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Helicobacter Pylori Infection and Coronary Artery Disease

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A B S T R A C T

The aim of this investigation was to determine the seroprevalence of H. pylori in patients with coronary artery disease (CAD). Patients with coronary artery disease (n=90) and control group (n=90) were enrolled into this randomized, multi-centre study. CAD risk factors analyzed included age, male gender, diabetes mellitus, systemic hypertension, cigarette smoking, hypercholesterolemia and socioeconomic status. The results of this study showed a higher seroprevalence of Helicobacter pylori infection in patients with CAD compared to controls (78,8% versus 58,3%, p<0.05). However, Helicobacter pylori seropositivity was not associated with coronary artery risk factors (smoking, body mass index, diabetes mellitus, hypertension, total cholesterol and socioeconomic status) either in the whole study population or in the patients and control subjects analyzed separately (P>0.05). Further study are needed to clarify the precise role of Helicobacter pylori infection on the development of coronary artery disease.

Key words: *Helicobacter pylori infection, coronary artery disease-CAD*

Introduction

Helicobacter pylori, a gram-negative, microaerophilic spiral bacterium, has been found to infect the gastric mucosa of over half the world s population[1]. Helicobacter pylori gastritis is associated with the development of peptic ulcer, gastric adenocarcinoma and gastric MALT lymphoma[2]. Helicobacter pylori infection may induce a chronic systemic inflammatory status of low degree, which may have repercussions for the whole organism. Systemic indices of inflammation, such as levels of polymorphs and monocytes, are increased in H. pylori-infected dyspeptic patients, and many vasoactive substances and cellular mediators, such as cytokines, which are produced in the gastric mucosa in response to H. pylori infection, may be transported in the blood-stream and promote an inflammatory response in organs distant from the stomach[3,4].

Several preliminary reports have suggested that chronic infections by H. pylori, as well as other chronic infections, may be associated with atherosclerosis and vascular diseases[5,6]. However, most prospective studies have not confirmed the association between chronic infections and coronary disease[7–10]. Furthermore, H. pylori infection is associated with several confounding factors, particularly low social class, which are also related to higher incidence of vascular diseases[5].

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The aim of this investigation was to determine the seroprevalence of H. pylori in patients with coronary artery disease.

Materials and Methods

Patients with coronary artery disease (n=90) and control group (n=90) were enrolled into this randomized, multi-centre study.

All subjects had given informed consent to inclusion in the study and the research was carried out in accordance with the principles of the Declaration of Helsinki.

The diagnosis of coronary artery disease (CAD) required the presence of one of following: a history of coronary artery bypass graft surgery, a history of myocardial infarction or a history of percutaneous transluminal coronary stent. Exclusion criteria were: prior H. pylori eradication therapy, consumption of acid-suppressive drugs or antibiotics in the preceding 12 months, history of vagotomy or operations on the upper gastrointestinal tract and a known history of gastrointestinal pathology.

CAD risk factors analyzed included age, male gender, diabetes mellitus, systemic hypertension, cigarette smoking, hypercholesterolemia and socioeconomic status. We used occupational status as the socioeconomic status indicator. Patients were considered to have systemic hypertension if they had received the diagnosis with an arterial pressure>140/90 mm Hg or were being treated with antihypertensive medications or dietary modification. A history of past and current smoking of each patient was obtained. Patients who had stopped smoking >20 years ago and who were <30 years of age when they stopped were considered not to have smoking as a risk factor. Patients were considered to have diabetes mellitus if they had a fasting plasma glucose >6.4 mmol/L, were taking insulin or oral hypoglycemic agents or had previously received such treatment, or were currently using dietary modification to control the condition. Patients were considered to have hyperlipidemia if they had a serum cholesterol value >5.2 mmol/L or were receiving cholesterol-lowering treatment.

Potential control subjects were excluded if they exhibited one or more of the following: a known history of CAD, a known history of gastrointestinal pathology, chest pain and dyspnea, prior Helicobacter pylori eradication therapy, consumption of acid-suppressive drugs or antibiotics in the preceding 12 months, a history of vagotomy or operations on the upper gastrointestinal tract or a known history of gastrointestinal pathology. We selected 90 controls from among the healthy subjects and matched them with the patients for sex, age and coronary artery risk factors.

