GASTROELECTRICAL STIMULATION FOR GASTROPARESIS

QUESTION(S) TO BE ADDRESSED:

1. Is gastroelectrical stimulation clinically effective and safe in controlling symptoms and improving quality of life in patients (children and adults) with intractable nausea and vomiting from idiopathic or diabetic gastroparesis refractory to conventional medical management?

2. Is gastroelectrical stimulation cost-effective in controlling symptoms and improving quality of life in patients (children and adults) with intractable nausea and vomiting from idiopathic or diabetic gastroparesis refractory to conventional medical management?

SUMMARY:

- **Background:** Gastroparesis is a chronic disorder characterised by delayed emptying of the stomach in the absence of mechanical obstruction. Symptoms include nausea and protracted vomiting. In severe cases, patients may suffer dehydration, poor nutritional status, and poor glycaemic control (in diabetics) which may require hospitalisation.
- Conventional management of gastroparesis includes dietary modification and prokinetic/anti-emetic medications. A proportion of patients will be refractory to these measures.
- Gastroelectrical stimulation (GES) is a treatment option for individuals with intractable gastroparesis. The treatment involves the insertion of electrodes, which are fixed to the muscle of the distal stomach. The connector end of each lead is then attached to the neurostimulator. When the neurostimulator is turned on, electrical impulses are delivered via the electrodes. The aim of GES is to reduce symptoms and enhance gastric emptying.
- The prevalence of gastroparesis is difficult to estimate due to diagnostic difficulties and inconsistencies between definitions, and is not reliably reported in the literature. In 2002, the prevalence of severe, symptomatic and medically refractory gastroparesis in the United States population was estimated at 0.017% or 17 per 100,000 people.[3]
- Women appear to be disproportionately susceptible to gastroparesis from any cause. We found no data on the prevalence of gastroparesis in children.
- Studies suggest that diabetic gastroparesis affects about 20% to 50% of patients with type 1 diabetes and up to 30% of patients with type 2 diabetes, especially those with long-standing disease.

- **Clinical Effectiveness:** We identified two systematic reviews (SRs) of GES in adult patients with gastroparesis; we also found one randomised controlled trial (RCT) and one comparative case series published subsequent to the SRs.
- The earlier SR found that GES was associated with statistically significant improvements from baseline in total symptom severity score, vomiting severity score, nausea severity score and the need for enteral or parenteral nutritional support. There were also statistically significant improvements in SF-36 physical composite and mental composite quality of life scores.
- The other SR reported that GES significantly improved symptoms and gastric emptying overall. However both total symptom severity score and gastric retention significantly improved in patients with diabetic gastroparesis (DG), while gastric retention in idiopathic gastroparesis (IG) patients and post-surgical gastroparesis (PSG patients) did not reach statistical significance.
- The RCT also suggests some improvement in symptom scores, gastric emptying and hospitalisation. The study also showed improvements in quality of life. However this study was so small that the results may not be valid and/or generalisable to a larger population of patients.
- The comparative case series which compared GES with gastrectomy found that, of the patients in the GES group, 63% rated their symptoms as improved versus 87% in the primary gastrectomy group. There was no significantly difference in mortality rates.
- We included two case series of GES in children with gastroparesis. The studies suggest that GES is effective in children with gastroparesis. These results should be interpreted with caution because both studies were very small (including a total of 25 patients), uncontrolled and from single centres.

- **Cost Effectiveness:** We did not find any cost-effectiveness studies of GES in patients with gastroparesis refractory to conventional medical management.

- **Safety:** The most commonly reported adverse event associated with GES is infection at the site of device implantation. Other complications related to the device include erosion, migration and stomach wall perforation.
- The frequency of device removal reported in the literature was around 10%. Two cases of death due to small bowel infarction and heart failure were reported in one study. No adverse effects were reported in the studies of GES in children.

- **Activity and Cost:** The North East Treatment Advisory Group produced a costing report on GES for gastroparesis in 2010. Their report estimated that the cost for implantation of an Enterra™ device is between £16,000 and £18,000 per patient. This included all pre-, peri- and postoperative care and hardware costs, although additional costs may arise where there are complications.

