HHS Public Access

Author manuscript

Dig Dis Sci. Author manuscript; available in PMC 2016 October 18.

Published in final edited form as:

Dig Dis Sci. 2009 May ; 54(5): 1003–1010. doi:10.1007/s10620-009-0717-4.

Gastroparesis and Gastroparesis-like Syndrome: Response to Therapy and its Predictors

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Abstract

Purpose—The natural history and outcome of patients with gastroparesis is not well known. The aim of this study was to identify the clinical or pathophysiological characteristics, if any, that may be helpful in predicting therapeutic response in this condition.

Methods—This is a retrospective study of a cohort of patients who presented to a tertiary referral center with symptoms suggestive of gastroparesis. All patients were evaluated by scintigraphic measurement of gastric emptying and symptoms were scored using a modification of the Gastroparesis Cardinal Symptom Index (GCSI). Treatment generally included conservative measures such as antiemetics, prokinetics, tricyclic antidepressants and analgesics as well as various more invasive interventions in selected patients. Response to treatment was defined as a change in the overall GCSI score of two-thirds or more as compared with baseline.

Results—Out of a total of 93 patients, 69 patients met the eligibility criteria. Of these, 29 patients had diabetes mellitus and 40 patients had gastroparesis of non-diabetic etiology. Out of 69 patients, 49 were responders (71%) and 20 were non responders (29%). The cause (diabetic vs. non-diabetic) of gastroparesis or the presence of delayed emptying did not correlate with response. However, the severity of stomach distension, bloating subscale score and the global GCSI score at baseline presentation were predictive of response by multivariate analysis.

Conclusion—Higher global GCSI score, bloating subscale score, and severity of stomach distension at baseline presentation correlate with an unfavorable response in gastroparetic patients. On the other hand, neither the etiology of gastroparesis nor associated delay in gastric emptying appeared to be important in the clinical response. Patients with symptoms of typical gastroparesis but without delays in gastric emptying may be a distinct syndrome with a greater proportion of males than classical gastroparesis.

Keywords

Diabetic gastroparesis; Response in gastroparesis; Bloating

Introduction

The management of patients with gastroparesis remains a therapeutic challenge owing to the heterogeneity of the patient population and multiple mechanisms that contribute to symptom

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generation, leading to inconsistencies in the therapeutic regimens. The two commonest forms of gastroparesis are diabetic and idiopathic, together comprising 90% or more of cases seen in most tertiary referral centers. Our clinical experience suggests that both forms of the syndrome are probably heterogeneous in nature, with subsets that differ in their response to treatment and long-term prognosis. However, little is known about the clinical or pathophysiological characteristics, if any, that may be helpful in predicting therapeutic response and thereby providing a practical and useful stratification of patients. In this study, our aim was to determine if demographic characteristics, pattern of gastric emptying, etiology of gastroparesis, symptom nature and severity are predictive of response.

Methods

Patient Population

This is a retrospective analysis in which the study population consisted of a cohort of patients presenting to a single experienced gastroenterologist at a tertiary referral center with symptoms consistent with a diagnosis of gastroparesis. At the time of each visit, patient symptoms were scored prospectively using the questionnaire described below. These were recorded in the chart, along with response, if any, to treatment. Charts were reviewed over a three year period (2003 to 2007) for pertinent clinical information (symptoms, past medical history, past surgical history) and demographic characteristics (age, sex, gender and ethnicity). Out of the total ninety three patients screened, sixty nine patients were eligible for the study. Inclusion criteria for patient selection included clinical suspicion of gastroparesis (based on symptoms of nausea, vomiting, early satiety, postprandial pain, stomach fullness or bloating), absence of gastric obstruction on endoscopy or upper GI series, documentation of gastric emptying by scintigraphy within 3 months of the first visit and a minimum of four clinic visits (including the first one). Exclusion criteria included presence of oesophagitis, erosive gastroduodenal lesions on endoscopy, absence of documented gastric emptying study. Although this number was somewhat arbitrary, it was felt that it was the minimum required to establish a robust physician-patient relationship essential for the treatment of a chronic disease such as gastroparesis.

