ENHANCING INTESTINAL REHABILITATION IN SBS-IF

Case Study

A 40-year-old male is referred for evaluation of short bowel syndrome (SBS)
- Over the past 12 years, he has had several intestinal resections due to Crohn’s disease
- He is sustained on parenteral nutrition (PN) after multiple hospital admits for dehydration due to severe diarrhea
- His weight is 20 lbs below his usual; appears cachectic
- He takes some Imodium to control the diarrhea, but it does not seem to help
- He was told to avoid dairy products

Why These Patients Are Worthy of Our Time and Care

- Risks are great:
  - Central line-related
  - PN-related
  - Altered bowel anatomy-related
  - Increased mortality
- Other important effects:
  - Quality of life
  - Loss of sleep
  - Equipment “appendages”
  - “Not normal”
  - Morbidity/mortality
  - Financial
  - Out of pocket
  - Health care

What Defines Short Bowel Syndrome?

- Wide-ranging small bowel length
  - 300 to 800 cm
- Tremendous functional reserve
  - Problems when >75% removed
  - Entire colon equivalent to 50-60 cm SB length
- <200 cm small bowel remaining

Etiology of SBS in Adults

- Postoperative (24%)
  - Bariatric surgery
- Radiation enteritis/tumors (24%)
- Mesenteric ischemic events (22%)
- Crohn’s disease (17%)
- Trauma (8%)
- Other (7%)

SBS Bowel Anatomy Types

- Rapid transit
  - Acid hypersecretion
  - Poor adaptation
  - Malabsorption
  - Worst prognosis
  - <100 cm
- Adequate absorption until about 75% resected
  - 85 cm
- Slower transit
  - Uncommon; best prognosis
  - <30 cm

Treatment Goals in SBS

- Maintain adequate nutrition and growth
- Prevent and correct nutritional deficiencies
- Prevent and correct bowel- and treatment-related complications
- Improve quality of life
- Restore enteral autonomy if possible

Where to Begin?

Initial Assessment

- Determine bowel anatomy
  - Past medical and surgical history
- Weight loss history
- 24hr urine and stool or ostomy output
- Treatment history
- Medical complications
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**SBS Diet “Code” – More Like Guidelines**

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<tr>
<th>Factor</th>
<th>Colon Present</th>
<th>Colon Absent</th>
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<td>Meals/snacks</td>
<td>• 3-4 smaller meals/d</td>
<td>• 6+ small meals/d or less</td>
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<tr>
<td>Fluids</td>
<td>• ORS and/or hypotonic (low sodium) fluids</td>
<td>• ORS/high sodium fluids as needed</td>
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<td>Carbohydrates</td>
<td>• 50%-60% of energy intake as complex CHO</td>
<td>• 60%-70% of energy intake as complex CHO</td>
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<td>• Limit simple sugars (foods/fluids)</td>
<td>• Limit simple sugars (ingredients)</td>
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<tr>
<td>Fat</td>
<td>• 20%-30% of energy intake</td>
<td>• 20%-30% of energy intake as essential fatty acids</td>
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<td>• Ensure adequate (essential fatty acids)</td>
<td>• Ensure adequate (essential fatty acids)</td>
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<tr>
<td>Fiber</td>
<td>• 5 to 10 g/day soluble fiber</td>
<td>• 15 g/day soluble fiber</td>
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<tr>
<td>Salt</td>
<td>• Usual intake</td>
<td>• Increased salt intake</td>
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**Practical Suggestions**

- Chew foods well
- Smaller, frequent meals, avoid simple sugars
  - Start with their usual and tailor it – prior 3-day diet record
  - Tell them what they CAN eat
- Lactose restriction?
- Low FODMAP/Avoid sugar alcohols?
- Diet for SBS available @ www.ginutrition.virginia.edu
  - Under Patient Education Materials link

**Fluids/Hydration**

- Separate solids from liquids
  - Take small amounts of fluids with meals
  - Sp more between meals
- Avoid hypertonic/hypotonic fluids such as:
  - Water, tea, coffee
  - Fruit juices/drinks
  - Alcohol
  - Sport drinks
  - Sodas
  - Sweetened liquid nutritional supplements

