DOES HELICOBACTER PYLORI ERADICATION IMPROVE INFLAMMATION AND LIPID PROFILE IN PATIENTS WITH CORONARY ARTERY DISEASE ?

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ABSTRACT

• ***Objective:*** *We aimed to evaluate the influences of H. pylori eradication on the inflammation and the lipid profile in the H.pylori positive patients with coronary artery disease (CAD).*

• ***Material and Method:*** *Ninety five patients were evaluated with coronary angiography initially H.pylori were tested by using urea breath test in 72 CAD patients. H. pylori an eradication therapy was applied to 30 patients with H.pylori infection for 14 days while 22 patients with H.pylori infection were not given eradication therapy. Lipid profile and high sensitive C-reactive protein levels were measured and compared in both eradicated and non-eradicated groups before and two months after the H.pylori eradication.*

• ***Results:*** *Seventy two patients had CAD and 23 patients were normal as an angiographically. Fifty two CAD (72%) patients and 15 non-CAD (65%) patients had H.pylori infection and the difference was statistically not significant. Total cholesterol, LDL-cholesterol and hs-CRP were significantly decreased in H. pylori eradication treated group (n=25) compared to non-treaked group (n=22). However, changes in HDL-cholesterol and triglyceride levels were not significant statistically.*

• ***Conclusion:*** *Eradication of H. pylori in patients with CAD decrease total cholesterol , LDL-cholesterol and high sensitive C-reactive protein levels. This may help to slow down the atherosclerotic process indirectly in these patients.*

• ***Key Words:*** *Helicobacter pylori, eradication, inflammation, lipid profile.* ***Nobel Med 2009; 5(3): 65-69***

ÖZET

KORONER ARTER HASTALARINDA HELİCOBACTER PYLORİ ERADİKASYONU İNFLAMASYON VE LİPİD PROFİLİNİ DÜZELTEBİLİR Mİ?

• **Amaç:** Koroner arter hastalığı olan *H. pylori* pozitif hastalarda *H. pylori* eradikasyonunun inflamasyon ve lipid profili üzerine etkilerini incelemeyi amaçladık.

• **Materyal ve Metod:** Çalışmaya alınan 95 hastaya koroner anjiografi yapıldı, 72 koroner arter hastasında üre nefes testi kullanılarak *H.pylori* test edildi. *H. pylori* infeksiyonlu 30 hastaya 14 gün süreyle *H. pylori* eradikasyon tedavisi uygulandı. *H. pylori* infeksiyonlu 22 hastaya ise eradikasyon tedavisi yapılmadı. *H. pylori* eradikasyonundan önce ve iki ay sonra tedavi edilen ve edilmeyen her iki grupta lipid profili ve yüksek duyarlıklı CRP düzeyleri ölçüldü ve karşılaştırıldı.

• **Bulgular:** Hastaların 72'sinde anjiografi ile koroner arter hastalığı (KAH) tespit edildi, 23'ü ise normal bulundu. KAH olan hastaların 52 (%72)' sinde, normal olanların 15 (%65)'inde *H. pylori* infeksiyonu saptandı.

Fark istatistiksel olarak anlamlı bulunmadı. *H. pylori* eradikasyonu sağlanan grupta (n=25) *H. pylori* eradikasyonu yapılmayan gruba (n=22) göre total kolesterol, LDL-kolesterol ve yüksek duyarlıklı-CRP anlamlı olarak düşüktü (p<0,05). Bununla beraber HDL-kolesterol ve trigliserit düzeyleri iki grup arasında anlamlı farklılık göstermemekteydi (p>0,05).

• **Sonuç:** KAH olan hastalarda *H. pylori* eradikasyonu total kolesterol, LDL-kolesterol ve CRP düzeylerini düşürür. Bu sonuç hastalarda, dolaylı olarak aterosklerotik sürecin yavaşlamasına yardımcı olabilir.

