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Long-term outcomes of gastric electrical stimulation in children with gastroparesis

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ABSTRACT

Background: Gastric electrical stimulation (GES) has been used in adults with gastroparesis. However its use has been limited in children. We describe the largest experience with GES in children with long-term outcomes.
Methods: Data were collected on children who underwent GES over a 10-year period. Data regarding demographics, medical history, hospital course, and outcomes were collected and analyzed. Symptom scores (validated Likert scores) were compared using a paired Student's t test.
Results: Overall, 97 patients underwent GES, and a majority were teenage Caucasian girls. Ninety-six had temporary GES (tGES), and 66 had improvement in their symptoms. A total of 67 underwent permanent implantation (pGES), and there was significant reduction in all individual symptoms ($p < 0.001$) as well as the total symptom score (TSS) ($p < 0.0001$) at 1, 6, 12, and >12 months. Recurrence of symptoms leading to device removal occurred in 7 cases. Forty-one patients had continued improvement in symptoms for over 12 months, with a mean follow-up of 3.5 years (range 1–9 years).
Conclusions: This study represents the largest experience of systematic application of GES in children. GES is a safe and effective therapy for selected children with intractable GP with continued symptomatic improvement at 1 year and beyond.

Gastroparesis is a disorder characterized by severe nausea, persistent emesis, early satiety, abdominal pain and bloating in the absence of a gastric outlet obstruction [1]. This causes a significant impact on the quality of life for these patients, with high medication usage and frequent hospitalizations to control symptoms, with one estimate suggesting a cost burden of over 1 billion dollars in the US per year [1,2]. While gastroparesis occurs in almost 4% of US adults, the prevalence in children remains unknown [3]. Waseem et al. [4] noted that delayed gastric emptying was a relatively frequent finding in children who underwent a gastric emptying scan for abdominal 'complaints', suggesting that it is not uncommon. Multiple reports in the pediatric and adolescent age groups note that the etiology of gastroparesis is mostly idiopathic as opposed to adults in whom long standing diabetes is the most common issue [1,5–8]. Gastroparesis likely continues to be under reported in children as it is not usually in the differential for chronic dyspeptic symptoms [1].

Current medical therapy for gastroparesis consists of dietary modification with small and frequent low fat, low fiber meals and symptomatic relief with antiemetic drugs and pain control [5,9,10]. Prokinetics are also used, however they have limited efficacy because of tachyphylaxis and a small therapeutic window [11]. For recalcitrant cases, a number of surgical procedures have been utilized such as pyloroplasty, gastrojejunostomy, intrapyloric botulinum toxin injection, and in extreme cases partial to subtotal gastrectomy [12–15]. Some of these operations have been performed in children, however the experience is very limited and long-term results are unknown [1].

Gastric electrical stimulation (GES) uses high frequency, low amplitude current and has been applied in adults for the past 15–20 years with multiple reports of improvement in symptoms [8,16]. The mechanism of action remains unclear, but is thought to ameliorate symptoms by improving gastric accommodation via stimulation of the enteric nervous system, in addition to central effects mediated through the vagus nerve [17,18]. There are very few reports of the use of this therapy in children, with no long term outcomes or effectiveness studies, and the device remains 'off label' for use in patients less than 18 years of age [7,8,19]. The purposes of this study are to report the largest series of children with intractable symptoms of gastroparesis in whom GES was utilized, and to describe long-term outcomes and efficacy.

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1. Methods

1.1. Patient selection

All children less than or equal to 18 years of age at the time of diagnosis of gastroparesis, who underwent permanent GES implantation were selected. The implants were performed from 2004 to 2014 at one of two institutions (University of Mississippi Medical Center, Jackson, MS; and University of Florida Health, Gainesville, FL). Patient data regarding demographics, etiology, comorbidities, duration and course of symptoms, hospital course and need for supplemental nutrition support, results of temporary and permanent GES, and complications were collected. Patients were considered a candidate for GES based on the symptoms of gastroparesis/chronic dyspepsia (Intractable nausea, post prandial pain, emesis, anorexia, and bloating), and a gastric emptying test showing disordered gastric emptying.

1.2. Gastroparesis symptom scores

The gastroparesis scores were calculated using a validated Likert based scale (Gastroparesis Cardinal Symptom Index, or GCSI) [20]. The five 'cardinal' symptoms were anorexia, nausea, emesis, pain, and bloating. Patients self-described the individual symptom scores on a five-point scale before and after any interventions. A combined total symptom scores was calculated as well. A number of patients were either too young or had developmental delay and could not do these scores, therefore they were excluded after the initial analysis.