Symptom Questionnaire

At each clinic visit, every patient in the study had completed a self reported measure of symptom severity. Symptoms were scored using the modified Gastroparesis Cardinal Symptom Index (GCSI),[1] a validated scale of severity in patients that utilizes three clusters (nausea/vomiting, post-prandial fullness/satiety, and bloating). Our modification consisted of removing the “retching” category from this scale, as most patients were unable to clearly distinguish this from vomiting. The nausea/vomiting cluster therefore consisted of nausea and vomiting only. The other clusters remained the same as originally described with the post-prandial fullness/early satiety cluster consisting of stomach fullness, inability to finish a normal-sized meal (early satiety), feeling excessively full after meals (postprandial fullness), and loss of appetite and bloating subscale consisting of bloating and stomach or belly visibly larger (stomach distension). The patients graded individual symptoms on a six point scale (0=none, 1=very mild, 2= mild, 3=moderate, 4=severe, 5=very severe). Subscale scores were calculated by averaging across the items within each subscale. The range of scores is 0–5,

where higher scores represent a subjective perception of higher severity. The GCSI total score is obtained as the average of the three symptom subscales. GCSI total score can range from 0 to 5, with higher scores reflecting greater symptom severity. Response to treatment was defined as an arbitrary change in the overall GCSI score of two-thirds or more as compared with baseline. Although an improvement of fifty percent would generally be considered clinically significant, we chose a more stringent criterion because of the uncontrolled nature of our observations, compensating partially for the expected placebo response.

Gastric emptying

Gastric emptying was assessed scintigraphically using a radioisotope-labeled low-fat solid meal according to the consensus criteria established by Tougas et al.[2] Gastric emptying scintigraphy was performed in the morning after an overnight fast as previously described with prokinetics stopped for at least 3 days, along with brief discontinuation of narcotics, if patients were using them regularly. Finally, the response rates may not be representative of the medical community as this study was done in a tertiary care referral center and the patients were evaluated by an expert gastroenterologist. Following the administration of 1 mCi ^{99m}Tc sulfur colloid in a low fat "Eggbeater"® meal, serial scintiphotos were obtained of the stomach over four hours. GE was defined as the percentage of gastric retention equal to or greater than 60% at 2 hours and equal to or greater than 10% at 4 hours or both.

Therapeutic Interventions

Patients were prescribed multiple medications with the primary goal being symptomatic control of nausea and to a lesser extent, pain. As to be expected from the referral nature of the practice, all patients had reportedly failed to respond satisfactorily to standard “prokinetic therapy” including metoclopramide, tegaserod and erythromycin at the time of initial presentation. If patients were still on these medications at the time of presentation and were tolerating them, they were usually continued. As has been the practice of the senior gastroenterologist for more than a decade, all patients were started on a tricyclic antidepressant in low doses, typically nortriptyline beginning at 10–25 mg/day and usually peaking at 75 mg/day. If patients did not respond to several weeks of escalating doses of nortriptyline, “second-line” medications were introduced. These include domperidone (typically up to 80 mg per day in divided doses, using an institutionally approved protocol requiring an investigational new drug application to the Food and Drug Administration), mirtazapine, a tetracyclic antidepressant with prominent anti-nauseant properties (up to 30 mg per day), dronabinol, a marijuana derivative with antinauseant and orexic effects (up to 20 mg per day) and short (three-day) courses of aprepitant (80 mg for the first two days and 120 mg the third day). “Rescue” medications for nausea typically included promethazine on an as necessary basis.

Many of these patients also complained prominently of epigastric pain, as has been described previously.[3] Symptomatic treatment was attempted with several agents incrementally. In addition to tricyclic antidepressants that had already been prescribed for nausea, these included (in typical order): gabapentin, duloxetine, pre-gabalin, tramadol and

methadone. Overall, patients were taking an average of four medications on a regular basis for symptoms of gastroparesis.

A total of fourteen patients in the cohort also received treatment with gastric electrical stimulation using the Enterra device (Medtronics Inc. St. Paul, MN). Gastric electrical stimulation was in most cases instituted at the beginning of the evaluation period. However, not all patients accepted or were approved for electrical stimulator placement and so most were followed conservatively. Of the fourteen patients on Enterra, eleven patients had evaluations with the device on. Three patients had either device malfunction (n=1) or side effects (n=2) and were evaluated with the device off.

Twenty five patients required nutritional support with enteral tube feeding. Most of these patients had enteral feeding already in place at the time of presentation or shortly thereafter.

