Short Bowel Syndrome

Medical Management & Intestinal Rehabilitation

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Discussion Outline

• Overview of SBS
• Normal gut physiology
• Short bowel pathophysiology
• Medical Management
  – Nutrition support
  – Pharmacotherapy
  – Trophic hormones
Short Bowel Syndrome

- Malabsorptive syndrome due to functional and/or anatomic loss of extensive small bowel
- Incidence and prevalence unclear
  - Estimates based on The Oley Foundation Home TPN Registry (1992)
    - 40,000 home TPN patients each year
    - 26% had short bowel syndrome

Gastro 2006;130:S3-4
SBS: Etiologies

- **Adults**
  - Mesenteric vascular accidents
  - Crohn’s disease
  - Radiation enteritis
  - Trauma
  - Recurrent intestinal obstruction
  - Volvulus

- **Children**
  - Necrotizing enterocolitis
  - Intestinal atresia
  - Volvulus
  - Extensive agangliosis
  - Gastrochisis
  - Congenital short bowel
  - Meconium peritonitis
SBS: Clinical Features

- Diarrhea
- Dehydration
- Electrolyte abnormalities
- Malnutrition
  - Weight loss
  - Vitamin deficiencies
  - Mineral deficiencies
- Complications
  - Peptic ulcer disease
  - Kidney stones
  - Gallstones
  - Small bowel bacterial overgrowth
  - Metabolic bone disease
  - Treatment related
    - Line infections
    - Hepatic dysfunction
Gut Physiology & Pathophysiology
The Healthy Intestine

- **Small bowel**: 6 meters (3-8 m) or 20 feet
  - Duodenum 25 cm
  - Jejunum 2.5 m
  - Ileum 3.5 m
- **Colon**: 1.5 meters or 5 feet
The Healthy Intestine

- Iron and folate
- Beginning of food breakdown
- Carbohydrates, fats, proteins, calcium, magnesium, trace elements, and vitamins
- Same as jejunum, but distal ileum is specific for vitamin B12 and bile salts
- Water, electrolytes, and short chain fatty acids
The Shortened Intestine

- **Jejunoileal anastomosis**
- **Jejunocolic anastomosis**
- **End-Jejunostomy**

Retained bowel:
- ♦ Jejunum
- ♦ Ileum
- ♦ Colon
- ♦ Jejunum
The Shortened Intestine

• Retained bowel anatomy determines functional capacity
  – Length of small bowel remaining
  – Health of small bowel remaining
  – Presence of colon and ileocecal valve
  – Type of small bowel and its capacity to adapt
The Shortened Intestine

- Cutoff values of small bowel lengths separating transient and permanent TPN dependence
  - End enterostomy: 100 cm
  - Jejunocolic: 65 cm
  - Jejunoileocolic: 30 cm

Messing B et al. Gastroenterology 1999; 117
Intestinal Adaptation

- **Structural changes**
  - Macroscopic
    - dilation, thickening, lengthening
  - Microscopic
    - Villus: increase height & diameter
    - Crypt: elongation
    - Lifecycle: increase proliferation, decrease apoptosis

- **Functional changes**
  - Slowed transit to promote absorption
  - Increased carb & protein absorption per unit length
  - Up-regulation of sodium/glucose transporter
Intestinal Adaptation
Intestinal Adaptation

- Factors affecting intestinal adaptation
  - Remaining anatomy
    - Adaptive capacity of ileum > jejunum
  - Luminal nutrients
    - Hyperplasia via contact
    - Stimulates trophic hormone secretion
    - Stimulation of trophic pancreaticobiliary enzymes
  - Hormones & growth factors
    - Growth hormone, GLP-2, enteroglucagon
SBS: Treatment Options

Intestinal Rehab

Surgical Augmentation

Long-term TPN

Intestinal Transplant
Intestinal Rehabilitation
Intestinal Rehabilitation

• The process of restoring enteral autonomy and decreasing TPN dependence

• Rehab modalities
  – Diet, nutrition support
  – Fluids/electrolytes
  – Pharmacotherapy
  – Growth hormones
Intestinal Rehab: Diet

• Caloric needs increase by at least 50%
  – Absorb only 1/2 to 2/3 of energy consumed

• Maximizing absorption
  – Meal pattern
    • 5 to 6 small, calorically-dense meals
    • Separate liquids and solids
  – Meal composition
Intestinal Rehab: Diet

• Diet composition:
  – Depends on presence/absence of colon
  – Colon present: Increase complex carbs
    • Soluble fiber & starches pass undigested into colon
    • Fermentation by bacteria yields SCFA
    • SCFA absorbed by colon, salvaging 310-740 kcal/d
  – Colon absent: Less carbs, more fat

