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Two-channel gastric pacing in patients with diabetic gastroparesis

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Abstract

Background—Our primary goals were to investigate the effects of two-channel gastric pacing on gastric myoelectrical activity, and energy consumption with the secondary intent to monitor gastric emptying and symptoms in patients with severe diabetic gastroparesis.

Methods—Four pairs of temporary pacing wires were inserted on the serosa of the stomach at the time of laparotomy to place the Enterra™ System in 19 patients with severe gastroparesis not responding to standard medical therapies. Two of the pairs were for electrical stimulation and the other two for recording. Five days after surgery the optimal pacing parameters for the entrainment of gastric slow waves in each patient were identified by serosal recordings. Two-channel gastric pacing was then initiated for 6 weeks using a newly developed external multi-channel pulse generator. Electrogastrogram (EGG), total symptom score (TSS), and a 4-hour gastric emptying test were assessed at baseline and after 6 weeks of active gastric pacing. Enterra™ device was turned OFF during the duration of this study.

Key Results—Two-channel gastric pacing at 1.1 times the intrinsic frequency entrained gastric slow waves and normalized gastric dysrhythmia. After 6 weeks of gastric pacing, tachygastria was decreased from 15 ± 3 to $5 \pm 1\%$ in the fasting state and from 10 ± 2 to $5 \pm 1\%$ postprandially ($P < 0.05$), mean TSS was reduced from 21.3 ± 1.1 to 7.0 ± 1.5 ($P < 0.05$) and mean 4-hour gastric retention improved from 42% to 28% ($P = 0.05$).

Conclusions & Inferences—Two-channel gastric pacing is a novel treatment approach which is able to normalize and enhance gastric slow wave activity as well as accelerate gastric emptying in patients with diabetic gastroparesis with a good safety profile.

Keywords

gastric electrical stimulation; gastric emptying; gastric pacing; gastric slow wave; gastroparesis

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INTRODUCTION

Gastroparesis is a chronic disorder of gastric motility, defined as delayed gastric emptying of a solid meal without evidence of mechanical obstruction. Patients with gastroparesis have frequent hospital admissions, lost employment, and poor quality of life (1, 2).

Approximately one third of gastroparesis cases are caused by diabetes mellitus. Diabetic gastroparesis may be attributed to impaired motor activity involving gastric hypomotility and non-propagated contractions (lack of peristalsis) and/or impaired myoelectrical activity explained by abnormal frequency of the gastric slow wave (dysrhythmia), low amplitude and/or uncoupling of slow waves (3–6).

The most common treatment for gastroparesis is the use of prokinetic agents, such as metoclopramide, erythromycin and domperidone. Those who are refractory or intolerant to anti-emetics and prokinetic agents, often require placement of a feeding jejunostomy tube that does not improve gastric motility, but does provide nutritional support, and a drug delivery option (8, 9).

Gastric electrical stimulation (GES) with short pulses (330 μ s) and low energy (Enterra™ Device) was FDA approved in 2000 as a therapeutic option in the management of refractory gastroparesis (10–13). Long-pulse and high energy stimulation, another approach to GES, achieves gastric slow wave entrainment (pacing) and represents a promising new treatment for gastric motility disorders (14–16). In this method, the electrical stimulus is composed of repetitive single pulses with a pulse width in the order of milliseconds (10–600 ms), and a stimulation frequency in the vicinity of the physiological frequency of the gastric slow wave, 3 cycles per minute. Single-channel gastric pacing with a pair of electrodes located in the mid-body of the stomach is able to normalize gastric dysrhythmia (14–17) and improve gastric emptying in both patients with gastroparesis and animal models of gastroparesis (15, 18, 19). Recently, two or four-channel gastric pacing investigated in canine models showed that, a multi-channel approach utilizing 2 channels for electrical stimulation is substantially more effective in entraining gastric slow waves and accelerating gastric emptying than single channel gastric pacing. (20–22). However, there are no data concerning the effects of two-channel gastric pacing on gastric myoelectrical activity, gastric emptying and symptoms of gastroparesis in humans.

