Gastrointestinal Complication of Diabetes

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Is Gastrointestinal Symptoms Common in Diabetes?

Diabetic Neuropathy
- Distal sensory motor neuropathy
- Painful neuropathy
- Mononeuritis multiplexa
- Diabetic amyotrophy
- Pressure neuropathy
- Autonomic neuropathy

Upper GI involvement in DM
- Oesophageal dysfunction
- Gastroparesis
- Tachygastria
- Gallbladder atony and enlargement

Lower GI involvement in DM
- Diarrhoea
- Constipation
- Fecal incontinence
Causes of GI Pathology in DM

- Autonomic neuropathy of gut
- Associated co-morbidities
  - Celiac disease
  - Blind loop syndrome
- Drugs
  - GLP 1 agonist, Acarbose, Metformin etc
- Diet
  - High fibre diet, Sorbitol
- Abnormal function of Interstitial Cell of Cajal

Interstitial Cells of Cajal

- Electrical pacemakers
- Generate spontaneous slow waves in GI tract.
- Waves spread to smooth muscle cells resulting in depolarization and start contraction.
- Gut contractions in phasic phase are the basis for peristalsis and segmentation.

Frequency of ICC Pacemaker Activity

- 3 per minute in the stomach
- 12 per minute in the duodenum
- 10 per minute in the ileum
- 3 per minute in the colon

ICC Pathology in DM

- Advanced glycation end-products can lead to loss of neuronal nitric oxide synthase (nNOS) & impaired neurotransmission
- Increased oxidative stress leads to damage and loss of ICCs
- Smooth muscle atrophy leads to loss of IGF-1, a survival factor for ICCs.

Clinical spectrum of GI involvement in Diabetes

- Decreased lower oesophageal sphincter pressure
- Reduced peristalsis
- Reduced amplitude and wave speed of oesophageal contractions
Clinical spectrum of oesophageal involvement

• ? GORD more common in diabetes
• Usually Clinically insignificant
• Dysphagia is rare and needs further investigation

Gastroparesis

• Present in 20 to 40% long duration of type 1 DM other complications
• May be asymptomatic
• Commonly present with early satiety, nausea, vomiting, bloating, and postprandial abdominal fullness
• May develop unrelated symptoms
  – Hypoglycaemia, Poor control, Weight loss

Physiology of Gastric motility

• Two distinct anatomical part
  – Gastric fundus stores swallowed food
  – Antrum churns and propels food
• Pacemaker of stomach below fundus
• Rate of contraction = 3/min
• Peristaltic wave sweeps down to the antrum which grind food and propel it further to the duodenum

Neuro-humoral control

• Vagus & sympathetic fibre affects gastric motility
• Vagal reflex by distension stimulates contraction
• Motility disturbance due to diabetic neuropathy or vagotomy
• Various gut hormones affect antral contraction (secretin, gastrin, motilin, vasoactive intestinal peptide, glucagons, neurotensin, somatomedin, and cholecystokinin)
• Only motilin has significant gastric emptying effect

Pathophysiology of Gastroparesis

• Nonobstructive impairment of gastric propulsive activity
• Bradygastria
• Pylorospasm

Complications of Gastroparesis

• Difficulty of controlling blood glucose
• Weight loss
• Bacterial over growth
• Electrolyte disturbance
• Bezoars formation which may cause obstruction
### Investigations for Gastroparesis

- **Routine Blood tests:** U&E, Amylase, FBC
- **Ultrasound:** to rule out gallbladder or pancreatic disease
- **Upper GI Endoscopy:** to check for any abnormalities

### Radioisotope gastric-emptying scan

- Food containing radioisotope given
- Isotopic image of food at various interval
- Gastroparesis diagnosed if more than half of the food remains in the stomach after 90 minutes.

### Gastric manometry

- Electrodes placed in stomach
- Measurement of electrical activity and pressure of stomach as it digests liquids and solid food
- The measurements show the physiological function of stomach and whether there is any delay in digestion.

### Electrogastrogram (EGG)

- Surface electrodes over abdomen
- Record the electrical waves that precede each contraction
- Many hardwares and softwares available for measurement

### Other investigations

- Scintigraphic breath test
- Dual isotope test for solid & liquid
- Dynamic ultrasound imaging

### Aims of Gastroparesis Treatment

- Control vomiting
- Correct electrolyte imbalance
- Regain control of blood glucose levels
- To improve quality of life
### Treatment in Severe cases
- Admit
- Nil by mouth
- IV fluids & sliding scale IV insulin
- Parenteral nutrition in some cases
- Continuous naso-gastric drainage
- Avoid anti-kinetic drugs (cyclizine, narcotics, TCA)
- Pro-kinetic drugs

### Pro-kinetic Drugs
- Domperidone & Metoclopramide
- Bethanechol
- Erythromycin
- Cisapride

### Drugs in Development
- Motilin Receptor Agonist
  - Mitemcinal (GM-611)
  - GSK962040
- 5-HT4 agonists
  - prucalopride
  - TD-5108
- Other prokinetic drugs
  - SK-951
  - epalrestat

