Management of Short Bowel Syndrome in Children

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SUNY DOWNSTATE MEDICAL CENTER
SURGERY GRAND ROUNDS 3/21/2013
Female newborn, born at 35+5 weeks gestation via c-section, birth weight 2780g, APGAR 9/9

DOL#0-1:
- admitted to NICU for respiratory distress requiring CPAP and r/o sepsis

DOL#2:
- no meconium, abdomen soft,
- AXR: scattered gas filled loops of bowel and dilated transverse colon
- drop in hct requiring transfusion of PRBC

DOL#3:
- abdominal distention and bilious drainage from OGT
- AXR: remained unchanged
- pediatric surgery consulted
Case Report

UGI:
- Obstruction at the second/third portion of the duodenum

BE:
- Patent colon with cecum in the right upper quadrant adjacent to the obstructed duodenal loop
Case Report

- **DOL#3:**
  - UGI/BE concerning for malrotation with volvulus
  - Urgent surgical exploration: malrotation with volvulus and necrosis of the small bowel from third portion of duodenum to terminal ileum
  - Detorsion of small bowel, closure of abdomen
  - Return to NICU for resuscitation
  - Planned second look in 24h

- **DOL#4:**
  - Second look: unchanged necrosis of small bowel

- **DOL#5-11 (POD#1/2-6/7):**
  - Awake, alert, on abx, TPN, NCPAP
Case Report

- **DOL#12 (POD#8/9):**
  - Exploratory laparotomy, resection of necrotic small bowel with anastomosis of mid duodenum to terminal ileum
  - Gastrostomy
  - Broviac placement
Case Report

- DOL#21 (POD#9/17/18)
  - Off abx, on RA, TPN, starting feeds via gastrostomy

- DOL#32 (POD#20/28/29)
  - Tolerating feeds at 3cc/h via gastrostomy
  - TPN
  - UGI: esophageal reflux, delayed passage of contrast into ileum

- DOL#72
  - Tolerating feeds at 12 cc/h via gastrostomy
  - Continuous TPN
  - Weight: 3905g
Intestinal Failure

- Inability of the GI tract to provide sufficient absorption capacities to cover nutritional requirements for maintenance in adults and growth in children
- Functional and structural adaption for 1-2 years after resection
- Permanent intestinal failure is determined after 2 years
- Parenteral nutrition is first line treatment, allowing satisfactory growth and acceptable quality of life
- Intestinal transplant is indicated for failure of PN
- 5 year survival rate on PN is 75%
<table>
<thead>
<tr>
<th>Causes of Intestinal Failure in Children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short bowel syndrome 68%</strong></td>
</tr>
<tr>
<td>- Volvulus 15%</td>
</tr>
<tr>
<td>- Gastrochisis 24%</td>
</tr>
<tr>
<td>- Necrotizing enterocolitis 16%</td>
</tr>
<tr>
<td>- Atresia 9%</td>
</tr>
<tr>
<td>- Other 4%</td>
</tr>
<tr>
<td><strong>Motility Disorders 14%</strong></td>
</tr>
<tr>
<td>- Long segment Hirschsprung disease, chronic intestinal pseudoobstruction</td>
</tr>
<tr>
<td><strong>Mucosal Defects 10%</strong></td>
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<tr>
<td>- microvillus inclusion disease, tufting enteropathy</td>
</tr>
<tr>
<td><strong>Retransplantation 5%</strong></td>
</tr>
<tr>
<td><strong>Others 3%</strong></td>
</tr>
<tr>
<td>- tumors</td>
</tr>
</tbody>
</table>
SBS: Pathophysiologic changes

- Loss of intestinal absorptive surface
- More rapid intestinal transit
- Gastric hypersecretion
- Inactivation of pancreatic enzymes
- Loss of bile salts

- Malnutrition
- Weight loss
- Diarrhea
- Steatorrhea
- Vitamin deficiency
- Electrolyte imbalance
- Cholelithiasis
- Nephrolithiasis
- Liver Disease
Factors influencing Outcome

