Gastroparesis in critically ill patients

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Control of stomach motility

- Proximal gastric basal tone
  - Vagus nerve (Cranial nerve X)
  - Sympathetic inhibition
- Proximal gastric contraction
  - Motilin
- Proximal gastric receptive relaxation
  - GRP
  - Gastrin
  - CCK
  - Secretin
  - VIP
  - Somatostatin
  - Glucagon
  - Bombesin
- Duodenal distention
  - Acid, protein and fat content
- Feedback
Control of stomach motility

Proximal stomach

Distal stomach
Proximal stomach

relaxes during swallowing accommodation process stomach assumes reservoir functions
Distal stomach

critical for the grinding, mixing, and emptying of solids from the stomach
Motility change of upper GI tract in critically ill patient

• Gastroesophageal reflux
  – 60% in ICU patients

• Delayed gastric emptying
  – 50% of mechanically ventilated patients
  – 80% of patients with increased intracranial pressures

• Small bowel motility

Pathophysiology

• Impaired autonomic and enteric nervous system (ENS)
• Smooth muscle disturbance
• Cytokine-mediated inflammation
• Medication effects
• Electrolyte disturbances
• Increased intracranial pressure
• Hyperglycemia.
Factors effect upper GI dysmotility in critically ill patients

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Medications</th>
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</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Opiates</td>
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<tr>
<td>Prior surgery</td>
<td>Midazolam</td>
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<tr>
<td>Sepsis</td>
<td>Dopamine</td>
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<tr>
<td>Trauma</td>
<td>High-dose catecholamine</td>
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<tr>
<td>Acute pancreatitis</td>
<td>Proton pump inhibitors</td>
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<tr>
<td>Intestinal ischemia</td>
<td>Tricyclic antidepressants</td>
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<td></td>
<td>Calcium channel blockers</td>
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</tbody>
</table>

Motility change of stomach in critically ill patient

- ↓ LES tone
- ↓ Fundic accommodation
- ↑ CCK level
- ↑ Pyloric activity
- ↑ Duodenogastric feedback
- ↓ Antral motor activity
Clinical manifestations

• Intolerance to enteral feeds
  – High gastric residuals
  – Abdominal distention
  – Vomiting or regurgitation
  – Small intestinal bacterial overgrowth

• Increased mucosal permeability
  – Bacteremia
  – Systemic inflammatory response syndrome
Complication of gastroparesis

• Malnutrition
• Infection
  – Ventilator-associated pneumonia
  – Bacterial overgrowth
  – Bacteremia
• GERD and esophagitis
• Prolong hospital stay
• Increase mortality
Diagnosis

• High index of clinical suspicion
• Measurement of gastric residual volumes (GRVs)
• Gastric scintography
• Paracetamol absorption tests
• Isotope breath tests
Measurement of gastric residual volumes (GRVs)

- Common method of assessing gastric function in ICU patients
- Association of GRVs and gastric emptying
  - Not well validated
  - No accepted level of GRVs that represents GI dysmotility
- Value for the halting of feeds varies
  - 120 to 250mL
  - up to 400 to 500mL.
## GRVs level effect to clinical outcome

<table>
<thead>
<tr>
<th>Study</th>
<th>Complications</th>
<th>%</th>
<th>%Goal Kcal</th>
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<tbody>
<tr>
<td><strong>British Study</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200cc GRV (n=41)</td>
<td>37% *</td>
<td>59% *</td>
<td></td>
</tr>
<tr>
<td>150cc GRV (n=41)</td>
<td>61%</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td><strong>Canadian Study</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Vomiting</td>
<td></td>
<td>Intolerance</td>
</tr>
<tr>
<td>250cc GRV (n=44)</td>
<td>7%</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>150cc GRV (n=36)</td>
<td>6%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td><strong>Louisville Study</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Regurgitation</td>
<td></td>
<td>Aspiration</td>
</tr>
<tr>
<td>400cc GRV (n=20)</td>
<td>27.8%</td>
<td>22.6%</td>
<td></td>
</tr>
<tr>
<td>200cc GRV (n=20)</td>
<td>35.0%</td>
<td>21.6%</td>
<td></td>
</tr>
<tr>
<td><strong>Spanish Study</strong>&lt;sup&gt;4&lt;/sup&gt;</td>
<td>GI Complications%</td>
<td>47.8% *</td>
<td>%Goal Feeds</td>
</tr>
<tr>
<td>500cc GRV (n=160)</td>
<td></td>
<td>89% *</td>
<td></td>
</tr>
<tr>
<td>200cc GRV (n=169)</td>
<td>63.6%</td>
<td>83%</td>
<td></td>
</tr>
</tbody>
</table>