**Oral Rehydration Solutions**

- Are not for everybody...
- Start with 500-1000 mL/d
  - If they won’t drink 1 L, they won’t drink 3
- Sipping is better than gulping
  - Maximize mL of ORS per cm of small bowel
- Try ice cubes/popsicles
- Via nocturnal feeding tube
- Commercial and ORT-like recipes
  - In: A Patient’s Guide to Managing a Short Bowel

**When to Consider Enteral?**

- Feed as high up as possible (i.e. stomach)
- Lower osmolality, polymeric (not elemental), some MCT-containing tube feeding
- Infuse via pump to decrease nutrient load per cm bowel
- If bile salt deficient, try lower fat semi-elemental
- Give some fiber if colon segment remaining

**Optimizing GI Function – Interventions**

- Medications – FRONT LINE
  - Considerations
    - Medication malabsorption
    - Timing in relation to meals
    - Availability at the patient’s pharmacy
  - Always consider the dosage form
Antisecretory Agents

- Massive enterectomy associated with transient (6-12 mo) hypergastrinemia and hypersecretion
  - H2RA (IV)
  - PPI (oral)
- Octreotide
  - subQ
  - IV

Discussion Points

- Net secretor vs osmotic diarrhea
  - How do you distinguish between the two?
- How much bowel do you need to utilize a PPI?
  - Dose
  - Form
  - Establishing efficacy?
  - When to go to IV route?
- When would one consider octreotide?

Antidiarrheal Use

- ↓ motility, ↑ contact time, ↑ absorption
  - Loperamide: minimal side effects; OTC
    - 2 to 4 mg every 6-8 hours
  - Diphenoxylate / atropine
    - 1 to 2 tablets every 6-8 hours

Discussion Points

- Are either more effective in patients with or without a colon?
- Any benefit to use both at the same time?
- What is the treatment endpoint?
- What if a patient does not have an ileum – can loperamide still be utilized?
- How many days before moving to narcotics?

Narcotics

- Codeine phosphate
  - 30 to 60 mg every 6-8 hours (vs pm)
- Opium tincture
  - 5 to 20 drops (0.25 mL to 1.25 mL) every 6-8 hours (vs pm)
  - (Note – 5 drops = 0.25 mL = 2.5 mg morphine)
  - Safer to dose in mL vs drops

Discussion Points

- Issues with narcotics:
  - “I don’t like to use narcotics” (patient or clinician)
    - Addiction potential
    - Are there any that are more addictive than others?
    - Other issues such as higher risk for being stolen?
    - Is this a higher risk than parenteral nutrition?
    - Pharmacogenetic issues of codeine
    - Requires monthly prescription
    - Prescriptions cannot be faxed/mailed
    - DEA concerns
    - What about using Pparegoric
    - Oxycodone, or other narcotics?
Other Therapies – Indications?

- Clonidine
- Bile salt binders
  - Not for use in patients without a colon
- Bile salt replacers
- Pancreatic enzymes
- Probiotics

Antimicrobial Use in SBS

- Small bowel bacterial overgrowth
- Multifactorial pathophysiology
- Variety of potential clinical consequences
  - May interfere with PN weaning and predispose to bacterial translocation
  - May be beneficial in CHO salvage
- Unique diagnostic challenge
  - Small bowel aspirate best test (?)
- Antibiotic therapy first line
  - Improved gas-related symptoms, reduction in stool output and/or weight gain

Case Study Continued

- He was determined to have about 90 cm of jejunum and half his colon; multiple micronutrient deficiencies also found
- Stool output was 3000 mL+ per day
- Urine output was ~ 890 mL per day
- PN was initiated, as were dietary/fluid modifications and aggressive use of antidiarrheals
  - Weight increased back to near his usual and previously identified micronutrient deficiencies were corrected
- Attempts to wean his PN stalled out at 5 nights/week

What should we do now?

