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• BRIEF REPORTS •

Type 2 diabetes mellitus affects eradication rate of *Helicobacter pylori*

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Abstract

AIM: To study the eradication rate of *Helicobacter pylori* (*Hp*) in a group of type 2 diabetes and compared it with an age and sex matched *non-diabetic* group.

METHODS: 40 diabetic patients (21 females, 19 males; 56±7 years) and 40 *non-diabetic* dyspeptic patients (20 females, 20 males; 54±9 years) were evaluated. Diabetic patients with dyspeptic complaints were referred for upper gastrointestinal endoscopies; 2 corpus and 2 antral gastric biopsy specimens were performed on each patient. Patients with positive *Hp* results on histopathological examination comprised the study group. Non-diabetic dyspeptic patients seen at the Gastroenterology Outpatient Clinic and with the same biopsy and treatment protocol formed the control group. A triple therapy with amoxycillin (1 g b.i.d), clarithromycin (500 mg b.i.d) and omeprazole (20 mg b.i.d.) was given to both groups for 10 days. Cure was defined as the absence of *Hp* infection assessed by corpus and antrum biopsies in control upper gastrointestinal endoscopies performed 6 weeks after completing the antimicrobial therapy.

RESULTS: The eradication rate was 50 % in the diabetic group versus 85 % in the non-diabetic control group ($P<0.001$).

CONCLUSION: Type 2 diabetic patients showed a significantly lower eradication rate than controls which may be due to changes in microvasculature of the stomach and to frequent antibiotic usage because of recurrent bacterial infections with the development of resistant strains.

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INTRODUCTION

Helicobacter pylori (*Hp*) is the most prevalent infection all over the world and has been considered as the causative agent of many gastrointestinal diseases[1,2]. Type 2 diabetes mellitus can present with many protean gastrointestinal symptoms and *Hp* can play a role in this context[3,4].

Although a number of studies has been performed on the association of *Hp* and diabetes mellitus, the results have been controversial. In a large study performed by Xia *et al*., the seroprevalance of *Hp* infection was not statistically different in patients with diabetes mellitus and non-diabetic controls[5]. In earlier studies, the prevalence of *Hp* was reported to be 62 % versus 21%, but according to Xia *et al*., the prevalence of *Hp* should be corrected for age and gender and there are no differences if an adjustment has been done for these variables[6].

The literature is even scarce about treatment regimens of *Hp* infection in diabetes mellitus. We also know that the eradication of *Hp* shows great differences between different ethnic groups and in patients with some chronic conditions[1,7]. Therefore we proposed that the eradication rate of *Hp* may be also different in type 2 diabetics in comparison to non-diabetic controls and we planned a prospective study to elucidate the eradication rate of *Hp* infection in type 2 diabetic subjects.

MATERIALS AND METHODS

Patients

Diabetic patients with dyspeptic complaints from Diabetes Outpatient Clinic were referred for upper gastrointestinal endoscopies in the Gastroenterology Department. Upper gastrointestinal endoscopies were performed in a standard fashion with a videoendoscope (Pentax G-2940, Japan) by the same endoscopist. Endoscopic findings were noted and *Hp* infection was assessed using 2 gastric antrum and 2 gastric corpus biopsy specimens, which were evaluated with the rapid urease test and the pathological examination (Haematoxylin-Eosin staining and Giemsa if the first stain was negative). Only patients with positive results for *Hp* in pathological specimens were included in the study. The study population consisted of 40 patients with type 2 diabetic (21 females and 19 males; mean age 56±7 years) and 40 *non-diabetic* dyspeptic patients as a control group from Gastroenterology Outpatient Clinic (20 females and 20 males; mean age 54±9 years) matched for sex and age (Table 1). All patients had detailed information about the study and written informed consent.

Table 1 Characteristics of the patients in diabetic and control groups

	Diabetics	Control	*P*
n (F / M)	40 (21 / 19)	63 (25 / 40)	>0.05
Age (y)	56±7	54±9	>0.05
Diabetes duration (y)	7.2±5	-	
HbA1c (%)	7.4±1.3	-	

Methods

At enrolment and at the end of the treatment, each patient completed a dyspepsia questionnaire proposed by Buckley *et al*., which had been slightly modified[8]. A triple therapy with amoxycillin (1 g b.i.d), clarithromycin (500 mg b.i.d) and omeprazole (20 mg b.i.d) was given for 10 days. After 10 days, the patients received 20 mg omeprazole for 5 weeks if a gastric or duodenal ulcer was identified in the initial endoscopy or 40 mg of famotidin if there was gastritis. Cure was defined as the

absence of *Hp* infection assessed by corpus and antrum biopsies in control upper gastrointestinal endoscopies performed 6 weeks after completing the antimicrobial therapy. Endoscopic findings were evaluated again in control endoscopy and compared with initial endoscopic findings. Any side effects due to the treatment were reported.

