Management of the short bowel syndrome

C R Pennington

Short bowel syndrome (SBS) represents a threat to the life of the patient and a challenge for the clinical nutritionist and gastroenterologist. A good understanding of the pathophysiology and principles of management reduce morbidity and improve the quality of life of patients with this condition.

Diagnosis and common causes of SBS

The length of the intestine in normal human subjects is variable, with the measured length *in vivo* depending on muscle tone. When measured from the duodeno-jejunal flexure the length ranges from 275 cm to 850 cm.[1,2] Clearly the clinical impact of any resection will be influenced by the initial intestinal length, which tends to be shorter in female subjects. The common reasons for intestinal resection resulting in SBS differ between countries. They include infarction due to volvulus or vascular occlusion, multiple resections for stricturing Crohn's disease, malignancy and radiation enteritis.[2] Trauma and gunshot wounds are common reasons for SBS in some communities, and a short bowel was previously created for the management of morbid obesity.

The residual capacity of the intestine is such that many patients with a short bowel are minimally inconvenienced. Clinical presentation and therapeutic needs are determined by several factors. These include the length and nature of the remaining small bowel, with particular reference to the presence or absence of ileum and normality of function. The presence or absence of the colon, and the time of adaptation for those patients with a colon in continuity also have an important influence on management.

The approximate intestinal length can be determined at surgery, or by radiological study of the small intestine. Such methods are not always accurate and do not reveal the functional mass of the intestine. Initial intestinal function will be governed by length, site and disease, which may alter and influence nutrition, biochemistry and renal function. Interest has focused on the measurement of citrulline for this purpose. Glutamine is converted to citrulline by the intestine; citrulline is further converted to arginine in the kidney. There is a correlation between small intestinal length and serum citrulline leading to the suggestion that citrulline may usefully detect those patients who will be dependent on parenteral nutrition.[3] Whereas prospective evaluation is required, changes in residual gut function through disease and adaptation, and the facility for nutrient absorption through the colon will make interpretation difficult in relation to the potential absorptive capacity of the gut and therefore the need for parenteral nutrition.

Influence of a short bowel on intestinal function

Reduction of the intestinal digestive and absorptive capacity after major resections is a reflection not only of the loss of intestinal length – many other factors contribute. Gastric acid hypersecretion follows intestinal resection due to the loss of inhibitory peptides.[4] This has unfavourable effects on residual gut function because of the volume and pH of gastric secretion. Not only does the acid environment impair digestion through the effect on pancreatic and other digestive enzymes, but the precipitation of bile acids increases the problem of fat malabsorption. Similarly the loss of peptides such glucagon-like peptide 2 and peptide YY results in the loss of the ileal break with hastened gastric emptying and intestinal transit.[5] Thus hypersecretion of gastric acid, impaired digestion, and more rapid intestinal transit combine to diminish the residual intestinal function.

The jejunum is relatively 'leaky'[6] and lacks the ability of the ileum and colon to absorb fluids against an osmotic or electrochemical gradient. Thus dehydration and electrolyte imbalance are a particular risk with an end jejunostomy when stomal volumes may measure many litres. The consumption of the usual oral hypotonic fluids will increase sodium loss. Hypertonic fluids will increase fluid loss.

The ileum is adapted for the absorption of bile acids and vitamin B_{12}. The loss of bile acids occurs for two main reasons: the break in the entero-hepatic circulation depletes the bile acid stores and availability, and the precipitation of bile acids in the intestinal lumen on account of an acid environment through gastric hypersecretion. In some patients with a colon in continuity and loss of the ileo-caecal valve, bacterial overgrowth can contribute to this process. Luminal bile acids play an important role in the digestion and absorption of fat; bile acid depletion increases the malabsorption of fat. This has important nutritional consequences for patients with both types of SBS, jejunostomy and colon in continuity. Patients with a colon in continuity have an additional problem with diarrhoea (and nephrolithiasis as discussed below). Bile acids that are not absorbed are deconjugated by the colonic bacteria. Deconjugated bile acids cause severe diarrhoea in the colon by

Department of Digestive Disease and Clinical Nutrition, Ninewells Hospital and Medical School, Dundee, Scotland

C R Pennington, BSc, MD, FRCP, FRCP

mechanisms including calcium-mediated and cyclic AMP-mediated stimulation of chloride secretion in the colon.[7] Resins such as colestipol and cholestyramine have been used to bind secondary bile acids with diminution of diarrhoea in these subjects.

The ileum and right colon are important for the process of intestinal adaptation. Adaptation is mediated through the release of peptides such as cholecystokinin and glucagon-like peptide 2[8,9] that are released by oral feeding and enteral feeding in which long-chain triglycerides have an important role. Adaptation is associated with an increase in the number and size of villi, and increase in crypt depth; there is also some increase in bowel length. This process increases the absorptive area of the intestine.[10] Unfortunately clinically significant adaptation is not a feature of the end jejunostomy probably through the loss of stimulatory peptide secretion; it is also a slow process and may take up to 2 years to complete.