Problem with Current Approaches

- PN still frequently necessary
  - Does not enhance bowel function
  - Costly (> $100K/yr)
  - Reduced quality of life
  - 1-2 hospitalizations annually/patient

Risk Factors for Permanent Intestinal Failure

- Remnant bowel length
  - \( \leq 100 \text{ cm end-jejunostomy} \)
  - \( \leq 65 \text{ cm jejunocolic anastomosis} \)
  - \( \leq 30 \text{ cm jejunoleocolic anastomosis} \)
- Residual disease in remnant bowel
- Absence of colon
- Time on PN
  - \( \geq 2 \text{ yrs adults}; \geq 4 \text{ yrs children} \)
- Degree to which adaptation has occurred
- Age
- Nutritional status

Enter: Trophic Factors
**Trophic Factors**

- Facilitate intestinal adaptation
  - Morphological and functional
  - Ileum > Colon > Jejunum
  - Begins immediately after surgery and continues for 2-3 years
  - Variety of stimulators of adaptation

**Intestinal Adaptation - Hyperplasia**

- Stimulation by Peptide Hormones
- Inhibitors: Somatostatin, TGF-

**PN Weaning – Trophic Factors**

- FDA approval of rhGH (Zorbtive; Serono Inc.) in December 2003
  - Adults on PN to aid weaning together with optimized diet ± oral glutamine
- FDA approval of teduglutide (Gattex; NPS Pharm.) in December 2012
  - Adults on parenteral support

**Combination Therapy in SBS Randomized, Controlled Trial Design**


- PN reduced during weeks 1-3 if:
  - positive enteral balance > 500 mL/d
  - urine output > 0.5 mL/kg/hr
  - stable weight and electrolytes

**RCT of r-hGH, Glutamine, and Specialized Oral Diet**


- Weight decreased from baseline to end of follow-up similarly in all groups

**Growth Hormone in SBS**

- Conflicting findings of this therapy in short-term, randomized, controlled, cross-over studies
  - Benefit mainly due to diet
  - Weight gain due to fluid retention
  - Maintain benefit long-term
- Methodological differences among studies limit definite conclusion regarding benefit of this therapy

**Growth Hormone Adverse Effects**

- Fluid retention (peripheral edema)
- Arthralgias
- Carpal tunnel
- Hyperglycemia
- Nausea
- Injection site reactions
- Intracranial hypertension
- Hypersensitivity reaction
- Acute pancreatitis

**Glucagon-like Peptide 2 and Teduglutide**

- Secreted from L-cells of distal ileum/prox colon
- GLP-2 analogue
  - Substitute glycine for alanine at position 2
- Resistant to degradation by dipeptidyl peptidase-4 (DPP-4)
  - Longer half-life of 2-3 hrs vs 7 min

**Randomized, Controlled Trial of Teduglutide in PN-Dependent SBS**

83 PN-dependent SBS patients

- **Optimize PN (0-8 wks)**
- **Stabilize PN**

**Endpoints**
- PN: % patients achieving PN reduction > 20% weekly needs b/w wks 20-24
- Lean body mass
- Plasma citrulline
- Adverse events

**Teduglutide Confirmatory Study**

- Multinational, multicenter, RDBPCT
- Similar design as prior study except only single dose teduglutide (0.05 mg/kg/d) vs placebo
- More aggressive PN/IVF weaning protocol
- % patients achieving 20 to 100% PN volume reduction by week 20-24

**Teduglutide #2 – Main Results**

- **Responder Rate Reduction in PN/IV Volume**
  - Teduglutide: 63%
  - Placebo: 30%
  - *P = 0.002

**Teduglutide – Adverse Events and Precautions**

- Increased AEs with teduglutide
  - Abdominal pain (31% vs 23%)
  - Nausea (28% vs. 19%)
  - Stomal complication (24% vs 7%)
  - Abdominal distension (21% vs 2%)
  - Peripheral edema (17% vs 5%)
  - Injection site reactions
  - Headaches

