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Pediatric Short Bowel Syndrome: Nutritional Care


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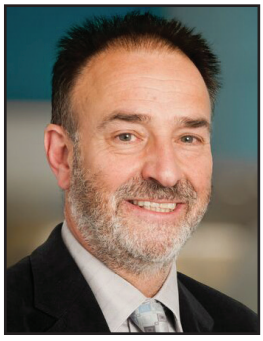
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Short bowel syndrome (SBS) is the most common cause of pediatric intestinal failure. The goal of treatment for SBS is intestinal rehabilitation involving the transition from parenteral nutrition to enteral autonomy. In order to achieve this, intestinal adaptation must occur with resulting structural and functional changes. Enteral feeds are a necessary factor in the promotion of adaptation. Children with SBS have significant malabsorption necessitating close monitoring of growth and laboratory studies in order to prevent deficiencies and maintain adequate growth. With the many complexities of this vulnerable population, it is important to have a multidisciplinary approach to their care as demonstrated by the success of intestinal rehabilitation programs.

INTRODUCTION

Intestinal failure occurs when the intestine is unable to absorb the necessary fluid and nutrition to support growth and development. The most common etiology of intestinal failure is short bowel syndrome (SBS), a term used to describe a critical loss of functional bowel length. Pediatric SBS often occurs as a result of surgical resection secondary to acquired gastrointestinal issues such as necrotizing enterocolitis or volvulus, or congenital anomalies such as gastroschisis and/or intestinal atresias (see Table 1). The goal of intestinal rehabilitation is to promote adaptation, the process by which the remaining intestine undergoes functional and histological changes in order to increase absorption after resection.[1] One of the most important stimulators of adaptation is intestinal exposure to nutrients. Over time, if carefully monitored and managed, most children with SBS will be able to transition from parenteral nutrition (PN) dependence to enteral autonomy.[2]

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Nutrition Assessment

A thorough nutrition assessment is important for the management of pediatric patients with SBS. See Table 2 for baseline nutrition evaluation components. Nutrition reassessment should occur regularly with frequent reevaluation for

the child on home PN. Evaluation can decrease in frequency according to the patient's specific needs, but even older children who have become enterally autonomous require a full nutritional assessment at least annually. Management by a multidisciplinary team (including physician, pediatric surgeon, registered nurse, registered dietitian, and pharmacist) has been shown to improve morbidity and mortality for patients with SBS as well as decrease reliance on PN.[3,4]

Growth goals for patients with SBS are the same as other pediatric patients although growth failure is common.[5-7] Weight gain at a lower percentile for age is acceptable while on PN if linear growth is tracking consistently along the child's established growth curve. Children with SBS are at particularly high risk for growth failure in the first two years of life and during their adolescent years, both periods of high-expected growth.[5,7] Some children who progress to enteral autonomy in their childhood years may require re-initiation of PN in their adolescent years if they demonstrate growth delays or other nutrient deficiencies.

Calculating Nutritional Needs

Provision of adequate calories and nutrients can promote age appropriate growth and development. Avoidance of overfeeding patients who are PN-dependent is also critical in the prevention of intestinal failure associated liver disease (IFALD).[8] Calories should be decreased for patients with excessive weight gain or those with weight-for-length or BMI >95th percentile for age. Generally, calories from PN are not reduced with introduction of enteral nutrition (EN) until tolerance and weight gain is established with feeds. As a result of malabsorption, enterally autonomous children with SBS may require enteral intake up to 200-250 kcal/kg/day in order to achieve adequate growth[9,10] (Table 3).

