Gastroparesis: Diagnosis and Management

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OBJECTIVES

• Brief review of the epidemiology

• Examine current mechanisms

• Provide cost-effective steps for the diagnosis of gastroparesis for practicing clinicians in a case based-approach

• Discuss tailored treatment strategies for the management of gastroparesis
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Epidemiology

Earlier reports: ~ 60% of patients with long-standing T1DM and gastrointestinal symptoms had diabetic gastroparesis \(^1\)

- these studies predated the routine use of intensive insulin therapy for T1DM

- Cumulative incidence of gastroparesis over 10 years in the only community-based study in Olmsted County \(^2\) (adjusted for age and gender):
  - 4.8% in T1DM
  - 1% in T2DM
  - 0.1% in non-diabetic people

Epidemiology

- The Rochester Diabetic Neuropathy Study from Olmsted County: 1% of patients had symptoms of gastroparesis
  
- Prevalence for nausea and/or vomiting or dyspepsia was not significantly different in type 1 or 2 diabetes relative to controls

- Symptoms of peripheral or autonomic neuropathy may not be associated with diabetic gastroparesis

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Mechanisms of Gastroparesis in Diabetes: Autonomic Dysfunction

Denervation
Gastroparesis Mechanisms: Gastrointestinal Cellular Defects- NIDDK Gastroparesis Consortium

Loss of M2 (anti-inflammatory) macrophages

Loss ICC cells

CD206

Mechanisms of Gastroparesis in Diabetes- Loss of nNOS

Control

Diabetic

Loss of nNOS expression stomach
Reduction nNOS number activity myenteric plexus

No effect on innervation
Chronic and Gastric Emptying DCCT/EDIC

Pilot Study subsample of DCCT

$^{13}$C spirulina meal

- Breath samples (15, 30, 45, 60, 90, 120, 150, 180, 240 min)
- Blood glucose (60, 120, 180, 240 min)
- Symptoms questionnaire

Delayed GE: greater DCCT baseline HbA1c, duration of DM, greater mean HbA1c over an average of 27 years of follow up (during DCCT-EDIC, $P = 0.01$), and lower R-R variability during deep breathing ($P=0.03$)
Hyperglycemia Slow Gastric Emptying

Euglycemic and hyperglycemic Clamp studies

Plumer et al, Diabetes Care 2015;38:1123–1129
Gastric Emptying, Incretin Hormones and Glycaemia

More rapid gastric emptying increases postprandial glycemia.

Acute hyperglycemia slows gastric emptying, while hypoglycemia accelerates it.

GLP-1 slows gastric emptying.

More rapid gastric emptying increases GLP-1 and GIP secretion.

GLP-1, GIP increase insulin.

GLP-1 suppresses glucagon.

Beta cell (insulin) decreases, Alpha cell (glucagon) increases.
Effects of Acute and Chronic Glycemia on Gastric Motility

Acute Hyperglycemia

- Retards gastric emptying in type 1 and type 2 diabetes:
  - Reduces proximal gastric tone
  - Suppresses antral motility
  - Stimulates piloric contractions

Acute Hypoglycemia

- Accelerates gastric emptying

Chronic Hyperglycemia

- Denervation
- Nitric oxide/ROS
- ICC
- Macrophages
- Ghrelin
- Incretins
- Slow-wave dysrhythmia

Gastroenterology. 1997;113(1):60–66
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Gastroparesis - Clinical Diagnosis

Symptoms:

- Nausea
- Bloating
- Loss of appetite
- Early satiety
- Postprandial vomiting

Examination

- Epigastric distention
- Presence of succussion splash

Gastroparesis Diagnosis

Gastric emptying with scintigraphy of digestible solids at 15-minute intervals for 4 hours after food intake

Emerging: 13C octanoic acid breath test or 13C-acetate simpler tests, safe, inexpensive and easier to use in practice

Metoclopramide

- FDA-approved for the treatment of gastroparesis
- Central and peripheral D2 receptor antagonist, but also actions on 5HT4 and 5HT3 receptor
- Weak level of evidence for benefits of metoclopramide for the management of gastroparesis
- Serious adverse effects: extrapyramidal symptoms (acute dystonic reactions; drug-induced parkinsonism; akathisia; and tardive dyskinesia)
- Use in the treatment of gastroparesis beyond 5 days is no longer recommended by the FDA and the European Medicines Agency.

Few Take Home Messages

- Prevalence of gastroparesis is changing and the pathogenesis is heterogeneous.

- If present may have important clinical consequences on nutritional status, glucose control, quality of life, depression and pain.

- Evaluate for gastroparesis in people with diabetic neuropathy, retinopathy, and/or nephropathy by assessing for symptoms of unexpected glycemic variability, early satiety, bloating, nausea, and vomiting.

- Exclusion of other causes documented to alter gastric emptying, such as use of opioids or GLP-RA receptor agonists and organic gastric outlet obstruction, is needed before performing specialized testing for gastroparesis.

Few Take Home Messages

- Gastric emptying shares an interdependent relationship with postprandial glycemia
- Optimal control of the latter is integral to the management of diabetic gastroparesis
- Metoclopramide therapy should be applied only short term