Gastro 2006;130:S5-15
Am J Gastro 2004;99:1823-32
# Intestinal Rehab: Diet

<table>
<thead>
<tr>
<th></th>
<th>Colon present</th>
<th>Colon absent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbohydrate</strong></td>
<td>• 50-60% of kcal • Complex carbs</td>
<td>• 40-50% of kcal • Complex carbs</td>
</tr>
<tr>
<td><strong>Fat</strong></td>
<td>• 20-30% of kcal • MCT/LCT</td>
<td>• 30-40% of kcal • LCT</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>• 20-30% of kcal</td>
<td>• 20-30% of kcal</td>
</tr>
</tbody>
</table>

MCT medium chain triglycerides, LCT long chain triglycerides
Complex carbs = starches (pasta, rice, potatoes, bread)

Am J Gastro 2004;99:1823-32
Intestinal Rehab: Diet

Percent Calories Absorbed

Colon Present | Colon Absent

High Carb | High Fat | High Carb | High Fat

Lancet 1994;343:373-6
Intestinal Rehab: Diet

• Food Choices
  – Carbohydrates:
    • Avoid simple sugars, favor complex carbs

<table>
<thead>
<tr>
<th>Simple Carbs</th>
<th>Complex Carbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular soda</td>
<td>Pasta</td>
</tr>
<tr>
<td>Juices</td>
<td>Rice</td>
</tr>
<tr>
<td>Candy</td>
<td>Potatoes</td>
</tr>
<tr>
<td>Cakes, cookies, pies</td>
<td>Breads</td>
</tr>
<tr>
<td>Ice cream</td>
<td>Cereals</td>
</tr>
</tbody>
</table>
Intestinal Rehab: Diet

• Food Choices
  – Dairy products
    • Lactose intolerance may be a problem
    • If symptomatic, substitute lactose free products
  – Fruits and vegetables
    • Gradual introduction
    • Well cooked veggies, peeled fruits
Intestinal Rehab: Fluids

• Avoid hypotonic fluids (water)
• Focus on oral rehydration solutions
  – Balanced ratio of salt and sugar
    • Sodium: 70-90 mMol/L
    • Sugar: 20 g/L
  – Products
    • WHO-ORS
    • Rice based formulas (Ceralyte)
    • G2 plus ½ tspn of salt per liter
Intestinal Rehab: Fluids

[Diagram showing intestinal cells and fluid transport mechanisms, including the movement of sodium (Na⁺), potassium (K⁺), and glucose.]
Intestinal Rehab: Fluids

• Home Recipe for ORS
  – 1 Liter of Water
  – 4 tablespoons of sugar
  – \( \frac{3}{4} \) teaspoon of salt
  – Sugar free artificial sweetener
  – Optional:
    • 1 tspn baking powder (1/2 tspn baking soda)
    • \( \frac{1}{2} \) tspn of 20% potassium chloride
Intestinal Rehab: Fluids

• Fluid intake
  – Sip throughout the day, do not guzzle
  – Separate from meals
  – Set volume targets
    • 1-2L per day to start, titrate as needed
Intestinal Rehab: Medications

- Antidiarrheals
  - Opiates
  - Octreotide
  - Pancreatic enzymes
  - Bile acid sequestrants, supplements
  - Clonidine
# Antidiarrheals: Opiates

<table>
<thead>
<tr>
<th>Medication</th>
<th>One dose</th>
<th>Typical dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loperamide (Imodium)</td>
<td>1 tab = 5 ml = 2mg</td>
<td>1-2 tabs 4 x per day</td>
</tr>
<tr>
<td>Diphenoxylate atropine</td>
<td>1 tab = 5 ml = 2.5mg</td>
<td>1-2 tabs 4 x per day</td>
</tr>
<tr>
<td>(Lomotil)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>1 tab = 15-60 mg</td>
<td>15-30 mg 3-4 x per day</td>
</tr>
<tr>
<td>Tincture of opium (DTO)</td>
<td>0.3 ml = 6 drops</td>
<td>6-20 drops (0.3 – 1ml) 4 x per day</td>
</tr>
</tbody>
</table>

**Timing of medication:**
30 min before meals and at bedtime
Acid Suppressive Therapy

• Indication
  – Acid hypersecretion after major resection increases risk of ulcers
  – Excess acid impairs fat digestion & absorption

• Agents
  
  **PPIs**
  - Omeprazole
  - Esomeprazole
  - Lansoprazole
  - Rabeprazole

  **H2 RAs**
  - Famotidine
  - Ranitidine
Pancreatic Enzymes

• Rationale:
  – Pancreatic enzymes critical to fat digestion
  – Loss of function post resection
    • Acid hypersecretion inactivates enzymes
    • Loss of intestinal cells which produce hormones that trigger pancreatic enzyme release
Pancreatic Enzymes

