Reprogramming of Gastric Motility with “Pulse Therapy” (Metoclopramide and Erythromycin) in Severe Gastroparesis

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Abstract

Gastroparesis is a very common condition, however many times it becomes difficult to manage even after long-term treatment due to multiple etiologies or improper therapy. Patients with severe gastroparesis are considered candidates for gastric electrical stimulants. The “Pulse Therapy” using metoclopramide and erythromycin to reprogram gastric motility can delay or even avoid the need for gastric electrical stimulants. This case report focuses on a patient with severe gastroparesis, who was considered for a gastric pacemaker implantation and was instead treated successfully with “Pulse Therapy.” As a part of this regimen, he was given metoclopramide continuously for 3 months along with pulses of erythromycin for 10 days a month for 3 months. Patient recovered dramatically that he no longer remained a candidate for gastric pacemaker implantation. This case study emphasizes on how the proper use of prokinetic agents based on symptoms and gastric emptying study can reprogram the stomach motility in these patients with severe gastroparesis.

Keywords: Diabetic gastroparesis, erythromycin, gastric emptying study, gastroparesis, Helicobacter pylori, idiopathic gastroparesis, metoclopramide, past Helicobacter pylori infection, prokinetic agents, severe gastroparesis

Introduction

Gastroparesis and its related symptoms are among the most common gastric problems faced by patients, which emphasizes the need for it to be addressed appropriately. Many etiologies are responsible for gastroparesis, such as diabetes, chronic renal failure (CRF), previous Helicobacter pylori infection, gastric surgery, low vitamin D level, hypothyroidism etc. Patients with no discernible etiology are labeled as “Idiopathic Gastroparesis.” The treatment varies depending on the etiology. In the presence of multiple etiologies and severe gastroparesis, as illustrated here, patients are then considered candidates for gastric electrical stimulants like gastric pacemakers. With the proper use of “Pulse Therapy,” one can improve symptoms of gastroparesis and possibly avoid such invasive procedures. We illustrate that “Pulse Therapy” with metoclopramide and erythromycin reprograms the gastric motility and restores the gastric rhythm.

Case Report

A 43-year-old man admitted to hospital on 05/08/2011 with severe nausea and vomiting and his past medical history including insulin dependent diabetes mellitus (DM), CRF, diabetic retinopathy and gastroparesis. At that time, gastric emptying scintigraphy revealed severe gastroparesis. Patient was referred for consultation for possible gastric pacemaker. Patient was initially treated with ondansetron 4 mg po qid, omeprazole magnesium 20 mg po daily, famotidine 20 mg po bid and metoclopramide HCL 5 mg po tid. His HbA1c at that time was 12. His DM was treated with insulin lispro 22 units before breakfast, insulin lispro 26-28 units at dinner and insulin glargine 15-18 units at bedtime. His HbA1c improved to six and his vomiting ceased. Patient also complained of weight loss and occasional nausea. He denied abdominal pain, postprandial fullness, bloating, heart burn, diarrhea, constipation or any other changes in bowel movements.

Patient was also being treated for high cholesterol, hypertension, vitamin D deficiency and hyperphosphatemia with Stage 4 and

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Gastroparesis is a clinical condition in which patients have symptoms of delayed gastric emptying with no evidence of physiological obstruction. The most common etiology for gastroparesis is idiopathic followed by DM, post-surgical, connective tissue disorders, neurological disorders such as parkinsonism, ischemic diseases, metabolic disorders and many other less common causes.

Diabetes is the second most common etiology for gastroparesis. Studies showed that 31% of patient with gastroparesis has a diabetic etiology. Diabetic patients often have more gastrointestinal (GI) complications than the general population due to their higher prevalence of gastroparesis.[10] Nearly, 18% of the diabetic patients experienced upper GI symptoms; specifically, delayed gastric emptying is found in 27-65% of patients with Type 1 diabetes while it is found in 30% of patients with Type 2 diabetes.[11] The etiology of diabetic gastroparesis itself is numerous and not clearly established. Certain important factors include autonomic neuropathy, acute hyperglycemia, abnormalities of gut hormones and neurotransmitters, thyroid function, gastric acid secretion and H. pylori infection.[12] A causal relationship linking DM and gastroparesis is poor glycemic control since postprandial blood glucose concentrations are both determined by and a determinant of the delivery of nutrients from the stomach into the small intestines.[13]

CRF may be the cause of delayed gastric emptying theoretically because of uremia-induced neuropathy, electrolyte disturbance, vitamin D deficiency, metabolic acidosis and anemia.[6] To conclude, CRF as a cause of delayed gastric emptying, we have to take into consideration several factors specific to patient such as current blood urea nitrogen and creatinine level, duration of renal failure, history of hemodialysis or peritoneal dialysis or conservative treatment and the study used for timing gastric emptying. There are conflicting reports for improvement of gastric retention after hemodialysis; while some report shows improvement.[18] Others showing no improvement.[19]

