Gastroenterology and Hepatology From Bed to Bench.

ORIGINAL ARTICLE

The effect of the treatment of *Helicobacter pylori* infection on the glycemic control in type 2 diabetes mellitus

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ABSTRACT

Aim: To evaluate the possible long-term effects of *Helicobacter pylori* infection on Hemoglobin A1c and fasting blood sugar levels in patients with type 2 diabetes.

Background: *Helicobacter pylori* causes the gastrointestinal tract inflammation, which *it* plays an important role in distortion of glucose and lipids absorption that altered lipid metabolism and energy harvesting and develops type 2 diabetes, insulin resistance and has been linked to impaired blood glucose.

Patients and methods: In this clinical trial, patients with type 2 diabetes and confirmed *Helicobacter pylori* infection were recruited from the endocrinology clinic of the Shahid Beheshti University Tehran, Iran. Before and after 3 months of eradication therapy fasting blood samples were taken and glycalated hemoglobin levels and fasting blood sugar levels were measured.

Results: 85 (27 male 31.8%, 58 female 68.2%) patients with the mean age of 52.±4.7 years were recruited. 52 (62%) had successful *Helicobacter pylori* eradication (16 male, 30.8% and 36 female, 69.2%). The mean glycalated haemoglobin levels before successful treatment was 8.7±1.1 and after treatment was 8.3±0.9 and difference was significant ($p<0.001$). Mean IgG level of serology was 3.3±1.1 and the correlation with glycalated haemoglobin was significant ($p=0.02$) ($r=0.4$).

Conclusion: Our results indicate that the *Helicobacter pylori* treatment can improve the mean glycalated haemoglobin in patients with type 2 diabetes. More investigations will be required to evaluate the effects of *Helicobacter pylori* eradication among different age groups and in relation to obesity status, diabetes and other disease, and it may be beneficial for patients at risk of diabetes to be checked for the presence of *Helicobacter pylori* infection.

Keywords: *Helicobacter pylori* infection, Type 2 diabetes, HbA1C, FBS, UBT, Glycemic control.

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Introduction

Helicobacter pylori (HP), a gram-negative bacillus, is the most common pathogenic bacteria in the world and infects and chronically colonises the mucous lining of the stomach (1). Approximately 50% of the world's population is thought to be infected by HP, the majority of infected people remain asymptomatic, and only a small portion develops illness, usually in adulthood (2, 3). HP causes gastrointestinal inflammation and this inflammation can influence glucose and lipids absorption. Glucose and lipid metabolism and energy utilization is abnormal in type 2 diabetes, insulin resistance (4). Previous studies provide conflicting conclusions regarding the association of HP infection with various clinical manifestations of diabetes (5-8). Xia et al

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reported no association between HP seroposivity and diabetes in their study, however, Guvener et al reported that the prevalence of HP gastritis in patients with type 2 diabetes was higher than age-matched healthy controls (9, 10). Moreover, El Hadidy et al. indicated that HP infection significantly increased triglyceride level in patients with type 2 diabetes (11). We postulated that the studying biomarkers of diabetes mellitus, such as glycated hemoglobin levels (HbA1c), fasting blood sugar (FBS) and insulin resistance, may improve the understanding of the etiologic role of HP infection in patients with type 2 diabetes. To address this issue we designed this study to evaluating the possible long-term effects of H.P. infection on HbA1c and FBS levels in patients with type 2 diabetes.

Patients and Methods

In this clinical trial, 85 patients referring to endocrinology clinic of Shahid Beheshti University of Medical Sciences in Tehran, Iran, were studied. The study protocol was approved by ethical committee of Shahid Beheshti University. The study procedure was explained to all patients and informed written consent was given. Patients with type 2 diabetes and confirmed HP infection (IgG positive serology) that had symptoms such as as dyspepsia and reflux were enrolled. Exclusion criteria were type 1 diabetes, withdrawing from treatment, previous gastroscopy or gastrectomy, current antibiotic therapy, H2 receptor antagonists, omeprazole or sucralfate therapy in the 12 preceding weeks.

One serum sample was obtained from each diabetic patient in the study for measurement of IgG anti-helicobacter pylori antibodies titres. The diagnosis of H.P infection was established by positive serology for IgG anti HP antibody. HP antibodies were determined using a commercial ELISA technique. In addition, before eradication therapy, blood samples were taken and glycated hemoglobin levels (HbA1c) and fasting blood sugar (FBS) were measured. All patients were treated with eradication therapy consisting of omeprazole 20 mg bid, clarythromycin 500 BID and amoxicillin 1 gr BID mg for 14 days. All patients were followed up within treatment duration and patients that discontinued drug consumption were excluded. One month after eradication treatment, a urease breath test (UBT) was performed to assess if HP eradication had been successful; Three months after eradication treatment, HbA1C and FBS were re-evaluated; HP infection was considered to have been eradicated when the UBT was negative. When HP infection persisted, patients were excluded from the study. Gastrointestinal symptoms and glycemic control were evaluated initially and 1 and 3 months after initial HP eradication treatment.

Data are expressed as mean and standard deviation (SD). Adjustment to normality was checked through the Kolmogorov–Smirnov test. Student's *t*-test was used for paired and unpaired data with quantitative variables. The level of significance was determined (P=0.05). All estimates were performed using the SPSS version 16.