### Other Treatments Tried
- 5 HT3 antagonist (Odanosterone)
- Levosulpiride (Dopamine antagonist used as antipsychotics)
- Viagra
- Tegaserod (US drug for IBS)
- Clonidine

### Long term management
- Frequent small meals (> 6 times /day)
- Avoid fatty and high-fibre foods
- Insulin analogues with each meal
- Improve diabetes control
- Pro-kinetic drugs

### Botulinum toxin injection
- 200 units injected at the pyloric sphincter during upper GI endoscopy
- Improved symptoms
- Reduction in gastric emptying
- No complication
- Not proven beneficial in RCT
Ghrelin agonist (TZP 101)
- Ghrelin secreted by stomach
- Increases appetite and stimulates gastric emptying
- 2 subjects with gastroparesis treated with TZP 101 IV infusion
- Significant reduction in gastric emptying measured by gastric scintigraphy
- Also being tried in paralytic ileus

Feeding tube
- Feeding jejunostomy tube
- Can be temporary and used only if necessary when gastroparesis is severe

Gastric pacemaker
- Two small electrodes implanted in the muscle wall of the stomach
- Leads connected to the neurostimulator placed beneath the skin in abdomen
- Can externally control and adjust the settings of neurostimulator
- Surgical procedure done under general anesthesia

Gastric Stimulation

Surgical treatment
- 3/4th gastrectomy
- Gastro-jejunostomy
- Long afferent loop

Prognosis
- Many cases improve symptomatically with occasional relapse
- Severe cases have other complications
- High mortality in severe cases
Indication of Gastric Pacing

Intractable (drug refractory) gastroparesis associated with
- type 1 diabetes
- After surgery
- in association with anorexia nervosa and abdominal migraine

Other treatment to consider:
- jejunostomy tube
- gastrostomy tube
- pyloroplasty

Safety of Gastric Pacemaker

In a series of 51 patients:
- Extra abdominal pain in 27%
- infection 4%
- device migration 2%
- stomach wall perforation 2%

No particular safety concerns but potentially:
- infection of the neurostimulator pocket
- erosion of leads into the stomach mucosa
- small bowel obstruction.

Tachygastria

- Usually asymptomatic
- Diagnosed with Isotope scanning & EGG
- Physiological response to hypoglycaemia
- ? Seen in early Type 2 DM

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Gall Bladder Atony

- Large Gall bladder volume in DM
- Impaired contraction to cholecystokinin
- ? More gall stone in people with DM
- Emphysematous cholecystitis more common in DM

Diarrhoea in Diabetes

- 8% of advanced DM
  - Watery and painless
  - occurs at night
  - may be associated with fecal incontinence
- Can alternate with normal or even constipation

http://hdl.handle.net/123456789/5437
**Pathophysiology of Diarrhoea**
- Impairment in fasting and fed intestinal motor function
- Impaired alpha 2 adrenergic regulation of mucosal transport of ions leading to reduced absorption of water and electrolytes in the ileum and colon
- Impaired transit causing small bowel bacterial overgrowth
- Do not forget sorbitol/metformin/caeliac disease

**Treatment of Diarrhoea**
- Review diet & medication
- Codein, loperamide and other agents
- Metronidazole for bacterial overgrowth
- Clonidine for secretory diarrhoea

**Fecal Incontinence**
- Caused by anorectal dysfunction
- Usually associated with diarrhoea
- Treatment:
  - Bio feed back
  - Bulk forming agent with anti diarrhoeal

**Pathophysiology of Constipation in Diabetes**
- Dysfunction of intrinsic and extrinsic intestinal neurons
- Decreased gastrocolic reflex
- Abnormal internal anal sphincter tone
- Impaired rectal sensation

**Constipation in Diabetes**
- Much common than diarrhoea
- ? Associated with diabetic neuropathy
- Can cause pseudo obstruction
- Treatment as in non-diabetic patients

**Non-Alcoholic Fatty Liver Disease & Diabetes**
- Abnormal LFT present in up to 80% T2DM
- Diabetic patients with high BMI more at risk of Fibrosis
- Cirrhosis related death 2.5 times more in people with diabetes

Details beyond scope of this Presentation
Is gastrointestinal symptoms more common in people with diabetes?

### Table: Prevalence Rates

<table>
<thead>
<tr>
<th>Symptom Complex</th>
<th>Controls (n = 8185)</th>
<th>Diabetes (n = 423)</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal symptoms‡</td>
<td>11.5</td>
<td>15.4</td>
<td>1.44 (1.09-1.91)</td>
</tr>
<tr>
<td>Upper dysmotility symptoms§</td>
<td>15.3</td>
<td>18.2</td>
<td>1.75 (1.34-2.29)</td>
</tr>
<tr>
<td>Any bowel symptom§</td>
<td>18.9</td>
<td>26.0</td>
<td>1.84 (1.46-2.33)</td>
</tr>
<tr>
<td>Diarrhea symptoms§</td>
<td>10.0</td>
<td>15.6</td>
<td>2.06 (1.56-2.74)</td>
</tr>
<tr>
<td>Constipation symptoms#</td>
<td>9.2</td>
<td>11.4</td>
<td>1.54 (1.12-2.13)</td>
</tr>
</tbody>
</table>


Questions?

Comments?