Clinical Response to Gastric Electrical Stimulation in Patients With Postsurgical Gastroparesis

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Background & Aims: **The aim of this study was to report the long-term clinical response to high-frequency gastric electrical stimulation (GES) in 16 patients with postsurgical gastroparesis who failed standard medical therapy.** ***Methods:*** **Clinical data collected at baseline and after 6 and 12 months of GES included (1) severity and frequency of 6 upper gastrointestinal (GI) symptoms by using a 5-point symptom interview questionnaire and total symptom score, (2) health-related quality of life including physical composite score and mental composite score, (3) 4-hour standardized gastric emptying of a solid meal by scintigraphy, and (4) nutritional status.** ***Results:*** **The severity and frequency of all 6 upper GI symptoms, total symptom score, physical composite score, and mental composite score were significantly improved after 6 months and sustained at 12 months ($P < .05$). All patients had delayed gastric emptying at baseline. Gastric emptying was not significantly faster at 12 months, although 3 normalized. At implantation, 7 of 16 patients required nutritional support with a feeding jejunostomy tube; after GES, 4 were able to discontinue jejunal feeding. The mean number of hospitalization days was significantly reduced by a mean 25 days compared with the prior year. One patient had the device removed after 12 months because of infection around the pulse generator.** ***Conclusions:*** **Long-term GES significantly improved upper GI symptoms, quality of life, the nutritional status, and hospitalization requirements of patients with postsurgical gastroparesis. Although vagal nerve damage or disruption was part of the underlying pathophysiology, GES therapy was still effective and is a potential treatment option for the long-term management of postsurgical gastroparesis. A controlled clinical trial of GES for PSG patients (who are refractory to medical therapy) is indicated given these encouraging results.**

Postsurgical gastroparesis (PSG), identified as a chronic form of gastric atony in the absence of mechanical obstruction that results from disruption of the normal mechanisms that govern gastric motility, develops in up to 10% of patients who undergo vagotomy (either deliberate or inadvertent) as part of their upper gastrointestinal (GI) surgery.[1–3] The incidence increases to as high as 50% in those with chronic gastric outlet obstruction before surgery.[4,5] Other surgeries that are associated with delayed gastric emptying (GE) include Billroth I and II antral resections, Roux-en-Y gastrojejunostomy, fundoplication, esophagectomy with colon or gastric pull-up, and pylorus-preserving Whipple procedure.[6] Associated symptoms include nausea, vomiting, early satiety, abdominal pain, and weight loss. Severe gastroparesis might result in recurrent hospitalizations, malnutrition, and significant mortality.[1,7]

Symptomatic management of PSG includes dietary manipulation and the combination of prokinetic and antiemetic agents.[3,8,9] However, only metoclopramide and erythromycin are commercially available in the United States, and both have side effects that make them intolerable for more than 40% of patients.[10] Without an antrum, medical therapies are less successful, and medications might not be reliably absorbed because of bezoar formation.[6,11] In severe cases, patients might be placed on a liquid caloric diet. For patients who fail these therapies, surgical interventions are often contemplated.[11] These include tube gastrostomy for gastric decompression and jejunostomy for enteral feedings. Total gastrectomy is reserved for intractable vomiting and weight loss after all other options have failed. This is usually in the patient after partial gastric resection with either a Billroth I or II with or without a Roux-en-Y reconstruction.

Recently, gastric electrical stimulation (GES) has been investigated as a new approach for treatment of medically refractory gastroparesis.[12,13] Several studies have shown that GES by an implantable device with high-frequency

Abbreviations used in this paper: GE, gastric emptying; GES, gastric electrical stimulation; HQOL, health-related quality of life; MCS, mental composite score; PCS, physical composite score; PSG, postsurgical gastroparesis; TPN, total parenteral nutrition.

1542-3565/05/$30.00

PII: 10.1053/S1542-3565(04)00605-6

(12 cycles/min) and low-energy stimulation parameters (330 μs and 5 mA) produced a significant and sustained improvement in symptoms and nutritional status in most patients with intractable symptomatic gastroparesis.[14–18] On the basis of the WAVESS data,[16] the US Food and Drug Administration approved GES with high frequency and low energy parameters (ENTERRA Therapy System; Medtronic, Minneapolis, MN) in March 2000 under a Humanitarian Device Exemption for symptomatic relief in patients with diabetic and idiopathic gastroparesis, but not for postsurgical etiologies.[19] There are only 2 preliminary reports of GES therapy in patients with PSG.[20,21] However, these 2 studies are performed in a small group of PSG patients with various durations of GES therapy, thus underpowering the statistical analysis of the clinical effects of GES. In this present report, we analyzed the clinical response after 12 months of GES therapy in patients with PSG, including symptoms, health-related quality of life (HQOL), nutritional status, and GE.