Non-pharmacological therapy should be tried first in patients who have less severe symptoms of gastroparesis. Non-pharmacological measures includes mainly dietary modifications such as small frequent meals, more liquid based diet and avoidance of solid foods and high fat meals.[13] Symptomatic gastroparesis requires pharmacological treatment mainly with prokinetic medications such as metoclopramide, erythromycin and domperidone.[7,8] Amongst these, domperidone is not approved for any medical condition in US.[9] Metoclopramide is a combined serotonin (5-hydroxytryptamine,) agonist and dopamine D2 antagonist.[7,9] It stimulates esophageal, stomach and small intestinal contractions and enhances gastric emptying. Erythromycin acts on motilin receptors present on neural and smooth muscles, which potentiates gastro-duodenal motility.[7,11]

Following two tables [Tables 1 and 2] are the proposed algorithms for the use of prokinetic agents in gastroparesis based on GES and severity of symptoms.

Erythromycin should be given 250 mg 3 times a day. Metoclopramide should be started 5 mg 2 times daily and can increase up to 40 mg/day according to symptoms. When taking metoclopramide, patient should be followed-up regularly every 2 weeks to monitor symptom control and to identify any development of side-effects of metoclopramide, especially those related to cardiac and central nervous system.

Our patient is diabetic, with end stage renal disease on dialysis and was also previously treated for H. pylori infection in the past. H. pylori infection damages the gastric neurons and may

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**Table 1: Gastroparesis grading and proposed treatment**

| Grade | GES t1/2 | Management recommendations* |
|-------|---------|----------------------------|
| Normal | 45-95 min | PPI and use erythromycin after correlating with clinical symptoms |
| Grade 1 | 96-120 min | PPI plus erythromycin |
| Grade 2 | 121-180 min | PPI plus erythromycin, if not improve add metoclopramide |
| Grade 3 | >180 min | “Pulse treatment” with metoclopramide and erythromycin |

*Proposed doses are discussed below; GES: Gastric emptying study
subsequently account for the delayed gastric emptying. Even after eradication of infection, gastroparesis can occur after few years due to initial damage of gastric nervous system. This effect is more pronounced with the presence of diabetes.\textsuperscript{11,12} Patient was referred to us after failing previous treatments for his gastroparesis. He continued to be symptomatic even after well management of his CRF and diabetes. Pulse Therapy for this patient would be beneficial since his stomach motility had also been altered by his previous \textit{H. pylori} infection. He was started with two prokinetic drugs, metoclopramide and erythromycin. He was given metoclopramide 10 mg 4 times daily continuously for 3 months along with 10 days of erythromycin 250 mg 3 times daily every month for 3 months. This “Pulse Treatment” showed dramatic improvement in symptoms, as well as in gastric emptying time. This proposed regimen reprograms the disturbed gastric and intestinal movements. Patients’ symptoms have improved, however he may require low dose of metoclopramide for one more month after the initial treatment.

**Conclusion**

This case report focuses on how “Pulse Treatment” with prokinetic agents improved severe gastroparesis-related symptoms and gastric emptying time in patient with past \textit{H. pylori} infection and well-controlled DM and CRF. We can avoid unnecessary endoscopic treatment or gastric electrical stimulants like pacemakers by modifying the medication approach and using two prokinetic agents as in our proposed “Pulse Therapy.”

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**Table 2: Gastroparesis grading and management plan according to symptoms and symptom score**

| Frequency of symptoms** | Symptom score** | Symptomatic grading | Symptom score range | Approximate GES t1/2 (min) | Management recommendations* |
|------------------------|----------------|---------------------|---------------------|----------------------------|----------------------------|
| None                   | 0              | None                | 1-7                 | 45-95                      | PPI and use erythromycin after correlating with clinical symptoms |
| <1/week                | 1              | Mild                | 8-14                | 96-120                     | PPI plus erythromycin     |
| 1-3/week               | 2              | Moderate            | 15-21               | 121-180                    | PPI plus erythromycin, if not improve add metoclopramide |
| >3/week                | 3              | Severe              | 22-28               | >180                       | “Pulse treatment” with metoclopramide and erythromycin |

*Proposed doses are discussed below; **Followings are the symptoms used for scoring based on their frequency as mentioned in the table – 1: Epigastric pain; 2: Postprandial fullness; 3: Early satiation; 4: Bloating; 5: Belching; 6: Nausea; 7: Heart burn; PPI: Proton Pump Inhibitor; GES: Gastric emptying study.

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