NEONATAL SHORT BOWEL SYNDROME

Neonatal short bowel syndrome is a consequence of small intestinal loss or resection, mucosal enteropathies, and motility disorders. There is shortened small intestines with malabsorption to a degree that standard feeding practices cannot support normal growth, and parenteral nutrition support is required for significant period of time. Bowel disease results in inability to sustain growth, hydration, and electrolyte homeostasis. The basic problem with small bowel syndrome is the loss of intestinal absorbing surface.

Causes of neonatal short bowel syndrome are necrotizing enterocolitis, volvulus, intestinal atresia, gastrochisis, and aganglionosis. Factors that have an impact on the neonate’s subsequent dependence on parenteral nutrition are the length of residual bowel, anatomical area of bowel resection, presence or absence of ileocecal valve and colon, viability of remaining intestines, and associated medical and surgical problems.

Small intestinal length is 115 cm +/- 21 cm in fetus between 19-27 weeks’ gestation. The intestine doubles in length during the last trimester.

Normal newborn intestinal length is 248 cm +/- 40 cm. The diameter of the newborn small intestines is 1.5 cm.

There is a direct relationship between the crown-heel length and intestinal length in normal infants from 32 weeks’ gestation through 3-4 years of age. There also is direct relationship between mucosal surface area and body weight and body surface area. The absorbing surface of 1 cm of intestines is approximately 600 cm2 as a result of villi and microvilli of the mucosal surface.

Pathophysiology of Short Gut Syndrome

Digestive and absorptive functions are not evenly distributed along the intestinal length. Mucosal villi of jejunum are longer with a greater absorbing surface than those of the ileum. The duodenum and jejunum are the main sites for digestion and absorption of carbohydrates, fats, protein, and fluids. The majority of electrolytes, minerals, and vitamins are absorbed in the proximal small bowel (except for vitamin B12). In intact intestines, ileum plays a lesser role in the same jejunal functions. The major nutritional complication of loss of jejunum is generalized malabsorption with calorie deficiency. Jejunum is principle site of iron absorption. Calcium and magnesium deficiency may be secondary to fat malabsorption with fatty acids forming insoluble salts with dietary calcium and magnesium.

Ileum is primary site for active absorption of vitamin B12 and conjugated bile salts. Jejunum cannot adapt and compensate for ileal functions. Unabsorbed conjugated bile salts reach the colon where bacterial deconjugation and dehydroxylation produce d-hydroxy bile acids. These abnormal bile acids provoke fluid and electrolyte secretion by
the colon. Fecal losses of malabsorbed conjugated bile acids deplete bile acid pool, impairing fat absorption and increasing potential for cholelithiasis. Steatorrhea increases concentration of unabsorbed long-chained fatty acids in the colon. These fatty acids are hydroxylated by colon flora and can stimulate fluid secretion by the colon. Ileal resection is also associated with hyperoxaluria and nephrolithiasis from oxalate stones.

The colon is the key site for retrieval of salt and water if their absorption has been inadequate in the small bowel. Colon is capable of absorbing free fatty acids, end product of bacterial fermentation of unabsorbed carbohydrates and, thus, may salvage carbohydrate calories lost through small intestinal malabsorption.

Adaptation to Small Bowel Resection

Adaptation to small bowel resection has three stages: early, intermediate, and late.

Early phase – hypertrophy and hyperplasia of residual intestine. This begins within 48 hours of intestinal resection, usually complete by 3-6 months after resection. Glucose and fluid absorption/cm increases. Ileum has greater capacity for these adaptive changes than does the jejunum. Exposure of intestinal mucosa to enteral nutrients, particularly glucose, provides fuel for the adaptive hyperplasia. Enteral nutrition is not only a luminal stimulant for intestinal adaptation, but also induces secretion of hormones that stimulate the process.

Gastrin levels often are increased at this time, and hypergastrinemia may produce clinically significant gastric hyperacidity.

Mucosal hypertrophy can be induced at any time after resection by starting feeds.

Intermediate phase – gradual dilatation of residual intestines and gradual increase in intestinal transient time. These changes are usually complete within the first 18-24 months after resection. Dilatation and delayed transient maximizes the contact of intestinal mucosa with luminal contents and improves nutrient absorption.

This could also be counterproductive; this could promote small bowel bacterial overgrowth with subsequent adverse events – such as bacterial translocation, deconjugation of bile acids, d-lactic acidemia, and hydroxylation of fatty acids.

