Is there Any Relationship Between Diabetic Gastroparesis and Mucosal Injury?

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Received date: June 4, 2016; Accepted date: August 2, 2016; Publication date: August 9, 2016

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Abstract

Objective: We aimed to show the relationship between diabetic gastroparesis and mucosal injury by comparing the findings of upper gastrointestinal system endoscopy between patients with and without diabetic gastroparesis.

Material and method: Upper gastrointestinal system endoscopy and gastric emptying scintigraphy were performed on the same day in 51 volunteer type 2 Diabetes Mellitus patients. 4-hour gastric emptying scintigraphy with 500 mCl Technetium (Tc) 99m diethylene triamine pentaacetic acid (DTPA) in semisolid foods for the determination of gastroparesis was performed in the patients. Upper gastrointestinal system endoscopy was compared between patients with and without gastroparesis by gastric emptying scintigraphy.

Results: The mean ages of patients with diabetic gastroparesis (20 Female (F)/10 Male (M)) and without (12F/9M) diabetic gastroparesis were 57.04 ± 9.41 and 53.35 ± 6.98 years, respectively. There was no statistically significant difference between groups in terms of age and gender distribution (p=0.192, p=0.489, respectively). There were no significant differences with respect to age, gender, body mass index (BMI), fasting blood glucose (FBG) and Hb A1c between groups (p=0.192, p=0.489, p=0.529, p=0.653, and p=0.707, respectively). Erosive (E) findings were more frequent in patients with (22 E/8 Nonerosive (NE)) than without (1 E/20 NE) diabetic gastroparesis, and the difference was statistically significant (p<0.05).

Conclusion: Erosive findings were significantly more frequent in patients with than in those without diabetic gastroparesis. This also suggested that mucosal injury results from motility disorder.

Keywords: Diabetic gastroparesis; Endoscopy; Gastric emptying scintigraphy; Mucosal injury

Introduction

Gastroparesis is a disorder characterized by delayed gastric emptying in the absence of mechanical obstruction of the stomach [1]. It was shown in several studies that, diabetes mellitus (DM) accounted for almost one third of gastroparesis cases [2-4]. Symptoms of gastroparesis usually include early satiety, nausea, vomiting, bloating, and upper abdominal pain. Diabetic gastroparesis can result in nutritional compromise, impaired glucose control and a poorer quality of life, independent of other factors such as age, tobacco and alcohol use, or type of diabetes [4-6]. Diabetic gastroparesis is a clinical syndrome that occurs in both type 1 and type 2 diabetes. It is associated with considerable morbidity among these patients and with the resultant economic burden on the health care system [6].

According to the studies, the pathogenesis of gastroparesis is still not well understood but involves abnormalities in multiple interacting cell types including the extrinsic nervous system, enteric nervous system, interstitial cells of Cajal (ICCs), smooth muscles and immune cells. The primary diagnostic test is gastric scintigraphy, although other modalities such as breath test, capsule, ultrasound, magnetic resonance imaging (MRI), and single-photon emission computerized tomography (SPECT) imaging show promise as alternative diagnostic modalities [7].

We aimed to compare the findings of upper gastrointestinal system endoscopy between patients with and without diabetic gastroparesis. To the best of our knowledge, no similar prospective randomized study has been published previously in the literature.

Material and Method

The study was approved by the local ethics committee and all subjects provided written informed consent. A total of 51 type 2 DM patients consecutively, who were agreed to be included in our study and admitted to Endocrinology and Metabolism polyclinic for glucose monitorisation, were enrolled in this study from December 2011 to February 2012.

Inclusion criteria were as follows: not usage of drugs that affect gastric motility or that are gastroprotective, absence of gastric outlet obstruction, absence of previous stomach and/or bowel surgery, absence of ileus and/or motility disorder, absence of hypothyroidism and/or psychological distress and absence of pregnancy or breast-feeding. Patients not fulfilling one of the above-mentioned criteria were excluded from the study. Each patient determined suitable for inclusion in the study underwent a physical examination, and detailed medical histories were recorded. The patients did not mention any dispeptic complaints at first, but when we questioned symptoms of gastroparesis (early satiety, nausea, vomiting, bloating, and upper abdominal pain) and reflux (heartburn, pyrosis) in voluntary patients, it was shown presence of some dispeptic complaints in these patients. Information including sex, age, height, body weight, body mass index
Gastric emptying scintigraphy

HbA1C was assayed with original kit (794-0412 SIGMA) using High pressure was measured in all patients with conventional correction.

Gastrointestinal system endoscopy was performed on the same day in using Friedewald formula \[LDL-chol=(T-chol) - (HDL-chol) - (TG/5)\].

