NEHA PAREKH, MS, RD, LD, CNSD
Intestinal Rehabilitation Program, Departments of Gastroenterology and General Surgery, The Cleveland Clinic Foundation

DOUGLAS SEIDNER, MD
Department of Gastroenterology, The Cleveland Clinic Foundation

EZRA STEIGER, MD
Department of General Surgery, The Cleveland Clinic Foundation

Managing short bowel syndrome: Making the most of what the patient still has

ABSTRACT

Short bowel syndrome (severe malabsorption after resection of the small bowel) is characterized clinically by chronic diarrhea, dehydration, electrolyte abnormalities, and malnutrition. The severity and management depend on the site and extent of the intestinal resection, whether the ileocecal valve remains, whether there is disease in the residual bowel, and the degree of adaptation of the remaining bowel.

KEY POINTS

Patients with an intact colon should follow a high-carbohydrate, low-fat diet. Those without a colon should eat a diet with moderate carbohydrates and moderate fat. Fruit juices and sweets exacerbate diarrhea and should be avoided.

Excess fluid loss should be replaced by sipping a glucose-and-salt solution, preferably the World Health Organization's oral rehydration solution or a similar commercially prepared solution.

Patients should eat five or more small meals a day, minimize concentrated sugars, maximize complex carbohydrates, and drink fluids between meals. Fiber, multiple vitamins (including vitamin B_{12}), calcium, and magnesium should be supplemented when indicated.

Various medications reduce intestinal fluid output. Restorative surgery and growth factors that enhance intestinal adaptation may reduce dependency on total parenteral nutrition.

PATIENTS WHO DEVELOP short bowel syndrome after surgical resection of the small intestine may be able to avoid or reduce their need for total parenteral nutrition (TPN) by following an individualized regimen of diet and medical therapy. If conservative measures fail, surgical options are available, including small bowel transplantation.

TPN and other intravenous fluids can now be given at home, but these measures can be complicated by life-threatening sepsis, liver failure, and metabolic bone disease. It is still better to eat and drink than to receive nutrition by the intravenous route.

ANATOMY OF SHORT BOWEL SYNDROME

Short bowel syndrome occurs in patients who have had extensive resection of the small intestine, commonly because of intestinal ischemia, Crohn disease, radiation enteritis, volvulus, or cancer. It is characterized by severe malabsorption, typically presenting with chronic diarrhea, dehydration, electrolyte abnormalities, and malnutrition.

The normal small intestine varies in length from 365 to 600 cm and has a surface area of 3,300 cm^2. However, when we include the Kerckring's folds (the numerous circular folds of the mucous membrane, also known as plicae circulares or valvulae conniventes) and the villi and microvilli, the true absorptive surface area is about 2 million cm^2, comparable to the size of a tennis court.

The large intestine, in contrast, is about 150 cm long in most people and does not have

villi or a markedly increased absorptive surface.

Mechanisms of malabsorption

A number of mechanisms contribute to malabsorption after massive resection, including acid hypersecretion, hypergastrinemia, rapid intestinal transit (especially likely when the distal ileum is resected, or parts of the colon containing peptide YY—the so-called "breaking hormone"—are lost), impaired residual bowel, loss of surface area, bacterial overgrowth in dilated segments of small bowel, and bile acid depletion.

How much of the intestine is left?

Whether a patient needs TPN depends, to a large extent, on how much intestine remains. To avoid TPN, a patient typically needs a minimum of either 60 to 90 cm of small intestine along with a portion of the colon, or 150 cm of combined jejunum and ileum if no colon is left.

Unfortunately, the length of intestine left intact is not often recorded in operative reports; usually only the amount resected is mentioned. Two methods can help estimate the amount of small intestine remaining:

The small intestine has a surface area as big as a tennis court

Plasma citrulline is believed to be a biological marker of enterocyte mass. Citrulline, an amino acid that is not incorporated into exogenous or endogenous proteins, is synthesized in enterocytes from muscle-derived glutamine and converted by the kidney into arginine. In one series,[1] all patients with a plasma citrulline level of 20 μmol/L or less required permanent home TPN.

An opisometer, a device used in map reading to measure curved lines, can be used by radiologists to assess the length of the small bowel.[2]

The remaining small bowel can adapt

With time, the remaining small bowel can increase its absorption to compensate for the missing segments. We used to believe that this adaptation occurred only within 6 months of a massive resection. Now with home TPN, adaptation may still occur as much as 3 years later. All patients with a preserved colon, no matter how little small bowel remains, should be given the chance to develop intestinal adaptation with careful nutritional support.[3]

Besides remnant length and an intact colon, other factors that favor intestinal absorption include having:

- Remnant ileum
- An intact ileocecal valve
- No mucosal disease
- An intact stomach, pancreas, and liver.