Protein needs for these patients are also higher than expected for age due to increased gastrointestinal losses. Infants who are PN dependent may require up to 4 g/kg/day while older children may require 2-3 g/kg/day of protein from a combination of intake types even into adolescent years to maintain appropriate growth and development.[9,10]

Fluid needs to maintain hydration are typically higher than age matched controls due to high GI losses. Actual fluid needs may vary depending on the length of remaining bowel, portion of remaining bowel (those with preserved colon often have lower fluid requirements), and total daily stool or ostomy output. Some patients who are enterally autonomous may have even higher fluid requirements of up to 150-200 mL/kg due to higher GI losses. Furthermore, these increased losses often necessitate a higher sodium provision, both parenterally while receiving PN, and enterally, after enteral autonomy is attained.

Table 1. Causes of Pediatric Intestinal Failure

- Short bowel syndrome
  - Necrotizing enterocolitis
  - Gastroschisis
  - Intestinal Atresia
  - Volvulus
  - Intestinal aganglionosis
  - Meconium Ileus
- Motility disorders
  - Chronic intestinal pseudoobstruction
- Congenital enteropathies
  - Microvillus inclusion disease
  - Tufting enteropathy

Laboratory Monitoring

With the significant risk of nutrient deficiencies, regular laboratory monitoring is required. This is especially important for patients who are on parenteral nutrition. There is significant variation in the frequency of lab monitoring recommended by different intestinal rehabilitation centers and authors.[11-13] See Table 4 for a suggested lab monitoring protocol.

Parenteral Nutrition

Careful management of PN by multidisciplinary intestinal rehabilitation teams has allowed for significant improvements in survival as a result of decreases in complications associated with PN

and the required central venous access.[14] Recent advances in PN include:

- New lipid formulations that have helped decrease IFALD and,
- Careful management of micronutrient delivery.

However, challenges remain with frequent product shortages of nearly all PN components.

Until recently, the only FDA-approved intravenous lipid emulsion (IVLE) in the U.S. was soybean oil-based Intralipid™ (Baxter/Fresenius Kabi). These products contain high levels of pro-inflammatory omega-6 fatty acids and hepatotoxic phytosterols shown to contribute to development and progression of IFALD.[15] In order to minimize these negative effects, Intralipid™ doses are often restricted to 0.5-1.0g/kg/day with improvement in liver disease. This change typically necessitates an increase in glucose infusion rates to make up for lost lipid calories. High glucose infusion rates can further contribute to IFALD. To help address these issues, Omegaven™ (Fresenius Kabi), a fish oil-based lipid emulsion consisting of only omega-3 fatty acids, was introduced in the early 2000s. Because it was found to successfully reverse cholestasis in IFALD,[16] Omegaven™ was FDA-approved in 2018 for use in children with PN-associated cholestasis. Concerns have been raised regarding development of fatty acid abnormalities related to the isolated provision of omega-3 fatty acids long-term. Recently the FDA approved SMOFlipid™ (Fresenius Kabi) for use in adults. It is currently being widely used off-label for children with SBS. SMOFlipid™ is a mixed-lipid emulsion consisting of 30% soy, 30% MCT, 25% olive, and 15% fish oil. Studies of children with intestinal failure have shown prevention of IFALD with SMOFlipid™.[17-19] Fish-oil lipid emulsion may still be necessary to treat cholestatic IFALD if it develops despite use of SMOFlipid™. While Omegaven™ is typically dosed at 1 gm/kg/day, SMOFlipid™ has been shown to be safe at higher doses allowing for an improved balance of calories. There is evidence that at least 2 g/kg/day of SMOFlipid™ is necessary to prevent and treat

Table 2. Baseline Nutrition Evaluation Components

- Review of medications and supplements
- Relevant medical history (including notation of the remaining portions and lengths of bowel)
- Laboratory measurements (see Table 4)
- Analysis of nutritional intake
- Stool output
- Anthropometric measurements (including age, weight, height, occipital frontal circumference for infants, and mid-upper arm circumference).