Thus both types of SBS, end jejunostomy and colon in continuity, are affected by gastric hypersecretion, rapid intestinal transit, and reduced function of the residual intestine, with the prospect of macronutrient and micronutrient deficiency. Patients with an end jejunostomy are at particular risk of fluid and electrolyte imbalance and need greater intestinal length if they are to be independent of parenteral nutrition, there is no intestinal adaptation, and they need vitamin B_{12} replacement. Intestinal adaptation can occur over time in patients with a colon in continuity. This may take up to 2 years, during which time artificial nutritional support will often be needed. The length of intestine needed for adequate intestinal function depends on the type of SBS, as does the complication profile.

Clinical management of the patient with SBS

When considering the management of this condition it is important to bear in mind the different implications of an end jejunostomy and colon in continuity. The immediate principles of management include the correction of fluid and electrolyte imbalance, optimising the residual intestinal function and the replacement of nutrient deficits.

Implications of intestinal length

Studies of cohorts of patients with SBS have investigated the length of intestine required to allow the patient freedom from intravenous therapy in different circumstances after possible adaptation has occurred and with optimal treatment and normal residual intestine. Patients with end jejunostomies need at least 100 cm of jejunum; for those patients with the colon in continuity 50 cm of jejunum may be sufficient but if some terminal ileum including the ileo-caecal valve has been preserved, as little as 35 cm of small intestine may be enough.[11,12]

Fluid balance and rehydration therapy

Before adaptation and with a shorter jejunal length, intravenous fluids and in many cases intravenous nutrition, are needed. Intravenous therapy is also necessary in patients with longer residual intestine in whom the residual bowel is diseased. Crohn's disease and radiation enteritis are such examples and contrast with the loss of otherwise normal intestine through volvulus or embolism.

Patients with an end jejunostomy are at particular risk of dehydration and electrolyte imbalance. The 'leaky' jejunum and fast transit means a high output stoma. Typically the patient is very thirsty and drinks increasing volumes of inappropriate fluids, increasing the stomal loss and thirst. Eventually severe dehydration and renal impairment ensue. Such patients usually require resuscitation with intravenous fluids. Thereafter they are given oral World Health Organisation (WHO) rehydration fluids, isotonic glucose-electrolyte solutions in which the sodium content is 90 - 120 mmol/l.[6] Patients are advised not to drink at meal times. The consumption of ordinary hypotonic drinks is limited to 500 ml until tolerance is ascertained. Such restrictions are usually unnecessary in patients with a retained colon. Depending on disease in the residual jejunum and jejunal length, some patients may need to continue with parenteral fluids (and even parenteral nutrition). Careful management and monitoring are required of the fluid balance with measurement of the daily weights, stomal and urinary output.

Optimising the residual gut function

Optimising the residual gut function is important for the management of diarrhoea, malabsorption and nutrition. Acid hypersecretion may only persist for 6 - 12 months but it causes impaired digestion in both types of short bowel patients. Acid suppression with proton pump inhibitor (PPI) drugs is required.

Antimotility drugs are used to retard gut transit and increase digestive time in most patients. Given the loss of the entero-hepatic circulation of active metabolites large doses of loperamide such as 16 mg a day may be needed. Octeotride has been employed as an alternative to these agents.[13] Long-acting derivatives are now available. Not only is it an expensive option, octeotride might reduce adaptation through the suppression of peptide release.

Bacterial overgrowth can be a problem with the colon *in situ*, especially in the absence of the ileocaecal valve. Under these circumstances treatment with intermittent courses of antibiotics may be helpful, but these drugs expose the patient to the risk of vitamin K deficiency (much of which is produced through bacterial metabolism in the colon) as well as *Clostidium difficile* toxin-induced diarrhoea and colitis.

Cholylsarcosine has been used to replace the endogenous bile acids, which are lost through malabsorption. This is a

synthetic bile acid in which the carboxyl group of cholic acid is conjugated with the amino group of sarcosine. The advantage of cholylsarcosine is resistance to bacterial deconjugation in the colon, and thus it avoids the secretory diarrhoea that accompanies the ileal malabsorption of bile acids.[14]

Nutritional management

Nutritional management of the patient with SBS requires careful attention. Generally patients are asked to eat frequently so they consume a high-energy diet, especially during the early phases of adaptation. The oral replacement of zinc and magnesium may be needed. Oral magnesium preparations can aggravate diarrhoea, magnesium oxide is the preferred formulation,[15] and absorption is dependent on satisfactory vitamin D status. Parenteral replacement of vitamin B_{12}, and fat-soluble vitamins may be needed.