*<sup>p</sup><0.05

GRVs level effect to clinical outcome

Soroksky A et al. IAMJ 2010; 12:543-8
Problems of GRVs

• No definite cut off level
• Depend on many factors
  – Position of tube
  – Tube characteristics
  – Volume of syringe used
  – Operator performing test
• Poor relationships between GRVs and gastric emptying

Zaloga GP Crit Care Med 2005
Gastric residual volumes guideline

- Canadian guideline: > 250 mL
- ESPEN guideline: Not addressed
- ASPEN/SCCM: > 500 mL

Trends to up to 300-400 mL in most guideline ASPEN/SCCM will remain at 500 mL
Scintigraphy

- Gold standard for the measurement of gastric emptying
- Measures the emptying of isotope from the stomach
- Disadvantage
  - limits its use in the ICU due to large size of equipment
  - Difficult to transport critically ill patients to nuclear medicine department
  - Impractical in the ICU setting due to solid nature of the isotope-labeled meal

Moreira TV, McQuiggan M Nutr Clin Pract. 2009
Paracetamol absorption test

• Paracetamol
  – Not absorbed in the stomach
  – Rapidly absorbed from the small intestine after passage through the pylorus

• Paracetamol absorption test
  – Inexpensive
  – Feasible technique used in the ICU
  – Simple to perform

• Factors affect measurement of paracetamol level
  – Sepsis (volume of distribution)
  – Abnormal hepatic and renal metabolism

Moreira TV, McQuiggan M Nutr Clin Pract. 2009
Nonradioactive isotope breath tests

• Minimally invasive
• require limited equipment
• Procedure
  – Ingestion of a meal labeled with a stable isotope, such as carbon-13, which is rapidly absorbed in the small bowel
  – Isotope is oxidized by the liver to produce 13-labeled CO2
  – Appearance of the 13-labeled CO2 in expired air is determined by gastric emptying rates
• Limitation
  – affected by the hepatic impairment found commonly among ICU patients.
Diagnosis in summary

• Gastric scintigraphy
  – Gold standard for gastric emptying measurements
  – Impractical for use in the ICU setting

• Other methods for diagnosing GI dysmotility in the critical care patient
  – Not validated or standardized

• Diagnosis of impaired motility in the critical care patient
  – High index of suspicion
  – Practical modality such as GRV measurement
Treatment

General measure
• Correct principle illness
• 30°-45° head up
• Minimize use of opiates, dopamine and catecholamines
• Correct electrolyte imbalance
• Control blood sugar

Medication and intervention
• Prokinetics
  – Metoclopramide
  – Motilin agonists: erythromycin
  – Nonantibiotic motilin agonists
  – Ghrelin agonists
  – CCK antagonists
• Opioid Antagonists
  – Naloxone
  – Methylnaltrexone

• Postpyloric Feeding

McClave SA et al. JPEN J Parenter Enteral Nutr 2009
Metoclopramide

• Mechanism
  – Serotonin 5-hydroxytryptamine (HT) 4 receptor agonism
  – Dopamine D2 receptor antagonism
  – Direct stimulation of gut smooth muscle contraction

• Action
  – Increases esophageal, fundic and antral contractile amplitudes
  – Elevates lower esophageal sphincter pressure
  – Improves antropyloroduodenal coordination

• Increased gastric emptying and improved enteral feeds in the critical care setting

Metoclopramide disadvantage

• Tachyphylaxis
• Side effects
  – Up to 30% of patients
  – Antidopaminergic effects on the CNS
  – Acute dystonic reactions: facial spasm, oculogyric crisis, trismus, and torticollis: 0.2%-6%
  – Drowsiness, fatigue, and lassitude: 10%
  – Restlessness, agitation, irritability
  – Hyperprolactinemia

• Tardive dyskinesia
  – 1% to 10% of cases
  – Taken for more than 3 mo

Nguyen NQ, et al.. Crit Care Med. 2007
Ganzini L, et al.. Arch Intern Med. 1993
Erythromycin

• Motilin receptor agonist
• Motilin
  – Polypeptide hormone in distal stomach and duodenum
  – Increases lower esophageal sphincter pressure
  – Initiating the MMC in the antrum of the stomach
• Action
  – Increases the amplitude of antral peristalsis
  – Triggers MMC phase III activity
  – Stimulates gastric emptying