Table 3. Estimated Calorie Needs for Pediatric Patients with SBS

Age	Exclusively PN Dependent	Enteral
Infants 0-6 months	85-105 kcal/kg	120-200+ kcal/kg*
Infants 6-12 months	80-100 kcal/kg	100+ kcal/kg*
Toddlers/Children	50-90 kcal/kg	80+ kcal/kg*
Adolescents	30-50 kcal/kg	REE x 2+*

*depending on degree of malabsorption and length of remaining bowel
Adapted from Mirtallo, 2004[10]

essential fatty acid deficiency.[20,21] With changes in the amount of fatty acids provided with various IVLE, it is suggested that the individual levels of fatty acids, specifically linoleic acid, alpha-linolenic acid, Mead acid, and the triene-to-tetraene ratio all be taken into account when considering the fatty acid status of a patient.[22] Table 5 compares the contents of the three IVLE commonly used in pediatric SBS.[23]

Enteral Nutrition

In order to promote adaptation and prevent intestinal atrophy, enteral feeds are started as soon as possible after intestinal resection.[24,25] Some children can achieve nutritional goals by mouth while others may require a feeding tube. With the heterogenous nature of SBS, there is no optimal feeding regimen or advancement schedule that is appropriate for all patients, although in general, initial trophic feeds are started and advanced slowly. Advancement is continued if stool frequency and volume does not drastically increase. For patients with an ostomy, goal output is typically <30-40ml/kg/day, although patients may tolerate higher amounts without significant dehydration or electrolyte imbalances as long as the output and laboratory studies are

Table 4. Suggested Lab Monitoring for Pediatric SBS Patients

Lab Parameters	Frequency			
	PN Dependent		Enterally Autonomous	
	Monthly*	Every 3 Months	At Each Visit	Every 3-12 Months
CBC	x		x	
Electrolytes, Glucose, BUN, Creatinine, Calcium, Magnesium, Phosphorus,	x		x	
AST, ALT, GGT, Alkaline phosphatase Bilirubin (direct, indirect and total), albumin	x		x	
Prothrombin time /INR	x		x	
Total Cholesterol		x		
Triglycerides		x		
Iron, % saturation, total iron binding capacity		x		x
Vitamins: A, D & E		x		x
Retinol Binding Protein		x		x
Zinc		x		x
Copper		x		
Selenium		x		
Essential Fatty Acid Profile		x		x**
Vitamin B12, methylmalonic acid		x**		x**
TSH, Free T4		x^		
Urine iodine		x^		
Urine sodium		x^^		

*If seen more frequently than monthly, check labs at each visit
**Check annually if last check was normal
^If receiving >70% of calories from parenteral nutrition
^^Check if high volume ostomy or stool output

Table 5. Comparison of Intravenous Lipid Emulsions

Source (%)	Intralipid™	SMOFlipid™	Omegaven™
Soybean	100	30	0
MCT*	0	30	0
Olive oil	0	25	0
Fish oil	0	15	100
Vitamin E (mg/L)	38	200	150-296
Phytosterols (mg/L)	348	47.6	0
	Fatty acids (%)		
Linoleic	44-62	21.4	4.4
α-Linolenic	4-11	2.5	1.8
DHA	0	2	12.1
EPA	0	3	19.2
Arachidonic	0	0.15-0.6	1-4

*MCT = medium chain triglycerides
Adapted from Vanek, 2012[23] and Fresenius Kabi the manufacturer of Intralipid™, SMOFlipid™, and Omegaven™.

carefully monitored.

Human breast milk is preferred as it contains growth factors, immunoglobulins, and other components that stimulate adaptation.[26] If breast milk is not available, elemental formula has historically been used, although there is evidence in animal studies that more complex nutrients promote adaptation.[27] Human studies have been small and do not clearly show benefit of one type of feeding over another.[25] With a lower osmotic load, children with SBS often tolerate larger volumes of lower caloric density formula, so it is our practice to start with dilute standard infant formula. Typically, this involves starting with 15 kcal/oz formula for infants and 20 kcal/oz for older children and delaying increasing caloric density until tolerating goal volume feeds and PN is being weaned.