- **Equity:** We did not identify any specific equity issues relating to gastroelectrical stimulation for gastroparesis.

1 Context

1.1 Introduction

Gastroparesis is a chronic disorder characterised by delayed emptying of the stomach in the absence of mechanical obstruction. The most common symptoms are nausea and protracted vomiting.[1] In severe cases, patients may suffer dehydration, poor nutritional status and poor glycaemic control (in diabetics) which may require hospitalisation.[2-4]

Although gastroparesis is often associated with diabetes,[5] it is also found in chronic pseudo-obstruction, connective tissue disorders, Parkinson's disease, and mental illness. [6] Conservative treatment options for gastroparesis include modification of dietary intake and pharmacological therapy with prokinetic agents, such as metoclopramide, and anti-emetic agents, such as metoclopramide, granisetron or ondansetron. Patients with severe (drug refractory) gastroparesis may require jejunostomy[a] tube insertion for nutritional support, gastrostomy[b] tube insertion for stomach compression and pyloroplasty[c].[1, 7]

Data on surgical therapy for gastroparesis are limited. Complete gastrectomy[d] may provide symptom relief in cases of post-surgical gastroparesis.[8] Gastric pacing and gastroelectrical stimulation (GES) are also options for treating refractory gastroparesis.

Gastric pacing with a gastric pacemaker involves the use of a set of pacing wires attached to the stomach and an external electrical device that provides a low-frequency, high-energy stimulation to entrain the stomach at a rhythm of three cycles per minute. However, the gastric pacemaker is cumbersome and problematic for chronic use because of external leads.[6]

GES is distinct from gastric pacing. It involves abdominal surgery to implant a neurostimulator into the abdomen. The Enterra™ system manufactured by Medtronic is currently the only GES device commercially available.[1, 6]

1.2 Existing national policies and guidance

In May 2014, the National Institute for Health and Care Excellence (NICE) issued interventional procedures guidance (IPG489)[1] on gastroelectrical stimulation for gastroparesis. The guidance recommends the following;

- Current evidence on the efficacy and safety of gastric electrical stimulation for gastroparesis is adequate to support the use of this procedure with normal arrangements for clinical governance, consent and audit.
- During the consent process, clinicians should inform patients considering gastric electrical stimulation for gastroparesis that some patients do not get any benefit from it. They should also give patients detailed written information about the risk of complications, which can be serious, including the need to remove the device.
- Patient selection and follow-up should be done in specialist gastroenterology units with expertise in gastrointestinal motility disorders, and the procedure should only be performed by surgeons working in these units.

[a] Jejunostomy is the surgical creation of an opening (fistula) through the skin at the front of the abdomen and the wall of the jejunum (part of the small intestine). It can be performed either endoscopically, or with formal surgery.
[b] Gastrostomy is the creation of an artificial external opening into the stomach for nutritional support or gastrointestinal compression
[c] Pyloroplasty is surgery to widen the opening in the lower part of the stomach (pylorus) so that stomach contents can empty into the small intestine (duodenum).
[d] Gastrectomy is a medical procedure that involves surgically removing all or part of the stomach.

- Further publications providing data about the effects of the procedure on symptoms in the long term and on device durability would be useful.

2 Epidemiology

The prevalence of gastroparesis is difficult to estimate due to diagnostic difficulties and inconsistencies between definitions. Women appear to be disproportionately susceptible to gastroparesis from any cause. Some commentators speculate that this may be because of higher levels of progesterone in women, which can affect smooth muscle motility.[9] We found no studies of the prevalence of gastroparesis in children.[10]

A high prevalence of gastroparesis has been reported in patients with diabetes, and the number of cases appears to be increasing due in part to the rise in the incidence of diabetes.[2] Studies suggest that diabetic gastroparesis affects about 20% to 50% of patients with type 1 diabetes and up to 30% of patients with type 2 diabetes, especially those with long-standing disease.[3] However, these studies were from tertiary academic medical centres where the prevalence is expected to be higher than the general population. In one community study, the prevalence was estimated to be about 5% among type 1 diabetics, 1% among type 2 diabetics and 0.2% in non-diabetics.[11] More community-based data are required to confirm or enhance the published figures.