Late adaptation – as infant grows in height, their bowel grows in length (at least until 3-4 years of age). Also, as child grows in height and weight, their calorie/kg body weight, and per cm2 of body surface area decreases. Requirement for calorie absorption per surface area of intestine decreases as the child grows. Key to this late adaptive process is maintenance of normal growth and nutrition, and prevention of complications of therapy that would hinder growth. Premature infants have small advantage since they have greater potential for bowel elongation than term infants. Intestines naturally doubles in length during the last trimester of gestation.
Management of Short Bowel Syndrome

The most important aspect of management of short bowel syndrome is assessment and replacement of fluid and electrolyte losses initially. Losses can be massive after surgery until adaptation occurs. Losses of sodium, potassium, calcium, phosphorus, magnesium, and zinc may be massive through diarrhea and, particularly, via stoma losses. Central alimentation is usually necessary with central line placement. IV nutrition to provide calorie, mineral, vitamin needs, and replace losses. Re-establish continuity between proximal and distal portion of the bowel as soon as possible as the colon plays critical role in salvage of water and sodium.

Any fever in patient with short bowel syndrome and central venous line should be considered line sepsis, and appropriate work-up and treatment initiated. Coverage for gram positive and negative bacteria should be instituted until culture results and sensitivities are available. Many episodes of bacterial sepsis can be treated without removal of central line. Fungal sepsis almost always requires removal of central lines.

Feedings

Enteral feedings should be initiated as soon as possible. The route (oral, NG, gastrostomy) and frequency (bolus versus continuous drip) depends on length of remaining small bowel. In patients with greater than 75% loss of small bowel, continuous enteral feedings by drip are most effective. Patients with more than 25% residual small bowel may do well with small bolus feeds by mouth. With feeding tolerance, small bolus feeds may be initiated. Daily assessment of infant’s tolerance to feedings is important. Volume of stool output relative to enteral intake, electrolyte losses in stool or stoma fluids, abdominal distention, emesis, presence of unabsorbed carbohydrates (reducing substance in stool) and integrity of perianal skin from loose stool.

Daily small increases in the amount of enteral feedings with evaluation of tolerance of tolerance allow goal of maximum utilization of infant’s residual absorbing surface without creating problems secondary to malabsorption. It is important to maintain IV nutrition as enteral nutrition is advanced.

Formula

Glucose polymer formulas are probably best tolerated. Lactose is least tolerated, although breast milk/colostrum is recommended. Combination of long chain triglyceride and medium chain triglycerides may be appropriate. Oligopeptides 2-5 amino acids are usually well tolerated. Choose formula with protein hydrolysate, MCT oil, and glucose polymers. Initiate at 1/4-1/2 strength, small volumes, bolus versus drip, assessing infant’s tolerance. Strength and volume may be increased, if tolerating previous feedings. Increased strength of formula is usually initiated first.
Supplements

Infants with short bowel syndrome need both fat and water soluble vitamin supplements. This is especially important after IV nutrition has been discontinued. An infant can have deficiencies even with normal growth. Mineral deficiencies may develop off of IV nutrition. Monitor sodium, potassium, calcium, magnesium, and zinc, especially with abnormal losses. Measure vitamin levels – A, D, E, K, vitamin B12. Iron requirements can be met after enteral feedings are started. Follow iron, iron-binding capacity, and ferritin.

Trace element deficiencies may occur on IV nutrition. Follow selenium, chromium, copper, and manganese. With cholestasis, copper and manganese will have to be limited.

Preservation of oral feeding function is a goal of short bowel syndrome. Prevent oral aversion. Some small oral feedings should be offered regularly, if possible. Avoid continuous use of pacifiers. Involve Speech/Feeding specialists for appropriate oral stimulation.

Soluble fiber, pectin, can be fermented in the colon, and may increase total calorie absorption through production of short chain fatty acids. Pectin may reduce fluidity of the stool. Little impact upon total water loss. Pectin, 1-3%, can be tried, especially with colon present.

Hyperacidity

Hypergastrinemia and hyperacidity can develop. H2 receptor antagonists and/or proton pump inhibitors may improve pancreatic lipolytic activity in fat absorption.

Gut Hypomotility

Nasojejunal feeding tube may be necessary with poor gastric motility.

Increased Gut Motility

Loperamide (Imodium) prolongs intestinal, mainly colon, transit time and may allow for better fluid and, possibly, nutrient absorption (0.1 mg/kg, given 2-3 times daily).

Cholestasis

Bile acid pool may be depleted, resulting in fat malabsorption. Ursodiol may increase fat absorption without causing diarrhea, and may decrease incidence of cholelithiasis by increasing bile flow.
Bile Acid-Induced Diarrhea

Cholestyramine and colestipol may be helpful with ileal resection. Resin therapy may deplete bile acid pool and exacerbate steatorrhea. Monitor for hyperchloremic acidosis and electrolyte abnormalities. Anion binders may decrease absorption of other anionic agents, like anticonvulsants and antibiotics.