The increased interest in whole food-based formulas has brought us commercially available, nutritionally complete products that resemble a blenderized feed. While some patients require blenderized feeds to be diluted, as they often have a high caloric density, others, especially those with a colon segment, tolerate them well. There is a likely benefit from the significant fiber content in many blenderized formulas which not only acts as a prebiotic, but slows down intestinal transit allowing more time for absorption, and provides the fuel for colonocytes to make short chain fatty acids providing additional calories to the patient.[28,29]

Children with SBS are at high risk for developing oral aversion due to their complicated medical history and the limitations on enteral feeds early on. It can also be a limiting factor in the ability to wean a patient off of PN as patients tend to tolerate larger amounts of food orally even if they do not tolerate larger volumes or more calorically dense formula. In order to avoid oral aversion, it is important to start oral feeds as early as possible even if the feed volume is minimal. With improvements in long-term PN management, there is less pressure to quickly advance enteral feeds allowing infants to develop the necessary oral

Table 6. Resources for Both Clinician's and Patient/Families

For Clinicians
• NASPGHAN patient education website (GIKids.org) • NASPGHAN clinician focused website (NASPGHAN.org) • Clinical Management of Intestinal Failure, Textbook, Christopher P. Duggan, MD, MPH, Kathleen M. Gura, PharmD, BCNSP, FASHP, and Tom Jaksic, MD, PhD (2011) • Pediatric Intestinal Failure, Christopher P. Duggan, MD, MPH and Tom Jaksic, MD, MPH, New England Journal of Medicine (2017)
For Patients/Families
• A Kid's Guide to Short Bowel Syndrome (sponsored by Takeda) o Available at no cost at: **https://www.shortbowelsyndrome.com/** o Go to "Sign Up" tab on top bar--takes you to section to order a free book

skills. Although many programs use gastrostomy tubes for slow continuous feeding, delay of gastrostomy placement may help achieve these early oral feeding goals and prevent development of oral aversion by focusing all feeding efforts on the oral route. If patients are being tube fed, feeds can be held to allow for bottle feeds several times per day. A nocturnal regimen can give the child time off the pump during the day and help to stimulate hunger to aid in oral intake.

As the child approaches 6 months corrected age, age-appropriate foods should be introduced with a focus on vegetables, proteins, and complex carbohydrates. Children with SBS need to follow a diet low in sugar (natural, added, sugar alcohols [sorbitol, mannitol, xylitol, erythritol], or artificial sweeteners) as sugars and sweeteners can create an osmotic load contributing to increased stool output. Sugars can also worsen small intestinal bacterial overgrowth which can cause diarrhea, abdominal distention, emesis, poor growth, intestinal bleeding, and may contribute to IFALD.[30] While some sugar and artificial sweeteners may be tolerated, following the recommendation to avoid sweet tasting food in young children may prevent them from developing a preference for sweet foods.

Micronutrient Deficiencies

Children with SBS are at high risk for multiple micronutrient deficiencies while receiving full PN, during the transition to enteral nutrition, and once enterally autonomous.[31] In recent years, PN component shortages have become more common resulting in deficiencies.[32] In order to address individual trace element deficiencies in PN-dependent patients, it is important to be able to adjust them individually. Use of commercially available standard pediatric PN trace element solutions can also result in manganese and chromium toxicity as these micronutrients are both found as contaminants in PN. For these reasons, separate dosing of trace elements is recommended for pediatric SBS patients.

The degree of micronutrient risk and deficiencies vary depending on the length of bowel and which portions of the intestine remain. Those with loss of the terminal ileum are at higher risk for fat soluble vitamin deficiencies, vitamin B12 deficiency, as well as essential fatty acid deficiency. With increased overall gastrointestinal losses, patients are also at risk of sodium, magnesium, and zinc deficiencies. While there are numerous deficiencies seen in SBS, some of the most common include iron, fat-soluble vitamins, vitamin B12, and iodine.

