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DIABETIC GASTROPARESIS – OBESE VERSUS NON OBESE PATIENTS

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Abstract: *Symptoms suggestive of gastroparesis are common in patients with type 2 diabetes mellitus (DM), associated with autonomic neuropathy. Gastric emptying abnormalities have also been reported in obese patients. An association between obesity and gastroparesis symptoms in diabetic patients with neuropathy has been recently investigated.*

In this study 50 patients with DM were selected. They were investigated for gastroparesis using gastric emptying scintigraphy (GES). Dyspeptic symptoms were assessed using Gastroparesis Cardinal Symptom Index (GCSI).

Obese subjects reported significantly more early satiety (6.01 ±1.25 vs 3.71 ±1.81, P<0.05), fullness (2.58 ±1.87 vs 1.08 ±1.47, P<0.05), nausea (3.42 ±1.99 vs 2.00 ±1.69, P<0.05) and not being able to finish a normal sized meal (4.55 ± 1.67 vs 2.74 ±1.58, P<0.05) than non-obese subjects.

Obesity emerged as an independent predictor of cardinal symptoms suggestive of gastroparesis in patients with type 2 DM. This finding suggests that there are more mechanisms in addition to neuropathy to play a role in symptom's presence in this patient population. Also, symptoms in entire group did not correlate well with GES and severity of gastroparesis.

Key words: *gastroparesis, diabetes mellitus, obese.*

1. Introduction

Gastroparesis is defined as the reduction in motor activity of antrum and fundus of the stomach, with gastric dysrrhythmia and pyloric spasm; it has an important impact on quality of life of the affected individual, but it is to often ignored by the clinician. The majority of cases are idiopathic, and long standing diabetes mellitus is responsible for about 25-30% of cases [1].

The exact onset of gastroparesis is hard to be established because the disease is asymptomatic in the first stages and for a long period of time, and the symptoms, when present, are highly uncharacteristic. The onset may be acute with symptoms mimicking pyloric stenosis. Its cardinal features include nausea, vomiting, bloating, early satiety and discomfort. Weight loss, dehydration, electrolyte disturbances and malnutrition may develop in severe cases [1, 2, 3]

Asymptomatic patients may present the association an insufficiently controlled disease with a higher incidence of hypoglycemic episodes secondary to unequal absorption of ingested food. Food retention results in acceleration of fermentation which can determine diarrhea and progressive weight loss [3].

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There are periods free of symptoms, but gastroparesis is progressive, chronic and may be disabilitating. There is no clear association between length of disease and the onset of delayed gastric emptying [3, 4].

According to Revicki DA, et al. [5] the assessment of severity is important appropriate management. One method is the Gastroparesis Cardinal Symptom Index, which is a sum of 3 subscales (ranging from 1–3) for the three main symptom complexes: postprandial fullness/early satiety, nausea/vomiting and bloating.

The diagnosis of gastroparesis may be confirmed by demonstrating gastric emptying delay during a 4-hour scintigraphy (gastric emptying scintigraphy-GES) [3], in patients with or without symptoms. Obesity is discussed lately as a risk factor for symptoms in diabetic patients with gastroparesis [6].

The aim of this study was to analyze the correlation between body mass index and gastroparesis symptoms in patients with type 2 diabetes mellitus, as obesity is considered a possible factor associated with symptom presence and/or intensity.

The format of the bulletin will be A4. The article, inclusively the tables and the figures, should be of 6-8 pages, an even number of pages being compulsorily. The last page will be filled at least 70%.

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2. Material and Methods

We included in our study 50 patients with diabetes mellitus (30F/ 20M; mean age 61.34 ±3.61 years) and 45 healthy controls (27F/18M; mean age 59.15 ±3.28 years), free of symptoms and any known gastrointestinal disease or diabetes mellitus. The mean duration of disease was 10.22 (±9.67) years; 15 (30%) patients required insulin treatment; 14 (28%) patients were treated with sulfonylurea; 26 (52%) patients were treated with biguanids. The gastric emptying was assessed, both in controls and in diabetic patients, using gastric emptying scintigraphy (GES). GE was measured at 0, 1 and 2 hr after ingestion of a 99mTc sulfur colloid-labeled egg meal. Normal values for the percent remaining in the stomach at the key time points were 37 to 90 percent at 1 hour and 30 to 60 percent at 2 hours.

Dyspeptic symptoms were assessed using Gastroparesis Cardinal Symptom Index (GCSI). The patients (both controls and the study group) filled the questionnaire, which include the following nine symptoms: nausea, retching, vomiting, stomach fullness, not able to finish a normal sized meal, feeling excessively full after meals, loss of appetite, bloating, stomach or belly visible larger.

Symptoms were rated by the patients among the choices none (0), very mild (1), mild (2), moderate (3), severe (4), and very severe (5). The GCSI total score equals the sum of the nausea / vomiting, bloating and fullness / early satiety subscales, divided by 3 (15). Mild symptoms are present but do not interfere with daily activities, moderate symptoms are present and interfere with, but do not preclude, daily

activities, severe symptoms seriously interfere with daily activities. Very mild and very severe are variations of these symptoms. Patients filled in the questionnaire one day before GES.

