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Gastric Electrical Stimulation (GES)

An Evidence Update

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About this Update

This report updates the following evidence-based analysis:

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Gastric Electrical Stimulation (GES)

Update to the 2006 Medical Advisory Secretariat (MAS) Evidence-Based Review

A literature search was conducted on July 21, 2009 to update the 2006 evidence-based review by the Medical Advisory Secretariat (MAS)[1] on the use of GES for the treatment of 1) gastroparesis and 2) morbid obesity (the search details described in the Appendix).

As of July 2009, the Enterra device continues to be licensed by Health Canada for "the treatment of chronic intractable (drug refractory) nausea and vomiting", however, no GES device is currently licensed by Health Canada for the treatment of morbid obesity.

The updated literature search identified six observational studies that met the inclusion criteria (Table 1).

Overall, the updated GRADE quality of evidence is unchanged from the 2006 evidence-based analysis (low) and the same uncertainties apply in terms of study quality, consistency, and directness of results. No new randomized controlled trials were identified in the literature search.

The conclusion from the 2006 MAS evidence-based review remains unchanged.

> *"For GP, the overall GRADE and strength of the recommendation is "weak" – the quality of the evidence is "low" (uncertainties due to methodological limitations in the study design in terms of study quality, consistency and directness). Further evidence of effectiveness should be available in the future since there is a RCT underway that is examining the use of GES in patients with severe refractory GP associated with diabetes and idiopathic etiologies (ClinicalTrials.gov identifier NCT00157755)."*

According to the ClinicalTrials.gov website, NCT00157755 "has been terminated" and no study results are available to date.[2] Correspondence with the manufacturer that sponsored the trial further confirmed that the trial was terminated.

[1] http://www.health.gov.on.ca/english/providers/program/mas/tech/ohtas/tech_ges_081806.html

[2] http://clinicaltrials.gov/ct2/show/NCT00157755.

Table 1: Results of Included Studies Identified in the Updated Literature Search for Gastric Electrical Stimulation

Study	Study Design	Primary Objective	Treatment & Follow-up	Results	Comments
Anand et al. 2007 (1)	Retrospective Patients with drug-refractory gastroparesis who consented to a variety of protocols at 3 centres in the United States between 1992 and 2005. Included patients that were reported in Abell et al. 2003 (the study with the highest quality evidence in the 2006 MAS evidence-based review). GES implanted n=156 Controls n=58 Idiopathic n=146 Diabetic n=45 Postsurgical n=23	No primary objective reported. Aims were: 1. Investigate long term effect of GES on GI symptoms, gastric emptying. 2. Evaluate long term adverse events 3. Assess survival of GES patients compared with historical controls. Sample size calculation or justification not reported. Total GI symptoms score (patient daily record) Vomiting frequency score (patient daily record) Gastric emptying (scintigraphy)	Patients stratified into 3 groups and further grouped by type of gastroparesis: **Group 1** Consented but never implanted n=25 **Group 2** Implanted with temporary followed by permanent GES n=49 Implanted with a permanent device only n=107 **Group 3** Temporary device awaiting a permanent device n=33 Median follow-up 4 years. No range reported. Dropouts not reported.	Significant reduction in symptoms for permanent GES patients at last follow-up compared with baseline. Total GI symptom score 15.6±0.3 to 10.9±0.2, p<0.001 Vomiting frequency score 2.9±0.1 to 1.9±0.2, p<0.001 Long term follow-up by 3 main symptoms (baseline vs. latest), no p values reported, definition of "improved" not reported: **Vomiting** 62% improved, 37% not improved **Nausea** 59% improved, 41% not improved **Total Symptom Score** 84% improved, 16% not improved 4 hr. Gastric Retention (before vs. after) Improved from 26% to 17%, p<0.001 (definition for delayed emptying is >10% at 4 hours)	~ 10% of patients underwent algorithmic adjustment of stimulation parameters to optimize their symptom response. Unclear if study designed to examine intragroup or intergroup comparisons. Unclear if temporary pacing same as permanent pacing. Unclear if concomitant prokinetic/ antiemetic therapy was discontinued during treatment. Subjective self-reported endpoints (symptom and frequency scores). 4 hour gastric retention was still considered delayed (>10%). Patient death rates were higher for diabetic patients than for non-diabetic patients. Confounders related to diabetes not discussed (e.g. antidiabetes drugs).
Brody et al. 2008 (2)	Prospective N=50 Diabetic n=20 Idiopathic n=25 Postsurgical n=2 Connective tissue disorder n=3	No primary objective reported. Aims were: Characterize the effect of GES on symptoms and gastric motor function. Sample size calculation or justification not reported. Total GI symptoms score (patient daily record) Gastric emptying (scintigraphy)	34/50 patients available for 6 and 12 month follow-up after receiving GES. 15 diabetic 19 idiopathic Median follow-up 28 months (range 3 to 51 months)	At 12 months Decrease in total severity symptom score 19.05±8.04 to 14.05±8.28, p≤0.01 Decrease in total frequency symptom score 20.39±8.08 to 15.71±7.40, p≤0.05 At 6 months Decrease in 4 hour gastric retention 35±24 to 21±21, not significant No difference in: Total symptom score between idiopathic (n=19) and diabetic (n=15) patients, p=0.70. Gastric retention between idiopathic (n=14) and diabetic (n=10) patients, p=0.30.	Unclear if study designed to examine effects before and after GES implantation in all patients or in patient subgroups. Possible type 2 error for analysis of idiopathic and diabetic patients. Unclear if concomitant prokinetic/antiemetic therapy was discontinued during GES treatment. Subjective self-reported endpoints (symptom and frequency scores). 4 hour gastric retention was still considered delayed (>10%).