COMMON RESECTIONS

Jejunal resection is often necessary for patients with ischemic bowel.

Under normal circumstances, the bulk of nutrient absorption takes place in the first 150 cm of the small bowel (the duodenum and proximal jejunum). Adequate macronutrient absorption is usually preserved unless more than 75% of the proximal bowel is resected. The distal small bowel and the colon have increased functional reserve and adaptive capacity to generally allow maintenance of normal intestinal transit time and absorption.

Ileocolic resection is commonly performed to manage ileocecal Crohn disease. After an ileal resection, adequate energy and fluid absorption can usually be maintained in the proximal small bowel and colon. However, the distal 100 cm of ileum is the only region that absorbs vitamin B_{12} and bile salts: resection of this area can cause significant fat and electrolyte malabsorption. Loss of the distal small bowel, ileocecal valve, and proximal colon also decreases intestinal transit time by accelerating gastric emptying of liquids and increasing proximal small bowel motility.

Extensive bowel resection, leaving less than 60 cm of small bowel, results in profound fluid, electrolyte, and nutrient losses. The remaining jejunum adapts to a minimal degree, and prolonged gastric acid hypersecretion can cause ulceration of the proximal small bowel, further aggravating malabsorption. Patients usually need long-term parenteral nutrition support and may need a small bowel transplant.

DIETARY MANAGEMENT

If the colon is intact, use a high-carbohydrate, low-fat diet

Several small reports show that the optimal dietary management of short bowel syndrome

depends on what part of the intestine was removed.

Nordgaard et al,[4] in a crossover trial, randomized 14 patients with short bowel syndrome (8 with an intact colon and 6 with jejunostomies and no functioning colon) to a diet high in carbohydrate or a diet high in fat. For patients with a colon, the high-carbohydrate diet increased energy absorption from 49% to 69% compared with the high-fat diet and did not affect fecal volume. For patients without a colon, manipulating the diet did not significantly affect energy absorption, but the high-carbohydrate diet increased stool output by more than 700 mL vs the high-fat diet.

In view of these findings, we recommend a high-carbohydrate, low-fat diet for patients with an intact colon. Patients without a colon may improve with a diet incorporating moderate carbohydrates and moderate amounts of fat. Simple sugars or concentrated sweets, especially fruit juices, should be minimized to avoid increasing the osmotic load of the gastrointestinal tract and exacerbating the underlying diarrhea.

A high-carbohydrate diet is helpful for patients with an intact colon for a number of reasons. Complex carbohydrates, in the form of soluble fiber, slow down intestinal transit time, stimulate mucosal growth, and increase colonic cell proliferation by functioning as a preferred fuel for the colon. Undigested carbohydrates pass into the colon, where they are fermented by bacteria into short-chain fatty acids. These fatty acids are absorbed by the colon to provide additional energy and enhance absorption of sodium and water.

Patients with high-output stomas (> 2 L/day) may benefit from an additional 5 to 10 g of soluble fiber per day, which can be obtained from over-the-counter fiber supplements.

Replacing fluids and electrolytes

The sodium concentration of small-bowel effluent is about 100 to 150 mmol/L. Sodium loss can become significant in patients with intestinal output of 3 L or more per day.

Oral rehydration solutions contain sodium and glucose. The concentrations of each are calculated to take advantage of the sodium-glucose cotransport system across the cell membrane of intestinal villi, in which sodium is actively transported by coupling with glucose.

Sodium absorption exceeds losses when the sodium content of the solution is more than 90 mmol/L. The best mix for sodium absorption is sodium 120 mmol/L (about 2.6 g/L) and glucose 56 mmol/L (about 10 g/L).

Nightingale et al[5] conducted a randomized crossover trial in six patients with high jejunostomies who, in 48-hour periods, took sodium chloride 120 mmol per day in three forms: in gelatin capsules, in an isotonic glucose electrolyte solution (280 mOsm/kg H_2O; 30 kcal), or in a glucose polymer solution (280 mOsm/kg H_2O; 200 kcal). Patients absorbed extra sodium with each form of supplementation. However, two patients vomited the salt capsules, and the authors determined that a sipped glucose-salt solution is the best way to replace salt in patients with short bowel syndrome.

Patients typically drink fluids that vary widely in their content (**TABLE 1**). The optimal fluid is isotonic (280 mOsm/kg H_2O). Maximum absorption occurs with glucose 10 g/L, but even the best solutions have more to increase palatability. Sports drinks, sodas, and juices contain too much glucose and not enough sodium, causing diarrhea to worsen.