Results

In this study, we evaluated 85 (27 male 31.8%, 58 female 68.2%) with a mean age of 52.3±4.7 years. Among the 85 patients recruited, 52(62%) had successful HP eradication – the responders (16 male 30.8% and 36 female 69.2%) (Table 1). In responders, the mean HbA1C before treatment was 8.7±1.1 and after treatment was 8.3±0.9 and difference was significant ($p<0.001$). Mean HbA1C in responders and non-responders to treatment were 8.7±1.1 mg/dl 8.8±1.3 respectively and analysis of these four variables (before and after treatment of responders and non-responders) with repeated measure ANOVA test was significant in two groups (between groups: p=0.03) and in responders group (within groups:

Table 1. The demographic and laboratory data in responders and non-responders

Variables		No –response	Response	Total	P-value
Age		53.6±5.6	40.4±4.9	52.3±4.7	0.25
Sex	Male	11(40.7)	16(30.8%)	27(31.8)	0.53
	Female	22(59.3)	36(69.2)	58(68.2)	
HbA1C		8.8±1.4	8.3±0.9		0.001
Duration		54±39	58±41	56±37	0.42
FBS		144±19	146±24	145±22	0.47
BMI		27.5±5.6	27.1±5.3	27.4±5.2	0.32

FBS: Fasting Blood Sugar,BMI: Body Mass Index

P=0.02) (Figure 1). Mean IgG level of serology was 3.3±1.1 and the correlation with HbA1C was significant (p=0.02) (r=0.4) (Table2 and 3).

Table 2. The value of HbA1c and FBS before and after treatment in responders

	Treatment		P value
	before	after	
FBS	145±22	133±18	NS
HbA1C	8.7±1.1	8.3±0.9	0.001

Table 3. The value of HbA1c and FBS before and after treatment

		Response	No-Response	P-value
HbA1C	before	8.7±1.1	8.8±1.3	0.02
	After	8.3±0.9	8.8±1.4	0.03

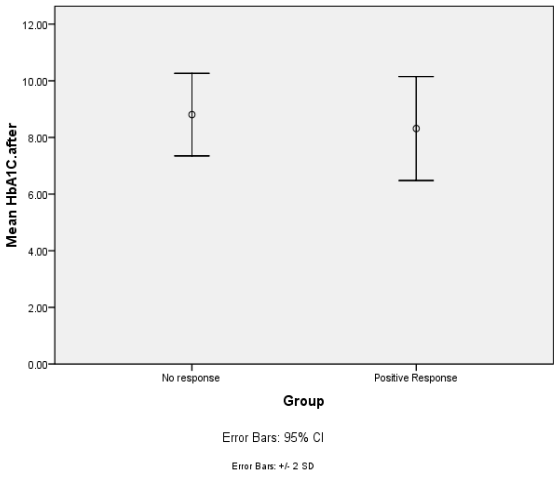

Figure 2. HbA1c after treatment in two groups (Mean & SD).

Discussion

Although DM is a risk for developing many infections because of their impaired immune status, the prevalence risk of HP infection among patients with diabetes remains uncertain, owing to both differences of selection criteria of the diabetic patients and to different criteria for the diagnosis of HP infection (12). Furthermore, preceding studies have made conflicting reports about the association between HP infection and type 2 diabetes. Results from this study revealed that for 85 patients with Type 2 diabetes and HP infection 52 patients (62%) responded to treatment (16 male 30.8% and 36female 69.2). Xia et al in a study did not report any association between HP immunoglobulin G seropositivity and diabetes mellitus (13) and a study by De Luis in 2001 on effect of the treatment of HP infection on gastric emptying and its influence on the glycaemic control in type 1 diabetes mellitus, indicated that HbA1c did not change remarkably after treatment (14). Chen et al. showed that HP may affect the levels of two stomach hormones that help regulate blood glucose, and they advocated that eradicating HP using antibiotics in some older obese individuals (4). Guvener et al. indicated a significant higher prevalence of HP gastritis in patients with type 2 diabetes (10). Additionally, in a review article by Polyzos et al., the epidemiological evidence regarding the association between HP infection and quantitative indexes of insulin resistance was reviewed and it was concluded that such an association may occur.

However this study recommended, that further studies are needed to define whether this is a fundamental association (15). In agreement to these mentioned studies and our results, some authors indicated that the HP infection is related to HbA1c and a possible mechanism for the association is the role of HP in the host metabolic homeostasis by disturbing the ghrelin and leptin production that affects the blood glucose level in diabetes patients (16–18). Moreover other studies revealed that HP infection is related to a various complications such as peptic ulcer as carcinoma, anaemia and gastric motor dysfunction (14). In this regard Chia Hung et al., evaluated 44 patients with type 2 diabetes and showed that the incidence of faster gastric emptying times in patients with HP infection was higher than in HP negative patients (19). A study by Cohen et al. demonstrated that adults infected with HP had higher BMI levels, even if asymptomatic, and suggested that HP therapy may lead to weight loss and improve diabetic control (20).

This study, we found that infections with HP affects the metabolic state in diabetic patients In our study, short term eradication of infection, a primary source of inflammation, caused an improvement in the metabolic state of diabetic patients. The main reason of this association was not found in our study, but according to the findings of this research and the previous similar studies, two main theories relating to eradication of inflammatory cytokines and reduction of antibiotic resistance have been proposed (21,22).

Therefore, in regard to the findings of our study and other similar studies, we can conclude that there is a significant relationship between HP infection and the metabolic control in diabetic patients. The mechanisms underlying this relationship remain uncertain but possible mechanisms include changes in gastrointestinal motility, acid secretion and inflammatory cytokines such as IL1, IL2, IL6 and IL8 (23).

The interpretation of our results was subject to some limitations: small sample size and lack of control group so, further controlled investigations are recommended with larger series to validate the findings reported here.

Our results indicated that the HP treatment can improve the metabolic abnormalities in type 2 diabetic patients. More investigations will be required to evaluate the effects of HP eradication among different age groups and in relation to obesity, diabetes and other disease status. It may be beneficial for patients at risk of diabetes to be checked for the presence of HP infection and considered for HP eradication.

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