



Case Study: The nutritional management of short bowel syndrome in a very low-birthweight neonate

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Introduction

Necrotising enterocolitis (NEC) is the most common gastrointestinal disease in preterm neonates.¹ The aetiology of NEC remains poorly understood. Proposed preventive strategies include the provision of breast milk as an enteral feed, monitoring the advancement of feeds and modulating the gut microbiome by providing probiotics.^{1,2}

Some patients who present with NEC require surgical intervention for the resection of a necrotic bowel which may result in short bowel syndrome (SBS). SBS may also result from congenital defects or disease-associated loss of absorption, and is characterised by the inability to maintain protein, energy, fluid, electrolyte or micronutrient balance when on a conventionally accepted, normal diet.³

The clinical course and nutritional management of a preterm infant with SBS is described in this case study. New developments in the prevention of NEC are briefly discussed. Relevant evidence with regard to nutritional management is reviewed, and practical aspects of the management discussed.

Case study

A 25-year-old multigravida mother presented in spontaneous preterm labour. She was tocolysed to delay delivery, and received two intramuscular steroid injections. A male infant was born via normal vertex delivery at 29 weeks' gestation. The Apgar (appearance, pulse, grimace, activity and respiration) scores documented at one and five minutes were 6 and 8, respectively. The infant presented with moderate respiratory distress, and required admission to the intensive care unit for continuous positive airway pressure (CPAP) support. On day 5 of life, the patient had neonatal jaundice, for which phototherapy was required, with the subsequent normalisation of total bilirubin levels. Phototherapy was stopped on day 7 of life. CPAP was stopped on day 2, and oxygen given via nasal cannula. Thereafter, on day 3 of life, he was weaned to room air.

Anthropometry

The infant's birthweight was 1 080g, which is classified as very low birthweight. His birth length was 37 cm and head circumference 27 cm. These measurements were plotted on a gender-specific Fenton growth chart.⁴ All measurements were below the 50th centile for gestational age and showed proportional growth in utero. After initial weight loss post delivery (12% of his birthweight) due to adaption processes after birth, his weight increased by 14 g/kg/day.

Management

The patient received donor-expressed breast milk and mother's expressed breast milk via an orogastric tube. The mother received intensive breastfeeding support in the hospital. Feeds were introduced at 22 ml/kg on day 1 of life, and increased by 35 ml/kg/day. Probiotics (Pro-B2[®], C Pharm) (0.2 ml/day) were started on day 3 of life. Once the patient achieved a feed of 150 ml/kg, providing an estimate of 101 kcal/kg and 1.8 g protein/kg daily, a multinutrient breast milk fortifier (FM 85[®], PreNAN) and multivitamin (Multi-Vitamin[®], Pharmachem) (0.3 ml/day) were initiated, providing a combined total of 118 kcal/kg, and 2.8 g protein/kg daily. To ensure adequate nutritional intake and growth, feeds were incrementally increased to 200 ml/kg, providing an estimate of 146 kcal/kg and 3.3 g protein/kg daily. No clinical signs of feeding intolerance were noted during the advancement of feeds. A preterm formula, which provided 136 kcal/kg and 4.02 g protein daily, was introduced on day 15 of life due to an inadequate breast milk supply.

On day 21 of life, the infant presented with abdominal distension, bile-stained vomit and bloody stools. All feeds, probiotics and multivitamins were stopped. He developed respiratory failure and required intubation and ventilator support. He was started on inotropes for hypotension. An abdominal X-ray showed *pneumatosis intestinalis*, indicating NEC. C-reactive protein was increased (Table I), and the patient was commenced on antibiotic treatment (meropenem, 20 mg/kg). Parenteral nutrition (PN) was started via a peripherally inserted central catheter at 64 ml/kg, providing 45 kcal



Table 1: The blood values of the monitored variables during the course of treatment

Monitored variables	Normal values	Day 20	Day 21	Day 40	Day 51	Day 58
Sodium (mmol/l)	136–145	131	118	141	136	129
Potassium (mmol/l)	4.1–5.3	-	7.2	3.9	4.7	3.8
Urea (mmol/l)	0.7–4.6	-	5.0	1.0	1.5	2.5
Creatinine (µmol/l)	14–34	-	32	-	20	13
Magnesium (mmol/l)	0.66–1.03	-	1.07	0.87	0.97	0.82
Calcium (corrected) (mmol/l)	2.17–2.62	-	2.18	2.08	2.09	2.02
Phosphate (mmol/l)	1.15–2.15	2.14	2.39	1.44	0.85	1.35
Albumin (g/l)	28–46	-	-	-	-	19
Total bilirubin (µmol/l)	5–21	-	-	49	44	53
Conjugated bilirubin (µmol/l)	0–5	-	-	46	-	48
Alkaline phosphatase (µmol/l)	82–383	-	-	-	777	822
Alanine transaminase (U/l)	4–35	367	-	10	6	11
Aspartate transaminase (U/l)	0–65	-	-	-	41	-
γ-glutamyl transferase (U/l)	12–122	-	-	180	178	-
C-reactive protein (mg/l)	≤ 10	-	32	-	19	8
Haemoglobin (g/dl)	9.1–13.0	11.6	-	8.0	7.2	7.9
White cell count (x 10 ⁹ /l)	5.5–18.0	-	-	13.26	194.80	11.26
Platelet count (x 10 ⁹ /l)	140–350	-	-	217	177	159

and 1.3 g protein/kg daily, and sodium-containing intravenous (IV) fluids were given for hyponatraemia. The infant was transferred to another tertiary institution for surgical intervention.