The diabetic patients also had an upper gastrointestinal endoscopy in order to exclude any potential obstruction which might explain their complaints or delayed gastric emptying. HbA1c was measured in all diabetic patients in order to establish a correlation between this value and the gastric emptying rate. We also measured in all diabetic patients and controls: cholesterol, triglycerides, and plasma glucose.

Patients were defined as obese if their body mass index (BMI) was over or equal 30 kg/m^2 , regardless their status as cases or controls.

Written informed consent was obtained from all patients and the study was conducted according to the Declaration of Helsinki and the local ethic committee.

3. Statistical analysis

Continuous variables were expressed as mean (SD). Differences were tested for significance by unpaired Student's *t* test which is sensitive even for small and unequal groups. Upper and lower 95% confidence limits for each variable were calculated from the two tails of the Student's *t* test distribution. We compared the results between the study groups and with control group. A p value <0.05 was considered significant. Pearson correlation coefficients were used to explore linear relationships between the study variables. Statistics were performed with SPSS for Windows, version 10.0.

4. Results

The demographic characteristics of the patients and controls are presented in Table 1.

Demographic characteristics of the study group Table 1

Parameter	Diabetes mellitus	Control	p
Number (F/M)	50 (30F/20M)	45 (27F/18M)	0.75
Age	61.34 ±3.61	59.15 ±3.28	0.66
Disease duration (years)	10.22 (±9.67)	NA	NA
Insulin treatment	15 (30%)	NA	NA
Per os treatment	40 (80%)	NA	NA
Cholesterol (mg%)	236.88 (±66.93)	165.21 (±38.91)	0.02
Tryglicerides (mg%)	183.45 (±93.07)	110.33 (±49.21)	0.06
Fasting plasma glucose (mg%)	159.42 (±53.63)	81.02 (±11.33)	0.01
HbA1 (%)	7.20 (±1.59)	4.1 (±2.1)	0.01

From the 50 patients, 24 (48%) reported one or more gastrointestinal symptoms from the scale, 15 (62.5%) of them being obese, and 26 (52%) of patients were asymptomatic, 19 (73%) of them being nonobese. From those with dyspeptic symptoms, 13 (54.2%) reported fullness and/or early satiety from very mild to

severe, 6 (25%) reported bloating from very mild to severe and 4 (16.6%) reported vomiting or nausea from very mild to moderate. All the subjects from the control group were asymptomatic, as they answered "none" or "very mild" in all the questions.

From the total group, 27 patients (54%) had abnormal gastric emptying on scintigraphy at 2 hr and 23 patients had normal GES. Nineteen patients from de group with abnormal gastric emptying (66.6%) were obese patients.

From subgroup with abnormal GES, only 14 (51.8%) reported gastrointestinal symptoms previous to the evaluation, and only 3 from the 9 symptoms of the GCSI had a significant correlation with the severity of the gastric emptying as evidenced by scintigraphy. From this group, 66% were obese with type 2 DM.

When analyzed individually, the scores for nausea, not being able to finish a normal sized meal and early satiety are the only significantly higher in patients with delayed gastric emptying (3.13 ±1.85 versus 2.02 ±1.77, 4.22 ±1.59 versus 2.66 ±1.48 and 5. 99 ±1.15 versus 3.21 ±1.61, respectively).

The scores are higher and also statistically significant when analyzed in obese diabetic patients versus nonobese diabetic patients, regarding nausea, not being able to finish a normal sized meal, early satiety and feeling excessively full after meals.

Nausea, not being able to finish a normal sized meal and early satiety significantly correlates with the severity of the gastric empting delaying ($r = - 0.65$, $r = - 0.71$, $r = - 0.58$, respectively, with $p<0.05$ in all cases).

The total symptom score for diabetic patients with delayed gastric emptying was 4.13 (± 1.08), higher than in diabetic patients with normal gastric emptying: 3.81 (± 0.97) but without statistical significance ($p>0.05$). The total symptom score for obese diabetic patients with delayed gastric emptying was 4.23 (± 1.18), higher than in obese diabetic patients with normal gastric emptying: 3.58 (± 0.87), with statistical significance ($p<0.05$).

Early satiety was more frequently present in diabetic patients with delayed gastric emptying as compared to those with normal gastric emptying ($p<0.05$). No significant association was established between vomiting/nausea and bloating and delayed gastric emptying (table 2).

