DIABETIC ENTEROPATHY: TWO DIFFICULT PROBLEMS

DIAGNOSIS AND TREATMENT

Gary L. Cornette, D.O., F.A.C.O.I
Medical Director Gastroenterology
Diabetic Enteropathy: What is it?

- Motility Disorders
  - Esophageal
  - Gastric
  - Small Bowel
  - Colon
Signs & Symptoms

- Dysphagia
- Chest Pain
- Reflux
- Abdominal Pain
- Nausea/Vomiting
- Abdominal Bloating
- Malabsorption
- Malnutrition
- Bacterial Overgrowth
- Chronic Diarrhea
- Chronic Constipation
Diabetic Gastroparesis

**Prevalence**
- 27% - 58% Type 1 Diabetes
- 30% Type 2 Diabetes
- Majority of cases are women

**Symptoms**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>90% +</td>
</tr>
<tr>
<td>Early Satiety</td>
<td>80% +</td>
</tr>
<tr>
<td>Vomiting</td>
<td>68%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>50% - 80%</td>
</tr>
<tr>
<td>Bloating</td>
<td>60%</td>
</tr>
</tbody>
</table>
# Symptom Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>76%</td>
</tr>
<tr>
<td>Upper Abdominal Location</td>
<td>36%</td>
</tr>
<tr>
<td>Constant</td>
<td>28%</td>
</tr>
<tr>
<td>Burning, Vague, or Crampy</td>
<td>64%</td>
</tr>
<tr>
<td>Nocturnal</td>
<td>80%</td>
</tr>
<tr>
<td>Exacerbated by Meals</td>
<td>60%</td>
</tr>
<tr>
<td>Relief by Meals</td>
<td>15%</td>
</tr>
</tbody>
</table>
Unpredictable Food Delivery

Affects Glycemic Control

Both Hypoglycemia and Hyperglycemia
# Pathogenesis

<table>
<thead>
<tr>
<th>Complicated</th>
<th>Aggravating Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic Neuropathy</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Central Effects</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Local Myopathy</td>
<td>Anticholinergic Meds</td>
</tr>
<tr>
<td></td>
<td>Narcotics</td>
</tr>
<tr>
<td></td>
<td>Autoimmune Disorders</td>
</tr>
<tr>
<td></td>
<td>Parkinson’s Disease</td>
</tr>
</tbody>
</table>
# Gastroparesis Severity Classification

| Grade I – Mild | • Intermittent, easily controlled symptoms with maintenance of weight and nutrition, treated with dietary modification and avoidance of medications that slow gastric emptying |
| Grade II – Compensated | • Moderate symptoms, rare hospitalizations, treated by prokinetic and antiemetic agents |
| Grade III – Gastric Failure | • Medication unresponsive, cannot maintain nutrition, frequent E.D. visits and hospitalizations |
Diagnosis and Evaluation

- Have a high index of suspicion
- Cornerstone of Diagnosis
- Nuclear Medicine
- Solid Phase Gastric Emptying Study
The Study

Recommended Meal: Toast, jam and egg whites (eggbeaters) with Tc-Sulfur

**All medications that could delay gastric emptying must be stopped 24 hours before test**
Gastroparesis – Gastric Retention

Greater than 60% at 2 hours

Greater than 10% at 4 hours

Positive Test
Reasosn for Upper Endoscopy

- High incidence of GERD in Gastroparesis may be relatively asymptomatic in Type I Diabetes – Screen for Barrett’s

- Biopsy for H. Pylori

- Rule out gastric outlet obstruction, ulcer disease, and infiltrative diseases

- Rule out gastric bezoars
IMAGES (Food in Stomach)
Type I Diabetes: Screen for Celiac Disease with Serologic Testing

- Anti-tissue transglutaminase antibody (TTG) IgA
- Anti-endomysial antibody (EMA) IgA
- Total IgA
- Patients with IgA deficiency:
  - Deamidated giladin peptide (DGP) IgG
  - Positive test should have small bowel biopsies
Treatment