• **Anahtar Kelimeler:** *Helikobakter pilori*, eradikasyon, inflamasyon, lipid profili. **Nobel Med 2009; 5(3): 65-69**

INTRODUCTION

Although the effects of *H. pylori* on gastrointestinal system are well known; the data on its observed non-gastrointestinal effects such as cardiac, vascular, hepatic and cutaneuos are conflicting. It is suggested that the increase of inflammatory mediators or cross-reaction with antigens may account for the extra-intestinal involvement.[1,2] The hypothesis that *H. pylori* facilitates atherosclerosis is still disputable. It was found that Apo B levels which is a good marker of risk of vascular disease were higher but not statistically significant in *H. pylori* antibody positive cases when compared with negatives, but Apo B levels increased with C. pneumoniae infection.[3]

It is suggested that acute and chronic infections stimulate atherosclerosis cascade by arterial inflammation via mechanisms such as macrophage adhesion, endothelial injury, chronic inflammation and thrombosis.[2] Also, it is reported that *H. pylori* promotes atherosclerosis by increasing total cholesterol, LDL cholesterol / HDL cholesterol ratio and atherogenic lipid profile.[4,5] Takashima reported that mean HDL-Cholesterol levels were lower in *H. pylori* seropositive individuals than seronegative individuals and the percentage of the elderly individuals with HDL-Cholesterol < 35 mg/dl were higher in *H. pylori* seropositive group than seronegative group.[6] Animal studies support the association between atherosclerosis and infectious agents.[7,8] Morover, it was also shown that bacterial DNAs of C. pneumonia and *H. pylori* were present in human atherosclerotic plaques.[9] *H. pylori* stimulates the release of inflammatory mediators such as Interleukin-1 (IL-1), Interleukin-8 (IL-8), Tumor Necrosis Factor-α (TNF-α) [10] in addition to production of free oxygen radicals by contacting of bacterial products like vacuole forming cytotoxin, liposaccharides, neutrophil activating factor, porin with gastric epithelial cells. *H. pylori* may also cause to increase the platelet activation.[11]

MATERIAL and METHOD

Patients selection

The study has been conducted from January 2005 to February 2006. From all patients eligible to the study informed consent form were taken and the study was approved by the Local Ethical Committee. Inclusion criteria were as follows: chronic dyspepsia indication for H pylori screening, who have indication for coronary angiography (history of angina, exercise treadmill test showing high-risk features, etc.), consent of patient to participate in the study and to be follow-up to two months, patients who are above 18 years of age. All the patients fulfilled these criteria. Exclusion criteria were: acute infection, malignancy, any chronic inflammatory disease (such as collagenous tissue disease). Initially ninety five patients were evaluated for the study. Coronary artery angiography was performed for all these patients. Patients who had more than 40% stenosis in at least one of three major coronary arteries were diagnosed as CAD. According to this criteria twenty three patients did not have CAD and they were evaluated in the second step of the study. Grouping→

of the patients: *H pylori* was investigated by urea breath test (UBT) in 72 patients. 52 were *H. pylori* positive and 20 H. pylori negative. H. pylori negative patients with CAD were also excluded from the study. Fifty two patients was divided into two groups. Thirty patients were given *H. pylori* eradication therapy and 25 of them could be which eradicated, constituted *H. pylori* eradication therapy (HET) group. 5 patients which couldn't be eradicateted excluded from the study. Twenty two patients which were not given any therapy for *H. pylori* infection constituted non-HET group. Age, sex, hypertension, diabetes mellitus, smoking and medications were evaluated. Lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride), high sensitive C-reactive protein (hs-CRP) (DADE Behring, Marburg-USA) were also determined at the beginning of the study. *H. pylori* eradication treatment was applied for 14 days to 30 *H. pylori* positive patients and urea breath test was performed after the eradication treatment as a second time. Lipid profile and hs-CRP levels measured two months later in HET and non-HET groups.

Urea breath test (UBT): Radioactive labeled urea is given orally and radioactive labeled carbon dioxide is detected in breathing air one hour later when *H.pylori* urease enzyme breaks urea which is forming carbon dioxide. This test has a specificity of 90-100% and a sensitivity of 90-95%.[14,15] Urea breath test was repeated after 14-days eradication therapy and negative UBT result was considered as successful eradication.