1.3. Temporary stimulation

The temporary GES (tGES) was performed by one of two methods — endoscopic or transgastrostomy site. Patients who did not have a gastrostomy underwent endoscopy with placement of a transvenous epicardial pacing lead (Model 6416, Medtronic, Minneapolis, MN) via the side port into the gastric mucosa as previously described [8,21]. Transgastrostomy leads were placed with endoscopic guidance and modified Fetal Scalp spiral electrodes (Covidien, Minneapolis, MN) as described [22].

Typical tGES settings were started at 5–7 volts, 14 Hz frequency, 1 second 'on' and 4 seconds 'off', and pulse width 330 microseconds. The duration of the tGES was typically 1–3 days for the endoscopic and 3–28 days for the trans gastrostomy leads. Responses were measured by the GCSI scores, parental assessment, and changes in oral intake amounts as well as type.

1.4. Permanent GES placement

The procedure was either performed with either open or laparoscopic technique, as previously described [8,21,22]. Leads were secured in the seromuscular layer of the stomach. Initial settings used were similar to tGES. Settings were typically maintained for a 4-week period to allow for the postsurgical effect.

1.5. Data analysis

Descriptive data were compiled and reported as such. Statistical analysis was performed between patients before and after GES (both temporary and permanent) as well as comparing baseline to the most recent scores. Scores were considered continuous variables and were analyzed with the Student's paired t test with each subject acting as their own control. Analysis between groups of patients was performed using Fishers exact test, chi-square, or Mann–Whitney U test for nonparametric data. A p value less than 0.05 was considered significant, and 95% confidence intervals were also reported. Statistical analysis was performed using "R" 2.8.0-statistical program (Vienna, Austria), as well as Minitab v16 (Cary, NC).

2. Results

2.1. Demographics

Between 2004 and 2014, a total of 97 children and adolescents underwent stimulation assessment, with 96 having a temporary trial and one had permanent stimulation without a trial (Table 1). The mean age was 13.7 years (range, 2–19), and a majority were Caucasian (85.6%) females (76.2%). Medicaid was the primary insurer in 53%, and a large number came from other states (54.6%). A majority of the patients had multiple other comorbidities (69.1%), the most common of which were genetic/congenital disease (24.7%) and autoimmune disease (16.8%). The most common etiology was idiopathic (54.7%).

2.2. Pre GES course

All patients had gastric emptying scintigraphy with either liquid (5.3%) or solid (94.7%) meals. A vast majority (95%) had delayed emptying (moderate or severe). Median emptying time recorded was a half time of greater than 120 minutes. Duration of symptoms before stimulation was 3.5 years (range between 1 month and 9.5 years). Two thirds (66%) had already undergone other procedures before consideration for stimulation, including 13 fundoplications. All patients had used promotility agents at the time of evaluation, and most patients were on antiemetic (71.6 percent), pain (51.9 percent), and antireflux medications (79.0 percent). Of the 97 patients (Fig. 1), baseline symptom scores were obtained in 86 patients. Eleven patients were unable to use the gastroparesis scale for a variety of reasons.

2.3. Temporary GES

96 patients (Fig. 1) underwent tGES for chronic symptoms of gastroparesis. Endoscopic trials were performed in 71 cases, while 25 had trans G-tube evaluation. Nine patients needed multiple trials of tGES because of either inability to tolerate the lead in the pharyngeal area, or unclear results. In two patients we performed greater than 3 temporary stimulations as we awaited approval of the permanent implantation. There was a significant reduction in the individual, as well as total symptom scores in the 66 responders to tGES ($p < 0.005$), while the 30 nonresponders had no effect when compared to baseline (Fig. 2).

2.4. Permanent GES

Sixty-seven patients underwent permanent implantation as 1 patient bypassed the tGES trial. Laparoscopic placement was performed in 46 cases, while 21 patients had open operations. For patients being able to provide symptom scores, they were obtained at 1 month ($n = 56$), 6 months ($n = 52$), 12 months ($n = 40$), and >12 months (last recorded symptom score) ($n = 34$). At all time points, there was a significant improvement in individual symptoms scores ($p < 0.005$) (Fig. 3) as well as in the total symptom scores when compared to baseline

Table 1
Summary of characteristics of patients undergoing GES.

Characteristics ($n = 97$)	N (percent)
Age (years) (mean and range)	13.7 (2–19)
Female gender	74 (76.2)
Caucasian race	83 (85.6)
Medicaid insurance	51 (53)
Out of state residence	53 (54.6)
Preceding viral illness[a]	23 (23.7)
Comorbidities[b]	67 (69.1)
Autoimmune disease	17 (17.5)
Genetic/Congenital issues	24 (24.7)
Previous surgical history	64 (66)

[a] Documented history of specific viral URI, or gastroenteritis before symptom onset.
[b] Patients may have more than one comorbidity.