As with electrolyte replacement the dietary management of patients with end jejunostomy and a colon in continuity differ. A diet with a high fat content usefully increases energy absorption for those patients with an end jejunostomy. The patient is not inconvenienced by the increasing fat content of the jejunostomy effluent. Conversely a high-fat diet in patients with a retained colon not only leads to unacceptable steatorrhoea, it exposes patients to the risk of oxalate renal stones. Unabsorbed fats bind calcium in the colon through which free oxalate is subsequently absorbed. Thus patients with a retained colon are traditionally advised to eat a diet with a high carbohydrate content, and to restrict dietary sources of oxalate. Such foods include spinach, celery, tea, cola, carrots and rhubarb. Furthermore, additional calcium in the form of supplements have been used to bind colonic fatty acids. In conjunction with adequate fluid intake this may reduce the risk of oxalate renal stones.

Enteral tube feeding is used in some patients, especially those with anorexia, undernutrition, and borderline intestinal function. If tolerated the residual intestinal function can be exploited over much of the 24 hours. There is a theoretical basis for prescribing enteral products that contain peptides and medium-chain triglycerides. Peptides are preferentially absorbed. Medium-chain triglycerides are directly absorbed without dependence on bile acids for micelle formation; furthermore the colonic capacity for the absorption of medium-chain triglycerides has recently been described.[16] However, there is no evidence that these more expensive products confer significant clinical advantage when compared with traditional cheap polymeric feeds, and medium-chain fats may have an adverse effect on gastric emptying and intestinal motility.[17]

Whereas patients with both types of SBS have an increased incidence of gallstones due to bile acid depletion, patients with a colon in continuity are also prone to the development of renal calculi through enhanced oxalate absorption. Unabsorbed carbohydrate entering the colon may be metabolised by colonic bacteria to D lactic acid.

Thus patients with a retained colon can present with D lactic acidosis. Clinical features include confusion, acidosis and features that are similar to Wernicke's encephalopathy. Diagnosis can be compromised through the inability of many laboratories to measure D lactic acid. Traditional treatment is with broad-spectrum antibiotics and thiamine; bicarbonate is reserved for those patients with severe acidosis.

When the residual intestinal function is not adequate intestinal failure causes progressive malnutrition. These patients require intravenous feeding, sometimes indefinitely, but at least until the process of adaptation is complete.

Intestinal failure and the SBS

Malnutrition will impair the intestinal structure and function, increasing the likelihood of dependence on parenteral nutrition,[18] thus the decision to feed the patient parenterally must not be deferred until severe malnutrition develops. Intestinal failure is recognised by electrolyte imbalance and/or nutritional depletion despite the use of drug and dietary management to exploit the residual intestinal function. For those patients with extreme short bowel, and those in whom the residual intestine is diseased, the dependence on parenteral nutrition is likely to be permanent; in other patients parenteral nutrition will continue at least until adaptation is complete. Thus where facilities exist and domestic circumstances permit, home parenteral nutrition (HPN) is considered for all patients with intestinal failure on a short or long-term basis. Under these circumstances parenteral nutrition is delivered through a central catheter, with many younger patients choosing subcutaneous ports which provide more freedom for leisure activities. Patients are encouraged to eat, with nutritional deficits being addressed by the parenteral route, usually with overnight infusions of complete nutrient mixes that contain amino-acids, glucose, lipid, trace elements, and vitamins. The number of nutrition bags administered each week is gradually reduced as intestinal adaptation occurs; ultimately some patients only require electrolyte infusions.

The key to success with such treatment is the observance of strict catheter care protocols to minimise the risk of potentially serious complications. Serious complications usually arise in relation to the catheter: infection, central vein thrombosis, and catheter occlusion.[19] However, long-term parenteral nutrition has been associated with effects on other organ systems, including hepatobiliary disease and bone disease. Furthermore, manganese deposition has been described in the brain of HPN patients in the absence of cholestasis; this implies excessive manganese provision in some of the commercially available trace element solutions.[20,21]

The prognosis of patients treated with HPN mainly depends on the underlying pathology; the 5-year survival ranges from

80 - 90% in patients with Crohn's disease, to 40 - 50% for patients with radiation enteritis and motility disorders.[21] Although most patients treated with HPN for SBS arising from cancer die within a year, it is worth bearing in mind that some patients with ovarian cancer have surprisingly and unpredictably lengthy survival. Generally prognosis is better with HPN than intestinal transplantation despite recent developments in immunosuppression.[22] Within the UK the only indications for referral for transplantation at present include concomitant intestinal and liver failure and loss of venous access. Less stringent criteria apply in other countries that offer transplantation more readily.

Conventional surgical techniques in the management of SBS are designed to optimise function, slow transit, and increase intestinal length.[23] With reference to function, the restoration of continuity and the relief of obstruction are most important; some authorities try tapering dilated bowel. Other techniques are used to slow intestinal transit. These include reversed segments, artificial valves and colonic interposition and there is less information about outcome. Intestinal-lengthening procedures have also been described. Only a minority of patients with SBS are candidates for such surgical approaches.

SBS is a serious clinical problem with important implications for the patient and the clinical team. Clinical management should include the problems associated with SBS, treatment of the underlying disease, and psychological support. With careful management and attention to detail most patients can enjoy a reasonable quality of life even with an extremely short bowel.

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