Study	Study Design	Primary Objective	Treatment & Follow-up	Results	Comments
De Csepel et al. 2006 (3)	Prospective N=16 Diabetic n=7 Idiopathic n=7 Postsurgical n=1 Brain trauma n=1	Safety and 6 month efficacy of GES Sample size calculation or justification not reported. GI symptom questionnaire	10 patients completed 6 month follow-up after receiving GES.	GI symptom score Baseline for all 16 patients: 11.2±3.97 At 6 months: 4.85±4.60, p=0.004 Half of all patients no longer required gastric prokinetic medications.	Confounders related to diabetes not discussed (antidiabetes drugs, glycemic control). Unclear why the patients were on prokinetic drugs if had refractory gastroparesis while on GES. No definition of delayed gastric emptying.
Maranki et al. 2008 (4)	Prospective N=29 Diabetic n=12 (all insulin dependent) Idiopathic n=16 Postsurgical n=0	No primary objective reported. Aims were: Determine the clinical response to GES in patients with refractory gastroparesis using the GCSI questionnaire and to identify factors that may be associated with a favourable response. Sample size calculation or justification not reported.	Follow-up available for 28 patients who received GES. Mean (SEM) follow-up 4.9±1.3 months.	**Global clinical response to symptoms** 14 (50%) felt improved 8 (29%) felt the same 6 (21%) felt worsened. Symptoms in Diabetic GP patients 7 (58%) felt improved 3 (25%) felt same 2 (17%) felt worse Symptoms in Idiopathic GP patients 7 (44%) felt improved 5 (31%) felt the same 4 (25%) felt worse **GCSI score (mean±SD)** Significant reduction from baseline (3.3±0.2) to 2.7±0.2, p<0.05. No significant reduction among diabetic or idiopathic subgroups. 15 patients not using narcotics experienced a significant decrease in GCSI while those on narcotics had no significant change. Authors reported no correlation between with baseline emptying scan and clinical response. Final gastric emptying times not reported.	Unclear if study designed to examine effects before and after GES implantation in all patients or in patient subgroups. Confounders related to diabetes not discussed (antidiabetes drugs, glycemic control). Unclear if patients were on prokinetic/antiemetic drugs. 13/28 patients were on narcotics (opioids are known to decrease gastric emptying). The study showed that the use of narcotics was associated with a decreased response to GES. Routine follow-up tests such as gastric emptying test and HbA1c were not obtained.

