Short bowel syndrome (SBS) is a malabsorption syndrome resulting from extensive intestinal resection. Although the diagnosis of SBS relies less on an anatomical definition and more on a functional definition, for practical purposes in adults SBS can be defined as the presence of <200cm of remaining small intestine. In infants, necrotizing enterocolitis and congenital intestinal anomalies are frequently responsible. In older children and adults, multiple resections for Crohn's disease and massive resections due to catastrophic mesenteric vascular events, radiation enteritis, adhesive obstruction, and trauma represent the more common causes of SBS. These patients frequently experience chronic diarrhea, dehydration, and macro- and micronutrient deficiencies often requiring enteral or parenteral nutrition support at home.

While SBS is uncommon, it remains an important clinical problem due to its effect on the quality and duration of life of these patients, the high rate of associated complications, and the subsequent high costs involved in their care. Survival studies from France and the US have demonstrated two-year and five-year survival rates for SBS at over 80 and 70%, respectively. Furthermore, the study from France reported parenteral nutrition (PN) dependency at two years of 49%, and 45% at five years. Survival rates were lowest in the end-jejunostomy and ultra-short small bowel groups. Other factors affecting survival include the patient's age, primary disease process, comorbid diseases, presence of chronic intestinal obstruction, and the experience of the team managing the patient. Knowledge of the small bowel length can be useful for predicting the clinical outcome in SBS patients. The large range of small bowel length in humans (300–800cm) underscores the importance of being aware of the small bowel length remaining following a resection rather than the length of small bowel removed. When an operative report is unavailable or incomplete, a barium contrast small bowel series may provide an estimate of bowel length and is useful to delineate other structural features, such as the presence of bowel dilatation.

The region of the remaining small intestine and the presence of the colon also affect the outcome of the SBS patient. In general, an SBS patient will have one of the following bowel anatomies: jejuno-colic anastomosis, end-jejunosotomy, or jejuno-ileoileocolic anastomosis. Patients with a jejuno-ileoileocolic anastomosis have the best prognosis; however, this anatomy is the least common. Patients with an end-jejunosotomy are the most difficult to manage and are the most likely to require permanent parenteral support. A jejunal resection is generally better tolerated than an ileal resection because the ileum is capable of both structural and functional adaptation, while the jejunum mainly adapts functionally. Intestinal adaptation refers to a process following intestinal resection in which the remaining bowel undergoes a variety of macroscopic and microscopic changes in response to a number of stimuli in order to increase its ability to absorb fluid and nutrients. This stage may last for up to two years and it is during this time that most PN weaning occurs. The presence of the colon is beneficial in SBS patients given its ability to absorb water, electrolytes, and short-chain fatty acids (as an additional energy source), slow intestinal transit, and stimulate intestinal adaptation. It has been suggested that, in terms of need for PN, the presence of at least half of the colon is equivalent to about 50cm of small bowel.

Intestinal Rehabilitation

The relatively recent concept of intestinal rehabilitation emphasizes strategies to reduce or eliminate the need for PN and small bowel transplantation and can be applied to both adult and pediatric populations. A major component of intestinal rehabilitation consists of medication and dietary and fluid manipulation and, as such, lifestyle changes and increased out-of-pocket expenses are required on the part of the patient. The provision of patient education relative to the underlying disease process and the treatments being prescribed is important to enhance compliance with the care plan. SBS patients differ in their response to dietary and fluid manipulation depending on their bowel anatomy—specifically, the presence or absence of a colon. A high-carbohydrate (60%), low-fat (20%) diet has been shown to reduce fecal calorie loss, increase overall energy absorption, and result in improved wet weight absorption in SBS patients with colon-in-continuity. In contrast, end-jejunosotomy patients do not seem to benefit from dietary modifications. Owing to regional differences in water and sodium handling, those SBS patients without a colon generally require the use of a glucose-electrolyte oral rehydration solution (ORS) to enhance absorption and reduce secretion. The ingestion of an ORS with a sodium concentration of 90–120mEq/l has been...
shown to provide optimal jejunal absorption. While fluid composition is less important in those with a colon, adequate dietary sodium should be provided. Regardless of bowel anatomy, hyperosmolar fluids such as regular soda and fruit juices should be avoided, as they will aggravate stool losses.