- Remnant Length
- Intestinal Disease
- Intestinal Adaptation
- Remnant Location
- Other Digestive Organs
- Pharmacologic Therapy
- Nutrition Support
- Patient Age, BMI
Prognosis

- 80% of children with neonatal onset SBS wean from PN between age 1-2
- 10% die from complications
- 10% remain on permanent PN
  - Remnant length <30-40 cm
  - Absent ileocecal valve
  - Colon resection
  - Tolerance of <25% of enteral calories at 3 months of age
- Multidisciplinary approach at specialized center improves outcome

Intestinal Rehabilitation

- Enhance intestinal absorption and function
- Eliminate long-term dependency on PN

Medical Rehabilitation
- Maintain nutritional status
- Maximize enteral nutrient absorption
- Prevent complications

Surgical Rehabilitation
- Preserve intestinal remnant length
- Improving intestinal motility
- Increasing absorptive area

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Maintain nutritional status

- Replacement of fluid and electrolyte losses
- Parenteral Nutrition
  - Continuous then cyclic PN
  - Lipid minimization and alternate lipid preparations to reduce IFALD
- Enteral Nutrition
  - Start as early as possible postop with hypoosmolar feeds
  - Gradually increase as enteral adaption occurs
  - Enteral independence is goal
### Table 2
Dietary recommendations for short bowel syndrome

<table>
<thead>
<tr>
<th></th>
<th>Colon in Continuity</th>
<th>No Colon in Continuity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluids</strong></td>
<td>Hypotonic and/or ORS</td>
<td>ORS</td>
</tr>
<tr>
<td><strong>Carbohydrate</strong></td>
<td>50%-60% of caloric intake</td>
<td>40%-50% of caloric intake</td>
</tr>
<tr>
<td></td>
<td>Complex carbohydrates</td>
<td>Complex carbohydrates</td>
</tr>
<tr>
<td></td>
<td>Limit simple sugars</td>
<td>Limit simple sugars</td>
</tr>
<tr>
<td></td>
<td>Low lactose</td>
<td></td>
</tr>
<tr>
<td><strong>Fat</strong></td>
<td>20%-30% of caloric intake</td>
<td>30%-40% of caloric intake</td>
</tr>
<tr>
<td></td>
<td>Adequate essential fats</td>
<td>Adequate essential fats</td>
</tr>
<tr>
<td></td>
<td>MCT/LCT</td>
<td>LCT</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>20%-30% of caloric intake</td>
<td>20%-30% of caloric intake</td>
</tr>
<tr>
<td><strong>Fiber</strong></td>
<td>5-10 g/d soluble fiber for net secretors</td>
<td>5-10 g/d soluble fiber for net secretors</td>
</tr>
<tr>
<td><strong>Oxalate</strong></td>
<td>Restriction</td>
<td>No restriction</td>
</tr>
</tbody>
</table>

*Abbreviations:* LCT, long-chain triglycerides; MCT, medium-chain triglycerides; ORS, oral rehydration solution.
Pharmacologic treatment

- **Slow transit / diarrhea**
  - Loperamide
  - Diphenoxylate
  - Narcotics
  - Cholestyramine
  - Pancreatic enzymes

- **Reduce GI secretion**
  - H$_2$ receptor antagonists
  - Proton pump inhibitors
  - Octreotide
  - Clonidine

- **Treat bacterial overgrowth**
  - Antibiotics
  - Probiotics
  - Prokinetics

- **Glutamine, hormonal treatment**
Hormonal Treatments

- Growth hormone combined with glutamine
  - Effects short lived, results inconclusive in metaanalysis

- GLP-2 and its analog teduglutide
  - Hormone strongly associated with intestinal growth and post resection intestinal adaptation
  - Reduction in PN compared to placebo in RCT over 52 weeks