The prevalence of severe, refractory gastroparesis is seldom reported in the literature. In 2002, the prevalence of severe, symptomatic and medically refractory gastroparesis in the United States population was estimated at 0.017% or 17 per 100,000 people.[3]

3 The intervention

The Enterra™ is an implantable device developed to provide GES. Unlike gastric pacing, the Enterra™ delivers a high-frequency (12 cycles per minute), low-energy stimulation to the stomach. This stimulating frequency does not entrain the stomach, and therefore does not normalise gastric dysrhythmias; hence, the term GES is employed to differentiate between the Enterra and gastric pacing.[7]
The Enterra System was designed to treat intractable nausea and vomiting secondary to gastroparesis. The Enterra™ implant has a neurostimulator and two intramuscular leads. Implantation is done by an open or laparoscopic approach under general anaesthesia. The stimulating electrode of each intramuscular lead is fixed to the muscle of the distal stomach. The connector end of each lead is then attached to the neurostimulator, which is placed in a pocket in the abdominal wall. When the neurostimulator is turned on, electrical impulses are delivered. The rate and amplitude of stimulation can be adjusted wirelessly with a hand-held external programmer. Patients may need to return to hospital for adjustment or reprogramming of the device, to optimise the effect on gastric emptying.[1]

4 Findings

We carried out a literature search on 19 December 2014. We searched Medline, Embase, the Cochrane Library, Trip, DARE and NHS Evidence for systematic reviews, clinical trials, comparative studies and economic evaluations of GES for gastroparesis in both adults and children. We also searched PubMed for the last three months for any recent e-publications ahead of print publication. The search was limited to English language and the last 10 years.

We identified two systematic reviews (SRs) [2, 9] of GES in adult patients with gastroparesis; we also found one randomised controlled trial (RCT) [12] and one comparative case series [14] published subsequent to the SRs.

We did not find any SRs or RCTs of GES in children with gastroparesis. We found three case series, [17-19] of which we included two, because the third[19] only included three patients. We also found a case series[20] which included patients with functional dyspepsia as well as those with gastroparesis. However we did not include this as the results of this study did not differentiate between those with or without gastroparesis.

4.1 Evidence of effectiveness

Evidence of effectiveness in adults (See Table 1 for summary of results)
O'Grady et al[2] conducted a SR and meta-analysis to examine the evidence for the effectiveness of GES, primarily in patients with medically refractory gastroparesis of diabetic or idiopathic origin. The review included 13 studies. Only one of these was a randomised comparison (n=33).[16] There were nine prospective case series and three retrospective case series.

This review reported that GES was associated with statistically significant improvements from baseline in total symptom severity score (3/13 studies, mean difference 6.52 [CI: 1.32, 11.73], p=0.01), vomiting severity score (4/13, 1.45 [CI: 0.99, 1.91], p<0.0001), nausea severity score (4/13, 1.69 [CI: 1.26, 2.12], p<0.0001) and the need for enteral or parenteral nutritional support (8/13, OR 5.53 [CI: 2.75, 11.13], p<0.001). There were also statistically significant improvements in SF-36 physical composite and mental composite quality of life scores.

Chu et al[9] carried out an SR and meta-analysis to assess the effects of GES on symptoms and gastric emptying in patients with gastroparesis, and the effects of GES on the three subgroups of gastroparesis (diabetic gastroparesis (DG), idiopathic gastroparesis (IG) and postsurgical gastroparesis (PSG)). This study included ten studies (*n* = 601); only two of which were randomised, double-blind trials,[8, 16] the others being uncontrolled observational studies.
The review reported that GES significantly improved symptoms and gastric emptying overall. However both total symptom severity score (TSS) ($P < 0.00001$) and gastric retention at 2 h ($P = 0.003$) and 4 h ($P < 0.0001$) significantly improved in patients with DG, while gastric retention at 2 h ($P = 0.18$) in IG patients, and gastric retention at 4 h ($P = 0.23$) in PSG patients, did not reach significance. The results from the RCT were not significant on their own. The authors concluded that GES is an effective and safe method for treating refractory gastroparesis. DG patients seem the most responsive to GES, both subjectively and objectively, while the IG and PSG subgroups are less responsive and need further research.