Study	Study Design	Primary Objective	Treatment & Follow-up	Results	Comments
Lin et al. 2008 (5)	Retrospective. N=63 Diabetic n=38 Idiopathic n=11 Postsurgical n=14	Investigate whether there is an association between gastric emptying rate and symptom improvement in patients with gastroparesis. Sample size calculation or justification not reported.	12 month follow-up. No dropouts reported in patients who received GES.	Significant decrease in symptom subscores and total symptom score ($p<0.001$). Mean 4 hour gastric retention reduced by 7% <u>Gastric Emptying (mean % retention [SD])</u> Baseline: 46±25 12 months: 39±29, p=0.10 14 (22%) had normalized gastric retention time and 49 were still delayed. Overall, nausea (one of 7 symptoms in the Symptom Interview Form) was significantly correlated with reduction in 4 hour gastric retention. No significant correlation was found with the other 6 symptoms or the total symptom score.	Unclear if consecutive patients enrolled. Confounders related to diabetes not discussed (antidiabetes drugs, glycemic control). Unclear if patients were using prokinetic drugs while on GES. Overall, the mean 4 hour gastric retention was still considered delayed (>10%).
McKenna et al. 2008 (6)	Retrospective N=19 Diabetic n=10 Idiopathic n=6 Postsurgical n=3	No primary objective reported. Total symptom scores, weekly vomiting frequency and gastric emptying times were assessed. Sample size calculation or justification not reported.	Mean follow-up 38 weeks (range 4 weeks to 35 months). Results reported up to 12 months post-implantation.	At 12 months post-implantation, there was significant improvement in total symptom score (p=0.01) Within 6 weeks, frequency of vomiting decreased in 6/8 diabetic and 4/4 idiopathic GP patients. No postsurgical GP patients reported vomiting preoperatively. At 6 months post implantation, gastric emptying times normalized in 4/5 diabetic GP patients and 1/6 patients with GP due to other causes.	Confounders related to diabetes not discussed (antidiabetes drugs, glycemic control). Unclear if patients were using prokinetic drugs if had refractory gastroparesis while on GES.

GCSI refers to Gastroparesis Cardinal Symptom Index; GES, gastric electrical stimulation; GI, gastrointestinal; GP, gastroparesis; MAS, Medical Advisory Secretariat; SD, standard deviation; SEM, standard error of the mean

Appendix

Final Search – Gastric Electrical Stimulation – July 2008 Update

Search date: July 21, 2009
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, Wiley Cochrane, Centre for Reviews and Dissemination/International Agency for Health Technology Assessment

Database: Ovid MEDLINE(R) <1950 to July Week 2 2009>
Search Strategy:

1 exp Gastroparesis/ (733)
2 exp gastrointestinal motility/ or exp gastric emptying/ (29095)
3 exp Obesity/ (93834)
4 or/1-3 (122911)
5 exp Electric Stimulation Therapy/ or exp Electric Stimulation/ (135829)
6 4 and 5 (1464)
7 ((gastric or intragastric or stomach) adj2 (stimulat* or electrostimulat*)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (3091)
8 gastric pacing.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (45)
9 or/6-8 (4366)
10 limit 9 to (english language and humans and yr="2006 -Current") (211)
11 limit 10 to (case reports or comment or editorial or letter) (23)
12 10 not 11 (188)

Database: EMBASE <1980 to 2009 Week 29>
Search Strategy:

1 exp electrostimulation therapy/ or exp electrostimulation/ (107416)
2 exp Stomach Paresis/ or exp Stomach Emptying/ or exp Stomach Motility/ (11454)
3 exp obesity/ (102346)
4 1 and (2 or 3) (1030)
5 ((gastric or intragastric or stomach) adj2 (stimulat* or electrostimulat*)).mp. (2550)
6 (gastric pacing or enterra).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (62)
7 or/4-6 (3408)
8 limit 7 to (human and english language and yr="2006 -Current") (422)
9 limit 8 to (editorial or letter or note) (41)
10 case report/ (1044935)
11 8 not (9 or 10) (352)

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(1) Anand C, Al-Juburi A, Familoni B, Rashed H, Cutts T, Abidi N et al. Gastric electrical stimulation is safe and effective: a long-term study in patients with drug-refractory gastroparesis in three regional centers. Digestion 2007; 75(2-3):83-9.

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(5) Lin Z, Hou Q, Sarosiek I, Forster J, McCallum RW. Association between changes in symptoms and gastric emptying in gastroparetic patients treated with gastric electrical stimulation. Neurogastroenterol Motil 2008; 20(5):464-70.

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