All subjects enrolled (CAD patients and controls) underwent an enzyme-linked Immulite (chemiluminescent) analyzer IgG serologic test for H. pylori diagnosis (Diagnostic Products Corp., Los Angeles, CA, USA), in accordance with the manufacturer s guidelines. This kit has a sensitivity of 97% and a specificity of 98.%.

Results are presented as mean ±SD (standard deviation). Statistical analysis was carried out using SPSS software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc., Chicago, IL,USA) and chi-square and Student t-tests. A value of $P<0.05$ was considered statistically significant.

Results

In Table 1. are listed demographic data on the patients and controls. There was no significant difference in age, sex or coronary artery risk factors between the two groups, but the prevalence of seropositivity for Helicobacter pylori was higher in patients compared to controls (78,8% versus 58,3%, $P<0.05$). However, Helicobacter pylori seropositivity was not associated with coronary artery risk factors (smoking, body mass index, diabetes mellitus, hypertension, total cholesterol and socioeconomic status) either in the whole study population or in the patients and control subjects analyzed separately ($P>0.05$) as reported in Tables 2 and 3.

Discussion

Since 1994, a considerable number of studies have been performed on the correlation between Helicobacter pylori infection and ischaemic heart disease. The exact

TABLE 1
DEMOGRAPHIC DATA OF PATIENTS AND CONTROL GROUP

	Patients (n=90)	Controls (n=90)	value*
Age (mean years)	49.2	50.8	NS
Male (%)	67.5	68.7	NS
Hypertension (%)	59.6	55.8	NS
widctlparSmoking (%)	67.2	62.9	NS
Diabetes mellitus (%)	19.7	15.2	NS
Body mass index (kg/m^2)	29.5	26.2	NS
Total cholesterol (mmol/L)	6.9	5.1	NS
Socioeconomic status (high, %)	45.7	49.1	NS
Seropositivity to Helicobacter pylori IgG antibody (%)	78.8	55.5	P<0.05

*NS, P>0.05

TABLE 2
MAIN CLINICAL FEATURES OF CAD PATIENTS WITH AND WITHOUT HELICOBACTER PYLORI INFECTION

	Helicobacter pylori status		
	Seropositivity (n=71)	Seronegativity (n=19)	P value*
Age (years)	50.1+9	48.6+6	NS
Men (%)	67.9	66.7	NS
Smoker (%)	67.5	66.1	NS
Diabetes mellitus	20.1	19.1	NS
Total cholesterol > 5,2mmol/L (%)	59.6	55.7	NS
Socioeconomic status (high,%)	43.9	47.8	NS

Data are presented as mean+SD or percentage of patients.
*NS, P>0.05

TABLE 3
MAIN CLINICAL FEATURES OF CONTROL SUBJECTS WITH AND WITHOUT HELICOBACTER PYLORI INFECTION

	Helicobacter pylori status		
	Seropositivity (n=50)	Seronegativity (n=40)	P value*
Age (years)	50.1+7	49.6+9	NS
Men (%)	69.5	67.9	NS
Smoker (%)	63.4	62.6	NS
Diabetes mellitus	20.3	19.1	NS
Total cholesterol > 5,2 mmol/L (%)	50.6	48.7	NS
Socioeconomic status (high, %)	48.9	49.8	NS

Data are presented as mean+SD or percentage of patients.
*NS, P>0.05

pathogenetic role of H. pylori infection in atherosclerosis is still a matter of debate, and the process that underlies this association is also unclear.

Epidemiological and molecular studies as well as some eradicating trials gave conflicting results.