The aims of this unblinded study therefore were to investigate the effects of two-channel gastric pacing on gastric myoelectrical activity, energy consumption of the device, gastric emptying, symptoms and adverse events in patients with severe diabetic gastroparesis who had failed standard medical therapies. We hypothesized that two-channel gastric pacing could achieve the following primary goals: 1) entrain gastric slow waves and thus normalize gastric dysrhythmias, and 2) reduce the energy consumption when compared to the energy required for a single channel gastric pacing. Additional secondary goals were to 1) measure gastric emptying of a solid meal; 2) assess changes in symptoms status during the gastric pacing trial and 3) monitor adverse events and confirm safety of the device.

METHODS

Patients

Nineteen patients (8M, 11F, mean age: 41 years, range: 27–60) with severe diabetic gastroparesis who failed standard medical therapies were enrolled in this unblinded study that was approved by the Human Subjects Committee at University of Kansas Medical Center, and written consent forms were obtained from all subjects. The key inclusion criteria were: (a) documented diagnosis of diabetic gastroparesis for more than one year and refractoriness to antiemetics and prokinetics after more than 6 months of a full regimen of

standard medical therapy; (b) over 7 emetic episodes per week or chronic daily nausea; (c) delayed gastric emptying (gastric retention > 10% at 4 hours) based on a 4-hour standardized radionuclide solid meal (23). Patients were excluded if they had an organic or pseudo obstruction, primary eating or swallowing disorders, rumination syndrome, psychogenic vomiting, cyclic vomiting syndrome or evidence of an active malignancy.

Placement of Serosal Electrodes

During implantation of permanent electrodes and the pulse generator for the Enterra™ Therapy (14) via laparotomy technique, four pairs of temporary electrodes were anchored on the serosa of the greater curvature of the stomach with an inter-electrode distance of 1 cm using a previously published method (12, 24). These four pairs of electrodes were TPW62 multifilament surgical steel temporary cardiac pacing wires (Ethicon, Inc, Somerville, NJ, USA). The most distal pair of electrodes was positioned 3–4 cm above the pylorus and the most proximal one, 15–16 cm above. The interval between the pairs of electrodes was 4 cm (Figure 1). The first pair (the most proximal pair) and the third pair of electrodes at 7 to 8 cm proximal to the pylorus were used to deliver the electrical stimulation. The second and the fourth pairs at 11 to 12 cm and at 3 to 4 cm proximal to the pylorus respectively were placed for recording of gastric electrical activity. Wires from the electrodes were brought out through the abdominal wall percutaneously and placed under a sterile dressing to be connected to an external multi-channel pulse generator (MPG) for the study. At the time of surgery, full thickness antral wall biopsies from the greater curvature were obtained and stained with c-kit for analysis of interstitial cells of Cajal (ICC). The detailed description of the method for analysis of ICC has been published previously (25). At all times care was taken to avoid any hypoxic injury to the tissue.

Enterra™ device was interrogated in the operating room to confirm its ability to function but it was turned OFF and kept inactivated for the duration of this trial.

Study Protocol

For two weeks prior to placement of serosal electrodes and Enterra™ system implantation procedure, each patient was asked to complete a symptom diary, a baseline gastric emptying test and electrogastrogram (EGG) recordings (Figure 2). Four to five days after surgery the function of the electrodes was validated by 4 channel-serosal recordings and the optimal pacing parameters for entrainment of gastric slow waves in each patient were identified using a newly developed external multi-channel pulse generator (MPG) (GI Stimulation Inc., Charlottesville, VA) (see Figure 1). Before being sent home with a portable MPG the patient was trained on how to connect the electrodes to the external pulse generator, activate and care for the device and for the skin site where the electrodes were exiting the abdomen. All devices were placed in a fanny pack for protection during the day and patients were instructed to self-administer gastric pacing 30 minutes before, during and 4 hours after each meal. Upon completion of this active stimulation the pulse generator was disconnected from the electrodes and patients were shown how to charge the battery at night. It has to be noted that all 4 pairs of electrodes were color-coded to match the tips of connectors plugged into the MPG, to assure the correct use of stimulating and recording channels. The parameters utilized were determined by an optimization session described below: two-channel pacing at 1.1 times the intrinsic frequency ranging from 3 to 3.5 cpm, a pulse width of 10 to 300 ms and the amplitude of 0.5 to 3 mA. The phase shift of electrical stimuli between the first and third stimulation channels was adjusted to be the same as the intrinsic phase shift calculated from the baseline slow wave recording and varied from 8 to 10 seconds. After 6 weeks of two-channel gastric pacing, a follow up visit was scheduled to measure the serosal electrical recording, and perform an electrogastrogram (EGG) and 4-hour gastric emptying test. Also

