

CURRENT TOPIC

Short bowel syndrome

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Short bowel syndrome (SBS) encompasses a spectrum of metabolic and physiological disturbances resulting from massive anatomical or functional loss of small bowel. The clinical course of an infant who has undergone extensive small bowel resection is characterised by an initial period of watery diarrhoea, which is exacerbated by enteral nutrition and gastric hypersecretion. This is gradually replaced by a phase of progressive intestinal adaptation which often continues for more than a year and during which incremental enteral feeding is possible. Initial management is aimed at promoting and maintaining growth in the expectation that subsequent adaptational changes in the residual bowel will, in most cases, eventually permit full enteral feeding to be established. Should there be insufficient residual small bowel, home parenteral feeding allows long term survival with a good quality of life. More recently small bowel transplantation has become a further option in management. Although intravenous nutrition has transformed the prognosis of patients with SBS, complications associated with this treatment represent an important cause of morbidity and mortality.

Aetiology of short bowel

The commonest causes are necrotising enterocolitis, multiple intestinal atresias and midgut volvulus but gastroschisis and extensive intestinal aganglionosis account for some cases. Although there are reliable estimates of the number of patients each year in the UK developing irreversible intestinal failure,¹ there are no accurate data on the incidence or prevalence of childhood SBS.

Pathophysiology of short bowel syndrome

The fundamental defect is a reduced small bowel surface area for absorption of nutrients together with a more rapid transit of intestinal contents. Early on in SBS excessive gastric acid secretion mediated by hypergastrinaemia sometimes occurs. The lowering of intraduodenal pH inactivates pancreatic digestive enzymes and stimulates peristalsis. Although this problem tends to resolve with time, treatment with an H₂ receptor antagonist may be required.

Loss of mucosa containing brush border hydrolases adversely affects carbohydrate digestion. Testing liquid stool for reducing substances is a useful indicator of carbohydrate

intolerance. Non-absorbed sugars produce an osmotic diarrhoea, and, rarely, severe metabolic acidosis through conversion of carbohydrate by lactobacilli to D-lactic acid. This is associated with a neurological syndrome including headache, drowsiness, behavioural disturbance, ataxia, and blurred vision. The basis for the neurological abnormalities (once thought to be due to the D-lactate itself) is uncertain as it is now known that lactate can be metabolised by pathways other than isomer specific tissue L-lactate dehydrogenase² and may, therefore, be a marker for some unidentified toxic substance.

Malabsorption, absence of the ileocaecal valve, and hypomotile dilated bowel segments increase the risk of small bowel bacterial overgrowth. This results in deconjugation of bile acids, mucosal inflammation, and further compromise of digestion and absorption. Reduced levels of cholecystokinin and secretin in association with loss of jejunum contribute to impaired pancreatic and biliary secretion. Malabsorption of peptides and amino acids leads to nitrogen deficiency and resulting malnutrition will further impair pancreatic exocrine function.

Iron, calcium, and magnesium are maximally absorbed in the proximal small bowel. Calcium and fat malabsorption together result in the formation of insoluble soaps. One consequence of this is increased absorption of dietary oxalate which, under normal circumstances, would form insoluble calcium oxalate in the bowel lumen; bile salts in the colon are also thought to increase calcium oxalate absorption. Those patients with colon in continuity with shortened bowel may therefore have hyperoxaluria and are at risk of forming renal oxalate stones. A quarter of adult patients with less than 200 cm jejunum anastomosed to colon developed symptomatic renal stones.³ The risk in children is uncertain but in small follow up series between one and two thirds of patients have had hyperoxaluria.^{4,5} There is also an increased prevalence of gall stones relating to interruption of enterohepatic circulation of bile salts, changes in gall bladder emptying, and cholestasis associated with parenteral nutrition.

Excessive loss of micronutrients such as magnesium, zinc, copper and selenium occur, particularly when there is a high stoma with fluid stools. Iron deficiency can result from loss of duodenal-jejunal absorptive area, or from perianastomotic ulceration as a late complication of ileocolic anastomosis.⁶ Deficiencies of

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water soluble vitamins such as B12 and other B group vitamins occur when there is extensive loss of jejunum, and ileal loss may prevent adequate absorption of intrinsic factor bound B12. Routine injections of B12 are recommended in adult patients who have lost their distal ileum,⁷ although the prevalence of B12 deficiency in children after ileal resection is uncertain. One study showed impaired absorption in seven out of 10 children who had ileal resections,⁸ while serum B12 concentrations sometimes took several years to fall below normal. However, vitamin B12 malabsorption can return to normal even as long as 6–8 years after resection.⁹ Clearly, long term follow up of B12 status is necessary.

Loss of ileum may also interfere with absorption of bile salts and vitamin D. When the circulating bile acid pool becomes depleted fat malabsorption results. Steatorrhoea in turn leads to deficiency of fat soluble vitamins A, D, E, and K. While bone disease during parenteral nutrition is common and multifactorial in aetiology,¹⁰ long term problems related to vitamin D deficiency in those who have achieved full enteral feeding appear rare, even when supplements have not been given.¹¹ Unabsorbed fatty acids are converted to hydroxy fatty acids by colonic bacteria, and, together with unabsorbed bile acids, induce colonic secretion exacerbating diarrhoea.

