IMPACT OF HELICOBACTER PYLORI ON PROGNOSIS OF PATIENTS WITH ACUTE CORONARY SYNDROME

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Abstract

INTRODUCTION: Coronary artery disease (CAD) is the main cause of mortality in industrial and developing countries. New risk factors including infections are under investigation as potential factors. One of these infectious agents is Helicobacter pylori, which has been investigated in numerous studies. This study was designed in view of the controversies surrounding the impact of Helicobacter pylori on the prognosis of patients with acute coronary syndrome (ACS).

METHODS: All patients with ACS including unstable angina and myocardial infarction who were referred to Fatemieh Hospital between 20 February 2003 and 19 February 2004 and were admitted to the CCU ward were enrolled in this cohort study. A total of 411 patients with ACS were evaluated for Helicobacter pylori serologically, and the occurrence of cardiac events needing angioplasty or coronary surgery was assessed.

RESULTS: Mean age of patients was 59.97±38.12 years and 56% of them were male. The serology test for Helicobacter pylori infection was positive in 45.6±12.38%, negative in 43.8%, and borderline in 10.6% of patients. 191 patients had unstable angina and 220 patients had myocardial infarction. In a one-month follow-up, 10% of the patients developed cardiac events and PCI or CABG was performed in 6.1% (16.1% totally). One-month occurrence of cardiac events in the group with Helicobacter pylori infection was 11.9% vs. 19.3% in the group without infection (χ^2 =3.078, P=0.079).

DISCUSSION: This prospective study showed that Helicobacter pylori infection has no effect on short term prognosis of patients with ACS.

Keywords • Helicobacter pylori • Acute coronary syndrome • Prognosis

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Introduction

Coronary artery disease (CAD) is the main cause of mortality in industrial and developing countries.[1,2] Several risk factors such as cigarette smoking, hypertension, hyperlipidemia and diabetes have been proposed.[3,4] In some patients, no risk factor is found. These patients should be investigated for other risk factors such as infections.

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Infectious agents like Chlamydia pneumonia, Cytomegalovirus, Herpes simplex and Helicobacter pylori (H. pylori) may have a probable role,[5,9] but no definitive cause and effect correlation between these agents and unstable angina (UA) or myocardial infection (MI) has yet been approved.[10,11]

The role of Chlamydia pneumonia as a potentially important and treatable cause for UA or MI is under investigation.[12-16]

Many researchers have probed the role of H. pylori as a potential risk factor for CAD[17-20] and some studies have pointed to an association between H. pylori and CAD.[3,6,7,16,23-30] After modification of other cardiac risk factors in some studies, the role of H. pylori

in the development of CAD weakened or disappeared.[5,32-34] A number of studies have ruled out H. pylori as a risk factor for coronary disease.[35-38]
In some studies, the rate of positive serology tests for H. pylori has been greater in the control group.[36]
Although H. pylori has been proposed as a probable cause of coronary disease in reference books,[3,5] much doubt remains.
Numerous studies have been conducted about the impact of H. pylori on the prognosis of patients with coronary artery disease.
In one study, MI or mortality rate in one-year follow-up in patients with H. pylori was 22% vs. 18% in normal persons (P=0.1).[38]
Another study measured six inflammatory factors, anti-chlamydia antibody, anti-cytomegalovirus antibody and anti-H. pylori antibody in patients with UA, as well as in controls.
In this study, one-year prognosis, as determined by such events as recurrent angina, MI, need for angioplasty, coronary surgery, and sudden death had no correlation with positive serologic results.[10] In another study, recurrence of acute coronary syndrome and sudden death apparently diminished in patients with history of MI or UA who had positive serology tests and were treated with erythromycin and roxytromycin.[15]
This study was designed in view of the controversies surrounding increased cardiac events in ACS in patients with positive serology tests for H. pylori.

Materials and methods

This is a cohort study of patients with acute coronary syndrome (UA or MI) admitted to CCU of Fatemieh Hospital, Semnan, Iran, between 20 Feb 2003 and 19 Feb 2004. Written informed consent was obtained from all patients. A questionnaire obtaining demographic data, type of ACS, main risk factors (hypertension, hyperlipidemia, cigarette smoking and family history of ischemic heart disease) was completed by each patient. Within the first 48 hours of admission, a blood sample (5 cc) was taken and centrifuged to assess IgA (marker of acute H. pylori infection) and IgG (marker of chronic H. pylori infection). We used Dialups kits to measure IgA; IgG was measured with ELISA. IgA or IgG levels greater than 30, between 15 and 30, and below 15 were considered as positive, borderline, and negative, respectively. Patients were followed for a month, and recurrent angina, MI, sudden death, PCI and CABG were evaluated in them.
Diagnosis of UA and MI was based on history, physical exam, EKG and cardiac enzymes (CPK, CK-MB and troponin). After sample collection, obtained data were analyzed using SPSS (v. 11.5) software with χ^2 and analytic regression tests (alpha=0.05).