GCSI according to scintigraphy (normal or delayed gastric emptying) Table 2

	Normal scintigraphy (46.6%)	**Abnormal scintigraphy (53.3%)**
Item	**Score (mean ± SD)**	**Score (mean ± SD)**
Fullness/early satiety	3.77 (±1.85)	5.13 (±1.57)*
Nausea/vomiting	1.96 (±1.38)	2.56 (±1.49)
Bloating	3.31 (±1.46)	3.88 (±1.41)
Total score	3.81 (±0.97)	4.13 (±1.08)

*$p<0.05$

There is a positive but non-significant (weak) correlation between disease duration and gastroparesis (r = 0.22, p = 0.02). There are no correlations, in our study, between gender, age, the value of the HbA1 and the severity of gastroparesis (r<0.20 in all cases). When analyzing the symptoms according to the presence of obesity we can see that the presence of at least one symptom suggestive of gastroparesis was more likely among obese patients, and obese patients reported significantly more symptoms, but mainly from the same categories (**table 3**).

Gastrointestinal symptoms by obesity Table 3

Symptom	**Obese - N = 22**	**Nonobese - N = 28**
Nausea	3.42 ±1.99	2.00 ±1.69*
Retching	0.99 ± 0.60	0.78 ± 0.55
Vomiting	0.87 ± 0.65	0.66 ± 0.43
Stomach fullness	2.58 ±1.87	1.08 ±1.47*
Not able to finish a normal sized meal	4.55 ±1.67	2.74 ±1.58*
Feeling excessively full after meals/early satiety	6.01 ±1.25	3.71 ±1.81*
Loss of appetite	1.73 ± 0.81	1.69 ± 1.00
Bloating	2.86 ± 1.29	1.98 ± 1.11
Stomach or belly visible larger	1.89 ± 1.01	2.11 ± 0.99

*p<0.05

5. Discussion

Gastroparesis is often suspected by history and physical examination and can be confirmed by the appropriate diagnostic testing. Patients with gastric stasis present with abdominal pain, nausea, vomiting, early satiety, bloating, and weight loss. The vomits may contain "old" food ingested several hours previously. As described in the literature the most frequent complains are abdominal pain and early satiety [7, 8, 9], which corresponds with our results, but only for the last one, as our questionnaire did not include abdominal pain evaluation.

Patients with diabetic gastroparesis may be asymptomatic or develop symptoms that are not directly related to gastroparesis, such as poor glycemic control, particularly in those who are treated with insulin. A high percentage of patients in our study were asymptomatic.

There is a proposed classification of gastroparesis severity which may be useful in the approach of a diabetes mellitus patient with gastrointestinal symptoms and in treatment decisions, in mild, compensated and severe (with gastric failure) [10, 11]. Diagnostic problems appear in mild, and even in compensated forms, when the symptoms may not be suggestive for the diagnosis. It is obvious that the diagnosis of diabetic gastroparesis should not be established based only upon symptoms alone.

Scintigraphy is regarded as the gold standard to measure gastric emptying [12, 13], but some discussions are still needed. For detection of delayed GE (gastroparesis), solid-phase GE is preferable to liquids, since normal GE of liquids is often preserved until there is very severe motor dysfunction of the stomach. The prevalence of delayed GE detected with solid-phase GES at 2 hr is variable, ranging from 12 to 75% [14, 15].

Consensus standards for performing and reporting gastric emptying scintigraphy have been published by the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine [11]. The suggested protocol involves an egg meal containing 99mTc with imaging at 0, 1, 2, and 4 hours after meal ingestion.

The magnitude of the delay is often modest and not well-correlated with symptoms, except possibly bloating [16, 17]. Our data also suggested that the presence or absence of symptoms is not a good indicator for when to perform GES; we find a significant correlation only with a minority of symptoms (3 out of 9), but not with bloating. One possible explanation for the poor correlation between delayed gastric emptying and symptoms in diabetes mellitus may be the involvement of the afferent sensory nerve fibers by autonomic neuropathy thereby decreasing perception of symptoms [18]. However, increased pain perception in patients with diabetes has also been described. Careful evaluation of diabetics with other "dyspeptic" symptoms such as epigastric pain, nausea, vomiting, early satiety, postprandial fullness and/or anorexia may reveal other causes of symptoms (e.g. peptic ulcer or reflux disease), with only a minority having significant abnormalities of gastric emptying [19]. So the main question still remains when to suspect gastroparesis and perform GES.

On the other hand, obesity seems to be a strong and independent factor of the presence of at least one symptom suggesting gastroparesis and also a predictor of the number of symptoms [20]. Our finding are consistent with the study of Boaz M et al [6] for some of the symptoms (early satiety and fullness) and for the fact that in obese patients there is a tendency for more symptoms to appear, as comapred to non-obese patients. This fact indicates that there are other mechanisms or in addition to neuropathy which could explain the variability in gastroparesis symptoms. The problem remains open and future studies are necesary to solve this problem.

6. Conclusion

Regarding the relationship between symptoms and delayed gastric emptying, our data was similar to data from literature; the correlation between symptoms evaluated with GCSI and gastric scintigraphy was significant only for few items from the symptom scales. Obesity shoul be seen as a risk factor for gastroparesis symptoms in type 2 DM. We can state that gastric emptying tests in patients with diabetes mellitus should be performed in those having a history of several years, if they have upper digestive symptoms not explained by upper digestive endoscopy, or if they have unstable diabetes while on insulin or oral therapy.

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