Data Analysis

Demographic characteristics, symptom prevalence, severity, and gastric emptying were calculated in each group. Similar analysis of symptom pattern and severity was done by dividing patients by cause (diabetic versus non-diabetic) and by gastric emptying (normal versus delayed). Data are presented as mean (SD). Responders and non-responders were compared in bivariate analyses using two-group *t*-tests for continuous data, and Fischer's exact test for categorical outcomes. Changes from baseline were assessed using paired t-tests. Logistic regression was used to model the binary outcome variable of response status in order to identify significant predictor variables that included symptoms and their severity, and demographic characteristics. A two-sided alpha level of significance of 0.05 was used for statistical significance. When indicated, odds ratios (OR) were computed with 95% confidence intervals (CI) and differences were considered significant at 5% level.

The study was approved by the institutional review board at UTMB.

Results

Patient characteristics

Out of the 93 patients screened, 69 patients met the inclusion criteria and data from these patients were analyzed. Of these, 29 (42%) cases were diabetic and 40 cases (58%) were non-diabetic. In the non-diabetic group, six patients had a history of Nissen fundoplication preceding the onset of their gastroparetic symptoms by a varying period of time. Further, other relevant co-morbidities in this group included small bowel dysmotility in one patient, colonic inertia and pelvic floor dysfunction in one and sphincter of Oddi dysfunction in two patients. In the diabetic group, one patient had associated biliary dyskinesia. Fifty-two of the total sixty nine patients (75%) had delayed gastric emptying. There were 13 (19%) males and 56 (81%) females. The mean age was 42.98±13.14 years. Fifty-five patients (80%) were Caucasian with the rest being African American (n= 10, 15%), Hispanic (n=2, 3%), Asian (n=1, 1.5%) and unknown (n=1, 1.5%) respectively.

Baseline symptoms

Nausea and vomiting were the most prevalent symptoms, present in 96% and 88% of the patients, respectively. Eight of the 69 patients had cyclic symptoms and eight of the forty idiopathic patients had an abrupt onset of their symptoms. Stomach fullness (74%), postprandial fullness (68%), and bloating (52%) were also frequently reported. Early satiety, stomach distension, loss of appetite were present in 42%, 30% and 26% of the patients respectively. Pain-postprandial/epigastric pain was present in 42% of the patients at the onset.

Global Response Rate

At the time of this analysis, patients had been followed for a median duration of 9 months (range: 4 months to 3 years) starting from their first clinical visit. According to the criteria specified above, a total of forty-nine patients were considered responders (71%) while 20 (29%) did not meet the definition of response. Amongst responders, the global GCSI score showed significant improvement from a baseline mean of 1.97± 0.79 to 0.36± 0.28 ($P < 0.001$) (corresponding median values of 2 and 0.33 respectively). The global GCSI score of non-responders also declined significantly from a baseline mean of 2.73±1.03 to 1.75±0.51 ($P < 0.001$) (corresponding median values of 2.62 and 1.83 respectively) (Table 1). Symptom improvements in the various clusters paralleled these global changes (Table 1). Thus, as compared with responders, non-responders failed to meet our criteria of improvement in all subcategories including nausea, early satiety and bloating.

Determinants of response

We next looked at a variety of measures that could predict the probability of response in a given patient. The response rates did not differ based on gender, gastric emptying (i.e. normal versus delayed), cause of gastroparesis (i.e. diabetic versus non-diabetic), requirement for enteral feeding or gastric electrical stimulation. Seven of eight non-diabetic gastroparetics (88%) with an abrupt onset responded as compared with 22 of 32 (67%) without an abrupt onset; this difference was not statistically significant. Importantly, the use of narcotic analgesics was similar in both groups (53% of responders and 50% of non-responders) (Table 2).

The baseline mean global GCSI score was significantly higher for non-responders (2.73±1.03 versus 1.97± 0.79 for responders; $P = 0.001$). Bivariate analysis of the mean subscale severity scores showed that nausea/vomiting subscale severity score did not differ significantly between the two groups (3.85±1.73 for non-responders versus 3.66±1.24 for responders). However, the early satiety/postprandial fullness subscale mean and bloating subscale means were significantly higher in non responders as compared to responders (2.16±1.22 versus1.41±1.14; $P = 0.02$ and 2.18±1.68 versus 0.85±1.13; $P = 0.0003$ respectively).

Multivariate logistic regression was then used to identify the association between response and explanatory variables of age, gender, cause of gastroparesis, pattern of gastric emptying, enteral tube feeding, gastric pacer placement, symptom severity, mean subscale scores and global GCSI scores at initial presentation. Age, gender, type of gastroparesis, pattern of

gastric emptying, enteral tube feeding and gastric pacer placement were not associated with response. Factors independently associated with response in gastroparesis was severity of stomach distension (95% CI: 0.257, 0.976), bloating subscale score (95% CI: 0.24, 0.76) and the global GCSI score at baseline presentation (95% CI: 0.437, 0.83). For each of these measures, a one-unit increase in the score reduces the likelihood of being a responder by 0.50, 0.43 and 0.60 on average, respectively.