Eradication Treatment: Lansoprazole (60 mg/day), amoxicilline (2 g/day), chlarithromycin (1000 mg/day) were given orally for 14 days.

Statistical analysis

Results are presented as absolute value (%) for qualitative and as median (range) for quantitative data. SPSS (Statistical Package for Social Sciences) For Windows 10.0 software was used for statistical analyses. Data were expressed as ±SD. Treatment results (pre and post treatment change) and lipid parameter were compared by Mann Whitney U Test. A P value of < 0.05 indicated statistical significance for all tests. Power of the study has been evaluated as "Effect Size (dz)" by using G power analysis (Franz Faul Universität Kiel, Germany 1992-2008).

RESULTS

Ninetyfive patients were evaluated with coronary angiography initially. Seventytwo patients had CAD and 23 patients were normal. Mean age of the study group were 62±8 years. Fiftytwo (72%) patients had *H. pylori*

Table 1: Demographic and laboratory parameters of the study groups before therapy

	HET Group (n=25)	Non-HET Group (n=22)	p
Age (years)	67±7	52± 4	NS
Sex (Female/Male)	8/17	166±7	NS
Hypertension	15 (60%)	73±11	NS
Diabetes mellitus	10 (40%)	18 (78)	NS
Smoking	12 (48%)	4 (17)	NS
Statin	13 (52%)	5 (22)	NS
Anti-ischemic drugs	20 (80%)	81±9	NS
Antiagregan	22 (88/)	0.79±0.13	NS
hs-CRP (mg/dl)	6.5±8.5	13.9±1.5	NS
Total cholesterol (mg/dl)	204.9±52.5	192±32	NS
HDL-cholesterol (mg/dl)	41.1±12.0	44±6	NS
LDL- cholesterol (mg/dl)	133.5±38.9	127±31	NS
Triglyceride (mg/dl)	160.9±136.4	127±36	NS

NS: Non-significant, HET: Helicobacter pylori eradication therapy , non-HETG: Helicobacter pylori eradication therapy were not given

Table 2: Lipid parameters and hs-CRP levels of the study groups two months after therapy

	Two months later HET group (n=25)	Two months later Non-HET group(n=22)	p
Total cholesterol (mg/dl)	168.4 ± 21.9	198.2±31.2	0.01
HDL-cholesterol (mg/dl)	40.09±11.8	39.7±14.3	NS
LDL-cholesterol (mg/dl)	105.9±24.4	124.3±24.5	0.001
Triglyceride (mg/dl)	145.9±102.8	143.5±47.3	NS
hs-CRP (mg/dl)	4.19±3.3	5.4±3.6	0.02

Baseline and hyperemic measurements. DPFV; diastolic peak flow velocity, DMFV; diastolic mean flow velocity, CFR; coronary flow velocity reserve.

difference was statistically not significant. Table 1 shows demographic and laboratory parameters of the study groups. Before therapy patients charecteristics (age,sex, comorbidity,smoking, drug therapies ,lipid parameters, hs-CRP) were not different in HET and non-HET groups. *H. pylori* eradication was achieved in 25 patients (83%). Total cholesterol, LDL-cholesterol and hs-CRP levels were decreased significantly ($p<0.05$) in HETG when compared with non-HETG, whereas levels of HDL-cholesterol and triglyceride reduced ($p>0.05$) nonsignificantly two months later (Table 2). Power of the study as effect size was dz=0.36.

DISCUSSION

The association between *Helicobacter pylori (H. pylori)* infection and serum lipid profile is still controversial. It was shown that among *H. pylori*-positive and *H. pylori*-negative patients there was no difference in lipid profile.[16] The main result of our study is the significant decrease in total cholesterol, LDL-cholesterol and hs-CRP in →

infection among CAD patients and 15 (65%) patients had *H. pylori* infection among normal individuals. The *H. pylori* eradicated patients.This may allow us to speculate that *H. pylori* infection can increase the speed of the progression of CAD, at least, *H. pylori* infection can influence risk factors of atherosclerosis, such as lipid profile and inflammation. Some infectious agents like M. pneumonia, C.pneumonia, Cytomegalo-virus and *H. pylori* promote atherosclerosis by inflammation.[17-19]

H. pylori infection is the most common bacterial disease world wide.[20] It is the main cause of chronic gastritis and *H. pylori* infection is present in 95% patients with duodenal disease and 70 to 80% of patients with gastric ulcer. In one study, *H. pylori* positivity rate in subjects with angiographically demonstrated three vessel disease and in subjects with normal angiograms was found 83% and 25%, respectively.

