Technology Response: Gastrointestinal System

Richard W. McCallum, MD

FACP,FRACP (Aust), FACG, AGAF Professor and Founding Chair, Department of Internal Medicine Director of Center for Neurogastroenterology and GI Motility Texas Tech University HSC El Paso TX, Paul Foster School of Medicine

Short term and Long-term electrical stimulation of the lower esophageal sphincter increases sphincter pressure in patients with GERD

Short laparoscopic procedure

Minimal impact on gastroesophageal junction (GEJ) minimizes GI side effects

Adjustable treatment algorithms

Default recommended settings with capability to noninvasively adjust to changes in patient symptoms over time

Pulse width 200us, frequency: 20Hz, Amp 5-15mA

<u>Rodríguez L¹, Rodríguez P</u>, <u>Neto MG</u>, <u>Ayola JC</u>, <u>Saba J</u>, <u>Berel D</u>, <u>Conklin J</u>, <u>Soffer E</u>. Neurogastroenterol Motil. 2012-2013 May:24(5):446-50

Gastroparesis: Diagnosis and Treatment Algorithm



<u>Gastric Electrical Stimulation</u> (GES) / Enterra Device





Implantable neurostimulator: Medtronic Itrel 3 Model 3116
Neuromuscular leads (2): Medtronic model 4351
Stimulation Parameters Amplitude: 5 millia Pulse Width: 330 µse Rate: 14 Hz Cycle On Time: 0.1 sec Cycle Off Time: 5.0 sec



Results of Double Blind Trials with Enterra in Gastroparesis.



Abell T, McCallum RW et al; Gastroenterology 2003; 421-8

McCallum RW et al; Clinical Gastroenterology and Hepatology 2010;8:947-54 McCallum RW et al; Neurogastroenterology and Motility 2013;25:10; 815-e636

Conclusions

- There were no significant symptom differences observed in the double-blind crossover phase between ON and OFF.
 - One explanation is that the initial 6 week ON period rendered the subsequent double-blind data null.
 - The magnitude and duration of symptom reduction suggest that regression to the mean or a placebo effect are unlikely explanations for the overall results.
 - Cross over design is not appropriate for future studies
 - Best trial design is to randomize patients at time of surgery for the gastric stimulator to be turned on or off in a parallel fashion for a period of 3-6 months.

Comparison of Total Symptom Scores (TSS)



(Thalamus) (Caudate nucleus)

(Thalamus) (Caudate nucleus)





During GES



Mechanisms of Action of Enterra

- No effects on gastric slow waves or gastric emptying
- Does not accelerate gastric emptying
- Increases vagal nerve activity
- Relaxes proximal stomach
- Main role is influencing CNS control of nausea and vomiting

Electrodes in gastric muscle Cerebrum

Cerebellum

Spinal cord with nerve tracts

Nerve stimulus from stomach to brain

Stomach with vagus nerves

Pulse generator in abdominal wall

Interstitial Cells of Cajal (ICC)



K.M. Sanders et al., Neurogastroenterol Mot. 1999; 11: 331-338

Interstitial Cells of Cajal



These images were taken at 160 magnification of formalin preserved full-thickness 1 cm² surgically obtained gastric biopsies with staining of CD117. (A) An example of normal numbers of interstitial cells of Cajal (ICC) which is 20 ± 10 (mean ± 2 SD) cells per high powered field (HPF). (B) An example of depleted numbers of ICC (less than 10 cells/HPF).

The addition of pyloroplasty as a new surgical approach to enhance effectiveness of gastric electrical stimulation therapy in patients with gastroparesis.





<u>Sarosiek I¹, Forster J, Lin Z, Cherry S, Sarosiek J, McCallum R.</u> <u>Neurogastroenterol Motil.</u> 2013 Feb;25(2):134-e80

Gastric Pacing vs. Neurostimulation



Serosal Recording Before, During and After Low-Frequency Stimulation (3 cpm, 4 mA, 300 ms)





Depiction of Location of Gastric Electrodes



Example of baseline tachygastric slow waves (4.5 cpm) recorded from 2nd and 4th pairs of serosal electrodes



(Time, MIN)

Transcutaneous Electrical Acupuncture (TEA) in Gastroparesis -**Nausea and Vomiting**



reconstruction during visual stimulation.

• A large activation of the right inferior frontal gyrus can be seen. Activation of parietal lobe is also evident



Irene Sarosiek¹, Yan Sun², Jiande Chen², Richard McCallum¹

Theoretical Approach to Treat Obesity through Electrical Stimulation



<u>Deb S¹, Tang SJ, Abell TL, McLawhorn T</u>, et al

What is InterStim[®] Therapy?

- Electrical stimulation of sacral nerves
- Sacral nerves provide the most distal common autonomic and somatic nerve supply to the pelvic floor, detrusor muscle and lower GI tract.
- Indicated for management of functional disorders of the lower urinary and intestinal tract such as urinary and <u>fecal</u> incontinence.

InterStim[®] Therapy for Fecal Incontinence



Step 1 - Temporary implant Simple outpatient procedure

• Evaluate nerve integrity and therapy benefit

InterStim[®] Therapy for Fecal Incontinence Step 2 – Permanent implant



• Lead implanted at level

S3 or S4

- Stimulator placed in subcutaneous pocket
- Generally one night

hospital stay

Follow-Up Results Fecal Incontinence Episodes (weekly average)



Paired t-test, p<0.05 is considered statistically

Matzel et al, The Lancet, Vol 363, Apr. 2004

Investigational Device: Not Approved in the U.S.

Gastrointestinal Electrical Stimulation Current and Future Directions

Dr. Richard McCallum Thank you



Conclusions:

- In drug-refractory GP the addition of pyloroplasty (PP) to GES substantially accelerated GET;
- 2) The GET response in post-vagotomy group was the most impressive;
- GES improves nausea and vomiting by central control effects while PP normalizes gastric emptying which improves the other postprandial symptoms;
- 4) PP added to GES may sustain better long term symptoms control in gastroparesis.