- Precautions
  - Risk for acceleration of neoplastic growth
  - Colonoscopy before treatment and 1 year later
  - Intestinal obstruction
  - Pancreaticobiliary disease
  - Labs before and every 6 months
  - Fluid overload
  - Potential to increase concomitant drug absorption
  - Reduce dose in mod-severe CKD

**Trophic Factors – Further Study Needed**

- Long-term safety and efficacy
- Optimal patient selection
- Cost-effectiveness
- Optimal timing of administration relative to onset of SBS
PN Weaning – Practical Aspects

- Stepwise approach to when and how much
  - Frequent monitoring of food/fluid intake and stool/urine output
  - Inpatient vs. outpatient (vs. outpatient intensive)
  - Meet daily calorie and fluid intake goals
  - Adjustments based on tolerance:
    - Symptoms
    - Stool/urine output
    - Electrolyte/micronutrient levels
    - Weight
    - Hydration status

Inpatient vs. outpatient (vs. outpatient intensive)

- Meet daily calorie and fluid intake goals
- Adjustments based on tolerance:
  - Symptoms
  - Stool/urine output
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“Tools” for our Patients

- Monitoring Parenteral Nutrition: At Home
  - Weekly
    - CMP, phosphorus, magnesium, bicarbonate, glucose, CBC
  - Every 3-6 months
    - Trace elements
      - Zinc, copper, chromium, selenium, manganese
    - Iron
      - Ferritin (positive acute-phase reactant)
    - Essential Fatty Acid Profile
    - Stool output, physical exam, signs/symptoms

- Monitoring cont.
  - Periodic assessment of:
    - Vitamin A (negative acute-phase reactant)
    - Vitamin E
    - Folate
    - Methylmalonic acid/B₁₂

Vitamins/Minerals: What Makes Sense

- Many recommendations in literature/texts; very little evidence
- Consider:
  - Osmotic drag from so many pills (and fluid to take them)
  - Sheer cost of the supplements
  - Time to take them all
  - Does not include patient’s prescription medications!
- Add therapeutic vitamin and mineral supplement
  - Daily, twice daily—½ to 1 tab
  - Chewable, crushed, liquid form

More Tools

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**Vitamin D and Bone Health**

- Vitamin D
  - 25 OH vitamin D/ intact PTH
  - Baseline DXA scan (bone density)
- Direct sunlight to arms and legs:
  - 5-10 minutes avg = 3000 IU D3
  - Depends on time of day, season, skin sensitivity, latitude
- Sperti lamp (DUV Lamp)
  - www.vitaminduv.com
  - Tanning beds (10 minutes, 3 x/wk x 6 months – arms and legs)
- Liquid vitamin D
  - Consider higher dose, twice-daily dose, etc

**Concluding Remarks**

- Care of the SBS patient is time intensive
- Significant education of patient/caregiver is necessary and must be allotted for to maximize outcomes
- When embarking on an intervention, it is important to:
  - Try one thing at a time
  - Determine endpoint and how long you will give it to work
  - Move on to next intervention if it doesn’t
- Monitoring is ongoing and goals can change
- We cannot expect these patients to be successful if we do not, by our actions and giving of our time, demonstrate to them that they ARE worthy of our time and intensive care

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**Enhancing Intestinal Rehabilitation in SBS-IF**

**Strategies for Collaborative Care**

Thank you!
Enhancing Intestinal Rehabilitation in Short Bowel Syndrome—Intestinal Failure

Evaluation and management of patients with short bowel syndrome (SBS) can be challenging. This reference tool has been designed to help guide you through this complex process. Included are practical strategies to assess patients with suspected SBS-IF and subsequently manage these patients, including optimization of hydration and conventional drug therapy; parenteral nutrition (PN) protocols and weaning procedures; as well as the introduction of trophic agents into the treatment regimen to improve structural and functional intestinal integrity for optimal outcomes.