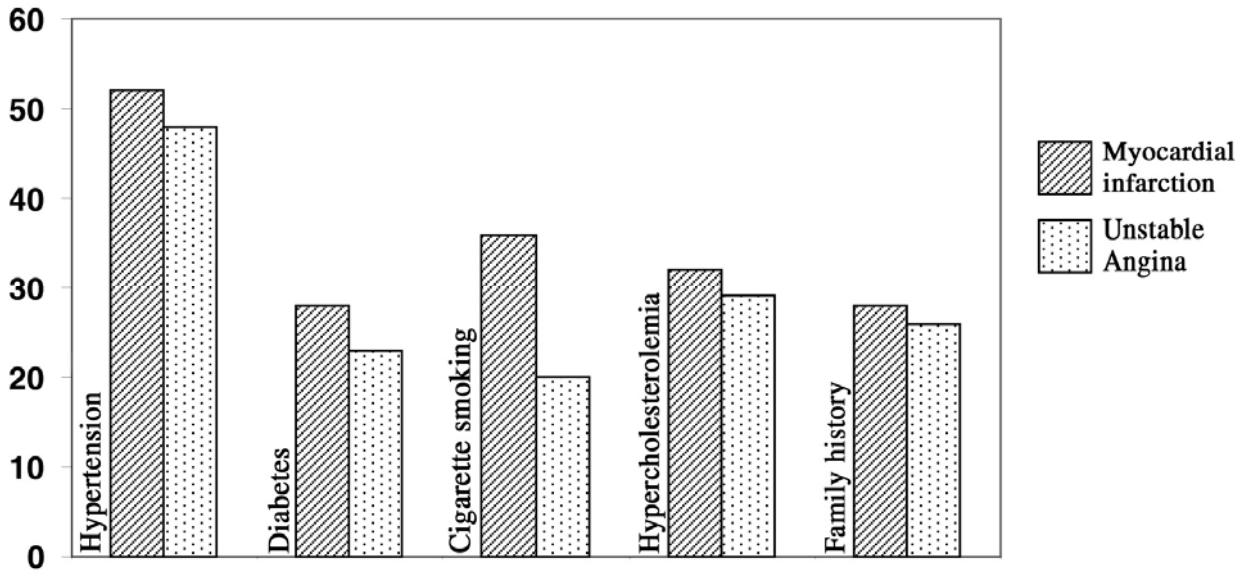

FIGURE 1. Prevalence of major risk factors of ischemic heart disease in patients with unstable angina and myocardial infarction

TABLE 1. Incidence of cardiac within one month of admission

Type of event	Prevalence	Percent	Total (%)
Unstable angina	34	8.3	51.5
Myocardial infarction	6	1.5	9.1
Sudden death	1	0.2	1.5
Angioplasty	13	3.2	19.7
CABG	12	2.9	18.2
total	66	16.1	100

TABLE 2. Association between cardiac events and serology of Helicobacter pylori

		One-month evaluation		Total
		Negative	Positive	
Anti H. pylori antibody (IgA or IgG)	Negative	117 80.7	28 19.3	145 100%
	Positive	133 88.1	18 11.9	151 100%
Total		250 84.5%	46 15.5%	296 100%

Results

A total of 411 patients were studied. Mean age of subjects was 59.97±38.12 years and 56% were male. The serology test for H. pylori infection was positive in 45.6±12.38%, negative in 43.8% and borderline in 10.6% of patients. The two groups of patients were not significantly different in terms of the main coronary risk factors (P>0.05). 191 patients had UA and 220 patients had MI.

Figure 1 shows the main coronary risk factors in the two groups. In a one-month follow-up, 10% of the patients were involved in cardiac events. PCI or CABG was performed in 6.1% of the patients (16.1% of total) (Table 1).