Allowable stool output is 40-50cc/kg/day. Monitor stool pH, stool-reducing substance (sugars), and stool fat.

Feedings may be increased by 1 cc/hour with continuous drip twice a week, monitoring stool output. When half energy requirements are provided by enteral nutrition in a continuous fashion, try small bolus feeds. If stool output increases by more than 50% or output significantly positive for reducing substances or fat, hold advancement.

Transition parenteral nutrition to cyclic increasing time off by 2-4 hour increments until parenteral nutrition can be given over 8-12 hours.

Surgery

PICC, Broviac
Central TPN
Fluids: Third Spacing – NS
  Maintenance
  Ongoing losses – measure electrolytes of fluid losses and replace q2 hours.

- Bladder catheter until urine established.
- Accurate intake and output.
- Morphine or fentanyl drip first three days, then wean.
- Ativan, 0.1 mg/kg IV q4 hours prn.
- OG to LIS.
- Monitor Na, K, Cl, HCO2, Ca, P, Mg, Zn – especially with diarrhea/massive stoma losses.

Re-establish continuity between proximal and distal portion of bowel (colon) as soon as possible.

Central TPN – Cycle TPN. (Try to limit macronutrients to prevent cholestasis.)
- Glucose increase to 12-14 mg/kg/day.
- May need insulin.
- Protein increase to 3-3.5 gm/kg/day (Prealbumin).
- Fat increase to 1.5-3 gm/kg/day.
- Optimize Ca/P ratio – use cysteine CaP,AP.
- Use acetate to treat SBS metabolic acidosis.
• May need extra selenium, chromium, less copper manganese. (Measure urinary NA (normal >10 mg).
• Trophemine should be used.
• Ranitidine in TPB for SBS gastric hyperactivity.

Adaptation – Enteral Nutrition

• Start feeds as soon as possible (3-5 days postop).
• Wean pain medications (narcotics).
• OG, continuous drip at 10 ml/kg/day.
• If very short length remaining, will need GT placed soon to prevent feeding aversion. NJ tube with gastric hypomotility.
• Breast milk, donor breast milk, formula with glucose polymers, protein hydrolysate, MCT oil/LCT, elemental AA formula, premature formula (<2500 grams), or fortification of term formula for premature.
• Start at 1/4-1/2 strength. Increase strength first. Increase rate of drip 1 ml/hour every 3-4 days.
• Monitor stool output (40-50 ml/kg/day), stool pH, reducing substance (glucose), fat, and perianal skin integrity.
• Hold volume increases if stool volume increases or increase in stool tests. Infuse stool into mucous fistula.
• Any fever, rule out sepsis with blood culture through line and peripheral. Start antibiotics for grams positive/negative organisms.
• Follow growth, weight, length, and OFC weekly.

Supplements

• H-2 receptor antagonists/proton pump inhibitor.
• Pectin, 1-3%, in feeds (with colon).
• Loperamide (Imodium) to slow transit time, mainly colon. Codeine, tincture of opium, and ursodeoxycholic acid may increase fat absorption if extensive ileal resection.
• Cholestyramine for ileal resection diarrhea.
• Acidosis – acetate, bicarbonate.

• Vitamins – fat and water-soluble vitamins, vitamin B12, especially of TPN. Iron evaluation and administration - Fe, TIBC, ferritin.

• Trace elements evaluation and administration. Zn – Zn levels, alkaline phosphatase.

• Calcium administration.
• Small oral feeds 2-3 times/day. One hour volume off drip.

• Speech to give oral stimulation.

• Skin protection perianally, peristomy.

• Bacterial overgrowth – abdominal pain, worsening motility, mucosal ulceration with bleeding, de-conjugation of bile acids (diarrhea), toxic by products (D-lactic acid), sepsis/guaiac stools, D-lactic acid level, acidosis.
Table 4  Micronutrient deficiency or overload syndromes in intestinal failure