symptoms assessment and the review of the symptom Diary pages for the last 2 weeks were performed in a similar fashion to data gathered at baseline prior to pacing.

Optimization of Pacing Parameters

A study to optimize pacing parameters was initiated when the patient was off all pain medications, and before discharge from the hospital (Figure 3). A series of stimulation sessions were conducted in the fasting state. Each session lasted 15 minutes. There was a recovery period of 5–10 minutes without stimulation between sessions. The stimulus provided by the MPG was a single constant current pulse, repeated periodically on each of two output channels with fixed phase relationship. Drawing upon previous GES studies on dogs (4, 14) and humans (6), pulse widths ranging from 100 microseconds (μ sec) to 500 milliseconds (msec) and pulse amplitudes ranging from 0.1 milliamperes (mA) to 6 mA were used. The pacing frequency was fixed at 1.1 times the intrinsic frequency (IF) of the patient's gastric slow wave. The IF is defined as the patient's baseline slow wave frequency without stimulation. The pacing frequency was set to 3 cycles/min (cmp) when the baseline IF was abnormal. Phase relationships among the channels were determined on the basis of the intrinsic characteristics of slow wave propagation as seen in the baseline recording.

During the first test session, stimulus was first applied to the most proximal electrode pair. Optimization experiments were conducted by first reducing pulse width and subsequently reducing pulse amplitude. The optimal setting of stimulation parameters was defined and set as the minimum pulse width and amplitude that were shown to entrain the gastric slow wave. During each subsequent test session, stimulus was applied to the third electrode pair. Electrode pairs on which stimulation parameters had previously been optimized continued to be stimulated, but the pulse width and amplitude of their signals might be reduced to the extent that such reduction was enabled by the addition of incremental channels of stimulation. Stimulation parameters were optimized using the procedures defined above.

Myoelectrical recordings were made after optimal parameters were identified for each number of active pacing electrodes (i.e. after optimizing the parameters for pacing via one channel and two channels). These recordings were made by using the electrodes that were not being stimulated during each session. The recordings were used to capture data concerning the frequency, amplitude, and propagation velocity of gastric slow waves, as well as the percent entrainment of slow waves. In determining entrainment, the criterion was phase-lock of the gastric slow wave with the pacing stimulus. This was determined by visual inspection of the recording.

Recording and Analysis of Gastric Electrical Activity

Gastric myoelectrical activity was measured with surface electrogastrgraphy (EGG) for 30 min in a supine position in the fasting state and for 1 hour after the ingestion of a liquid meal (Boost, 250 calories, Novartis Medical Health, Inc., Fremont, MI). Before the placement of EGG electrodes, the epigastric skin was shaved, cleaned, and abraded with sandy skin-prep jelly (Omni Prep, Weaver & Co., Aurora, Colorado) to reduce the impedance. Two silver-silver chloride ECG electrodes (BioTac® Ultra 7305, The Ludlow Company, Chicopee, MA) were placed on the abdominal skin: the first one at the midpoint between the xiphoid process and the umbilicus and the second on the subject's left side, just below the ribcage and above the level of the first electrode. A reference electrode was placed on the left costal margin, horizontal to the first active electrode. These electrodes were connected to a portable battery-operated recorder (Synectics Medical Inc., Irving, Texas) with cutoff frequencies of 1 and 18 cycles per minute (cpm). On-line digitization was done at a sampling frequency of 4 Hz and digitized samples were stored on the recorder. All

recordings were made in a quiet room and the subject was asked not to talk and to remain as still as possible during the recording to avoid motion artifacts.