Differences between patients with diabetic and non-diabetic gastroparesis

Twenty nine of the total sixty nine patients had diabetic gastroparesis and forty patients had non-diabetic gastroparesis. The two groups were similar with respect to response to treatment (69% versus 73%) as well as a variety of other parameters (Table 3). However, analysis of baseline symptom severity in patients with diabetic or non-diabetic gastroparesis showed that diabetic patients had significantly higher mean global GCSI scores (2.04±0.92 as compared with 1.60±0.75 in the non-diabetic group; $P = 0.04$). This was mainly due to an increase in the severity of postprandial fullness/early satiety cluster scores; the groups did not however, differ in the severity of the nausea or bloating cluster scores (Table 4).

Differences between patients with delayed gastric emptying as compared with those with normal emptying

Seventeen patients in our cohort had normal gastric emptying while in 52 patients gastric emptying was impaired. Only two of the patients in the former group had cyclic symptoms. The two groups were similar with respect to prevalence of diabetes (41% versus 42.3%), and response to treatment (65% versus 74%) (Table 5). Analysis of baseline symptom severity did not reveal any significant differences in either the subscale clusters or the global GCSI (Table 6). There was no significant difference in age among two groups (46.9 ± 13.04 years versus 41.7 ± 13.05 years). However, a striking difference was found in the gender distribution of patients; 41% of the group with normal gastric emptying were males as compared with 11.5% of those with delayed gastric emptying ($P = 0.01$).

Discussion

Gastroparesis is a heterogeneous disorder with limited knowledge of the pathophysiological mechanisms that contribute to phenotypic presentation. Further, there is a paucity of studies identifying the clinical characteristics of patients that distinguish responders from nonresponders. Previous studies that looked at symptom profiles of patients were focused on the association between predominant symptoms and putative pathophysiological mechanisms. Impaired gastric accommodation has been associated with early satiety and weight loss,[4–6] delayed gastric emptying with nausea, vomiting and postprandial fullness,[7,8] unsuppressed phasic contractility with bloating,[9] and hypersensitivity to gastric distension with postprandial epigastric pain and weight loss.[10] Overall, these studies have been hampered by lack of distinction between gastroparesis and functional dyspepsia,[11] and the varied and overlapping nature of the findings. Our current state of knowledge therefore suggests that more sensitive biomarkers or functional tests are needed to make substantive progress in the pathophysiological classification of gastroparesis. Until then, it

may prove clinically more useful to apply measures that predict therapeutic responsiveness based on validated questionnaires and readily available clinical information.

In this study, we evaluated the predictors of response in a group of patients with gastroparesis and report several important findings. First, nearly 70% of patients with gastroparesis responded to our treatment regimen. The response rates in our study are remarkable, particularly given the fact that most of these patients had been considered “refractory” prior to referral and that nearly half of them used narcotic analgesics. In a previous study of 146 patients seen in a tertiary practice, Soykan et al reported a response rate of 74% to prokinetic therapy.[12] Although these authors did not clearly define response, this figure is comparable to the response rates in our study. We acknowledge that several caveats have to be emphasized about our study, including the lack of control groups and the arbitrary definition of a response. Nevertheless, the high-response rate also suggests that aggressive measures such as the use of gastric electrical stimulation (at least according to the currently available methods) are probably indicated only in a small minority of patients. Finally, our results suggest that an important message for both patients and physicians is that severe gastroparesis is not a “hopeless” disease.

A significant minority of our patients had normal gastric emptying but could not be distinguished from those with delayed emptying on the basis of clinical features. Only two of these patients (of a total of 17) had cyclic symptoms. Although a gastric emptying test is the gold standard for the diagnosis of gastroparesis, the correlation between individual symptoms and delayed gastric emptying is poor and high intersubject and intrasubject variability has been reported.[15–17] Prospective studies have shown that delayed gastric emptying may have partial correlation with complaints of fullness, upper abdominal pain and reduced hunger but not with nausea and vomiting.[18,19] It is not clear what to call the patients who present with all the symptoms of gastroparesis but whose gastric emptying is normal. Although the term functional dyspepsia has been used in the past, it is not appropriate particularly in light of the recent reclassification using the Rome criteria. A better term may be gastroparesis-like syndrome (GLS); whether this represents a form-fruste of the classic syndrome or a different disease category altogether cannot be ascertained with complete confidence. However, the latter is suggested by the fact that the proportion of males was much higher in this subset compared to the group with delayed emptying (41% versus 11.5%). An alternative explanation is that males may be more resistant to changes in gastric emptying, even when affected by the same pathological process.