There was no correlation between H. pylori infection and main coronary risk factors (hypertension, hyperlipidemia, diabetes and cigarette smoking) (P>0.05). Besides, these risk factors had no significant correlation with one-month cardiac events (P>0.05). In the H. pylori infected group, the one-month incidence of cardiac events was 11.9% vs. 19.3% in the non-infected group (χ^2=3.078, P=0.079) (Table 2).

Discussion

Several studies have shown that inflammation is involved in the formation and progression of atherosclerosis. H. pylori is a known cause of inflammation. Both CAD and H. pylori infection are prevalent in the population and are closely associated with socioeconomic status.[37] On the other hand, if the correlation of H. pylori and CAD with the prognosis of patients is verified, the treatment of this infection would likely reduce the incidence of CAD and its related cardiovascular events.[37] Since H. pylori is acquired during childhood, development of a vaccine for children might be considered.[37]

H. pylori, which is colonized from childhood years may be in close association with CAD.[1,3-5,7] But recent studies have shown a weak association, or no association between H. pylori and CAD.[5,32-38]

In a large-scale study, patients were followed for 13 years and were examined at 5-year intervals. Mean follow-up period was 13.7 years. This study did not show any clear association between serology test positive for H. pylori and the incidence of CAD (at the start or during the study), but there was an apparent correlation between H. pylori infection and the risk of fatal CAD (OR=1.54, CI 95%: 1.30-2.30). Thus after heart attack, the ratio of patients with positive serology test who died was higher than that of patients with negative serology test (57% vs. 45%, OR=2, CI 95%: 1.19-3.36).[40] In another study, six inflammatory factors and serologic markers of Chlamydia pneumonia, Cytomegalovirus and Helicobacter pylori were measured in patients with history of acute coronary syndrome. There was no association between level of inflammatory markers and serologic states. The percentage of cardiac events and the need for coronary revascularization in one year showed no difference based on serologic tests.[10] However, antibiotic treatment can reduce future cardiac events in patient with acute coronary syndrome.

This effect is independent of positive serology for Chlamydia and H. pylori.[15]

In addition, an association has been shown between the number of infectious agents (such as Chlamydia, Hemophilus influenza, Epstein bar virus, Helicobacter pylori and Herpes simplex) and the extent of atherosclerosis and risk of future events.[41]

In the United States, the incidence of MI or death in patients with H. pylori was 22% vs. 18% in normal individuals (P=0.1).

The results of the above-mentioned studies are in concordance with our study.

Meanwhile, some studies resulted in controversial effects. The probability of coronary events was greater in patients who were not treated for H. pylori.[42] During a 3-year follow-up, the incidence of recurrent MI and death was greater in patients with positive serology. The probability of adjusted risk for MI or death (related to positive H. pylori serology) was 1.12.[38] Two studies were conducted on the effects of erythromycin and roxithromycin on the incidence of acute coronary syndrome after MI or UA. Based on these surveys, the incidence of coronary disease had decreased significantly during subsequent follow-ups.[16] In another study, prognosis of patients with H. pylori infection who were treated improved during the follow up period.[42]

Consequently, in spite of the short follow-up period in our study, concordance of results was noted.[10,15,40]

Mortality rate, recurrent angina or infarction, and the need for revascularization (PCI or CABG) showed no significant difference between the two groups.

Since no clear association has yet been shown between the prognosis of CAD and positive serology test, the difference between our results and those of other studies[16,38,42] may originate from certain problems.

Interactions between chronic H. pylori infection and the coronary arteries which is mainly due to immunologic reactions, can change lipid metabolism and cause hypercholesterolemia and increase the risk of consequent atherosclerosis.

Therefore if confounding factors are not matched between the two groups, they can influence the prognosis. In studies with well-controlled confounding factors, positive serology of H. pylori had no association with prognosis.[10,15,40] Type of diagnostic test for H. pylori infection can affect the results, hence that we assessed IgA and IgG as markers of acute and chronic infection in our study.

On the other hand, since these antibiotics have widespread antimicrobial effects, they probably eliminate other germs such as the bacterial causes of chronic bronchitis, pyorrhea and even normal gastric flora, and may reduce cardiac events via this mechanism. Recent data point to the importance of the total amount of bacteria in the development of atherosclerosis.

Although improvement in the prognosis of acute coronary syndrome after antibiotic medication may be due to anti-inflammatory, anti-oxidant and anti-thrombotic effects of these drugs which reinforce and fix atherosclerotic plaques, further studies are needed to assess the long-term effects of shorter-term antibiotic treatments.

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