Adaptation of the residual intestine

Massive small bowel resection is followed by a process of adaptation¹² involving cell hyperplasia and leading to increased mucosal surface area. There is, however, less potential for adaptation in the jejunum than in the ileum. Other changes include increases in bowel circumference, length and bowel wall thickness, villus height, crypt depth, cell proliferation, and rate of cell migration up the villus. These adaptive processes begin immediately after loss of bowel, continue for some years, and are accompanied by adaptive changes in the stomach, pancreas, and colon.

Luminal nutrition is essential for the full development of adaptational changes and should begin as early as possible. Other trophic influences include pancreaticobiliary secretions and gut hormones such as enteroglucagon, gastrin, epidermal growth factor, and insulin-like growth factor.

Nutritional management

Good nutritional management is the key factor in achieving an optimal outcome in SBS. The goals of nutritional support should be to maintain normal growth, promote adaptation, and avoid complications. This is best done in a regional unit with a multidisciplinary nutritional care team¹³ where there is regular experience of such patients. Total parenteral nutrition is necessary in the early stages, with only occasional exceptions,¹⁴ and expert central venous catheter access and maintenance are essential. Replacement of excess fluid and electrolyte losses is important. During the

change over to enteral feeding, attention must be given to providing adequate supply of micronutrients such as zinc, calcium, and magnesium. Cholestatic jaundice is common, with the danger of progression to hepatic cirrhosis. The aetiology of parenteral nutrition associated cholestasis is multifactorial but major risk factors include lack of enteral nutrition, prematurity, sepsis, and short residual bowel. Cyclical parenteral nutrition (overnight feeding) may decrease the risk of hepatic complications,¹⁵ as may treatment with oral antibiotics such as neomycin or metronidazole which may reduce harmful bacterial translocation across the gut.¹⁶ As low plasma concentrations of cholecystokinin during parenteral nutrition may be associated with risk of cholestasis,¹⁷ treatment with intravenous cholecystokinin would seem to be a logical approach to prophylaxis. So far, there is only very limited experience in adult patients receiving short term parenteral nutrition.¹⁸

In the newborn, enteral feeds are often introduced in the form of a lactose free protein hydrolysate such as Pregestimil (Mead Johnson) or Peptijunior (Cow and Gate). Initial nasogastric flow rates are set at 1 ml/hour, and slowly increased over weeks or months as parenteral feed is reduced. The speed with which enteral nutrition can be increased depends upon the nature and length of the residual bowel. The ileal mucosa is more able to absorb solutes against a concentration gradient than jejunal mucosa. Loss of ileum is therefore likely to result in major fluid and electrolyte losses. The colon is important for energy salvage since unabsorbed carbohydrate is fermented by bacteria to produce short chain fatty acids. These are not only used by the mucosa as a major energy source but also have a trophic effect. Increasing the carbohydrate rather than the fat content of enteral feed may improve energy balance in patients with colon in continuity with small bowel.¹⁹

Although enteral feed is better absorbed if given as a continuous infusion rather than by bolus, it is important to introduce some oral feeding as early as possible in order to avoid poor feeding and delayed speech development later on. The advice of a speech therapist should be sought at an early stage. Insertion of a percutaneous gastrostomy may be valuable in the older infant who is dependent upon nasogastric tube feeding.

As an alternative to a defined formula, a modular feed based on comminuted chicken (Chix, Cow and Gate) has the advantage of flexibility such that carbohydrate and fat content can be manipulated to suit individual requirements. For example, a combination of glucose polymer and sucrose may be better tolerated by an infant who has had necrotising enterocolitis with widespread mucosal damage. When there is fat maldigestion partial substitution of medium chain triglycerides for long chain triglycerides may be better tolerated, although feed osmolality will increase. Fat tolerance can be simply monitored using the steatocrit test²⁰ in a way analogous to monitoring of carbohydrate intolerance by the presence of reducing substances in the stool.

Pectin is a water soluble, non-cellulose dietary fibre which in animal studies has been shown to promote intestinal adaptation.²¹ When there is almost full adaptation to enteral feeds but a persisting and very limited residual requirement for parenteral nutrition, or if weight is maintained but does not increase once parenteral nutrition is discontinued, there are a number of strategies which can be tried to promote further absorption. Glutamine may exert a trophic effect on the bowel and can be added to provide up to 25% of enteral nitrogen. *Saccharomyces boulardii* is a yeast which is used to treat pseudomembranous colitis and has been shown to enhance sucrase and maltase activities in the rat, producing a trophic effect probably mediated by release of polyamines.²² There is, however, relatively little experience with these kinds of dietary modifications in human subjects.²³

Some complications can be successfully managed by manipulating diet. In one patient D-lactic acidosis was prevented by substituting starch for monosaccharides and oligosaccharides in the feed so that lactobacilli were deprived of their substrate for making D-lactic acid.²⁴ In view of the long term risk of renal oxalate stones³ patients should be advised to avoid oxalate containing foods such as chocolate, tea, cocoa, cola, spinach, parsley, rhubarb, celery, beetroot, and carrots as much as possible.