- EGF
  - Transiently increased carbohydrate absorption and improved tolerance to enteral feeding in pediatric patients
  - Under investigation

- GLP-1 agonist exenatide
  - GLP-1 receptor agonist approved for type 2 DM
  - Improvement in intestinal transit in case series
Surgical Rehabilitation

- Preserve intestinal remnant length
  - Minimize resection (tapering, stricturoplasty)
  - Restore continuity
  - Recruit additional intestine

- Improve motility
  - Relieve obstruction
  - Taper dilated bowel
  - Prolong intestinal transit (reversed segments, artificial valve, colon interposition)

- Increase absorptive area
  - STEP
  - Bianchi
Surgical Rehabilitation

- **Bianchi enteroplasty (1980)**
  - Longitudinal division of loop of distended bowel
  - Each mesenteric leaf supplies one of the divided segments
  - Divided segments are anastomosed
  - Early complication rate 20%
  - 50-80% sustained clinical improvement

- **STEP: Stepwise transverse enteroplasty (2003)**
  - Alternating staple lines
  - Reducing diameter while increasing length
  - Mortality 8%
  - 80% clinical improvement
  - Can be done more than once on same segment
Bianchi vs STEP

- Single Center review of lengthening procedures over 24 years
- Comparing survival, TPN weaning, complications
- 64 patients (14 adults)
- Complications 10%

<table>
<thead>
<tr>
<th></th>
<th>Bianchi</th>
<th>STEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures (#)</td>
<td>43</td>
<td>34</td>
</tr>
<tr>
<td>Remnant length before lengthening</td>
<td>44 cm</td>
<td>45 cm</td>
</tr>
<tr>
<td>Remnant length after lengthening</td>
<td>68 cm</td>
<td>65 cm</td>
</tr>
<tr>
<td>Overall survival (3.8y)</td>
<td>88%</td>
<td>95%</td>
</tr>
<tr>
<td>Time to discontinuation of TPN (months)</td>
<td>8.4</td>
<td>4.8</td>
</tr>
<tr>
<td>TPN weaning</td>
<td>55%</td>
<td>60%</td>
</tr>
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</table>

## Complications of Short Bowel Syndrome

<table>
<thead>
<tr>
<th>Catheter related</th>
<th>Hepatobiliary</th>
<th>Metabolic</th>
<th>Renal</th>
<th>Gastrointestinal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Intestinal failure associated liver disease</td>
<td>Fluid and electrolyte abnormalities</td>
<td>Chronic renal failure</td>
<td>Gastric hypersecretion</td>
</tr>
<tr>
<td>Loss of vascular access</td>
<td>Cholelithiasis</td>
<td>D-Lactic acidosis</td>
<td>Nephrolithiasis</td>
<td>Small bowel bacterial overgrowth</td>
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<tr>
<td></td>
<td>Micronutrient deficiency</td>
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<td></td>
<td>Changes in colonic flora</td>
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<td></td>
<td>Metabolic bone disease</td>
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<tr>
<td></td>
<td>Osteoporosis and osteomalacea</td>
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1989: first successful intestinal transplant
2011: 2067 intestinal transplants and 629 liver-pancreas-intestine transplants performed in the USA (75% in children)
Cost-effective compared to PN at 2 years
Early referral and listing are important to ensure greatest opportunity to obtain a transplant
Indications for Intestinal Transplantation in children

- **Failure of TPN (impending life-threatening complications)**
  - Intestinal failure-associated liver failure
  - Thrombosis of ≥2 central veins
  - ≥2 episodes/yr severe sepsis especially fungemia

- **Intestinal failure that virtually always results in early death despite optimal parenteral nutrition**
  - Extreme short bowel syndrome
  - Congenital intractable epithelial disorders

- **Controversial indications**
  - Intestinal failure with frequent hospitalizations, high enteric fluid losses or pseudoobstruction
  - Patient unwillingness to accept long-term parenteral nutrition (PN)