Herbert MK, Holzer P. Clin Nutr. 2008
Erythromycin disadvantage

• Tachyphylaxis
• side effects
  – IV infusion over 45 min to avoid sclerosing veins
  – skin rashes, nausea, cramping and abdominal pain.
  – increases the risk of sudden cardiac arrest with QT prolongation in those patients who were on CYP3A inhibitors such as antipsychotics, cardiac antiarrythmics drug, antifungals, calcium antagonists

Relationship between plasma erythromycin and durability of prokinetic action

- Down regulation of motilin receptor after high level of erythromycin
- Strategy to minimize tachyphylaxis
  - Reduce the dose to 70 mg twice daily
  - Adjusting the dose based on plasma concentrations

Nguyen NQ et al. Crit Care Med 2011
Rescue combination therapy

combination therapy with erythromycin and metoclopramide was highly effective and tachyphylaxis was less prominent

Domperidone

- Dopamine2-receptor agonist
- Actions as metoclopramide with fewer CNS side effects
- Not been extensively studied in the ICU setting
- Potential cardiotoxicity
- Need further studies in critical care patients.

Opioid antagonist

• Naloxone
  – Increased the volume of infused nutrition
  – Reduced GRVs
  – Decreased the incidence of ventilator-associated pneumonia
  – Reversal of analgesia and withdrawal symptoms

• Methylnaltrexone
  – Less cross the blood-brain barrier than naloxone
  – Less reverse the CNS effects of the medication

Meissner W, et Crit CareMed. 2003
CCK Receptor Antagonists

• CCK
  – Negative feedback effect to gastric emptying time
  – Causing antral hypomotility and pyloric hyperactivity
  – Elevated levels in critically ill patients

• CCK Receptor Antagonists
  – Increased gastric emptying in healthy subjects and those with irritable bowel syndrome.

• Further studies are needed
  – To assess effectiveness in ICU patients.

Elevated plasma CCK in feed-intolerant ICU patients

Postpyloric Feeding

• Delivery of nutrient directly into the small intestine using a small intestinal feeding catheter
• When gastric feeding in combination with prokinetic therapy has failed
• Current studies
  – Increase energy delivery
  – Not improve clinical outcomes

A multicenter, randomized controlled trial comparing early nasojejunal with nasogastric nutrition in critical illness.

No difference in target energy reached, pneumonia but higher GI bleeding rate in nasojejunostomy group (P=0.02)

Comparison of Postpyloric Tube Feeding and Gastric Tube Feeding in Intensive Care Unit Patients A Meta-Analysis

• Postpyloric tube feeding
  – Higher proportions of estimated energy requirement (weighted mean difference (WMD), 12%; 95% confidence interval [CI], 5%–18%)
  – Reduce GRV (WMD, −169.1 mL; 95% CI, −291.995 to −46.196 mL)

• Failed to demonstrate any benefits in
  – Mortality (OR, 1.05; 95% CI, 0.77–1.44)
  – New-onset pneumonia (OR, 0.77; 95% CI, 0.53–1.13)
  – Aspiration (OR, 1.20; 95% CI, 0.64–2.25)

Recommendation for management of gastroparesis in critical ill patients

• Assure that the feeding tube is in the proper position
• Keep the head of the bed elevated at 30°-45° at all times during the enteral feedings
• Use a large-bore sump tube for the first 1-2 days of enteral feeding
• Evaluate gastric residuals using at least a 60 mL syringe.
• Check gastric residuals every 4 hours especially in critically ill patients
• If the gastric residual volume (GRV) is >250 mL after a second gastric residual check
  – Prokinetic agent should be considered

Hurt RT., McClave SA. Crit Care Clin 2010
Recommendation for management of gastroparesis in critical ill patients

• GRV >500 mL
  – Holding enteral nutrition
  – Reassessing patient: physical assessment, gastrointestinal (GI) assessment, evaluation of glycemic control, minimization of sedation, and consideration of promotility agent use, if not already prescribed

• Consideration of a feeding tube placed below the ligament of Treitz if GRVs are consistently measured at >500 mL.

Hurt RT., McClave SA. Crit Care Clin 2010
Summary

• Gastroparesis in critical illness
  – Common problems
  – A lot of complication eg malnutrition, reflux and aspiration resulting in reduced lung function and ventilator associated pneumonia, bacterial overgrowth and sepsis
  – Prokinetic agents can improve gastric emptying and caloric delivery
  – Postpyloric delivery of nutrition may increase caloric intake but not improve clinical outcomes.
Thank you