang C-H, Lee K-T, Wang W-M, et al. Changes of coronary risk factors after eradication of Helicobacter pylori infection. The Kaohsiung journal of medical sciences. 2002;18(6):266-72.
13. Park SH, Jeon WK, Kim SH, Kim HJ, Park DI, Cho YK, et al. Helicobacter pylori eradication has no effect on metabolic and inflammatory parameters. Journal of the National Medical Association. 2005;97(4):508.
14. He C, Yang Z, Lu N-H. Helicobacter pylori—an infectious risk factor for atherosclerosis? Journal of atherosclerosis and thrombosis. 2014;21(12):1229-42.
15. MORIEL P, PLAVNIK FL, ZANELLA MT, BERTOLAMI MC, ABDALLA DS. Lipid peroxidation and antioxidants in hyperlipidemia and hypertension. Biological research. 2000;33(2):105-12.
16. Harmon ME, Campen MJ, Miller C, Shuey C, Cajero M, Lucas S, et al. Associations of circulating oxidized LDL and conventional biomarkers of cardiovascular disease in a cross-sectional study of the Navajo population. PloS one. 2016;11(3):e0143102.
17. Kanbay M, Gür G, Arslan H, Yilmaz U, Boyacioğlu S. Does eradication of Helicobacter pylori infection help normalize serum lipid and CRP levels? Digestive diseases and sciences. 2005;50(7):1228-31.
18. Majka J, Róg T, Konturek PC, Konturek SJ, Bielański W, Kowalsky M, et al. Influence of chronic Helicobacter pylori infection on ischemic cerebral stroke risk factors. Medical Science Monitor. 2002;8(10):CR675-CR84.
19. Karbasi-Afshar R, Khedmat H, Izadi M. Helicobacter pylori Infection and atherosclerosis: a systematic review. Acta Medica Iranica. 2015;53(2):78-88.
20. Ozder A. Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipids in health and disease. 2014;13(1):183.
21. Otsuka T, Takada H, Nishiyama Y, Kodani E, Saiki Y, Kato K, et al. Dyslipidemia and the Risk of Developing Hypertension in a Working-Age Male Population. Journal of the American Heart Association. 2016;5(3):e003053.
22. Mouhamed DH, Ezzaher A, Neffati F, Gaha L, Douki W, Najjar M. Association between cigarette smoking and dyslipidemia. Immunoanalyse & Biologie Spécialisée. 2013;28(4):195-200.