Medical management

Diarrhoea early in SBS should raise the possibility of gastric hypersecretion. The demonstration of an increased basal acid output confirms the diagnosis. Treatment with an H₂ blocker such as ranitidine should be tried, although hyperacidity is usually a transient early problem. Loperamide hydrochloride can be used to slow transit time and reduce secretion, but this in turn may increase the risk of bacterial overgrowth. Cholestyramine improves diarrhoea by binding bile acids and reducing their secretory effect in the colon. Cholestyramine may, however, reduce vitamin D absorption, and if diarrhoea is due to fat intolerance rather than bile salt malabsorption, cholestyramine may worsen matters by depleting the bile salt pool. In patients without a colon who remain at least partially dependent on parenteral fluids, stool losses can be reduced with gastric antisecretory drugs and octreotide, a synthetic analogue of somatostatin.²⁵ Urinary electrolytes should be monitored periodically and sodium maintained above 10 mmol/l in order to avoid growth failure and metabolic acidosis associated with total body sodium depletion.²⁶

Surgical management

At the initial laparotomy, as much viable bowel as possible should be salvaged. After restoration of intestinal continuity, contrast studies may be necessary to exclude correctable complications such as anastomotic or intestinal strictures. Numerous surgical procedures have

been described to alter intestinal transit and promote intestinal adaptation in SBS (see table) but considering the wide individual variation in the potential for intestinal adaptation, none of these procedures should be employed within 6–12 months of massive gut resection unless life threatening parenteral nutrition related complications develop.

Small bowel dilatation resulting in stasis and defective peristalsis can be treated by intestinal plication which preserves the mucosal surface area, or by tapering enteroplasty in which part of the bowel circumference is excised. The functional results of both techniques are similar,²⁷ but recurrent dilatation occurs frequently after plication. With the Bianchi technique, dilated bowel is bisected longitudinally and reconstructed to produce two parallel segments of twice the length and half the circumference.²⁸ Although this technique has been used in approximately 40 children with SBS and half have achieved successful weaning from parenteral nutrition,²⁹ major complications, principally anastomotic breakdown and vascular compromise, have been reported,^{30 31} and there is a paucity of objective evidence demonstrating improved intestinal absorption. Recent surgical modifications have been described which enable the Bianchi technique to be applied to initially undilated bowel³¹ and to the duodenum, where there is no suitable mesentery for the procedure.³²

Insertion of a reversed small bowel segment or a short length of colon (iso or antiperistaltic) into the small bowel can result in prolonged intestinal transit and improved nutrient absorption. Despite the difficulties in gauging the optimum length of interposed bowel, some encouraging reports have been published.^{33 34} However few infants have undergone this procedure and there are some concerns that short term results may not be sustained. These surgical techniques have been used in relatively small numbers of patients in whom the contribution of ongoing spontaneous enteral adaptation is uncertain. Furthermore, some of the procedures may risk compromising residual gut. Unless parenteral nutrition associated complications dictate otherwise, they are best reserved for patients in whom there is no evidence of continuing intestinal adaptation.

Techniques such as retrograde electrical pacing of the intestine, the use of a recirculating intestinal loop, construction of an intestinal valve, and the growth of small bowel neomucosa remain largely experimental at the present time.

With the advent of cyclosporin, long term successful small bowel transplantation became possible in the late 1980s and further progress

Surgical approaches to short bowel syndrome

Tapering or plication
 Intestinal lengthening
 Reversed small bowel segment
 Colon segment interposition
 Formation of an intestinal valve
 Retrograde intestinal electrical pacing
 Recirculating loop of intestine
 Growth of small bowel neomucosa
 Small bowel transplantation

followed the use of FK-506 immunosuppression. Isolated intestinal grafts have allowed successful weaning from parenteral nutrition³⁵ but long term results, particularly in children, are awaited. However, children who are permanently dependent on parenteral nutrition and who have life threatening complications related to parenteral nutrition should be considered for isolated small bowel or liver-small bowel grafting.³⁶

Outcome

The development of parenteral nutrition and its continuing refinement has revolutionised the treatment of SBS. Nevertheless, progressive liver dysfunction and parenteral nutrition associated sepsis remain the leading causes of death in patients with SBS. The outcome of SBS is determined by many factors which include length and type of remaining small bowel, the presence of an ileocaecal valve and colon, and whether the remaining gut is healthy. Recent reviews of experience with neonatal SBS in single centres show survival rates of over 80% and a progressive reduction in morbidity over the last decade.^{16 37 38} Successful weaning from parenteral nutrition has recently been described in an infant left with only 7 cm of jejunum anastomosed to ascending colon.³⁹ However, in the absence of an ileocaecal valve, at least 10–20 cm of small bowel are usually required to achieve satisfactory long term enteral nutrition in infants. As small bowel length more than doubles in the fetus during the last trimester of pregnancy, gestational age may be a factor in subsequent adaptation.

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