SASPEN Case Study

This case study was presented and discussed at the recent SASPEN 2010 Congress by Prof O Goulet, University of Paris Descartes.
The summarised discussion of the proceedings was prepared by Annette Prinsloo.

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Background information

Prenatally, the patient was diagnosed with dilated intestinal loops. The patient, born at term, was diagnosed with gastroschisis during the neonatal term.

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Patient's course

The patient was born at 39 weeks gestation, weighing 2 860 g. He was diagnosed with gastroschisis type III. He also presented with multiple intestinal atresias, a dilated duodenum and proximal jejunum as well as a left microcolon. On day 4 of life, the patient underwent surgery during which a small bowel resection and hemicolectomy were done. A jejunostomy, 30 cm from the ligament of Treitz, as well as a colostomy in the transverse colon were performed. On day 38 of life the patient developed a volvulus with subsequent jejunal necrosis leading to a perforation and resulting in peritonitis. This necessitated further surgery to create a new jejunostomy. On day 53 a jejuno-colic anastomosis was performed. Post surgery a small bowel follow through study showed that the anastomosis was not functioning. On day 72 of life the anastomosis was redone. During this period, the patient developed recurrent episodes of catheter related sepsis and cholestasis. The patient was subsequently transferred to the Necker-Enfants Malades Hospital in France where a combined liver-intestinal transplant was done.

Diagnosis

Short bowel syndrome with cholestasis.

Anthropometry

The patient's weight gain and growth was suboptimal during his clinical course. On admission to the Necker-Enfants Malades Hospital his weight was at -5SD and his length at -4SD.

Nutritional management

Postoperatively parenteral nutrition in combination with enteral nutrition using an elemental (amino acid based) milk formula was given.

Discussion of case study

Growth of the small intestine reaches a peak at 25–35 weeks after conception, doubling in length during the last 15 weeks of pregnancy.[1] Further rapid elongation takes place during the neonatal period until a crown-heel length of 60 cm is reached; after this, the rate of growth of the small intestine slows down until mature intestinal length is achieved at a body length of 100–140 cm.[1]

Short bowel syndrome (SBS) results from surgical resection, a congenital defect or disease-associated loss of absorptive capacity, and is characterised by the inability to maintain protein, energy, fluid, electrolyte and micronutrient balance when on a conventionally accepted normal diet.[2,3] The most common causes of SBS include necrotising enterocolitis (NEC) and congenital malformations such as intestinal atresias, gastroschisis or midgut volvulus.[3,4,5]

Despite multiple attempts, the minimum small bowel length needed to facilitate normal absorption has not yet been defined.[2] The functional ability of the small bowel is determined by the intrinsic characteristics of the remainder of the small bowel post surgery.[2] Patients at the greatest nutritional risk generally have a duodenostomy or a jejunoileal anastomosis with less than 35 cm

	Birth	6 months	13 months	21 months	26 months	27 months	28 months	29 months	30 months
Weight (kg)	2.86	5.5	6.0	6.5	6.75	7.5	8.0	8.5	9.0
Length (cm)	47	60	66	72	74	75	77	78	80
Head circumference (cm)	32	Not available							

of residual small bowel, jejunocolic or ileocolic anastomosis with less than 60 cm of residual small bowel or an end jejunostomy with 115 cm of residual small bowel.[2]

The goals in the treatment of infants with SBS are to keep the infant well nourished and growing proportionally, to keep fluid and electrolyte status stable, to minimise faecal loss of fluid, electrolytes and nutrients, and to maximise the process of bowel adaptation.[3]

The management of SBS is a multistage process.[2] It begins with a process of total parenteral nutrition (TPN), followed by a combination of enteral feeds and parenteral nutrition (PN), continuous enteral feeding only, weaning to bolus feeding and solid foods, and finally dietary modification alone.[2]