At the end of the recording, the EGG data were downloaded to an IBM 586 personal computer for data analysis. After the EGG segments with some inadvertent motion artifacts were identified by visual analysis and removed by using a locally developed program, the following parameters were computed from the EGG data using spectral analysis methods (26): (a) EGG dominant frequency: the frequency at which the power spectrum of the EGG recording had peak power (range of 0.5 to 9 cpm); (b) EGG dominant power: the power at the dominant frequency in the power spectrum of the EGG recording; (c) The percentage of normal slow waves (2–4 cpm), the percentage of tachygastria (4–9 cpm), and the percentage of bradygastria (0.5–2 cpm) present over the entire observation period. An EGG was considered to be abnormal if dysrhythmias presented for more than 30% of the recording time during either pre- or postprandial tracings (26, 27).

Symptom Assessment and Total Symptom Scores (TSS)

Each patient completed a self assessment Symptom Interview Form at baseline and after 6 weeks of active gastric pacing. This form assessed the symptoms of gastroparesis occurring during the 2 weeks before the interview and the two last weeks of a total of 6 weeks of gastric pacing study for severity of vomiting, nausea, early satiety, bloating, postprandial fullness, epigastric pain, and epigastric burning. 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). The sum of the severity ratings of the 7 symptom sub-scores comprised the overall total symptom score (TSS) for severity.

The Diary pages previously mentioned captured patient's daily symptoms such as: early satiety, postprandial fullness, bloating, presence of nausea and vomiting. Subjects were also asked to assess the exit site for the wires, MPG light indicator status and they were required to make a note if MPG device was turned ON with every meal. Numbers of meals per day, description of diet (did not eat at all; liquids only, solid only; mix diet) and use of nutritional support were noted by patients. These diary pages were designed to measure the patient's compliance regarding utilization of the MPG system.

Gastric emptying test

Gastric emptying (GE) scintigraphy test was performed in the morning after an overnight fast as previously described (23) with proton pump inhibition and prokinetics stopped for at least 3 days and narcotic medications being with hold for at least 12 to 18 hours if possible. The standardized method for gastric emptying using a low fat (2%) isotope labeled egg beater meal was utilized (23). Blood glucose was measured before the GE and the test was not started until glucose levels were > 75 and < 275 mg/dL.

Delayed gastric emptying was defined as the percentage of gastric retention equal to or greater than 10% at 4 hours (23). The rate of gastric retention at 2 hours was also recorded as abnormal if more than 60% of isotope was retained in a stomach at that time.

Statistical Analysis

Results are reported as means $\pm$ SEM if not otherwise specified. Analysis of variance (ANOVA) and Student's t-test were performed as appropriate to investigate the difference of the EGG parameters, symptom severity scores and gastric retention between baseline and during two-channel gastric pacing at 6 weeks (Microsoft Excel, Redmond, WA). $P < 0.05$

was considered significant. Post hoc power analysis (28) based on percent 4-hour gastric retention at baseline and during two-channel gastric pacing at follow-up for all 19 subjects was performed to assess the statistical power of this study.

RESULTS

Mean duration of diabetes for the 19 patients was 18 years (range: 7–39) and mean duration of gastroparesis was 7 years (range: 2–16). Five patients had previously required abdominal surgery for the placement of a jejunostomy tube for nutritional support. One patient had received both a kidney and pancreas transplant, while one other patient had undergone renal transplant only. Two patients were on hemodialysis. Three patients had documented coronary artery disease, and one had a history of myocardial infarction. Ten patients had diabetic peripheral neuropathy, 5 had been diagnosed with retinopathy and 6 were noted to have hyper-cholesterolemia/lipidemia. Eight patients had a previous cholecystectomy, and 10 patients were diagnosed with gastroesophageal reflux disease.