Although a detailed discussion of optimal SBS diet is not possible here, the provision of complex macronutrients in the diet of SBS patients is preferred; lactose is generally well tolerated and need not be restricted unless the patient is clearly intolerant; concentrated sugars should be avoided as they generate a high osmotic load and potentiate stool output; and restricted use is important only in those SBS patients with a colon in order to decrease the risk of oxalate nephropathy. The long-term success of an optimized diet requires extensive education and monitoring to maintain compliance and needs to be translated into foods and meal patterns that meet the individual’s preferences, lifestyle, and, in children, developmental age. Massive enterectomy is associated with a transient gastric hypergastrinemia and hypersecretion, which can result in increased stool output, peptic complications, and/or impairment in the function of digestive enzymes. H2-receptor antagonists and proton pump inhibitors may be beneficial, particularly during the first year following resection. Patients with high-output jejunostomies may occasionally benefit from treatment with the somatostatin analog octreotide. Open-label studies suggest a clinical benefit of both short-acting (e.g., 100μg given subcutaneously three times daily for 30 minutes before meals) and long-acting forms. However, this beneficial effect is often short-lasting, and the use of octreotide has not been shown to improve absorption or lead to the elimination of the need for PN.

Antidiarrheals work mainly to reduce intestinal motility, but also cause a slight reduction in intestinal secretion. Commonly used agents include loperamide, diphenoxylate, codeine, and tincture of opium. The use of codeine and tincture of opium tends to be limited by their sedating effect, potential for addiction when used long-term, and cost. In adults, loperamide 4mg four times daily has been shown to be more effective than codeine 60mg four times daily; however, there may be a synergistic effect when these agents are used together. In the setting of SBS, these agents seem to be most effective when administered before meals and at bedtime. Clonidine, which can be administered transdermally, may also be useful to treat high-output stool losses via its effects on intestinal motility and secretion. With the loss of significant portions of the ileum (i.e., >100cm in adults), bile acid malabsorption may exceed maximal hepatic synthesis, leading to a decrease in the bile acid pool and resulting in impairment of luminal fat digestion. Uncontrolled case studies using ox bile supplements and the synthetic conjugated bile acid cholytricosine have demonstrated improvements in fat absorption. While the initial reports are encouraging, these agents are not readily available at present. The use of bile acid sequestrants such as cholestyramine may worsen steatorrhea and fat-soluble vitamin losses in those with >100cm of distal ileum resected, and should generally be avoided in the SBS patient.

The development of small intestinal bacterial overgrowth (SIBO) appears to be common in SBS patients and may affect their ability to be successfully weaned off PN because of symptoms that impede oral intake and exacerbate malabsorption. When suspected, collection of small bowel fluid for quantitative culture is recommended to diagnose SIBO in the setting of SBS. Once pathological SIBO has been identified, oral antimicrobial treatment incorporating a broad spectrum of coverage is generally prescribed, with success being judged by an improvement in symptoms, reduction in stool output, and/or weight gain. Micronutrient, and sometimes electrolyte (e.g., magnesium), supplementation becomes necessary as PN is weaned and levels require periodic monitoring. The frequency of monitoring will depend on the stage of PN weaning and the presence of existing or prior deficiencies. As water-soluble vitamins are absorbed in the proximal small bowel, deficiencies in SBS patients are uncommon. In contrast, fat-soluble vitamin and essential fatty acid deficiencies are more commonly encountered. Supplemental zinc, and occasionally selenium, may be required in the presence of excessive stool losses. Lifetime administration of supplemental vitamin B12 is needed in those with more than 50–60cm of terminal ileum removed.

**Trophic Factors**

Many SBS patients are unable to be weaned completely from PN even after implementation of an optimized diet and medical care as described. Despite advances in the provision of PN, this mode of nutritional support carries with it significant risks to the patient such as catheter sepsis, venous thrombosis, and liver disease. As a consequence, there has been intense investigation to identify treatments that maximize intestinal absorption/adaptation with the goal of eliminating or at least minimizing the need for PN. Recent investigations in humans have focused on the use of growth hormone (GH) and glucagon-like peptide-2 (GLP-2).