# Referral and Listing Criteria for IT

<table>
<thead>
<tr>
<th>Referral Criteria</th>
<th>Listing Criteria</th>
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<tbody>
<tr>
<td>Children with massive intestine resection</td>
<td>Small bowel length of &lt;25 cm without an ileocecal valve</td>
</tr>
<tr>
<td>Children with severely diseased bowel and unacceptable morbidity</td>
<td>Intestinal failure with high morbidity and poor QOL</td>
</tr>
<tr>
<td>Microvillous inclusion disease or intestinal epithelial dysplasia</td>
<td>Congenital intractable mucosal disorder such as microvillous inclusion disease or tufting enteropathy</td>
</tr>
<tr>
<td>Persistent hyperbilirubinemia (&gt;6 mg/dL)</td>
<td>Persistent hyperbilirubinemia (&gt;3–6 mg/dL) and signs of portal hypertension, or synthetic liver dysfunction with coagulopathy</td>
</tr>
<tr>
<td>Thrombosis of 2 of 4 upper body central veins</td>
<td>Loss of more than 50% of the standard central venous access sites</td>
</tr>
<tr>
<td>Continuing prognostic or diagnostic uncertainty</td>
<td>Recurrent life-threatening episodes of sepsis resulting in multiorgan failure, metastatic infectious foci, or acquisition of flora with limited antibiotic sensitivities</td>
</tr>
<tr>
<td>Request of the patient or family</td>
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</tbody>
</table>
Types of Intestinal Transplant

- Isolated intestinal transplant
- Intestine plus liver transplant
- Multivisceral transplant
Complications after Transplant

- **Acute rejection**
  - Breakdown of gut barrier function leading to bacterial translocation and infection
  - Main cause of graft loss and death

- **Infections**
  - Sepsis one of the main cause of death post-transplant
  - Immune suppression, breakdown of gut barrier and ischemia reperfusion injury contribute to high incidence
  - Viral infections can lead to severe and prolonged diarrhea

- **Chronic renal failure**

- **PTLD**
  - More common in ITx than in other solid organ transplant

- **GVHD 5%**
Outcomes

- Patient survival:
  - 1y: 80-94% (worse if <1y of age)
  - 3y: 65-84%
  - 5y: 50-70%
- Graft survival:
  - 1y: 88%
  - 3y: 74%
  - 5y: 58%
- 80-100% of pediatric recipients develop enteral autonomy within 1-3 months
Outcomes

- Single center retrospective review of 123 patients from 1994-2006
- Median age 16m (4m-17y)
- Median weight 9.5kg (4.4-67kg)
- Irreversible intestinal failure and complications of TPN
- Multivisceral or isolated intestine

Outcomes

- Single Center retrospective review of 87 children (93 transplants) from 1994-2010
- Patient survival (1/5/10y) 73%/69%/61%
- Graft survival (1/5/10y) 59%/46%/34%

Outcomes

- Multicenter cross-sectional survey of candidates and non-candidates for ITx (adult and pediatric)
- Evaluation of validity of AST listing criteria (failure of home PN/ high risk of death/ high morbidity)

Pironi et al. Survival of patients identified as candidates for intestinal transplantation: a 3 year prospective follow-up. Gastroenterol.2008;135:61-71
Summary

- Multidisciplinary approach to SBS and progress in all aspects of management have greatly improved outcomes over the past 20 years
- Home PN is first line treatment
- Medical intestinal rehabilitation is initial treatment focus
- Surgical intestinal rehabilitation (lengthening procedures) may further improve function
- Short- and long-term survival for intestinal transplantation are improving
- Intestinal transplant is accepted treatment for patients with failure of PN
References

- Sabiston Textbook of Surgery 19th edition
- Pironi et al. Survival of patients identified as candidates for intestinal transplantation: a 3 year prospective follow-up. Gatroenterol.2008;135:61-71