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Pathophysiology</th>
<th>Clinical deficiency syndrome</th>
<th>Clinical overload syndrome</th>
<th>Laboratory evaluation</th>
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</thead>
<tbody>
<tr>
<td>Minerals and trace elements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>Fat malabsorption</td>
<td>Paresthesias, tetany. bone demineralization</td>
<td>*GI, GU. bone complaints</td>
<td>Serum Ca, PTH, DEXA scan</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Fat malabsorption and high GI fluid losses</td>
<td>Weakness, cardiac, CNS</td>
<td>*Weakness, cardiac</td>
<td>Serum Mg</td>
</tr>
<tr>
<td>Zinc</td>
<td>GI fluid losses</td>
<td>Poor growth, skin, hair, diarrhea</td>
<td>*Vomiting, headache, diarrhea, Cu deficiency</td>
<td>Serum Zn, low alkaline phosphatase</td>
</tr>
<tr>
<td>Copper</td>
<td>Overload more common in cholestasis</td>
<td>*Hemolytic anemia, neutropenia</td>
<td>Hepatic overload, neuropsychiatric Neurotoxicity</td>
<td>Serum Cu</td>
</tr>
<tr>
<td>Manganese</td>
<td>Overload more common in cholestasis</td>
<td>*Poor growth, ataxia, skeletal</td>
<td></td>
<td>Serum Mn</td>
</tr>
<tr>
<td>Iron</td>
<td>Absorbed proximally; not routinely in TPN</td>
<td>Microcytic anemia, irritability</td>
<td>Hepatotoxicity, GI bleeding, vomiting</td>
<td>Ferritin, TIBC, Iron Binding Cap, Hgb, HCT, peripheral smear</td>
</tr>
<tr>
<td>Selenium</td>
<td>Absorbed throughout small bowel</td>
<td>Myopathy, cardiomyopathy</td>
<td>*Thyroid enlargement</td>
<td>Serum selenium</td>
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</tbody>
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Fat-soluble vitamins

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Pathophysiology</th>
<th>Clinical deficiency syndrome</th>
<th>Clinical overload syndrome</th>
<th>Laboratory evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Fat malabsorption, cholestasis</td>
<td>Xerophthalmia, blindness</td>
<td>Increased ICP, hepatitis, vomiting</td>
<td>Vitamin A: retinol binding protein ratio 25-OH vitamin D</td>
</tr>
<tr>
<td>D</td>
<td>Fat malabsorption, cholestasis</td>
<td>Hypocalcemia, hypophosphatemia, rickets</td>
<td>Emesis, renal impairment</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Fat malabsorption, cholestasis</td>
<td>Myopathy, neuropathy, ataxia, hemolytic anemia</td>
<td>Coagulopathy</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>Fat malabsorption, cholestasis</td>
<td>Bleeding</td>
<td>Hemolytic anemia</td>
<td>Vitamin E: total serum lipid ratio Prothrombin time, PIVKA assay</td>
</tr>
</tbody>
</table>

Water-soluble vitamins

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Pathophysiology</th>
<th>Clinical deficiency syndrome</th>
<th>Clinical overload syndrome</th>
<th>Laboratory evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>B12</td>
<td>Gastric or ileal resection</td>
<td>Megaloblastic anemia, CNS including ataxia</td>
<td>None known</td>
<td>Serum B12, methylmalonic acid, homocysteine</td>
</tr>
<tr>
<td>Folate</td>
<td>Absorbed proximally</td>
<td>Anemia, thrombocytopenia, stomatitis, glossitis</td>
<td>None known</td>
<td>Serum Folate</td>
</tr>
</tbody>
</table>

*Rare in pediatric intestinal failure.

Summary of clinical deficiency syndromes and recommended laboratory evaluations.

In patients who receive parenteral lipid therapy, serum triglyceride levels should be routinely followed up. Surveillance for essential fatty acid deficiency is advised for patients who are either on omega-3 fatty acid-based lipid solutions or with significant fat malabsorption that has been weaned off parenteral lipids. Essential fatty acid deficiency may present clinically in an infant with sparse hair, poor weight gain, poor wound healing, and thrombocytopenia, and laboratory evaluation confirms an elevated ratio of eicosatrienoic acid: arachidonic acid (triene: tetraene).46

Assessment of bowel length and function

Along with the nutritional evaluation of the IF patient, the clinical assessment should involve an estimation of the child’s residual bowel function. The relevance of posturgical bowel length and anatomy in the SBS patient has been previously emphasized, and the physical and radiographic examinations may help to assess bowel dilation, motility, and length. In the setting of SBS or primary motility disorders, abdominal radiographs may demonstrate dilated loops of a small bowel. Air fluid levels may be demonstrated in areas of mechanical obstruction, or in chronic intestinal pseudo-obstruction. Other objective evaluations of bowel motility including manometry and transit studies may provide insight into pathophysiology or bowel function in suspected primary motility disorders with IF.47 Patients with SBS may have disordered motility due to the disruption in normal neuroendocrine patterns in the postsurgical bowel. When indicated, contrast radiology may be used as a clinical tool to assess dilation, motility, and length. Nightingale et al48 reported a high correlation between radiographic and surgical measurements of small bowel length in 18 adult SBS patients. Recently, Rossi et al49 reported their experience in estimation of small bowel length on radiological