Sports drinks, sodas, and juices contain too much glucose and not enough sodium

Of the commercially prepared oral rehydration solutions, the World Health Organization's oral rehydration solution contains the best mixture of glucose and sodium, and it costs the least. It comes in packets of powder that can be mixed at home with water and a sugar-free flavoring such as Kool-Aid or Crystal Light. Other commercially prepared oral solutions are available in over-the-counter premixed bottles and closely approximate the World Health Organization solution.

Frequent, small meals; supplements

Patients should eat five or more small meals a day consisting mostly of complex carbohydrates, eg, bread, pasta, rice, potatoes, and low-sugar cereals. Concentrated sugars should be kept to a minimum. Fluids should be reserved for between meals.

Fiber supplements, along with antidiarrheal medications, can be used as needed to

TABLE 1

Composition of various drinks and oral rehydration solutions

	SODIUM (MMOL/L)	CARBOHYDRATE (G/L)	OSMOLALITY (MOSM/KG H_2O)	COST ($/L)
Apple juice	3	124	730	1.44
Ginger ale	3	90	540	0.55
Chicken broth	250	0	450	2.49
Sports drink (eg, Gatorade)	20	60	300	1.58
Pediatric electrolyte oral maintenance solution	45	25	230	3.99
Parent's Choice	45	25	230	2.77
Enfalyte	78	32	170	13.18
Pedialyte	45	25	250	6.00
World Health Organization ORS*	90	20	310	0.55
Rice-based ORS* (eg, Ceralyte)	90	40	275	3.00

*Oral rehydration solution: optimal for sodium absorption

prolong intestinal transit time. Multivitamins with minerals should be taken orally two or three times a day by patients not receiving parenteral nutrition. Monthly vitamin B_{12} injections are recommended for patients who have had more than 100 cm of terminal ileum resected.

The WHO solution has the best mix of sodium and glucose, and it costs the least

Additional oral supplementation of several essential minerals is often necessary to replace excessive losses in patients with short bowel syndrome. Many of these patients will need calcium in carbonate, citrate, or gluconate form, taken in divided doses two to four times per day. Magnesium should be supplemented in the form of chloride, lactate, or gluconate salts, taken 1 hour before meals on an empty stomach. Serum trace elements should be checked in patients with suspected deficiency and supplemented as necessary.

MEDICAL MANAGEMENT

Antidiarrheal medications (eg, diphenoxylate, loperamide, codeine, and opium tincture) are often the foundation of management. Patients need to take them 30 minutes to 1 hour before meals and at bedtime.

Histamine-2 (H_2) receptor blockers (eg, famotidine, ranitidine) and **proton pump inhibitors** (eg, omeprazole, lansoprazole) help manage the excess acid secretion that occurs from hypergastrinemia. The H_2 blockers are usually compatible with parenteral nutrition solutions. It is important to start patients on moderate to high doses of H_2 blockers immediately after extensive surgical resection, because the high acid output makes them particularly susceptible to developing an ulcer. Some patients can discontinue these medications after 3 to 6 months.

Pancreatic enzyme replacement with pancrelipase is useful because of the rapid emptying and diminished transit time through the bowel that results in poor mixing with pancreatic and biliary secretions. For patients on H_2 blockers, an uncoated form of replacement is best to ensure it will dissolve quickly enough to be effective. The dosage is 1 to 8 capsules with meals and snacks.

Bile-acid resins (eg, cholestyramine) must be used carefully because they efficiently absorb many micronutrients and medications. They help patients who have at least half of their terminal ileum remaining and an intact colon: in such cases, bile-acid salt pools are maintained and spill into the colon, causing a choleretic diarrhea. On the other hand, bile-acid resins are not useful for patients with more than 100 cm of terminal ileum removed or who have no colon.

To quickly assess whether bile-acid resins might be helpful, the stool can be stained with a Sudan stain for steatorrhea. Significant steatorrhea indicates that bile salt pools are diminished and that bile-acid resins will not help.

Cholylsarcosine, a conjugated bile acid, is used for replacement therapy in patients with diminished circulating levels of bile salts, and it can help with fat absorption. Unfortunately, it is not available in the United States.

Antimicrobial medications (eg, metronidazole, cephalosporins) help improve absorption for patients with bacterial overgrowth, a problem that occurs in only a minority of patients.

Octreotide, a somatostatin analogue, is a double-edged sword: it can help some patients with very high fluid outputs but can also diminish adaptation because it inhibits important hormonal secretions. It should be used only in patients with very high fluid output who are doing poorly.