The state, area, motility and length of remaining bowel predicts the infant's ability to tolerate enteral nutrition.[3] The dependence on total parenteral nutrition (TPN) depends on the remaining length of bowel and the presence of the ileo caecal valve (ICV).[3] The process of bowel adaptation is the key to achieving independence from TPN. Adaptation is characterised by cellular hyperplasia, villus hypertrophy and increased crypt depth and bowel dilation.[3] This process may begin almost 24–48 hours post resection, and may continue for months to years. Some of the factors associated with adaptation include epidermal growth factor, GLP-2, glutamine, growth hormone and long chain polyunsaturated fatty acids from fish oils.[3]

Long term TPN is associated with the development of intestinal failure associated liver disease (IFALD), comprising hepatic steatosis, cholelithiasis or hepatic fibrosis.[3,5,6] Cholestasis is common amongst infants receiving PN from birth onward. Multifactorial risk factors have been implicated in the development of TPN-associated cholestasis, including prematurity, low birth weight, duration of TPN, multiple surgical procedures, recurrent sepsis, excessive energy intake, excessive protein and excessive parenteral lipids, lack of enteral feeding, systemic or portal endotoxaemia, reduced levels of gastrointestinal hormones, as well as the presence of phytosterols in intravenous fat emulsions.[3,6]

Commercially available intravenous fat emulsions are soy based preparations containing phytosterols such as sitosterol, campesterol and sigmasterol.[6] The observation of high plasma levels of phytosterols in patients with TPN-associated cholestasis receiving intravenous fat emulsions led to the hypothesis that accumulation of these substances contributes to cholestasis.[2,6] Their intravenous route of administration can lead to their accumulation in the hepatocyte because they are inefficiently metabolised by the liver.[6] Incorporation into hepatocyte membranes can then affect membrane fluidity and membrane-bound transport proteins such as the canalicular adenosine triphosphate-dependant bile acid transporters and sodium potassium-adenosine triphosphate.[6] Evidence from both animal and clinical studies indicates that omega-3 polyunsaturated fatty acids and their specific lipid mediators can reduce not only the activity of inflammatory processes but may also lower inflammatory susceptibility in general.[6] Thus, they can also lessen the inflammatory response in liver tissue probably by regulating Kupffer cell activation and suppressing cytokine production.[6] Omega-3 supplementation in addition to conventional lipids (to prevent essential fatty acid deficiency) may be advantageous in the prevention and treatment of TPN-associated cholestasis.[3,6]

Prevention of IFALD can be achieved by limiting total energy overload.[2] Excessive non-protein energy has been associated with increased sepsis risk. The risk of sepsis may be a result of hyperinsulinism and hyperglycaemia, the facilitation of bacterial growth in a lipid rich solution, or an increased propensity for bacterial translocation.[3] TPN with excessive glucose intake may induce insulin resistance and subsequent steatosis.[2] Furthermore, IFALD can be prevented by using parenteral solutions containing taurine.[2,5] Taurine increases bile flow and protects against toxic bile salts, such as lithocholic acid, which has been shown to produce bile duct hyperplasia, gallstone formation and intrahepatic cholestasis. Other worthwhile strategies to prevent IFALD include intermittent infusion of TPN,[2] prevention of other catheter-related sepsis and reduction of intra-luminal bacterial overgrowth.[5]

Lack of enteral nutrition with a subsequent reduction of gastrointestinal hormones such as cholecystokinin, motilin, glucose dependant insulinotropic polypeptide, secretin, pancreatic polypeptide, glucagons and vasoactive intestinal peptide may reduce gallbladder contractibility and the development of intestinal stasis.[2] Disrupted enterohepatic circulation caused by ileal disease, resection and lack of enteral nutrition with a subsequent reduction of hepatocellular bile acid, bile secretion, and gallbladder contraction increases the likelihood of progressive liver injury.[2]

In a recent study done on TPN-dependant infants ($N = 10$) with SBS, Cole and co-workers studied the impact of feeding route and intestinal permeability on blood stream infection (BSI), small bowel bacterial overgrowth (SBBO) and systemic immune responses.[4] They found that BSI incidence was high (80%) and SBBO was common (50%). SBBO increased the odds for BSI (> 7-fold; $p = 0.009$).[4] Serum TNF-α and interleukin-1 ß, -6, and -8 levels diminished with increased enteral nutrition.[4] The authors thus concluded that in children with SBS, SBBO increases the risk for BSI, and systemic proinflammatory response decreases with increasing enteral feeding and weaning of TPN.[4]