Five of the 19 patients (26%) had reduced numbers of ICC in the antrum based on full thickness biopsy samples obtained at surgery and processed with c-kit staining. Twelve patients had abnormal patterns of EGG at baseline (7 with >30% dysrhythmias - tachygastria) and 10 with a decrease in EGG power postprandially). Four of the 5 patients with reduced numbers of ICC determined by the c-kit methodology had abnormal EGGs.

The gastric slow wave was entrained in every patient by two-channel gastric pacing, with a mean pulse width of 350 msec and an amplitude of 4 mA for single-channel gastric pacing (1st pair of electrodes only) or a mean pulse width of 150 msec and amplitude of 2 mA (first channel) and 0.5 mA (third channel) for two-channel gastric pacing. Figure 4 shows typical recordings from the serosal electrodes at baseline and during entrainment of gastric slow waves with two-channel gastric pacing. The entrainment of the gastric slow wave was demonstrated by the fact that the slow waves were phase-locked with the stimuli (pacing signal).

Two-channel gastric pacing improved gastric slow waves and normalized gastric dysrhythmias (Figure 5). After 1.5 months of gastric pacing, tachygastria was significantly decreased from $15\pm3\%$ to $5\pm1\%$ ($P<0.05$) in the fasting state and from $10\pm2\%$ to $5\pm1\%$ postprandially ($P<0.05$). The percentage of normal slow waves (2–4 cpm) was significantly increased after 6 weeks of gastric pacing ($75\pm3\%$ vs. $85\pm2\%$). The mean postprandial EGG power change was substantially increased from 0.3 ± 0.6 dB to 1.0 ± 0.6 dB ($P=0.2$).

Severity for each GP symptom (nausea, vomiting, early satiety, bloating, postprandial fullness, epigastric pain, and epigastric burning) was significantly reduced after 6 weeks of two-channel gastric pacing ($P<0.01$, Figure 6). A significant reduction of TSS from 21.3 ± 1.1 at baseline to 7.0 ± 1.5 after 6 weeks of two-channel gastric pacing was observed.

For all 19 patients enrolled in this study, mean gastric retention at 4-hour was reduced from 42% at baseline to 28% after 6 weeks of gastric pacing ($P\geq0.05$, Figure 7). There were 3 patients whose chronic high dose of narcotic use could not be stopped for the emptying test. In the remaining 16 patients the mean 4-hour gastric retention decreased significantly from 43% at baseline to 25% after 6 weeks of two-channel gastric pacing ($P=0.012$) and the GE was accelerated in 70% of patients and actually normalized in 25%. The mean glucose level before each gastric emptying test was similar, 160 mg/dL at baseline and 174 mg/dL after 6 weeks of gastric pacing.

Based on the formula for the calculation of the stimulation energy (E): $E = \text{pulse width (ms)} \times \text{pulse amplitude}^2 (\text{mA}^2)$ as published by Chen et al (21), we found that the minimum

stimulation energy required to entrain the gastric slow wave by single-channel gastric pacing was 5600 ms mA² whereas it was 850 ms mA² for two-channel gastric pacing (see Table 1).

No unanticipated adverse events were observed in this study. Patients tolerated the external pacing wires well with no significant infections and only mild skin irritation. They were removed with gentle pulling and the addition of Xylocaine spray to the skin. No malfunctioning or technical difficulties related to the use of the external MPG device were noted.

DISCUSSION

All of the previous studies on GES in humans were performed using single-channel electrical stimulation (10–16). To date, researchers have mainly employed two different sets of GES parameters for treatment of gastroparesis. One of them is utilizing a high-frequency and low-energy or short pulse parameters, i.e., with four times or much higher frequency than the established physiologic rate of the gastric slow wave and the width of stimulation pulse in the order of a few hundreds of microseconds (e.g., 330 μ sec) (11–13). This high-frequency and low-energy GES is capable of preventing symptoms of nausea and vomiting but has minimal effects on gastric emptying and does not entrain or change the electrical rhythm in gastroparetic patients (11, 15, 16, 24). The other GES technique is a low-frequency and high-energy or long-pulse parameters, i.e., using stimulation frequency similar to the physiologic frequency of the gastric slow wave (3 cycles/min) and the width of stimulation pulse in the order of milliseconds (10 – 600 msec) (14–16, 29, 30). The majority of the previous studies indicate that single-channel high energy GES technique is able to entrain gastric slow waves, normalize dysrhythmias (10, 12, 13), and improve gastric emptying rate and symptoms of gastroparesis (12).