During the same study period, dyspeptic patients seen at the Gastroenterology Outpatient Clinic were taken as the control group if there was no history of type 2 diabetes, and their fasting plasma glucose levels were in normal limits (between 80-110 mg/dl) and pathological *Hp* positivity was found in gastric antrum and corpus specimens. The same triple therapy and a control upper gastrointestinal endoscopy after 6 weeks were also applied to the control group.

Statistical analysis

Results were expressed as means ± SEM. Statistically significant differences between groups were assessed using either Student *t* test, Fischer' s exact test or ANOVA test, as appropriate. $P<0.05$ was considered to be significant.

RESULTS

All enrolled patients completed the study. *Hp* was eradicated in 50 % (20/40) type 2 diabetic patients and in 85 % (34/40) *non-diabetic* dyspeptic patients. The eradication rate was significantly lower in diabetics in comparison to the controls ($P<0.05$).

There were no side effects in both groups, which led to discontinuation of the treatment.

At baseline, type 2 diabetic patients infected with *Hp* showed a high prevalence of gastrointestinal symptoms. There was a statistically significant decrease in epigastric pain, nausea and belching after *Hp* eradication treatment (Table 2).

Table 2 Prevalence of gastrointestinal symptoms in type 2 diabetic patients before and after the treatment

	Before (%)	After (%)	*P*
Epigastric pain	75 (30 / 40)	30 (12 / 40)	<0.05
Bloating	68 (27 / 40)	43 (17 / 40)	NS
Pyrosis	63 (25 / 40)	38 (15 / 40)	NS
Nausea	55 (22 / 40)	23 (9 / 40)	<0.05
Belching	63 (25 / 40)	30 (12 / 40)	<0.05
Early satiety	30 (12 / 40)	20 (8 / 40)	NS

Denotes: NS=not significant

Age, duration of the diabetes and Haemoglobin A1c levels were not significantly different between the diabetics in whose *Hp* was eradicated and whose *Hp* was not eradicated (Table 3).

Table 3 Comparison of demographic data of diabetic patients in whom *Hp* was eradicated and *Hp* was not eradicated

	Hp (+) at control endoscopy	*Hp* (-) at control endoscopy	*P*
Female sex (%)	53	47	>0.05
Age (y)	56.2±8	55.8±8	>0.05
Diabetes duration (y)	7.3±5	7.2±5	>0.05
HbA1c (%)	7.2±1.2	7.2±1.2	>0.05

DISCUSSION

Hp infection is responsible for up to 90 % of upper gastrointestinal diseases and is linked to the development of gastric carcinoma, MALT associated lymphoma and has to be eradicated whenever it' s possible[9,10].

Standard triple therapy (Omeprazole, Clarithromycine and Amoxycillin) has been shown to be highly effective in the eradication of *Hp* in *non-diabetic* subjects in many previous studies (91 %)[11,12]. In our control group, we found an eradication rate of 85 %, which was compatible with the results in the literature.

Many authors have extensively explored the relationship between *Hp* and diabetes mellitus. There has been controversial results in previous studies but in a larger, well-designed study of Xia *et al*., there was no difference of the seroprevalence of *Hp* infection between patients with diabetes mellitus and *non-diabetic* controls[5]. But there were no studies which explored the efficacy of anti *Hp* protocols in type 2 diabetics, whereas in a study of Gasbarrini *et al*. in type 1 diabetics, the *Hp* eradication rate was 65 % in comparison to 92 % in controls[13]. In another study performed on type 1 diabetics, the eradication rate was 62 % with different triple antibiotic regimens and this could be increased by quadruple regimen to 88 %[14]. In the present study performed on type 2 diabetics, a much lower eradication rate of *Hp* (50 %) was found. Histopathological examination was used in this study for the detection of pre and post treatment *Hp* and as the gold standard, it was more reliable and reproducible than the ^{13}C urea breath test, which has been used in the studies by Gasbarrini *et al*[13,14].

Immunosuppression in diabetes might predispose to the low eradication rate of *Hp* infection but other mechanisms may also explain the low eradication rate of *Hp* in type 2 diabetics. Type 2 diabetics are more susceptible to many bacterial and mycotic infections, which may lead to frequent use of antibiotics, and to the development of resistance[15-18].

Due to absorption problems in gastric mucosa, the extent of antibiotic absorption may be less[19]. This study showed a high rate of pathological endoscopic findings in type 2 diabetics, which may lead to disorders in gastrointestinal motility and to insufficient absorption of the drugs. Autonomic neuropathy has also been accused as a culprit. But studies in the literature suggested that there was no correlation between *Hp* positivity and delay in gastric emptying.

A standard 10 days triple therapy with conventional antibiotics seems not to be warranted in diabetics. Due to problems of absorption and motility, alternative regimens with longer duration seem to be necessary for a higher eradication rate. In particular, if we take into consideration that gastrointestinal symptoms, which are quite frequent in diabetics, are significantly improving when it is possible to eradicate *Hp*, we should try to eradicate *Hp* in diabetic subjects. But this is a new area of research and the larger prospective studies with different anti *Hp* regimens for type 2 diabetics are needed.

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