Difficult and Disappointing

- Discontinue medications that inhibit gastrointestinal motility
- Dietary Modification (Dietician referral)
  - Smaller, more frequent meals
  - Reduced fat meals
  - Reduced bulk meals - remove hard to digest foods like seeds, nuts, corn, popcorn, and fiber
## Prokinetic Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism(s) of Action</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>Dopamine $D_2$ receptor antagonist, 5-HT$_4$ receptor facilitation of acetylcholine release from enteric nerves</td>
<td>5-20 mg qid</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Motilin receptor agonist</td>
<td>50-250 mg qid</td>
</tr>
<tr>
<td>Domperidone</td>
<td>Peripheral dopamine $D_2$ receptor antagonist</td>
<td>10-30 mg qid</td>
</tr>
<tr>
<td>Bethanechol</td>
<td>Muscarinic receptor agonist</td>
<td>25 mg qid</td>
</tr>
<tr>
<td>Pyridostigmine</td>
<td>Acetylcholinesterase inhibitor</td>
<td>30-60 mg tid</td>
</tr>
</tbody>
</table>
Metaclopramide

- Is it worth a trial of metaclopramide in moderate to severe Gastroparesis?

- Side effects (30% of patients experience side effects)
  - Fatigue
  - Agitation
  - Sleep disturbances
  - Hyper prolactinemia
  - Dystonia
  - Irreversible Tardive Dyskinesia

“Black Box Warning”
Erythromycin

- Beneficial for short term use only
- Tachyphylaxis occurs in almost all patients – relates to motilin receptors down regulation
Domperidone

- Not approved by FDA
- Available from Europe, Canada, and the internet
- Antiemetic effects are stronger than prokinetic effects
- Can prolong QTc interval (same as Cisapride)
## Antiemetic Medications

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Examples</th>
<th>Effects on Gastric Emptying</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine antagonists</td>
<td>Prochlorperazine, thiethylperazine</td>
<td>Variable</td>
</tr>
<tr>
<td>Muscarinic antagonists</td>
<td>Scopolamine</td>
<td>Delay</td>
</tr>
<tr>
<td>Histamine H&lt;sub&gt;1&lt;/sub&gt; antagonists</td>
<td>Dimenhydrinate, Meclinzine</td>
<td>Delay</td>
</tr>
<tr>
<td>Serotonin 5-HT&lt;sub&gt;3&lt;/sub&gt; antagonists</td>
<td>Ondansetron, Granisetron</td>
<td>Variable</td>
</tr>
<tr>
<td>Neurokinin NK&lt;sub&gt;1&lt;/sub&gt; antagonists</td>
<td>Aprepitant</td>
<td>Delay</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>Dronabinol</td>
<td>Delay</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline, Nortriptyline</td>
<td>Delay</td>
</tr>
<tr>
<td>Other antidepressants</td>
<td>Mirtazapine</td>
<td>?</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Lorazepam</td>
<td>?</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisone</td>
<td>?</td>
</tr>
</tbody>
</table>
Severe Gastroparesis

Symptoms

- Unrelenting symptoms
- Failed medical therapy
Gastric Electrical Stimulation

Medtronic
Gastric Electrical Stimulation Cont…

- Enterra Brand
  - FDA approved for “Humanitarian use devise exemption”
  - Use restricted to clinical trials in institutions with IRB and physician trained in use and implantation
### Case Study

- 35 to 38 patients with severe gastroparesis experienced an 80% reduction in nausea and vomiting

### Complications

- Infection
- Lead dislodgement
- Bowel obstruction
- 10%-20% lead to device removal
Conclusion

- Gastroparesis common in Type I and Type II Diabetes
- Can adversely affect glycemic control
- Solid phase gastric emptying study and upper endoscopy are cornerstones of diagnosis and evaluation
- Non-medication and medication treatment is disappointing
- For severe gastroparesis, gastric stimulation may hold promise