

PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

Gastroparesis: Patient Case and Brief Review

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PATIENT CASE

WD is a 69-year-old woman with a primary diagnosis of COPD with hypertension, hyperlipidemia, major depressive disorder and Type II diabetes as comorbid conditions. She lives at home with her husband who is primary caregiver.

Medications:

- Albuterol-ipratropium inhaled via nebulizer 4 times daily
- Prednisone 20mg by mouth daily
- Morphine long-acting 60mg by mouth every 12 hours
- Morphine concentrate 15mg by mouth every 3 hours as needed for pain or shortness of breath
- Venlafaxine extended-release 112.5mg (75mg + 37.5mg) by mouth every 12 hours
- Senna 2 tablets by mouth at bedtime

WD is being seen for the first time by the home hospice nurse. She is in no pain and morphine alleviates her breathless episodes. However, over the past few months she has felt bloated and increasingly nauseous. When the nausea progresses to vomiting, remnants of meals she has eaten several hours earlier are amongst the vomitus. WD reports having a regular bowel movement every other day and a recent 10-pound weight loss attributed to her nausea and vomiting. In prior weeks, her primary doctor tapered and discontinued a number of medications, including her blood pressure medications, cholesterol-lowering agent and oral hypoglycemics, to align with her goals of care. Currently her blood pressure is 115/78 and glucose is 130 by finger-stick.

INTRODUCTION

Gastroparesis is a syndrome of delayed gastric emptying of solids, in the absence of an obstruction, with main symptoms of nausea, vomiting, early satiety, belching, bloating and/or upper abdominal pain. Etiology can be idiopathic in nature but may also be due to a virus, medications (e.g., opioids, alpha-2 agonists, tricyclic antidepressants, calcium channel blockers, dopamine agonists, anticholinergics), injury to the vagus nerves (e.g., post-surgical, cancer-related) or due a chronic condition such as diabetes mellitus, neurological disease (e.g., Parkinson disease) or autoimmune disease (e.g., AIDS).^{1,2}

INITIAL MANAGEMENT

Dietary modification³

- Avoid fatty, acidic and spicy foods, alcohol and carbonated beverage consumption and smoking
- Diet should be low in non-digestible (insoluble) fiber (e.g., fresh fruits and vegetables)
- Choose soluble fiber or fiber that is cooked and reduced in particle size (e.g., mashed or pureed)
- Small, frequent meals as tolerated

Hydration and vitamin supplementation in mild severity gastroparesis only³

- Prevents resulting hypokalemia, metabolic alkalosis and dehydration from vomiting and reduced oral intake

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Improve glycemic control³

- Acute hyperglycemia may slow gastric emptying in diabetes
- Hyperglycemia may interfere with the efficacy of prokinetic medications

In patients with continued symptoms, initiate pharmacologic therapy:

Prokinetics to increase the rate of gastric emptying³

- Metoclopramide (Reglan®) – 5 to 10mg PO/IV/IM/SQ four times daily 10-15 minutes before meals and at bedtime. Initiate with 5mg dose, adjust as tolerated and continue for up to 12 weeks before providing a drug holiday. Monitor for side effects including anxiety, restlessness, depression, QT interval prolongation, dystonia and tardive dyskinesia. Metoclopramide is a dopamine antagonist and interacts with Parkinson-type medications. It is contraindicated in complete bowel obstruction.
- Erythromycin – For patients that fail a metoclopramide trial, 40 to 250mg by mouth or 3mg/kg/dose IV three times daily before meals. Continue therapy for up to 4 weeks before providing a drug holiday. Monitor for side effects including tachyphylaxis, gastrointestinal toxicity, ototoxicity, resistant bacterial growth and QT prolongation. Erythromycin is a macrolide antibiotic, but its effects on gastroparesis are not deemed a class effect—azithromycin (Zithromax®) is not a suitable substitute.

