Management of Short Bowel Syndrome: Beyond TPN

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CASE

- 47 y.o. male, lawyer
- Inflammatory/fistulizing Crohn’s Disease
- Multiple small bowel resections
- 100 cm jejunum to transverse colon remaining
- On parenteral nutrition for 32 years
- Course complicated by:
  - line infections
  - decreasing venous access
  - abnormal liver tests
Etiology of SBS

University of Chicago
n = 98

- Radiation: 13%
- Ischemia: 15%
- Post-op: 22%
- Crohn's: 44%

University of Nebraska
n = 500

- Post-op: 35%
- Crohn's: 16%
- Ischemia: 17%
- Radiation: 19%

Thompson et al. JPEN 2015:DOI
Rapid Dehydration output > 2 L/day

Must Know:
- Resection - site
- extent
- Residual health

Length of Small Bowel
~ 600 cm

- carbohydrates
- fats
- proteins
- calcium
- magnesium
- trace elements
- vitamins

- vitamin B₁₂
- bile salts
- short chain fatty acids

Water and electrolytes
Small Bowel Response to Resection: Adaptive Dilation

Normal Bowel

Short Bowel

Nutrient/Fluid Absorption

Slows Transit

Intestinal Adaptation

Stimulators of Hyperplasia

Luminal Factors
- Nutrients
- Non-nutrients
  - Secretions
    - pancreatic
    - biliary

Local Factors
- Trefoil peptides
- Prostaglandins
- Polyamines

Hormones & Peptides
- Enteroglucagon
- Growth hormone
- Gastrin, EGF, GLP-2
- IGF-1, TGFα, IL11

↑ Nutrient/Fluid Absorption
Short Bowel Syndrome

Clinical Consequences

- Diarrhea / steatorrhea
- Dehydration
- Weight loss
- Manifestations of vitamin and mineral deficiencies

Bile salt, B₁₂ malabsorption

Risks of resection:
- <100 cm bile-salt diarrhea
  - cholestyramine tx
- >100 cm fat malabsorption
  - vit A, D, E, K, LCFA + B₁₂
  - bone disease
  - oxalate stones

Large fluid losses
All nutrients malabsorbed
Rapid transit

Best tolerated
Good adaptation
Fe/Ca/folate absorption
Reconnect Colon when Possible

Messing et al. Gastroenterology 1999;117:1043
Short Bowel Syndrome
Basics of Management

• Block endogenous secretions
  - Proton Pump Inhibitor
  - Try octreotide if > 3 L/day output
• Slow motility to improve contact time
  - Loperamide, diphenoxylate
  - Liquid opiate
• Diet – multiple small meals, ORS
  - Jejunostomy (high salt, nutrient dense)
  - Colon present (low fat, low oxalate)
• Supplement vitamin/minerals
  - Vitamin B12 and fat-solubles, Ca, Zn, Mg
• Monitor wt, hydration, bone, stones, vit/minerals
  - Life-long

Parenteral Nutrition

- Dextrose
- Lipids
- Amino acids
- Electrolytes & minerals
- Vitamins
- Trace elements
- TPN

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**Short Bowel Syndrome/Intestinal Failure**

<table>
<thead>
<tr>
<th></th>
<th>Home Parenteral Nutrition</th>
<th>Small Bowel Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr survival</td>
<td>89%</td>
<td>78%</td>
</tr>
<tr>
<td>5 yr survival</td>
<td>75%</td>
<td>63%</td>
</tr>
<tr>
<td>Morbidity</td>
<td>line infection</td>
<td>rejection</td>
</tr>
<tr>
<td></td>
<td>liver disease</td>
<td>GVHD</td>
</tr>
<tr>
<td></td>
<td>osteoporosis</td>
<td>infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lymphoma</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>60-70% good</td>
<td>80-90% good at 6mo</td>
</tr>
<tr>
<td>Long Term Cost</td>
<td>$70-120,000/yr</td>
<td>$332,827/person/yr</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ 2 yrs post transplant</td>
</tr>
</tbody>
</table>

Howard Gastroenterology 2006;130:552
Abu-Elmagd Gastroenterology 2006;130:5132
Smith et al. OPTN/SRTR Am J Transplant 2014;1:97

Ethanol line locks decrease infection

Oliveira et al. Pediatrics 2012;129:318
Badia-Tahull et al. Nutrition 2015;31:1109
Short Bowel Syndrome
Other Therapies

• Growth Hormone
  - conflicting results
  - ? main effect on colon
  - side effects (edema, arthralgia, sleep)
  - contraindications (infection, cancer)
• Night-time G tube feeding
• Bowel lengthening surgeries
  - mainly in children
  - Bianchi, STEP
Serial Transverse Enteroplasty (STEP)

Outcomes
• 16 children
• increased length 80 to 110 cm
• 60% tapered off EN/PN
• less favorable in gastroschisis

Novel Drug - Short Bowel Syndrome
Clinical Observation
• Gleeson 1971, Stevens 1984
  - glucagon-secreting tumor alters SB structure
  - glucagonoma syndrome and giant duodenal villi

Basic Science
• Drucker 1996 (Proc Natl Acad Sci 93:7911)
  - glucagon-like peptide 2 (GLP-2)
  - induced intestinal epithelial cell proliferation

Translational Human Pilot Study
• Jeppesen 2001 (Gastroenterology 120:806)
  - GLP2 increased absorption/decreased ostomy output

Stevens. Gut 1984;25:784
Glucagon-Like Peptide 2

Teduglutide is a Novel GLP-2 Analogue

GLP-2 (short-acting)

HADGSFSDEMNTILDNLAAARDFINWLIQTKITD
HGDGSFSDEMNTILDNLAAARDFINWLIQTKITD
Teduglutide

Teuscher, Jeppesen, Mortensen et al 2005
Teduglutide Clinical Trials - Summary

- Safe (0.03 - 0.15 mg/kg SQ daily)
- PRCT in SBS, 83 pts, extended 52 wks
- Results:
  - increased villous height, crypt depth
  - increased absorption, lean body mass
  - decreased outputs
  - decreased PN needs in 68%, some stopped or day off PN (dose 0.05 mg/kg/day)

- Side effects: stoma hyperplasia, abd pain, inj site pain

- FDA approved, no contraindications, no time limit
  - Short bowel, PN/IV fluid-dependent, on optimal care

Jeppesen et al Gut 2005;54:1224 and 2011;60:902

Real Time Experience in Short Bowel/Intestinal Failure

Change in PN Volume on Teduglutide

Pt #1 – Case Patient
- Off PN after 32 yrs!
- Line free – dove into swimming pool
- Sleeps through the night

Wall et al. Abstract, Clinical Nutrition Week, Savannah Georgia 2014
Teduglutide
Unanswered Questions

- ? Needed daily
- ? Cancer risk
  - colon cancer
  - pancreatic cancer
- ? What about the small stuff
  - vitamin/mineral/essential fatty acid deficiencies
- Will price come down
  - novel, orphan drug

Short Bowel Syndrome Management
Take Home Points

- Know site/length resected to guide therapy
- Optimize medical regimen
  - multiple small meals, ORS
  - block acid, slow motility
  - extensive resections likely need PN
- Teduglutide (GLP-2 analogue) improves uptake
- Consider lengthening surgery if dilated bowel
- Small Bowel Transplant when
  - loss of vascular access, liver disease
- Monitor for nutrient deficiencies, bones, stones