The two systematic reviews were well conducted; the questions were well defined and eligibility criteria were clear. However, they were limited by the lack of high-quality studies available. Most of the studies were uncontrolled case series, so the results may be affected by changes in the symptoms attributable to other factors, such as the natural history of the condition or the placebo effect.

McCallum et al[12] carried out an RCT of 32 patients with gastroparesis of idiopathic origin (see Figure 1 for study design). The primary objective of their study was to test for an improvement in weekly vomiting frequency (WVF) when the device was turned on, compared to when the device was turned off, during blinded, three-month, crossover phases. The secondary goal was to demonstrate a reduction in symptom scores and to assess changes in quality of life, gastric

emptying, number of days in hospital, and body mass index (BMI) in the idiopathic gastroparesis cohort when receiving active stimulation for up to 12 months.

They reported that during the unblinded on period, there was a significant reduction in WVF from baseline (61.2%, P <0.001). At one year after the blinded phase, the mean WVF was 87% lower, (P < 0.001). This was accompanied by improvements in gastroparesis symptoms, gastric emptying and days of hospitalisation (P < 0.05).

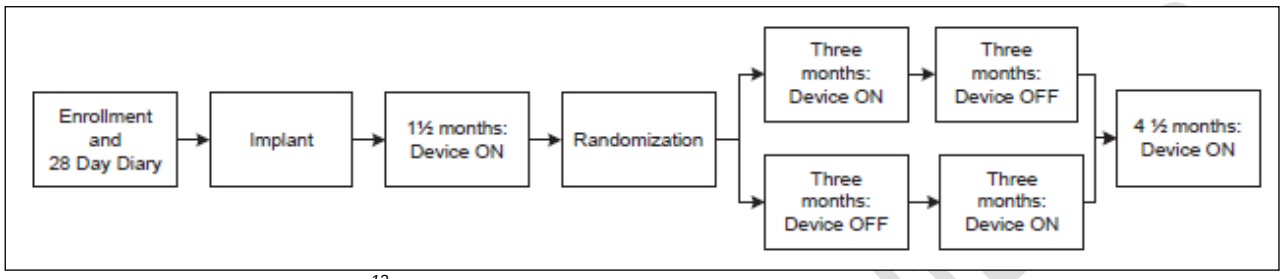

Figure 1: Design of McCallum et al[12]

The study had a number of limitations. The question was well defined and eligibility criteria were clear. However, the study only included a small number of patients. The authors pointed out that the lack of wash-out period between the on and off periods may have masked the effect of GES. The carry-over effect induced by GES for first 1½ months in all participants, and 4½ months in half of them, may have biased the study.

All the authors received funding from Medtronic, who also paid for the study and were involved in its design and analysis.

Zehetner et al[14] carried out a retrospective chart review of 103 patients who had surgical treatment for medically refractory gastroparesis. 72 patients had GES implanted and 31 had either subtotal or total gastrectomy. Of the GES group, 63% of the patients rated their symptoms as improved versus 87% in the primary gastrectomy group (p=0.02). There was no significant difference in mortality rates. Some patients who did not respond to GES had subtotal gastrectomy. The authors concluded that GES is an effective treatment for medically refractory gastroparesis but that subtotal gastrectomy should also be considered.

The study only included a small number of patients from one centre and the data were collected retrospectively. One of the authors was a consultant for Medtronic.

<u>*Evidence of effectiveness in children*</u> (*See Table 2 for summary of results)*
Islam et al[17] reported on an uncontrolled study of nine consecutive patients younger than 18 years old with gastroparesis who underwent temporary and/or permanent GES.