Plica angularis region for evaluation of Helicobacter pylori (HP) based classification

Biochemical parameters

Venous blood samples were taken after 12 hours of fasting and then at 2 hours post-prandial. Biochemical assays were done in ABBOTT-ARCHITECT C16000 devices. Glucose, T-chol, TG, HDL, and creatinine were assayed with original kits (GAGO-20 SIGMA, MAKO43 SIGMA, TR 0010 SIGMA, L 2014 SIGMA), respectively, using enzymatic UV (Hexokinase), enzymatic colorimetric (cholesterol-oxidase), enzymatic colorimetric (Glycerol-P oxidase), enzymatic colorimetric, and colorimetric (kinetic alkaline picrate) methods. HbA1C was assayed with original kit (794-0412 SIGMA) using High Performance Liquid Chromatography (HPLC) method in TOSOH G8 device. LDL-chol was calculated from T-chol, HDL-chol and TG levels using Friedewald formula \[LDL-chol=(T-chol) - (HDL-chol) - (TG/5)\].

Gastric emptying scintigraphy

After fasted overnight, Test Meal consisting of egg substitute (equal to 2 large egg), two slices bread, strawberry jam (30 gm), 120 ml water with 500 mCi Tc-99m DTPA ingested within 10-15 min, and then gastric emptying time was performed on supine position by 1 min images at time 0, 1, 2, and 4 hrs and geometric mean attenuation correction.

Gamma camera images were recorded in 4 hours in Siemens Scintiview SP device, after patients were given semisolid foods with Tc 99 m DTPA. Gastric emptying time-activity curves were obtained, and gastric emptying time was calculated by a single blinded nuclear medicine specialist. Normal value of 4-hour gastric emptying scintigraphy was T1/2: 55 ± 15 minutes.

Upper gastrointestinal system endoscopy: Upper gastrointestinal system endoscopy (Esophago gastro duodenoscopy (EGD)) was performed in Fujinon device by a single blinded endoscopist.

Statistical analysis

Data entry and analysis were performed using the Statistical Package for the Social Sciences (SPSS) for Windows version 17.0 program. Chi-Square and Mann-Whitney-U tests were used for comparisons of means of the groups. Results having a p value lower than 0.05 were accepted as significant.

Results

The mean ages of patients with (20 F/10 M) and without (12F/9M) diabetic gastroparesis were 57.04 ± 9.41 and 53.35 ± 6.98 years, respectively. There were no significant differences with respect to age, gender, BMI, FBG, and HbA1c between groups (p=0.192, p=0.489, p=0.529, p=0.653, and p=0.707, respectively) (Table 1).

Regarding diabetic complications, nephropathy and neuropathy (n: 1 patient), retinopathy (n: 1), coronary artery disease (n: 1) and neuropathy (n: 2) were present in the patients without gastroparesis, while retinopathy (n: 2), neuropathy (n: 4), coronary artery disease (n: 2), and retinopathy and neuropathy (n: 2) were noted in patients with diabetic gastroparesis.

There was no significant difference between the groups for presence of retinopathy, neuropathy, coronary artery disease, retinopathy and neuropathy, nephropathy and neuropathy, respectively (p=0.655, p=0.498, p=0.562, p=0.564, p=0.562) (Figure 1). There was no significant difference between the groups for presence of retinopathy, neuropathy, coronary artery disease, retinopathy and neuropathy, nephropathy and neuropathy, respectively (p=0.655, p=0.498, p=0.562, p=0.564, p=0.562).

There was no statistically significant difference between the groups in terms of education level (p=0.082). None of the patients consumed alcohol. There was no statistically significant difference between the groups regarding smoking habit (p=0.194), familial history of DM (p=0.602) (Figure 2).
**Table 1**: Demographic and clinical features. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBG: Fasting Blood Glucose, BMI: Body mass index, HbA1c: Hemoglobin A1c, PPG: Post-prandial glucose, TG: Triglyceride, T-Chol: Total cholesterol, HDL: High density lipoprotein, LDL: Low density lipoprotein, Cre: Creatinine, HP: Helicobacter pylori.

![Figure 1](https://example.com/diabetic-complications.png)

**Figure 1**: Distribution of Diabetic Complications in the Groups. There was no significant difference between the groups for retinopathy, neuropathy, coronary artery disease, retinopathy and neuropathy, nephropathy and neuropathy, respectively (p = 0.655, p = 0.498, p = 0.562, p = 0.564, p = 0.562).