I. Initial Assessment

1. Determine:
   - Bowel anatomy: op note, small bowel follow through
   - Weight loss history
   - Presence of GI and other symptoms that may affect oral intake or fluid loss
   - Potential signs/symptoms of micronutrient deficiencies
   - Signs of dehydration and malnutrition
   - Pertinent past medical, psychiatric and surgical history
   - Education, motivation, support system and potential economic or other barriers

2. Evaluate:
   - Surgical complications
     - Anastomotic strictures, chronic obstruction, enterocutaneous fistulae
   - Medical complications
     - Chronic diarrhea (multiple causes, especially *Clostridium difficile* ["C. Diff."] infection)
     - Fluid/electrolyte disturbances
     - Oxalate nephropathy
     - D-lactic acidosis
     - Renal dysfunction
     - Metabolic bone disease
     - Peptic ulcer disease

Define treatment history:

3. Diet
   - 3-day diet record
     - What and amounts of ALL food/beverages consumed
   - Supplements used (Ensure, Boost, herbals, protein, probiotics, etc.)
   - Vitamins and minerals used – dose/form
   - Nutrition support history
     - Enteral and/or central venous access device
     - Formula used, route and method of administration
     - Prior complications
   - Current medications – Review ALL
     - Dosing
     - Check for liquid meds (sugar alcohols)
     - Form (tab, capsule, suspension, sustained or delayed-release)
     - Include ALL over-the-counters

II. Moving Forward

- Differentiate between osmotic vs. secretory diarrhea
  - Clinical history, 24-hour fast
- Obtain baseline data on patient's "normal regimen" (diet, IV fluids, medications, etc.):
  - Urine output
  - Stool output
  - Weight
III. Optimizing GI Function - Interventions

1. Diet
   - Educate patient to:
     - Chew foods well
     - Take smaller, frequent meals – Tell them what they CAN eat.
     - Start with patient’s usual (refer to 3 day written diet record, if possible) and tailor it
     - Avoid simple sugars
     - Consider lactose restriction
     - Consider low FODMAP/Avoid sugar alcohols
     - Avoid oxalate if colon segment
     - Separate solids from liquids
     - Take small amounts of fluids with meals
     - Sip more between meals
     - Avoid hypertonic/hypotonic fluids
     - Oral rehydration solutions

2. Medications
   - Considerations
     - Scheduled dosing: NOT “PRN”
       - Every 4, 6 or 8 hours?
       - Before, during, after meals?
       - Available at the patient’s pharmacy?
       - Dosage form
     - Front line
       - Antisecretory agent
         - Proton pump inhibitor, H2-blocker
       - Gut slowing agents
         - Loperamide, diphenoxylate with atropine, Paregoric, tincture of opium, codeine
       - Other therapies
         - Clonidine
         - Bile salt binders?
         - Bile salt replacers
         - Pancreatic enzymes?
         - Antimicrobials
         - Probiotics?
       - Trophic agents
         - r-hGH
         - Teduglutide

IV. Stepwise Approach to Rehabilitate Intestinal Function in SBS Patients with Intestinal Failure

- Wean from parenteral nutrition
  - Optimize oral diet and fluids
  - Aggressive use of antisecretory and antimotility agents
  - Surgically maximize remnant bowel function if possible
  - Careful monitoring of status
  - Micronutrient monitoring and supplementation, as needed
- Meet daily calorie and fluid intake goals
- Inpatient vs. outpatient
- Frequent monitoring and adjustments based on
  - Symptoms
  - Stool/urine output
  - Electrolyte/micronutrient levels
  - Weight
  - Hydration status

V. Resources

- UVAHS GI Nutrition Website (www.ginutrition.virginia.edu) with links to:
  - Nutrition Articles in Practical Gastroenterology including:

- New SBS Pocket Guide for Patients
  - Abbreviated version of guide above
  - Contact Maureen Stellwag at MStellwag@npsp.com to obtain

- Oley Foundation
  - http://www.oley.org or (800) 776-OLEY

This reference tool is a companion to “Enhancing Intestinal Rehabilitation in SBS-IF: Strategies for Collaborative Care,” a CME/CE-certified program jointly sponsored by Potomac Center for Medical Education and Rockpointe. Supported by an educational grant from NPS Pharmaceuticals, Inc. © 2014 Rockpointe