In our study, the *H. pylori* positivity rate in CAD and non-CAD groups were 72% and 65% respectively, and on the contrary, there was no statistical significant difference between groups. Honda and coworkers reported that *H. pylori* infection does not accelerate the age-related progression of arteriosclerosis in their 4-year follow-up study.[21] At the other hand in one study it was reported that 37.9% of the patients of the *H. pylori* negative group and 45.5% of the patients of the *H. pylor*i positive group were treated with reintervention.

These data indicated that *H. pylori* infection had a modest influence on CAD and progressive atheroma, but the showed a tendency to increase.[22]

Some investiga-tors suggested that the gastrointestinal *H. pylori* coloniz-ation increased cardiovascular risk and eradication treatment may reduce this risk,[16] like the results in the present study. Examining *H. pylori* IgG serologically, Kanbay et al. reported that *H. pylori* IgG levels in CAD patients and control group are not different.[20] Although there is methodologic difference with respect of detecting *H. pylori* by UBT in our study we observed similar results. It was reported that H. pylori leads to development of atherosclerosis by facilitating an atherogenic lipid profile through an increase of total cholesterol, LDL cholesterol and total cholesterol/HDL cholesterol ratio.[4]

In another study, lower HDL choles-terol levels were detected in *H. pylori* (+) patients but this difference was not significant in patients <60 years old.[5] In our study urea breath test was positive in 72% of patients with CAD and in 65% of patients without CAD. Adiloglu et al.[23] found that the association of CAD and the presence of *H. pylori* was statistically significant. Chimienti et al.[4] reported that Anti-*H. pylori* Cag A IgG is similar in patients with cardiovascular disorders and in healthy control group and there is no statistically significant difference between them. Indeed, Chimienti et al. studied a sample of healthy subjects, free of any symptoms of cardiovascular disorders.[4] These findings are consistent with the present study although our patients have symptomatic CAD. Studies examining the changes in coronary risk factors following *H. pylori* infection are limited and their results are contradictory.

Lu et al[12] reported that fasting blood sugar, lipid profile and fibrinolytic profile were not altered following eradi-cation therapy. But a recently published new study adds evidence for supporting of the association of seropositivity of *H. pylori* with cardiovascular diseases.

Many components of metabolic syndrome such as levels of uric acid, plasma glucose, total cholesterol, fibrinogen were lower than their baseline levels after 3 weeks antibiotics duration, triglyceride levels did not change.[25] Another study no significant difference in LDL, TC, or TG serum levels were found between eradicated and non-eradicated groups although CRP and HDL serum levels were found to be the same before and after treatment in non-eradicated group, CRP levels were found to decrease and HDL levels to increase significantly in eradicated group.[26] These findings suggest that *H. pylori* infection per se might generate atherosclerosis or metabolic syndrome, and *H. pylori* infection might be one of the risk factors of athero-sclerosis thorough inflammation and modulation of glucose and lipid profiles, which may be prevented by antibiotics.[24, 25]

These findings are concordant with the present study becouse we also observed a decrease in total cholesterol, LDL-cholesterol and CRP levels with antibiotic therapy.

However, our study has some limitations. First our study sample size is small to make such a certain con-clusion. Second, urea breath test has a high sensitivity but low specifity, so endoscopic studies may give futher results.

CONCLUSION

H. pylori infection cannot be considered as an indepen-dent risk factor for CAD. However, it may contribute to atherosclerosis by enhancing the impact of risk factors on endothelial cells. So the effect of *H. pylori* eradication treatment on atherogenic lipid profile should be kept in mind.

Nevertheless we believe that more comprehensive and long-term follow up studies are required to examine the effect of *H. pylori* eradication on atherosclerosis.

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