O'Keefe et al[6] studied patients with very high-output jejunostomies (about 3 L/day), requiring tremendous amounts of intravenous fluids with parenteral nutritional formula day and night. After 10 days, patients given octreotide 100 μg three times a day subcutaneously had significantly reduced stomal fluid and electrolyte losses. They were less thirsty, needed smaller amounts of oral fluids, gained weight because of better hydration, and had better urine output and renal function. As expected, hormonally stimulated gastric acid and pancreatic lipase secretions were significantly reduced. The risk of accelerated gallstone formation increased, and the risk of bowel obstruction was nil.

Recombinant growth hormone (somatotropin) promotes adaptation and is the only growth factor approved by the US Food and Drug Administration for treating patients with short bowel syndrome.

Seguy et al[7] studied 12 patients with short bowel syndrome who had an average of 38 cm of jejunum remaining; most had an intact colon, and all were medically stable on parenteral nutrition formula. Patients were randomized to receive injections of either recombinant human growth hormone 0.05 mg/kg/day or placebo for 3 weeks. After a 1-week washout period, the groups were switched. Treated patients absorbed significantly more energy, nitrogen, carbohydrate, and fat, accounting for 37% of their parenteral nutrition requirements. Body composition also improved, even within the short study period.

Byrne et al[8] randomized 41 patients with short bowel syndrome to three treatments: a specialized oral diet with glutamine; a recombinant growth hormone and the specialized diet without glutamine; or growth hormone and the diet with glutamine. Patients were treated for 4 weeks, then discharged home. Growth hormone injections were stopped at this point, but patients on specialized diets and glutamine continued them for 12 weeks. Only the group receiving the combined diet, growth hormone, and glutamine improved significantly throughout the study: their TPN requirement was reduced by an average of more than 7 L and 5,000 Kcal per week (nearly 4 fewer days of TPN required per week).

Glucagon-like peptide 2 (GLP-2) has been used in clinical studies in Europe and is now being tested in the United States.

Jeppesen et al[9] treated eight patients with short bowel syndrome whose terminal ileum and colon had been removed. GLP-2 400 μg subcutaneously twice a day for 35 days resulted in improved intestinal absorption and body weight composition, including increased body weight, lean body mass, and bone mass. Bone density loss is a problem in many patients with short bowel syndrome, possibly from underlying disease, medications, or parenteral nutrition.

An H_2 blocker should be started immediately after extensive intestinal resection

SURGICAL MANAGEMENT

A number of attempts have been made to manage short bowel syndrome surgically.

Reversed segment procedures, which involved reversing a 10-cm segment of small bowel, were used 30 years ago to produce a functional partial small bowel obstruction to slow intestinal transit time. The results were mixed, and these procedures are rarely used today.

Stricturoplasty, the widening of a narrowed area of bowel, is done in patients with Crohn disease to avoid large or multiple resections.

Intestinal lengthening (Bianchi) proce-

dures and the creation of **artificial enteric valves** are sometimes used, but are only of variable benefit. Bianchi procedures are used mostly in children with a dilated segment of small intestine.

Reconnecting small or large bowel that is out of circuit to reestablish continuity results in the greatest benefit: it is essential to know each patient's exact anatomy to assess such options.

Small bowel transplantation

For patients who cannot continue on home TPN, small bowel transplantation offers a chance to resume a more normal lifestyle. Indications for intestinal transplantation include:

- Impending or overt liver failure from parenteral nutrition
- Loss of vascular access (thrombosis in two major vessels)
- Recurrent line sepsis, fungal line sepsis, or a single episode of sepsis with hemodynamic instability
- Patients with a gastrointestinal tract that cannot be reconstructed
- Recurrent severe dehydration
- Inability to maintain patients safely and reliably on TPN.

Different types of small bowel transplantation include isolated intestine, combined liver and intestine, and multivisceral transplants.

Survival statistics show that patients with intestinal transplants are only slightly worse off than those on home TPN.[10] Survival is increasing as surgical procedures and immunosuppression regimens improve.

Cost of bowel transplantation is estimated to be $150,000 in the first year, including workup and hospitalization of the donor, hospitalization of the recipient, follow-up tests and visits, and immunosuppressive therapy.[11] In comparison, home TPN costs between $100,000 and $150,000 annually. In the long run, transplantation is more economical for a patient who cannot be maintained on home TPN.

Some transplants take some time to start working, and some do not survive for the duration of a patient's lifetime, so patients may still need TPN for varying periods.

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ADDRESS: Douglas Seidner, MD, Department of Gastroenterology, A30, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.