The high response rate in our study could reflect one or more of the following factors: (1) general supportive care, an effective physician-patient relationship and close follow-up (2) spontaneous resolution of symptoms with time (3) specific interventions such as the institution of low-dose tricyclic antidepressants. In the absence of a randomized controlled trial, this cannot be asserted with complete confidence. However, given the fact that the presence of delayed gastric emptying did not appear to affect the response rate, our findings add to an emerging consensus amongst experts that therapies directed towards sensory mechanisms (putatively targeted by TCAs) may be more important for effective palliation of symptoms.[13] This is supported by a recent study in patients with idiopathic gastroparesis in whom symptoms did not correlate with delayed gastric emptying but to changes in gastric

accommodation (early satiety and weight loss) and hypersensitivity to gastric distention (epigastric) pain, early satiety and weight loss). Overall symptom severity was not correlated with gastric emptying or accommodation, but only with sensitivity to gastric distension.[14]

The main goal of this study was to identify predictors of response, regardless of the specific treatment instituted. We first looked at differences between diabetic and non-diabetic patients. We did not find differences in demographics; however, diabetic patients had higher baseline GCSI scores, mainly due to differences in the fullness/satiety subscale. There have been no direct comparisons of these two subgroups although a previous report did suggest a higher association with pain and history of sexual/physical abuse in idiopathic patients.[12] We did not objectively evaluate pain severity in our study, but there was no difference between the two groups with respect to the use of narcotic analgesics. A subset of idiopathic gastroparetics, distinguished by an abrupt onset, are thought to be post-viral and may have a better prognosis.[20] We did not have enough patients to confirm this in our study. On the whole, however, patients with non-diabetic gastroparesis appeared to have similar response rates to diabetic patients (see below).

Therefore, neither the etiology nor associated delay in gastric emptying appeared to be important for the clinical response of gastroparetic patients. On the other hand, we found that the “bloater” phenotype is highly indicative of the response to treatment. Bloating is one of the least understood of gastrointestinal symptoms. It has been most well studied in patients with irritable bowel syndrome where it has been attributed to several pathophysiological phenomena, including hypersensitivity, abdominal distention and/or abdominal wall dystony, and impaired handling of intestinal gas.[21, 22] The pathogenesis of bloating in gastroparesis is unknown but of all symptoms, appears to be best predictive of delayed gastric emptying, a finding that is also true in patients with functional dyspepsia.[23,24] Further, in patients with dyspeptic symptoms and delayed gastric emptying, acute administration of erythromycin improves gastric emptying and bloating but not any of the other symptoms such as nausea, fullness or pain.[25] Erythromycin is not useful as long-term treatment and it can therefore be argued therefore that the lack of responsiveness of the bloater phenotype is because of the lack of effective prokinetics. Thus, if bloating but none of the other clusters, results from delayed gastric emptying, patients with this as a predominant symptom will not respond since we may not be able to improve gastric emptying. However, bloating did improve significantly in both responders and non-responders (although not the same extent). Further the reduction in nausea and other satiety clusters was also proportionately much less in non-responders. This suggests that bloating by itself is not the cause of refractoriness but simply a marker for the same.

The limitations of our study need to be considered. Most patients included had undergone evaluations and therapies for gastroparesis at other institutions, reflecting a referral bias in our patient population. The lack of standardization of the medication regimen makes it difficult to evaluate its role in the therapeutic response. Although the questionnaire was prospectively administered, the clinical data were retrospectively abstracted. Thus, the role of other factors of possible relevance such as BMI, could not be assessed.

In conclusion, our study has several important outcomes. First, the symptoms of even severe gastroparesis can be reasonably controlled in the majority of patients by a regimen that uses a combination of several symptomatic medications including tricyclic antidepressants. Further, responsiveness is not dependent on the type of gastroparesis or delayed gastric emptying but correlates well with a simple clinical measure viz. bloating. The “bloater” phenotype thus may be an important subtype to characterize further in terms of the underlying pathophysiology and pathogenesis. Future pharmaceutical trials may need to stratify patient subsets according to the severity of both global scores and bloating at baseline.