To date, only trials using a combination of GH, glutamine, and an optimized diet with PN weaning as the primary end-point have been published. In an open-label trial, Byrne et al. treated 47 patients, most of whom had a colon-in-continuity, with a combination of GH, oral glutamine, and an optimized diet for three weeks followed by continued use of the diet and glutamine. With follow-up for as long as five years, 40% of patients could be weaned completely from PN while another 40% could make significant reductions in their PN use. A more recent randomized, controlled study of this combination treatment approach in 41 PN-dependent SBS patients (most with colon-in-continuity) demonstrated a significant reduction in PN requirements in all groups studied; however, the extent of reduction was greatest and longest-lasting in the group in which GH was administered in addition to the diet and glutamine. On the basis of this evidence and the safety of the treatment program, the US Food and Drug Administration (FDA) approved the use of recombinant human GH in patients with SBS on PN as an aid for PN weaning. Nevertheless, due to conflicting findings on nutrient absorption reported in three prospective, randomized, controlled trials, the role of this combination therapy remains controversial. Further controlled studies investigating the optimal dose, duration, and timing of administration in relation to the onset of SBS are needed before this therapy can be routinely advocated for SBS patients.

GLP-2 appears to be a promising gut hormone that plays a role in intestinal adaptation. In a small, open-label trial investigating the effects of GLP-2 in humans with SBS, the administration of 400μg GLP-2 twice daily for 35 days resulted in an increase in overall energy absorption, a decrease in fecal wet weight, a slowing of gastric emptying, and a non-significant trend toward increased jejunal villus height and crypt depth. More recently, a longer-acting GLP-2 analogue, tegludotide, was shown to be safe, well-tolerated, and intestinotrophic, and significantly increased intestinal wet weight but not energy absorption in 16 SBS patients. Although there are currently no data on tegludotide’s utility in PN weaning, a large, multinational, randomized, controlled trial to study this issue is currently in progress.
Short Bowel Syndrome

Autologous Gastrointestinal Reconstruction

Non-transplant surgical procedures have been devised with the goal of maximizing the function of the SBS patient’s existing intestine. These procedures are sometimes referred to as surgical intestinal rehabilitation or autologous gastrointestinal reconstruction. The choice of surgery is influenced by the existing bowel length, function, and caliber and can be divided into procedures that optimize function (e.g., lengthen, taper) or slow transit (e.g., reversed segment). These procedures should be considered only after the initial adaptive period and with specific goals in mind. Additionally, operations such as these should be considered only when the patient is stable and medical and dietary management has been maximized. While there are encouraging results from case series, evidence of long-term success has not yet been documented and only a small proportion of SBS patients are candidates for these procedures.

Small Bowel Transplantation

Small bowel transplantation (SBT) may be considered in SBS patients with a lifelong need for PN when complications of PN such as liver disease, loss of venous access sites, or recurrent episodes of life-threatening catheter sepsis occur. SBT can be performed in isolation, in combination with liver transplantation, or in combination with transplantation of multiple organs. The outcome following intestinal transplantation has improved considerably with the development of more potent immunosuppressants and improvements in surgical techniques and other aspects of care following transplantation. SBT patient survival rates are beginning to approach those of liver transplant patients, particularly in those who are well enough to wait at home for their transplant. Nevertheless, graft survival rates remain significantly lower than patient survival rates and a considerable percentage of patients with a functioning graft may still require PN. Therefore, while transplantation remains a promising and exciting therapeutic option, improved patient and graft survival and an increased likelihood of graft function in order to ensure the discontinuation of PN are necessary before it can be recommended to more SBS patients.

Conclusion

Management of SBS patients is complex, requiring a comprehensive, multidisciplinary approach. Specific dietary intervention combined with careful medical management and, sometimes, surgical strategies offers the potential of PN reduction and overall improved clinical outcome. While still controversial, the administration of trophic factors alone or combined with diet modification may allow enhanced adaptation and PN reduction. Small bowel transplantation remains a promising treatment for appropriate candidates.

References