In our present unblinded study, we assessed the efficacy of a novel approach, two-channel gastric pacing as a potential treatment for refractory diabetic gastroparesis. One of the parameters analyzed was gastric myoelectrical activity before and after active two-channel gastric pacing. It was found that two-channel pacing at 1.1 times the intrinsic frequency significantly enhanced gastric slow waves and normalized gastric dysrhythmia assessed by EGG recordings. This observation is also in agreement with the results on multi-channel gastric pacing recently published in both healthy and diseased canine models (20–22). Also, for the first time, we observed that two-channel gastric pacing accelerated gastric emptying of a solid meal although reduction in gastric retention after 6 weeks of gastric pacing was not statistically significant. Taking alpha level as 0.05 and observed effect size as 0.723 based on percent 4-hour gastric retention at baseline and during two-channel gastric pacing at follow-up from all 19 subjects, we identified the observation power as 0.58 for a two-tailed t-test. This post hoc analysis (28) indicated that the statistically nonsignificant finding on the effect of two-channel gastric pacing on percent 4-hour gastric retention was due at least in part to a lack of statistical power. Thus the sample size in the present study may have been too small to detect the effect of two-channel gastric pacing on gastric emptying.

One of the major drawbacks for single-channel gastric pacing with long pulses is that it needs high stimulation energy to entrain gastric slow waves and normalize dysrhythmias. This is because the electrodes which are designed to provide stimulation have to be placed in the proximal stomach to avoid reverse pacing (18, 21). To entrain gastric slow waves, the stimulation energy for the single-channel gastric pacing has to be high enough to ensure the stimulation pulses are propagated a distance of 20 cm or greater from the proximal stomach to the distal antrum. In contrast, multi-channel GES was designed to mimic the natural propagation and characteristics of the gastric slow waves. For two-channel gastric pacing with long-pulses used in this study, each stimulation channel was responsible to entrain slow

waves at a distance of 8 cm. As a result, the consumption of stimulation energy with two-channel gastric pacing was much less than that with single-channel gastric pacing. It was found that the energy required by two-channel gastric pacing represents about 15% of the energy consumed by single-channel gastric pacing. This result is consistent with the previous studies on multi-channel GES in both healthy and diseased models of canines (20–22). The efficiency of multi-channel GES not only saves battery life but also makes it more feasible to use a permanent implantable device. The superiority of two-channel gastric pacing over the conventional single channel gastric pacing was shown in a previous dog model of gastroparesis (22). Therefore the next step is to pursue the challenge of an implantable multipoint pacemaker as a new device for the treatment of gastroparesis in humans.

One of limitations of this study is the lack of sham-GES data. Thus, a favorable placebo response during two-channel gastric pacing could not be ruled out. All patients enrolled in our study were diagnosed with a profoundly delayed emptying of the stomach, very severe symptoms of gastroparesis not responding to numerous medications given over years necessitating frequent hospitalizations, malnutrition requiring jejunal tube feeding support, as well as having other complications of chronic diabetes including renal failure and cardiovascular disease. Thus, the fact that we observed a symptom improvement in this very challenging group of patients, beginning within the first week of starting gastric pacing therapy, and which was able to be sustained over 6 weeks is scientifically and clinically very meaningful. However a randomized placebo-controlled study will be needed to investigate the efficacy of two-channel gastric pacing.

Under our protocol, the interrogation of Enterra™ System that was OFF for the duration of this study, was performed at each clinical visit to document its integrity for its future use. At the end of the study all pacing wires were generally easily removed from the serosa with gentle pressure. Although at this time the placement of temporary wires is invasive, the electrodes could be potentially placed endoscopically in the future (31). Certainly if laparoscopic surgery is utilized patients will need to stay in the hospital for only one or two days to recover or could even be discharged on the same day. In addition, gastric pacing using a external multi-channel pulse generator could be used as temporary treatment of gastroparesis to observe improvement of GP symptoms in the future. Hence it could be a valuable technique to act as a predictor of efficacy and whether a permanent implantation would be appropriate.