At baseline, all the patients were symptomatic. The authors reported significant improvements in combined symptoms score (p=0.04), nausea (p=0.039), and vomiting (p=0.0016) at follow-up (8 to 42 months). However there was no change in the rates of gastric emptying. The authors concluded that GES can be successfully applied to adolescents with intractable nausea and gastroparesis symptoms who fail to respond to medical therapy.

Teich et al[18] carried out a retrospective review of 16 consecutive children with functional dyspepsia and gastroparesis refractory to medical therapy implanted with the Enterra system to assess the feasibility and clinical outcomes of the intervention.

The authors found that, after permanent GES, there was significant improvement in symptom score compared to baseline for severity of vomiting 2.57 vs. 0.46, frequency of vomiting 2.42 vs. 0.39, frequency of nausea 3.79 vs. 1.57 and severity of nausea 3.29 vs. 1.07. They conclude that GES improves health in children with functional dyspepsia and gastroparesis who did not respond to medical therapy.

These studies suggest that GES is effective in children with gastroparesis. However, the results should be interpreted with caution because both studies were very small, uncontrolled and carried out at single centres. Therefore the findings reported may not be valid and/or generalisable to a larger population of patients.

4.2 Trials in progress

NCT00903799: A randomised study of the clinical efficacy and efficiency of gastric electrical stimulation (Enterra®) for refractory nausea and/or vomiting is ongoing, but not recruiting. The estimated study completion date is February 2016.

NCT00568373: An open-label study of gastric electric stimulation-Enterra Therapy for the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology is currently recruiting. The estimated study completion date is December 2016.

4.3 Evidence of cost-effectiveness

We did not find any cost-effectiveness studies of GES in patients with gastroparesis refractory to conventional medical management.

4.4 Safety

Adverse effects and other post-operative treatment sequelae were not consistently reported in the studies. The reported complications relate to the insertion of the device. The most common adverse event associated with GES appears to be infection at the site of device implantation. Other complications related to the device include erosion, migration and stomach wall perforations.

The frequency of device removal reported in the literature was around 10%.[2,3,9,12] Infection was reported to occur in about 5% to 10% of cases,[3] skin and lead erosion in 1% [13] and one study reported a case of gastric perforation. One study[14] reported two cases of death due to small bowel infarction and heart failure.

No adverse effects were reported in the studies of GES in children.

Table 1: Summary of evidence for effectiveness of GES in adult patients with gastroparesis

Study	Patients	Intervention	Control	Outcomes
O'Grady et al 2009[2] SR with MA 13 studies	Adult patients with medically refractory gastroparesis N=364	High frequency GES Only studies evaluating permanently implanted high frequency GES were included	Any	12 Month outcomes preferred **Symptom Improvement - Total Severity Score (TSS) – 3 Studies** GES demonstrated significant benefit over sham GES or baseline – WMD for TSS change = 6.52 [CI 1.32 to 11.73, p=0.01] However significant heterogeneity noted between studies **Vomiting Severity Scores – 4 Studies** WMD for change from baseline =1.45 [CI 0.99 to 1.91, p<0.0001] **Nausea Severity Scores – 4 Studies** WMD for change from baseline =1.69 [CI 1.26 to 2.12, p<0.0001] **SF 36 PCS (Physical) - 4 Studies** WMD for change from baseline = 8.05 [CI 5.01 to 11.10, p=<0.0001] **SF 35 MSC (Mental) - 4 Studies** Mean difference = 8.16 [CI 4.85 to 11.47, p=<0.0001] **Requirement for enteral or parenteral nutrition – 8 Studies** Baseline 96 Patients reduced to 21 patients after GES 78% reduction [p<0.001] **Weight gain in kg – 4 Studies** Non-significant result 3.68kg [CI -0.23 to 7.58, p=0.07] **Solid gastric emptying 2 hours - 4 Studies (highly heterogeneous)** WMD at 2 hours = 23.2% [CI 7.9 to 38.4%, p=0.003] **Solid gastric emptying 4 hours - 5 Studies** WMD at 4 hours = 12.7% [CI 9.8 to 15.6%, p<0.0001 **Device Complications - 10 Studies** Device removal 22/265 patients (8.3%)
Chu et al 2012[9] SR and MA 10 studies	Adult patients with gastroparesis N=601	High frequency GES Only studies evaluating permanently implanted high frequency GES were included therefore studies using GES for <1 month were excluded	Any	**Symptom Improvement - Total Severity Score (TSS) – 6 Studies** Summary weighted mean difference (WMD) 6.80 [CI 4.04 to 9.57, p<0.00001] **Vomiting Severity Scores – 5 Studies** WMD from baseline 1.42 [CI 1.22 to 1.62, p<0.00001] **Nausea Severity Scores – 5 Studies** WMD from baseline = 1.47 [CI 1.82 to 2.11, p<0.0001] **Solid gastric emptying 6 Studies** WMD at 2 hours = 22.6% [CI 11.82 to 33.37%, p=0.0001] **Solid gastric emptying 4 hours 7 Studies** WMD at 4 hours = 13.04% [CI 7.44 to 18.64%, p<0.00001 **Device complications - 8 Studies** Infection = 3.87%; Pain at site =0.67%; Lead or device migration = 2.69%; 1.18% had complications of peptic ulcer disease, penetration of electrode into