• Dosing
  – Need at least 30,000 IU of pancreatic lipase per meal
  – Avoid delayed release, encapsulated formulations
  – Use non-encapsulated forms with acid suppressive therapy (e.g., Viokase 16)
Bile Acid Therapy

bile salts via enterohepatic circulation stimulate hepatocytes to secrete more bile salts

95% of bile salts reabsorbed into intestinal capillaries

5% of bile salts lost in feces
Bile Acid Therapy

**Bile Acid Resin**
- Loss of <100 cm of ileum
  - Malabsorb bile acids
  - Bile acids in colon trigger secretory diarrhea
  - Treatment = Cholestyramine

**Bile Acid Replacement**
- Loss of >100 cm of ileum
  - Malabsorb bile acids to greater extent
  - Liver synthesis of bile acids can’t keep up
  - Develop bile acid deficiency
  - Treatment = Cholylsarcosine
Bacterial Overgrowth Rx

- Overgrowth of bacteria common
  - Post surgical anatomic hold ups
  - Loss of ICV
  - Adaptive bowel dilation

- Treatment:
  - Antibiotics +/- probiotics
  - Cyclical use encouraged
    • Use first 7-10 days each month
    • Rotate antibiotic used
Intestinal Rehab: Trophic factors

• Trophic Factors
  – Promote structural changes in the intestine that enhance absorption
  – Available agents
    • Growth Hormone
    • GLP 2 Analog (Teduglitide)
Growth Hormone

- Evaluated in a number of small open label and randomized trials with mixed methodology and mixed results
- Randomized control trial in 2005 established efficacy and resulted in FDA approval for use in SBS

Growth Hormone

• Phase 3 clinical trial
  – Randomized 41 patients
  – 3 groups
    • Modified diet plus glutamine
    • Modified diet plus GH (0.1 mg/kg/d)
    • Modified diet plus both glutamine and GH
  – Treated for 28 days total
  – Primary endpoint: Reduction in PN/IVF

GLP-2 Analog: Teduglutide

- GLP-2 is a hormone produced by L cells in the ileum and colon
- Functions
  - Decreases acid secretion
  - Delays gastric emptying
  - Increases intestinal blood flow
  - Increases villus length
GLP-2 Analog: Teduglutide

- Open label pilot study
  - 16 patients (10 no colon, 6 portion colon)
  - Treated for 21 days with varying doses
- Results:
  - Increased wet weight absorption
  - Increased urine output
  - Decreased fecal weight and energy excretion
  - Increased villus height

Gut 2005;54:1224-1231
GLP-2 Analog: Teduglutide

• Multicenter RCT completed
  – Included 83 patients
  – Randomized to Placebo vs. Teduglutide (Doses 0.05 mg/kg/d or 0.1 mg/kg/d)
  – Primary Endpoint: Reduction of PN volume ≥ 20%
GLP-2 Analog: Teduglitide

Percent of patients achieving 20% PN reduction

Week 24 RCT
- Placebo: 6%
- Low dose: 46%
- High dose: 25%

Week 52 Open label extension
- Placebo: 6%
- Low dose: 68%
- High dose: 52%

(RCT = Randomized Controlled Trial)
GLP-2 Analog: Teduglutide

• Repeat multicenter RCT in progress
  – Validation study
  – Mount Sinai Hospital actively enrolling

• Inclusion criteria
  – Adults
  – ≥12 mos PN/IVF dependent SBS
  – PN/IVF ≥ 3x per week
  – Serum cr, BUN <1.5x ULN
  – LFTs <2x ULN
Intestinal Rehab: Weaning

• Consider weaning TPN if
  – Stable at optimal weight
  – Adequate fluid and calorie intake
  – Stable BUN and creatinine
  – Vitamin and mineral status normal

• Tube feed transition may be necessary
Intestinal Rehab: Expectations

• Transition from TPN to enteral nutrition is a gradual process that requires close follow up with an experienced team of providers

• Medical therapy is not always enough and surgery to augment intestinal length and function may be necessary
Summary

- Intestinal rehabilitation is aimed at reducing TPN dependence and increasing enteral autonomy
- Medical rehab options focus on symptom control, maximizing absorptive capacity, and optimizing nutritional status
Summary

• Modalities of medical therapy include
  – Nutrition support (TPN, tube feeds) and dietary modification
  – Medications to reduce diarrhea and enhance digestion
  – Trophic agents aimed at augmenting bowel adaptation
Summary

• A multidisciplinary team is most effective at guiding the rehab process
  – Gastroenterologists
  – Surgeons
  – Dieticians
  – Nurse coordinators