Methods

Patients

There were 16 patients (15 women and 1 man; mean age, 46 years; range, 21–66 years) who underwent GES implantation for documented refractory PSG between 2000 and 2003 at the University of Kansas Medical Center, Kansas City, Kansas. The key inclusion criteria were (1) documented diagnosis of gastroparesis for more than 1 year and refractoriness to antiemetics and prokinetics; (2) more than 7 emetic episodes per week; (3) in the setting of fundoplication where patients can not vomit then chronic daily nausea was the criterion; and (4) delayed GE (gastric retention greater than 60% at 2 hours and greater than 10% at 4 hours) based on a 4-hour standardized radionuclide solid meal.[22] Patients were excluded if they had organic obstruction or pseudo-obstruction, primary eating or swallowing disorders, chemical dependency, positive pregnancy test result, or psychogenic vomiting. The study protocol was approved by the Human Subjects Committee at University of Kansas Medical Center, and written consent forms were obtained from all subjects before the study.

Study Protocol

This study consisted of (1) a baseline (the 4-week period before surgery) evaluation of medical history and upper GI symptoms, GE test, HQOL, assessment of nutritional status, pregnancy testing, and blood chemistries to determine the qualification for enrollment; (2) surgical placement of the GES system by laparotomy as previously described if the stomach is intact[15,16] or position of the 2 electrodes in the muscularis propria of the greater curvature at 2 and 3 cm proximal to the gastric anastomosis in the case of antrectomy; (3) removal of any parenteral nutrition, gastric decompression devices, or gastrically placed jejunal feeding tubes and (4) in cases of malnutrition placement of a feeding jejunostomy tube if not already in place; and (5) follow-up at 6 and 12 months after implantation to repeat baseline measurements. In addition, adverse events, including hospitalizations, were monitored throughout the follow-up period. The detailed descriptions of the GES system and surgical and stimulation techniques have been published previously.[15,16]

Assessment of Symptoms

Each patient completed a Symptoms Interview Form at baseline and at 6- and 12-month follow-up visits. This form assessed the symptoms of gastroparesis occurring during the last 2 weeks before the interview for severity and frequency of vomiting, nausea, early satiety, bloating, postprandial fullness, and epigastric pain. The severity of each symptom was graded by the patients as 0, absent; 1, mild (not influencing the usual activities); 2, moderate (diverting from, but not urging modifications of, usual activities); 3, severe (influencing usual activities, severely enough to urge modifications); and 4, extremely severe (requiring bed rest). Also the frequency of each symptom was graded as 0, absent; 1, rare (1/wk); 2, occasional (2–3/wk); 3, frequent (4–6/wk); and 4, extremely frequent (≥7/wk). The sum of the severity ratings of the 6 symptom subscores comprised the overall total symptom score (TSS) for severity, and the sum of the frequency ratings of the 6 symptom subscores comprised the overall TSS for frequency.

Assessment of Health-Related Quality of Life

HQOL was assessed by using the previously validated SF-36 Health Status Survey (acute) questionnaire.[23] Two summary scores were derived from the 8 subscores of the SF-36 questionnaire and reported as the physical composite score (PCS) and the mental composite score (MCS). PCS and MCS are norm-based measures for which the mean ± standard deviation for the general US population is 50 ± 10.[24]

Measurement of Gastric Emptying

GE scintigraphy was performed in the morning after an overnight fast as previously described[22] with prokinetics stopped for at least 3 days. This standardized method for GE consists of a scrambled egg substitute (120 g of Free Cholesterol & Fat Free Egg; Sunny Fresh Foods, Inc, Monticello, MN) (60 kcal) labeled with ^{99m}Tc sulfur-colloid (1 mCi), 2 slices of whole wheat bread (120 kcal), 30 g jelly (75 kcal), and 120 mL of water.[22] The meal has a total caloric value of 255 kcal (nutritional composition: 72% carbohydrate, 24% protein, 2% fat, and 2% fiber). Anterior and posterior images of the stomach were taken immediately after eating and then hourly for 4 hours. Gastric retention of gamma counts was calculated by the Department of Nuclear Medicine by using geometric and decay correction. Delayed 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.[22]