![Figure 2](https://example.com/treatments-diabetes.png)

**Figure 2**: Treatments of Diabetes Mellitus in the Groups. There was no statistically significant difference between the groups regarding dietary, insulin, metformin, insulin and metformin, sulfonylurea and metformin and pioglitazone an metformin medications for DM, respectively (p = 0.476, p = 0.478, p = 0.496, p = 0.566, p = 0.475, p = 0.426).
Diabetic gastroparesis was described as "gastroparesis diabeticorum" in patients with type 1 diabetes with gastric retention by Kassander in 1958. Diabetic gastroparesis has been associated with advanced type 1 diabetes with poor glycemic control, it is increasingly being recognized in patients with type 2 diabetes. Gastroparesis is characterized by delayed gastric emptying in the absence of mechanical obstruction of the stomach [13]. Symptoms of gastroparesis are variable but may include early satiety, nausea, vomiting, bloating, and upper abdominal pain. Patients with gastroparesis admit to hospital and require more procedures [14].

The predictors for diabetic gastroparesis remain poorly defined, although duration of disease and the presence of diabetic complications are thought to be potentially important [4,15,16]. In one study, no significant association was shown between DM duration and the development of gastroparesis, and there was also no significant association between neuropathy and the development of gastroparesis [17]. Another study suggested that coexisting peripheral neuropathy was significantly associated with the development of gastroparesis, while autonomic neuropathy was not [18]. Those researchers also showed that poor glycemic control measured both by self-report and HbA1c was an independent risk factor for upper gastrointestinal symptoms, but the duration and type of diabetes were not significant [18]. A two-year prospective follow-up study observed no clear association between gastrointestinal symptoms and autonomic neuropathy or glycemic control [19]. In our study, we also found no significant association between the two groups regarding duration of DM, presence of diabetic complications or HbA1c (p>0.05).

In a consortium study, cellular changes were shown in the pathogenesis of diabetic gastroparesis [7]. Results of our study suggested that these cellular changes can cause mucosal injury.
macroscopically. Thus, in one study showed that the pathogenesis of diabetic gastroparesis was as follows: autonomic neuropathy, loss of neuronal nitric oxide synthase leading to loss of nitric oxide, increased oxidative stress with loss of upregulation of protective enzymes such as heme oxygenase-1, loss of ICCs with resultant gastric arrhythmia and delayed gastric emptying, smooth muscle atrophy, loss of insulin-like growth factor (IGF)-1 from smooth muscle, and loss of macrophages expressing heme oxygenase-1 [7]. However, another study showed that there was also a significant correlation between loss of ICCs and enteric nerves in diabetic gastroparesis. In diabetic gastroparesis, loss of ICCs was associated with delayed gastric emptying. It was shown that ICC or enteric nerve loss did not correlate with symptom severity [20-27]. Overall clinical severity and nausea in idiopathic gastroparesis were associated with a myenteric immune infiltrate [28]. Thus, some authors have suggested that full-thickness gastric biopsies could help define specific cellular abnormalities in gastroparesis, some of which are associated with the physiological and clinical characteristics of gastroparesis [27,28]. In our study, it was shown that the spectrum caused by the cellular changes can lead to mucosal damage macroscopically.

HP associated gastritis, peptic ulcer and gastric malignancy are known diseases. When investigating the relationship between HP positivity and presence of gastroparesis, the studies were showed that there was not related to the HP positivity and presence of gastroparesis [29,30]. In another study suggested that there was no relationship between HP positivity and presence of dyspepsia or gastroparesis in uremic patients [31]. In Caballero-Plasencia’s study showed that, there was no relation neither symptoms of dyspepsia nor HP positivity and presence of gastroparesis [27,28]. In our study, it was shown that the spectrum caused by the cellular changes can lead to mucosal damage macroscopically.

In Parkman’s study, upper gastrointestinal endoscopies were examined retrospectively in 20 patients with diabetic gastroparesis. Nine patients had normal upper gastrointestinal system endoscopy, while 11 patients had pathologic findings [34]. The aim of the present study was to evaluate the relationship between presence of diabetic gastroparesis and erosive findings on endoscopic examination. We found no similar prospective study in the literature in which endoscopic findings in patients with and without diabetic gastroparesis were compared.

In all the studies on the pathogenesis, management and treatment of diabetic gastroparesis, upper gastrointestinal endoscopic examination studies are lacking in patients with diabetic gastroparesis. We aimed to show the effect of diabetic gastroparesis on endoscopic findings, and we showed that diabetic gastroparesis may cause macroscopic mucosal injury. In that case, motility disorders such as diabetic gastroparesis can cause cellular changes and inflammatory process. In course of time, mucosal injury may lead to macroscopic findings.

In conclusion, the presence of HP positive may not be associated with diabetic gastroparesis. We suggest that, the patients with DM would be benefit from screening EGD for signs of developing gastroparesis. Finally, we would suggest that non-erosive findings at EGD may be a precursor to development of gastroparesis. High volume studies in the future must clarify the relationship between diabetic gastroparesis and mucosal injury.

Acknowledgement

Our study is presented as an abstract in American Diabetes Association scientific sessions in 5-9 June 2015 Diabetes vol.64, ADA, 2015.

References