Mendall et al.[5] in 1994 reported a higher prevalence of H. pylori infections in patients with ischaemic heart disease (IHD). This finding has since been verified by several other authors. Danesh et al.[11] showed evidence of strong association between IHD and serological markers of persistent infection sustained by H. pylori. These results were confirmed by other studies in which higher levels of anti H. pylori antibodies were found in patients with IHD or who had died of myocardial infarction (MI) than in normal controls[12,13]. Pasceri et al.[14] have demonstrated a higher prevalence of either H. pylori infection or CagA-positive strains in patients with IHD than in controls. Singh et al.[15] in a similar study, found a prevalence of H. pylori CagA-positive strains in 52% of the IHD patients compared to 43% of the controls. The association remained significant even after the adjustment for blood pressure values, body mass indeks, plasma concentrations of low-density lipoprotein and high-density lipoprotein cholesterol, history of hypertension and diabetes, statin treatment and socioeconomic status. Kowalski et al.[16] reported a higher prevalence of H. pylori infection in patients with unstable angina or MI as well as an evidence of H. pylori-related DNA in atherosclerotic lesions of 47,8% patients with coronary heart disease.

Some epidemiological study did not show any clear correlation between H. pylori infection and IHD[17,18]. No significant association was found concering H. pylori infection among patients with angiographically documented coronary artery disease[19–21], and in patients with high risk of restenosis after coronary intervention[22]. In Koenig et al.[23] and Whincup et al.[24] studies none of the inflammatory markers (CRP, fibrinogen, plasma viscosity or leucocyte counts) was significantly different in patients with H. pylori infection and in controls, thus denying any positive correlation between those events.

Kowalski et al.[25] proved that H. pylori eradication significantly attenuates the reduction in coronary artery lumen in patients with coronary artery disease after percutaneous coronary angioplasty, possibly by reducing the effect of proinflammatory cytokines. Another study[26] has evaluated the effect of the eradication of H. pylori infection on the plasma levels of total cholesterol, LDL choles-

terol, fibrinogen and IL-8. In particular, all those factors were significantly decreased after the administration of the eradicating treatment.

Other studies did not confirm any beneficial effect of the eradicating treatment on the known risk for ischaemic heart disease. Schweeger et al.[27] demonstrated that successful eradication of H. pylori do not determine any change in either fibrinogen or other proteins of the acute phase levels. Stone et al.[28] did not find any correlation between eradication of H. pylori infection and risk factors for ischaemic heart disease.

In conclusion, the results of this study showed a higher seroprevalence of Helicobacter pylori infection in patients with CAD compared to controls (78,8% versus 58,3%, $p<0.05$). However, Helicobacter pylori seropositivity was not associated with coronary artery risk factors (smoking, body mass index, diabetes mellitus, hypertension, total cholesterol and socioeconomic status) either in the whole study population or in the patients and control subjects analyzed separately ($P>0.05$). Further study are needed to clarify the precise role of Helicobacter pylori infection on the development of coronary artery disease

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HELICOBACTER PYLORI INFEKCIJA I KORONARNA ARTERIJSKA BOLEST

SAŽETAK

Cilj ovog rada je bio odrediti seroprevalenciju Helicobacter pylori infekcije u bolesnika s koronarnom arterijskom bolešću. U ovu randomiziranu multicentričnu studiju uključeno je 90 bolesnika s koronarnom arterijskom bolešću i 90 zdravih osoba u kontrolnoj skupini. Analizirani su rizični čimbenici za koronarnu arterijsku bolest i to: dob, spol, pušenje, prekomjerna tjelesna težina, arterijska hipertenzija, ukupni kolesterol u krvi, šećerna bolest i socioekonomski status ispitanika. Rezultati su pokazali statistički značajnu veću seroprevalenciju H. pylori infekcije u bolesnika s koronarnom arterijskom bolešću nego u ispitanika kontrolne skupine (79,1% nasuprot 58,3%, $P<0,05$). Međutim, H. pylori seropozitivnost nije bila udružena s čimbenicima rizika za koronarnu arterijsku bolest gledajući ukupan broj ispitanika ($n=180$) ili gledajući posebno bolesnike, a posebno ispitanike u kontrolnoj skupini ($P>0,05$). Potrebne su buduće studije kako bi se precizno odredila uloga H. pylori infekcije u nastanku koronarne arterijske bolesti