Other Medication Considerations

Domperidone, a dopamine antagonist, is available in Canada and some other countries. In the U.S., as an investigational antiemetic for cancer chemotherapy, it is only available to those enrolled in investigational studies.⁴

Cisapride promotes acetylcholine release in the gastrointestinal tract and is available in a number of countries. In the U.S., it was FDA-approved in 1993 for gastroesophageal reflux disease (GERD) and removed in 2000 due to reports of serious cardiac events. Today it is used in a limited capacity in investigational protocols for adults (with GERD, gastroparesis, pseudo-obstruction or severe chronic constipation), pediatrics (with GERD or pseudo-obstruction) and neonates (with feeding intolerance) who are unresponsive to other medications.⁴

Tegaserod, a selective serotonin (5HT-4) partial agonist, was approved for constipation-predominant irritable bowel syndrome (IBS-C) before it was withdrawn in 2007 due to reports of increased rate of heart attack, stroke, and worsening heart-related chest pain. It was then made available briefly for investigational protocols before the company stopped manufacturing. In March 2019, after a complete safety review, the FDA approved and re-introduced tegaserod for the treatment of adult women < 65 years of age with IBS-C.⁴ There is limited published data on the benefits of tegaserod in patients with gastroparesis^{5,6} but there is expert consensus for off-label use consideration for patients with malignancy-associated gastroparesis who are not responsive or have side effects with metoclopramide.⁷

Antiemetics – for persistent nausea and vomiting despite prokinetic therapy³

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- Antihistamines (e.g., diphenhydramine)
- Serotonin (5HT-3) antagonists (e.g., ondansetron)
- Phenothiazines (e.g., prochlorperazine) for symptoms despite the use of the agents above

In patients with refractory symptoms:³

- Re-evaluate compliance with dietary modification and pharmacotherapy
- Ensure nutritional support; consider jejunostomy and venting gastrostomy tube for enteral nutrition and decompression, respectively
- Parenteral nutrition can be considered but only in patients who cannot tolerate enteral nutrition despite concomitant pharmacotherapy

PATIENT CASE CONTINUED

WD's history of Type II diabetes, recent weight loss due to nausea, and vomitus containing food eaten several hours earlier are indicative of gastroparesis.^{1,2} Initial management instructions, as outlined above, are provided to WD and her husband.

WD has adhered to dietary modifications and maintained adequate hydration. It's difficult for WD and her husband to manage pureeing foods so she has opted for liquid nutrition shakes 3 times daily. She has also moved to liquid dexamethasone, in place of prednisone tablets, and liquid senna. Her long-acting morphine tablet was converted to transdermal fentanyl and venlafaxine extended-release tablet to regular-release tablets that can be crushed.

Two weeks following initial intervention for gastroparesis, WD is no longer vomiting and has not lost any more weight however the bloating and nausea continue. At this point, it is appropriate to begin a regimen of metoclopramide at 5mg by mouth before meals and at bedtime. A follow-up visit with WD four days later finds her much more comfortable with significantly less nausea.

For additional information on this topic, please review these references:

1. Longstreth GF. Approach to the adult with nausea and vomiting In: UpToDate. Talley NJ, Grover S, eds. Waltham, MA: UpToDate, Inc; Updated September 11, 2018.
2. Camilleri M. Gastroparesis: Etiology, clinical manifestations, and diagnosis In: UpToDate. Talley NJ, Grover S, eds. Waltham, MA: UpToDate, Inc; Updated September 24, 2018.
3. Camilleri M. Treatment of gastroparesis In: UpToDate. Talley NJ, Grover S, eds. Waltham, MA: UpToDate, Inc; Updated February 21, 2019.
4. Clinical Pharmacology [database online]. Tampa, FL: Elsevier/Gold Standard, Inc.; 2020.
5. Banh HL, MacLean C, Topp T, Hall R. The use of tegaserod in critically ill patients with impaired gastric motility. *Clin Pharmacol Ther.* 2005; 77:583.
6. Tougas G, Earnest DL, Chen Y, et al. Omeprazole delays gastric emptying in healthy volunteers: An effect prevented by tegaserod. *Aliment Pharmacol Ther.* 2005; 22:59.
7. Shafi MA, Nasser E, Javle M. Malignancy-associated gastroparesis: Pathophysiology and management In: UpToDate. Drews RE, Bruera E, Savarese DME, eds. Waltham, MA: UpToDate, Inc; Updated April 11, 2019.

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8. Camilleri M, et al. Clinical Guideline: Management of Gastroparesis. *Am J Gastroenterol*. 2013 Jan; 108(1): 18–38. [PDF link](#)
9. Parkman HP, Hasler WL, Fisher RS. American Gastroenterological Association. American Gastroenterological Association technical review on the diagnosis and treatment of gastroparesis. *Gastroenterology*. 2004; 127:1592. [PDF link](#)