In general, SBBO is a complication that frequently occurs after resection of the ileocaecal valve, when a tight anastomosis is present or with poor motility of a dilated small bowel segment. It is responsible for mucosal inflammation which can lead to nutrient malabsorption and a depleted bile acid pool. This results in steatorrhoea and malabsorption of fat-soluble vitamins.[5]

Aggressive enteral nutrition ensuring at least 20–30% of total daily energy intake through the enteral route promotes enterohepatic circulation, decreases biliary disease and stimulates the release of

gut hormones.[2] The choice of an appropriate enteral feed continues to be debated in the literature and has not been determined yet. Colostrum and breast milk may offer some advantages when available.[3] In animal models, colostrum and colostrum protein concentrate have been shown to stimulate mucosal growth. Whether the same results will be achieved with pasteurised donor breast milk need to be investigated.[3] Amino acid based and protein hydrolysate formulae have traditionally been used to shorten the duration of TPN.[3] The calcium and phosphorus content of these formulae may not be ideal, but they are typically better than that which can be delivered by TPN.[3]

The ileocaecal valve (ICV), located between the small and large bowel, acts to slow the transit time of intestinal contents and bacteria into the ileum.[3] Bacterial colonisation of the small bowel, in the absence of the ICV, can reduce absorption of vitamin $B_{12,}$ deconjugate bile salts, reduce bile salt absorption, and impair gut function.[2,3] With the preservation of the ICV, it would be reasonable to expect that the absorption of fluid or nutrients would improve by delaying the transit time of the intestinal contents.[2] This concept has not been supported by experimental evidence.[2] In cases of SBBO carbohydrate restriction, an increase in fat and protein intake is useful to decrease the development of gas-related symptoms and osmotic diarrhoea, because most bacteria ferment only carbohydrate. In patients with significant bile acid losses, a high fat diet may increase stool output and increase risk of oxalate nephropathy.[2]

During transition from TPN to enteral nutrition careful attention should be paid to monitoring serum electrolytes and hydration status.[2] Excessive osmotic fluid is the most common cause of diarrhoea.[2] Normal or half normal saline, as well as different intravenous electrolytes (potassium, sodium and bicarbonate) can be added to the patient's formula to meet their fluid and electrolyte requirements.[2] Continuous enteral nutrition as well as the use of diluted enteral formulae could also be employed to maintain adequate electrolyte and hydration status.[2]

Achievement of normal developmental goals is often overlooked in children with SBS. In an attempt to optimise nutritional intake various strategies are used including TPN as well as alternative feeding routes such as nasogastric tubes and gastrostomies. Oral intake is usually delayed, which could lead to feeding difficulties later in life. Non-nutritive, oral motor therapy and early oral feedings are important in intestinal rehabilitation.[3] An oral motor stimulation programme should be initiated when feasible and early small enteral feeds should be given orally when developmentally appropriate and safe.[3]

The following factors contributed to the clinical course of the patient:

- The lack of breastfeeding after birth deprived the patient of the immunological factors which were needed to support his immune system.
- The loss of the ICV created the ideal environment for SBBO, which contributed to recurrent episodes of sepsis.
- Aggressive continuous enteral nutrition predisposed the patient to the development of complications e.g. volvulus and jejunal necrosis.
- Long term TPN with high osmolar intravenous solutions led to vascular thrombosis.
- Continuous TPN, with an excessive glucose intake, reduced lipid intake, lack of additional α-tocopherol and possible aluminium contamination lead to repeated episodes of cholestasis.

In retrospect, Professor Goulet concluded that the ideal treatment for this patient, as supported by the literature, would have been intermittent TPN containing an omega-3 lipid infusion. Oral feeding using either breastmilk or a protein hydrolysate formula should have been instituted timeously. A liver transplant could have been avoided. By reversing the cholestasis and improving the patient's nutritional status, an isolated intestinal transplant could have been done.

References

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