Iron

Iron deficiency is the most common deficiency seen in SBS. Iron infusions are often needed for those receiving significant amounts of PN and enteral supplementation in those off PN. Iron is not typically included in PN, although iron dextran

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has been added to lipid-free PN by some groups.[33] While children who have reached enteral autonomy will likely tolerate enteral iron supplementation, children receiving full PN support will likely require IV iron infusions to treat and prevent iron deficiency. Iron sucrose has traditionally been used anywhere from weekly to monthly in order to replete and maintain iron stores. More recently ferric carboxymaltose has been used in patients with inflammatory bowel disease with iron deficiency. It is given at a higher dose than iron sucrose and has structural alterations that lead to longer duration of drug activity.[34] Hypophosphatemia, which can be severe and symptomatic, has been associated with ferric carboxymaltose making it essential to follow patient labs and clinical status in the weeks following infusion.[35,36] With careful monitoring, ferric carboxymaltose may help SBS patients require less frequent infusions (and line access) with improved iron status.

Fat-soluble Vitamins

Fat malabsorption is a common complication of SBS and a factor in the development of fat-soluble vitamin deficiencies. The doses of fat-soluble vitamins required for enterally autonomous patients can be quite high secondary to significant malabsorption. Vitamin A deficiency tends to respond well to enteral supplementation while vitamin E often requires a water-soluble formulation to optimize absorption. The dose of vitamin D included in the parenteral multivitamin is rarely enough to prevent vitamin D deficiency requiring additional supplementation.[37] With no separate parenteral form of vitamin D available in the United States, vitamin D deficiency that is refractory to enteral supplementation may require transition to calcitriol. There is a significant amount of vitamin E in both SMOFlipid™ and Omegaven™, typically preventing vitamin E deficiency until patients are off intravenous lipids (Table 5).

Vitamin B12

Vitamin B12 requires the terminal ileum for food-bound B12 absorption. Deficiency can lead to megaloblastic anemia and irreversible neurologic changes. As it is supplemented in PN, deficiency is often not an issue until patients are enterally autonomous. For monitoring, it is important to check both a B12 and methylmalonic acid level, as serum B12 levels can be unreliable.[38] Elevated methylmalonic acid levels are found in B12 deficiency, but can also be seen in small intestinal bacterial overgrowth so it is important to evaluate the patient's entire clinical picture when interpreting these labs.[39,40] Supplementation for children with SBS is most reliable in the injectable and nasal forms although sublingual preparations may be used as well. Oral B12 supplements are typically not useful in SBS due to significant malabsorption, the loss of the distal ileum in many patients, and the small amount of B12 that is passively absorbed when given in high doses via the oral route.[38]

Iodine

Iodine is another micronutrient of concern for children who are fully dependent on PN (>70% of calories provided by PN) as it is not routinely included in PN solutions in the United States and is important for growth and development. Monitoring of thyroid hormones, thyroglobulin, as well as urine iodine levels can help identify patients with iodine deficiency.[11,41] Iodine deficiency should be considered for urinary iodine levels <100 mcg/L; <50 mcg/L indicates moderate, and <20 mcg/L, severe deficiency.[42] Repletion of iodine can be difficult to achieve in children who are fully PN dependent, as they will not likely absorb an enteral supplement such as iodized salt. The use of ultra-dilute potassium iodide or topical iodine may be useful.[43]

CONCLUSION

Nutritional management is a major focus of intestinal rehabilitation in children with pediatric SBS. Multidisciplinary intestinal rehabilitation programs have been shown to improve the care and outcomes for this medically and surgically complex population. With careful monitoring of growth and nutritional lab values, prevention of complications associated with PN, and transition to enteral feeds with slow advancement, intestinal adaptation and enteral autonomy is achievable in most children with SBS. ■

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