				lumen of stomach, skin erosion, small bowel obstruction caused by the wires and other effects related to the physical effects of the device.
McCallum et al 2013[12] Cross over RCT (8 centres) USA **All authors received funding from manufacturer**	Adult patients with gastroparesis of idiopathic origin n=32 (n=25 analysed)	GES Baseline scores (pre-GES symptom scores were compared to post-GES results)	None	**Unblinded on period prior to randomisation** Median reduction in WVF 61.2% (P < 0.001) - 17.3 episodes at baseline vs. 5.5 at 1½ months. Mean TSS for frequency decreased (14.6%, p<0.001) from 21.4 to 16.1 points. **Reduction in WVF and TSS in crossover phase (for 3 months) -** on state vs. off state Median WVF 6.4 vs. 9.8, p=1.000* Frequency of TSS (mean ±SD) 16.0± 6.29 vs. 17.19±6.98, p=0.932 Severity of TSS (mean ±SD) 12.10± 5.83 vs. 13.81±6.95, p=0.556 Within-patient median reduction in WVF was 17% (P > 0.10). **Reduction in WVF at 12 months (12 months with ON stimulation)** Median % reduction 87.1% p<0.001 (17.3 episodes at baseline vs. 2 at 12 months) **Improvements in GP symptoms, QOL, gastric emptying and days of hospitalisation at 12 months (baseline vs. 12 months)** Frequency of TSS (mean ±SD) 21.74± 5.16 vs. 13±7.92, p<0.001 Severity of TSS (mean ±SD) 18.05± 6.34 vs. 1.16±1.42, p=0.114 QoL - PCS (mean ±SD) 32.66± 8.8 vs. 37.86±13.28, p=0.043 QoL - MCS (mean ±SD) 34.11± 11.67 vs. 41.27±12.29, p=0.001 Gastric retention at 2h (median) 63.5 vs.49, p=0.016 Gastric retention at 4h (median) 28 vs. 16.5, p=0.236 Days in hospital (median) 2 vs. 0, p=0.006
Zehetner et al 2013.[14] Controlled unrandomised study USA	Adult patients with medically refractory gastroparesis n= 103	GES n=72	Gastrectomy n=31	**Treatment effect (GES vs. Gastrectomy) -** Median follow-up time was 33.3 months Symptoms improved 63% vs. 87% p=0.02 Symptoms same 15% vs. 10% (p values not reported) Mortality 2.7% vs. 3.2% (no significant difference; p =1.00)

GES-gastroelectrical stimulation; IG- idiopathic gastroparesis; MCS-mental component score; NSS-nausea severity score; PCS-physical component score; PSG-post-surgical gastroparesis; QoL-quality of life; SMW – symptom monitor worksheet; TSS-total symptom severity score; VSS-vomiting severity score; WMD-weighted mean difference; WVF-Weekly vomiting frequency.