In conclusion, this was a novel study to determine the feasibility of two-channel gastric electrical pacing in diabetic patients with severe gastroparesis. Our major finding was that this method is able to normalize and enhance gastric slow waves. This goal can be achieved with good safety and with substantial reduction in the consumption of energy compared to a single channel gastric pacing system. The additional benefit of acceleration of gastric emptying also justifies the scientific basis for two-channel electrical stimulation as a promising therapeutic direction for the future. While our data does show that an improvement in symptoms accompanied the pacing period, further assessment of clinical efficacy would be best done in a double blind study design.

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Abbreviations used in this paper

EKG	electrogastrogram
GI	gastrointestinal
GES	gastric electrical stimulation
ICC	interstitial cells of Cajal
MPG	multi-channel pulse generator

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Depiction of Location of Gastric Electrodes

Figure 1.

Depiction of serosal electrodes location for external stimulation by a multi-channel gastric pulse generator (MPG). The electrodes utilized for stimulation were at 15–16 cm (channel 1) and 7–8 cm (channel 3) from the pylorus respectively whereas the electrodes for recordings the signal were located at 11–12 cm (channel 2) and 3–4 cm (channel 4) from the pylorus respectively. The pacing electrodes were positioned at time of laparotomy to place a permanent gastric neurostimulator (Enterra™ Device) whose electrodes were implanted into the gastric muscle at 9 and 10 cm from the pylorus on the greater curvature of the stomach.

Figure 2.
A flow diagram of the study protocol (replacing original Figure 2).

Figure 3.
(a) Connection of the external wires and Multi-channel Pulse Generator (MPG); (b) Depiction of the interrogation equipment, electrodes, MPG, signal amplifier and computer system during a typical session with the patient.

Figure 4.

Gastric myoelectrical recordings from serosal electrodes (a) Baseline recordings from the 4 leads (regular intrinsic slow wave frequency: 3 cpm) and (b) Entrainment of the gastric slow waves demonstrated in leads 2 and 4 after 6 weeks of two-channel pacing (frequency of 3.3 cpm).

Figure 5.

The percentage of fasting and postprandial (a) tachygastria and (b) normal slow waves based on surface EGG before and after initiating gastric pacing.

Figure 6. Comparison of individual upper gastrointestinal symptoms (vomiting, nausea, early satiety, bloating, postprandial fullness, epigastric pain and epigastric burning) using a severity grading scale of 0 to 4 with a maximum of 28 points between baseline and after 6 weeks of two-channel pacing. There was a significant reduction in all symptoms ($P < 0.01$) after 6 weeks of two-channel gastric pacing.

Figure 7.

Assessment of gastric emptying results at baseline and after 6 weeks of two-channel gastric pacing (N=19, P=0.12 for 2-hour gastric retention and P=0.05 for 4-hour gastric retention). Sixty-three percent of patients had an accelerated rate compared to their baseline and 4 normalized their gastric emptying (<10% retention of the meal at 4 hours).

Table 1

The stimulation parameters required for entraining gastric slow waves with two-channel gastric pacing and comparison of the energy used for a standard single-channel versus the new two-channel method. Channels 1 and 3 were utilized for stimulation and channel two and four served for recording purposes only.

Method of gastric pacing	Mean $\pm$ SEM pulse width (range) (ms)	Mean $\pm$ SEM pulse amplitude (range) (mA ²)	Energy (ms mA ²)
Two-channel:			850- total
First channel	200 $\pm$ 90 (10–300)	2.0 $\pm$ 0.1 (1–3)	800 $\pm$ 9 (10–2700)
Third channel	200 $\pm$ 90 (10–300)	0.50 $\pm$ 0.05 (0.4–0.6)	50 $\pm$ 0.225 (1.6–108)
Single-channel (for comparison only)	350	4	5600