Gastric Pacing For Diabetic Gastroparesis - Does It Work?

Abstract:

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Abstract
The management of diabetic gastroparesis resistant to medical therapy is very difficult. Gastric electrical stimulation (GES) is a relatively new therapeutic modality which has shown some promise in international trials. It has seen use in four patients in Ireland. Our aim was to determine if GES improved patientsâ outcomes in terms of duration and cost of inpatient stay and glycaemic control. We reviewed the patientsâ case notes and calculated the number of days spent as an inpatient with symptomatic gastroparesis pre and post pacemaker, the total cost of these admissions, and patientsâ average HbA1c pre and post GES. Mean length of stay in the year pre GES was 81.75 days and 62.25 days in the year post GES (p=0.89). There was also no improvement in glycaemic control following GES. GES has been ineffective in improving length of inpatient stay and glycaemic control in our small patient cohort.

Introduction
Gastrointestinal symptoms are common among patients with diabetes mellitus [1]. The main cause of these symptoms is thought to be delayed gastric emptying, or gastroparesis. Gastroparesis is usually multifactorial, with factors such as autonomic neuropathy, enteric neuropathy and sudden fluctuations in blood glucose all playing a role. Chronically elevated blood glucose levels are associated with increased rates of gastrointestinal symptoms [2], and acute hyperglycemia may also contribute to motor dysfunction in patients with diabetes [3].

Although about 50% of patients with longstanding diabetes mellitus have delayed gastric emptying when formally assessed, only a minority are symptomatic [4]. Symptoms consist of early satiety, anorexia, nausea, vomiting, epigastric discomfort, and bloating. Episodes of vomiting may occur in cycles leading to dehydration often necessitating prolonged hospital admission. Up to 12% of patients with type 1 diabetes mellitus report some symptoms of gastroparesis [5,6]. The finding of retained food in the stomach after an 8- to 12-hr fast in the absence of obstruction is diagnostic of gastroparesis [7]. All patients should have an oesophagogastroduodenoscopy to rule out structural abnormalities in the gastrointestinal tract. Gastric nuclear imaging (scintigraphy) is necessary to document delayed gastric emptying but the blood glucose should be normal at the time of testing because hyperglycemia decreases gastric motility. Scintiscanning at 15-minute intervals for 4 hours after food intake is considered the gold standard for measuring gastric emptying in detail. However, a simplified approach involving hourly scans to quantify residual gastric content is often used in practice; retention of over 10% of the meal after 4 hours is abnormal [7].

In most patients, promotility agents can reduce symptoms to a manageable level. Erythromycin is very useful when given intravenously (3 mg/kg over 45 minutes) to terminate episodes of acute gastroparesis [8], but the evidence for its use as a long term oral maintenance agent is weak [9]. Cisapride is effective in some patients but can lead to cardiac arrhythmias and cytochrome p450 interactions; its availability is therefore severely limited. Parenteral metoclopramide is an alternative to erythromycin but can have central side effects related to its antagonistic effects on dopaminergic neurons. However, its use as an oral maintenance agent may be safer than previously thought [10]. Domperidone is probably as useful as metoclopramide but current data are very limited [11].

In the most severely affected patients, who do not respond to promotility agents, gastric pacing (also known as gastric electrical stimulation (GES)) is an option. The gastric pacing device is approximately the size of a cardiac pacemaker and is implanted subcutaneously in the abdominal wall; laparoscopy is used to place electrodes in the smooth muscle about 10 cm from the pylorus along the greater curvature of the antrum. The 2 electrodes are placed 1 cm apart, tangentially, deep in the muscularis propria and connected to the operating device. There are three main methods of GES; the method in use in our institution involves the use of a low energy (300 microsecond pulse width), high frequency (12 cycles per minute) stimulator [12]. GES for diabetic gastroparesis has been used in only 4 patients in Ireland to date. The aim of our study was to determine if GES improved these patientsâ outcomes in terms of duration and cost of inpatient stay and glycaemic control.

Methods
The records of all four patients with gastric pacemakers inserted were reviewed. The number of inpatient days which each patient spent (in either Cork University Hospital or their local hospitals) due to gastroparesis in the year before pacemaker insertion was calculated and compared with the number of inpatient days spent by each patient since pacemaker insertion. Each patientâ s medical records were reviewed to confirm that the cause of admission was gastroparesis. From these figures, a cost benefit analysis was performed to see if the commencement of GES led to a reduction in the costs incurred due to inpatient admission for gastroparesis. The bed day costs were calculated using 2008 bed day costs from the Irish Health Service Executive (HSE) for Cork University Hospital (CUH). The average HbA1C for each patient for the twelve months before pacemaker was calculated and compared with the average HbA1C post

pacemaker insertion. The number of attendances which each patient had with the dietician / nutritionist was also noted. Data collection was terminated at the end of September 2007.

Results

Four patients in Ireland have had gastric pacemakers inserted; all were patients with type one diabetes mellitus. The first patient was 37 at presentation and had suffered from type one diabetes mellitus for twelve years. He had an eighteen month history of recurrent symptomatic gastroparesis, each episode lasting up to two weeks. Each episode began with nausea and bloating which were then followed by severe, intractable vomiting. He also suffered from erectile dysfunction and non nephrotic range proteinuria at diagnosis.