** This appears anomalous and we can't find any explanation for this, it may be a computational or other error.*

Table 2: Summary of evidence for effectiveness of GES in children with gastroparesis

Study	Patients	Intervention	Control	Outcomes
Islam et al 2008[17] Open label prospective case series	Patients ≤ 18 years old with gastroparesis n=9	Temporary and permanent GES Baseline scores (pre-GES symptom scores were compared to post-GES results)	None	**Symptom scores - Baseline vs. Temporary stimulation vs. Permanent stimulation** **VSS** (mean±SD)- 1.9±1.7 vs. 0.13±0.35 (p=0.03) vs. 0.44±1.01 (p=0.016) **NSS** (mean±SD)- 3.1±0.8 vs. 1.13±1.0 (p=0.06) vs. 1.6±1.5 (p=0.03) **TSS** (mean±SD)- 11.1±3.6 vs. 5.4±3.9 (p=0.06) vs. 6.7±3.2 (p=0.045) **IDIOMS**[e] (mean±SD)-15.7±2.6 vs. not performed vs.8.8±5.3 (p=0.001 No change in gastric emptying
Teich et al 2013[18] Retrospective case series	Patients ≤ 19 years old with functional dyspepsia and gastroparesis n=16	Permanent ± temporary GES Baseline scores (pre-GES symptom scores were compared to post-GES results)	None	**Symptom scores for severity of symptoms – baseline vs. post GES** **VSS** - 2.57±1.45 vs. 0.46±1.08 (p=0.05) **NSS** - 3.29±0.83 vs. 1.07±1.00 (p=0.05) **TSS** - 16.50±4.88 vs. 6.00±4.66 (p=0.05) **Symptom scores for frequency of symptoms – baseline vs. post GES** **VSS** - 2.42±1.55 vs. 0.39±0.83 (p=0.001) **NSS** - 3.79±0.43 vs. 1.57±1.55 (p=0.001) **TSS** - 18.64±5.58 vs. 7.50±6.05 (p=0.001)

GES-gastroelectrical stimulation; IDIOMS- investigator-derived independent outcome measure scores; NSS-nausea severity score; QoL-quality of life; SMW-symptom monitor worksheet; TSS-total symptom severity score; VSS-vomiting severity score; WMD-weighted mean difference; WVF-Weekly vomiting frequency.

[e] IDIOMS- investigator-derived independent outcome measure scores: this was used to evaluate the intensity of hospital service, severity of illness and number of nongastrointestinal organ systems involved.

4.5 Summary of section 4

We identified two systematic reviews of GES in adult patients with gastroparesis; we also found one randomised trial and one comparative case series published subsequent to the SRs.

The earlier SR reported that GES was associated with statistically significant improvements from baseline in total symptom severity score, vomiting severity score, nausea severity score and the need for enteral or parenteral nutritional support. There were also statistically significant improvements in SF-36 physical composite and mental composite quality of life scores.

The other SR reported that GES significantly improved symptoms and gastric emptying overall. However both TSS and gastric retention significantly improved in patients with DG, while gastric retention in IG and PSG patients did not reach significance.

These findings should be interpreted with caution because of number of methodological shortcomings, including the lack of well-conducted controlled studies, and heterogeneity in the way that studies were conducted and outcomes measured. These factors limit the confidence in meta-analytic results and greatly limit interpretation of the clinical impact of results.

The RCT also suggests some improvement in symptom scores, gastric emptying, hospitalisation and quality of life. However this study was so small that the results may not be valid and/or generalisable to a larger population of patients.

The comparative case series which compared GES with gastrectomy found a statistically significant difference between patients who rate their symptoms as improved in favour of the gastrectomy group. There was no significant difference in mortality rates.

We did not find any SRs or RCTs of GES in children with gastroparesis however we identified three but included two case series as the third only studied three patients. The studies suggest that GES is effective in children with gastroparesis again these results should be interpreted with caution because both are very small (total of only 25 patients), uncontrolled and single centre studies. The inherent biases mean that the findings reported may not be valid and/or generalisable to a larger population of patients.