Acknowledgments

Dr. Pasricha is partly supported by NIDDK grant U01 DK073983 (PJ Pasricha, PI)

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Table 1

Change in the mean global GCSI and mean cluster scores from baseline presentation to final follow up visit (B= baseline; F= follow-up). Responders N=49, Non-Responders N=20

	Responders			Non- Responders		
	Mean±SD		% Reduction	Mean±SD		% Reduction
	B	F		B	F	
Global GCSI	1.97±0.79	0.36±0.28	82	2.73±1.03	1.75±0.51	36
Nausea	3.66±1.24	0.81±0.63	78	3.85±1.73	2.75±1.41	29
Early Satiety	1.41±1.14	0.20±0.35	86	2.16±1.22	1.34±0.77	38
Bloating	0.85±1.13	0.09±0.24	89	2.18±1.68	1.25±1.05	43

Table 2

Response rates according to various patient characteristics

	% of Responders	% of NonResponders	P Value
Female Gender	71%	69%	NS
Delayed Gastric Emptying	73%	65%	NS
Diabetes	69%	73%	NS
Enteral Feeding	34.7%	42%	NS
Gastric Electrical Stimulation	20.4%	21%	NS
Narcotic Usage	53%	50%	NS

Values are Mean±SD

P value <0.05 is considered significant

Table 3

Baseline characteristics in Diabetic and Non-diabetic gastroparetic patients

	Diabetic N=29	Non-diabetic N=40	P Value
Age in years (Mean±SD)	44.8± 10.62	41.6± 14.6	NS
Males (%)	21	17.5	NS
Females (%)	79	82.5	NS
Caucasians (%)	72	85	NS
Delayed Emptying %	76	75	NS
Responders %	69	73	NS

Values are Mean±SD

P value <0.05 is considered significant

Table 4

Mean severity of the symptoms at baseline in Diabetic and Non-Diabetic gastroparetic patients

	Diabetic N=29	Non-diabetic N=40	P Value
Nausea	4.20±1.23	3.80±1.41	NS
Vomiting	3.86±1.38	3.10±1.85	NS
--Mean of Nausea Cluster	2.68±0.85	2.35±0.97	NS
Early Satiety	1.58±1.78	1.95±1.35	NS
Postprandial Fullness	3.03±1.93	2.05±1.83	**0.03**
Stomach Fullness	2.65±1.61	1.90±1.49	NS
Loss of Appetite	0.75±1.35	0.52±0.98	NS
--Mean of Postprandial cluster	2.00±1.25	1.35±1.10	**0.02**
Stomach Distension	0.82±1.56	0.92±1.52	NS
Bloating	2.00±1.76	1.27±1.52	NS
--Mean of Bloating Cluster	1.41±1.53	1.10±1.37	NS
Total GCSI Score	2.04±0.92	1.60±0.75	**0.04**

Values are Mean±SD

P value <0.05 is considered significant

Table 5

Baseline characteristics in patients with and without normal gastric emptying

	Normal Emptying N=17	Delayed Emptying N=52	P Value
Age in years (Mean±SD)	46.9± 13.04	41.7± 13.05	NS
Males (%)	41	11.5	
Females (%)	59	88.5	<0.01
Caucasians (%)	70.5	82.6	NS
Diabetic (%)	41	42	NS
Responders (%)	65	74	NS

Values are Mean±SD

P value <0.05 is considered significant

Table 6

Mean severity of the symptoms at baseline in Normal and Delayed gastric emptiers

	Normal Emptying N=17	Delayed Emptying N=52	P Value
Nausea	3.64±1.76	4.13±1.17	NS
Vomiting	3.23±1.98	3.48±1.61	NS
--Mean	2.35±1.24	2.54±0.81	NS
Early Satiety	0.76±1.39	1.36±1.60	NS
Postprandial Fullness	2.58±1.76	2.42±1.99	NS
Stomach Fullness	2.11±1.49	2.25±1.61	NS
Loss of Appetite	0.41±0.79	0.69±1.24	NS
--Mean	1.47±1.00	1.68±1.27	NS
Stomach Distension	0.82±1.56	0.92±1.52	NS
Bloating	1.00±1.76	0.84±1.46	NS
--Mean	1.64±1.76	1.55±1.68	NS
Total GCSI Score	1.72±0.81	1.81±0.86	NS

Values are Mean±SD

P value <0.05 is considered significant