Our second patient was a 25 year old female with type one diabetes mellitus for twelve years also. She had a one year history of the same symptom complex as the above patient, and also suffered from nocturnal diarrhoea and faecal incontinence. She had numerous diabetic complications at diagnosis â bilateral cataracts and preproliferative diabetic retinopathy. Our third patient was a 25 year old male with type one diabetes mellitus of nineteen yearsâ duration. He presented with an eighteen month history of intractable nausea and vomiting, as well as diabetic retinopathy and stage 2 chronic kidney disease. Our fourth patient is a 60 year old female who presented with frequent episodic vomiting for two years. She had type one diabetes mellitus for over twenty years.

* patient 4 deceased

nine months post commencement of GES
** bed day cost calculated 2008 costs from the HSE for Cork University Hospital

All of these patients were resistant to promotility agents. All had an oesophagogastroduodenoscopy performed on several occasions; this revealed that all patients had severe erosive gastritis, often with superimposed candidal infection and a large residual volume of gastric secretions. Gastric scintigraphy studies were performed in all patients using a 99-Tc sulphur colloid labelled scrambled egg meal, with a normal Gastric Emptying Half-Time (GET1/2) defined as 60 to 100 mins; all patients had delayed gastric emptying. All patients had gastric pacemakers inserted in a combined procedure by the departments of gastroenterology and cardiothoracic surgery. The table below documents their outcomes in terms of number of days of hospital admission and glycaemic control (as measured by HbA1C) pre and post procedure. Patient 3 has had longer follow up than the others; in his third year of follow up (March 2006 to February 2007) he was admitted for 26 bed days and between months 37 and 43 (March 2007 to September 2007) he was admitted for 7 bed days.

As outlined in the table, there was no significant difference in the numbers of days of admission to hospital pre-GES versus post-GES for any of our patients (p = 0.89 when lengths of stay pre and post GES were compared). Glycaemic control was not significantly affected either. None of the patients have had repeat gastric emptying studies. There was no significant difference in the number of attendances each patient had with the dietician / nutritionist pre and post GES. When each patientâ s case notes were reviewed in more detail, each patient was on broadly similar nutritional supplementation pre and post GES. Symptomatology pre and post GES was not formally assessed but only patient 3 reported any subjective improvement in his symptoms after GES.

Discussion

It is clear from the above that gastroparesis places a large burden on the Irish healthcare system. In 2008, the cost of a general medical bed in Cork University Hospital per patient per day was 990 euro. Therefore (using 2008 costs), it cost 118100 euro to keep patient 3 as an inpatient for the year preceding his gastric pacemaker insertion. This huge cost has also been shown in the United States where, in just one state (North Carolina), diabetic gastroparesis accounted for 7850 bed days in one year which had a total cost of $11,378,446 [13]. (For the purposes of comparison the

population of North Carolina is approximately 9.4 million). Our study also showed that the amount of time that patients with gastric pacemakers spent as inpatients did not decrease significantly after pacing. Also, the glycaemic control of all four patients remained static despite pacemaker placement.

Very few trials internationally have used an objective measure of patient improvement such as number of days spent as an inpatient, although some studies have shown that GES improves symptoms and quality of life [14-18]. Most studies which show an improvement in quality of life following gastric pacing have been unable to show any acceleration in gastric emptying rate. This is particularly relevant as it has been shown that delayed gastric emptying as detected radiologically predicts morbidity in gastroparesis patients [19]. Our patient cohort had no improvement in glycaemic control post GES. One study has shown an improvement in HbA1C at 6 and 12 months post GES, as well as symptomatic patient improvement [20]; however most studies have focussed almost entirely on symptomatic improvement rather than improvements in metabolic control.

Long-term open-label studies of gastric stimulation (3 to 4 years follow up) have reported relief of symptoms and a reduced need for nutritional support [21-23]. One of the longest and largest studies on GES followed 156 patients for a median of 4 years, and demonstrated general symptomatic improvement but no objective measure of patient illness such as bed-days was used [24]. Our patient with the longest duration of illness is showing progressive reductions in the number of bed days he is admitted for each year and is also feeling slightly better (self reported), but it is difficult to use this as evidence of long-term benefit with GES. Lin et al showed sustained reductions in severity of illness and length of hospital stay in patients receiving gastric electrical stimulation therapy beyond three years; however their improvements were sustained and persistent rather than additive [21]. Meta-analyses have urged caution as the long term benefit of GES is as yet unproven [25]. Reflecting the difficulties inherent in conducting trials in this area, the United Kingdom National Institute for Clinical Excellence, in their 2004 review of diabetic gastroparesis, stated that there were â uncertainties about the efficacy of this procedure, in particular about whether the procedure benefits patients solely by altering symptoms or by accelerating gastric emptyingâ . Also, techniques for calculating the correct electrical stimulus for each patient have not been developed yet [22] and therefore GES is likely to remain an experimental tool in the majority of centres.

In summary, we concluded that the long term cost effectiveness of GES (in terms of the number of patient admissions) and its benefits for glycaemic control have yet to be proven in the Irish healthcare setting. Although the number of patients in our study was small and follow-up was limited, we cannot recommend the use of GES in patients with symptomatic diabetic gastroparesis based on our evidence to date. However, larger studies, refinement of current GES technologies and further development of new GES systems may lead to benefits for patients with this condition.

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