The reported complications of the procedure relate to the surgical nature of the insertion of the leads and neurostimulator. The most common adverse event associated with GES appears to be infection at the site of device implantation. Other complications include erosion, migration and stomach wall perforations. The frequency of device removal reported in the literature was around 10%. Two cases of death due to small bowel infarction and heart failure were reported in one study. No adverse effects were reported in the studies of GES in children.

We did not find any cost-effectiveness studies of GES in patients with gastroparesis refractory to conventional medical management.

5 Cost and Activity

The North East Treatment Advisory Group produced a costing report on GES for gastroparesis for the North East Specialised Commissioning Team in 2010. Their report estimated that the cost for implantation of an Enterra™ device is between £16,000 and £18,000 per patient. This included all pre-, peri- and postoperative care and hardware costs, although noting additional costs may arise where there are complications.[15] This estimate was calculated based on the HRG tariff price in 2010 and the cost of the device.

6 Equity issues

We did not identify any specific equity issues relating to gastroelectrical stimulation for gastroparesis.

7 Discussion and conclusions

Is gastroelectrical stimulation clinically effective and safe in controlling symptoms and improving quality of life in patients with intractable nausea and vomiting from idiopathic or diabetic gastroparesis refractory to conventional medical management?

The current but limited evidence particularly in children suggests that GES produces significant symptomatic relief and improvements in two- and four-hour gastric emptying rates in patients with gastroparesis refractory to conventional medical management. Reductions in healthcare use such as enteral and parenteral nutrition were also reported.

However, the evidence is largely derived from lower quality studies. The lack of well-conducted, controlled studies and heterogeneity in the way that studies were conducted as well as the outcomes measured limit the confidence in the conclusions drawn from these studies. These factors also greatly limit interpretation of the clinical impact of results.

Is gastroelectrical stimulation cost-effective in controlling symptoms and improving quality of life in patients with intractable nausea and vomiting from idiopathic or diabetic gastroparesis refractory to conventional medical management?

We do not know. We did not find any cost-effectiveness studies of GES in patients with gastroparesis refractory to conventional medical management.

8 References

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9 Search Strategy

Search date: 19 December 2014
Databases searched: Medline, Embase, Cochrane, TRIP and NICE Evidence

Medline search:
1. ((gastroelectric* or gastro electric* or gastric electric*) adj3 stimulat*).ti,ab.
2. (gastr* nerve adj3 stimulat*).ti,ab.
3. (gastr* adj3 neurostimulat*).ti,ab.
4. enterra.ti,ab.
5. (Electric Stimulation Therapy/ or Electric Stimulation/) and (gastroparesis or gastric empty*).mp.

6. 1 or 2 or 3 or 4 or 5
7. limit 6 to (english language and yr="2004 -Current")

Population	Intervention	Comparator	Outcomes	Studies

Adults with intractable nausea and vomiting from idiopathic or diabetic gastroparesis refractory to conventional medical management	Gastroelectrical stimulation	Conservative and/or pharmacological therapies	Clinical effectiveness
			• Symptom Improvement measured by Total Severity Score (TSS)
			  ○ Vomiting Severity Scores
			  ○ Nausea Severity Scores
			  ○ Solid Gastric Emptying
			• Requirement for prokinetic and antiemetic use
			• Requirement for enteral or parenteral nutrition
			• Weight gain
			
			Device Complications
			
			Quality of life
			• SF 36 PCS (Physical)
			• SF 35 MSC (Mental)
			
			Cost effectiveness
				Meta-analyses
				Systematic reviews
				RCTs
				Other controlled studies
				Cohort studies
				Case series (excluding single patient case reports or studies with <5 patients)
				
				Health economic analyses
				Resource utilisation studies

Children with intractable nausea and vomiting from idiopathic or diabetic gastroparesis refractory to conventional medical management	Gastroelectrical stimulation	Conservative and/or pharmacological therapies		