During surgery, resection of a short segment of proximal jejunum 25 cm after the duodenojejunal flexure, and the terminal ileum and ileocaecal valve, was performed, as well as a total colectomy. Twenty-five centimetres of jejunum proximal to the duodenojejunal flexure, and 27 cm of distal jejunum and ileum, were viable, providing a total of 52 cm of viable small bowel remaining. A primary jejunojejunal anastomosis was performed and an end-ileostomy fashioned.

Post surgery, the patient was intubated and required ventilator support. He presented with hypocalcaemia and hypokalaemia, which was treated with IV calcium gluconate (5 ml/kg/day) and potassium chloride (KCl) (0.2 mmol/kg/hour), titrated to normal levels. PN continued at 60 ml/kg, providing 43 kcal and 1.2 g protein/kg daily, and IV fluids at 40 ml/kg. Fluids were restricted to 100 ml/kg because of mild oedema. Adrenaline (0.6 mg/kg/minute) was started postoperatively for hypovolaemia, and weaned on day 3 postoperatively. The patient was thrombocytopenic and received platelet transfusions.

The patient was kept *nil per os* for three days postoperatively owing to increased nasogastric aspirates. PN was continued at 60 ml/kg, and then increased to 80 ml/kg on day 3 postoperatively. Nasogastric feeds were started on day 3 post surgery at 1 ml/hour (20 ml/kg) of breast milk expressed by the mother. The oedema improved, and PN was increased to 100 ml/kg, providing 71 kcal/kg and 2.1 g protein/kg, on day 4. Magnesium sulphate (0.1 ml/kg) and KCl (0.2 mmol/kg/hour), were supplemented as the blood levels were low on day 5 post surgery. Feeds were incrementally increased by 1 ml/hour/day (18 ml/kg). A casein-dominant extensively hydrolysed

formula was provided when the mother could not provide adequate breast milk. She received breastfeeding support at regular intervals at both institutions. On day 8 post surgery, PN was increased to 120 ml/kg (85 kcal/kg and 2.5 g protein/kg). Enteral feeds were set at 40 ml/kg, providing 27 kcal/kg and 0.7 g protein/kg daily. The patient was transferred back to the original facility.

The enteral feeds were increased by 1 ml/hour/day (16 ml/kg) per day, and titrated against PN at a fluid volume of 160 ml/kg. Electrolyte-containing replacement fluid (100 ml of 0.45% normal saline with 1ml KCl) was given when the stoma losses were ≥ 30 ml/kg. Stoma losses increased on day 15 postoperatively to 80 ml/kg, and an amino acid-based formula was introduced. Loperamide (0.1 mg/kg) was given to reduce gut motility, and a proton-pump inhibitor (omeprazole) (0.5 mg/kg) prescribed to reduce gastric secretions. Poor growth was experienced, and the weight plateaued at 1 540 g. Losses remained high, and the enteral feeds were reduced to 16 ml/kg, with a subsequent decrease in ileostomy losses to ≤ 30 ml/kg.

The enteral feeds were again increased incrementally by 1 ml/hour/day (16 ml/kg) when the stoma losses were ≤ 30 ml/kg. Small oral feeds of breast milk expressed by the mother, when available, were introduced for oral stimulation. Neonatal cholestasis and elevated liver enzymes were shown in routine PN blood samples on day 14 postoperatively. As a PN regimen containing fish oil lipid emulsions was not routinely available at the institution, the pharmacy was tasked to procure these PN products. Ursodeoxycholic acid (20 mg/kg/day), a hydrophilic derivative of chenodeoxycholic acid, which acts by displacing toxic bile salts, was recommended.⁵ On day 51 of life, the C-reactive protein and white blood cells were raised. Antibiotics (vancomycin 10 mg/kg, and meropenem 20 mg/kg) were prescribed. Phosphate supplementation (1 mmol/



Table II: Enteral and parenteral requirements of the very low-birthweight premature infant^{6,7}

Nutrient	Parenteral (unit/kg/day)	Enteral (unit/kg/day)
Energy (kcal/kg)	110–120	110–135
Protein (g/kg)	1.5–4.0	3.5–4.0
Carbohydrate (g/kg)	13–18	11.6–13.2
Fat (g/kg)	3–4	4.8–6.6
Na (mmol/kg)	3.5–5.0	3.0–5.0
K (mmol/kg)	2.5–5.0	1.7–3.4
Cl (mmol/kg)	2.0–3.0	3.0–5.0
Ca (mmol/kg)	1.5–2.0	3.0–3.5
PO ₄ (mmol/kg)	1.5–1.9	1.9–2.9

kg/day) for hypophosphataemia was started on day 21, and an oral multivitamin (0.3 ml, twice daily) started once 75% of the enteral feeds were tolerated. As the primary site of vitamin B₁₂ absorption, i.e. the terminal ileum, had been resected, intramuscular vitamin B₁₂ supplementation (20 µg) was recommended. PN and EN were titrated at 160–180 ml/kg, providing full nutritional requirements. Enteral feeds provided 75% of nutritional requirements on day 32 postoperatively. The patient's weight was 1 920 g, and he was gaining weight at 16 g/kg/day. The patient was referred back to a specialised paediatric centre for further management on day 32.

By day 77 of life, the patient had received 60% of his requirements via the enteral route and 40% parenterally, and his weight has increased to 2.2 kg.

Nutritional requirements

According to the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guidelines, the enteral energy

requirements for neonates is 110–135 kcal/kg, with protein requirements of 3.5–4.0 g protein/kg for very low-birthweight preterm neonates between 1 000 g and 1 800 g (Table II).⁶ The parenteral energy requirement is 10% less than the enteral requirement because of the contribution of dietary-induced thermogenesis. When nutrition is provided via the parenteral route, 110–120 kcal/kg of energy, 3–4 g of lipids/kg, 1.5–4.0 g amino acids/kg and up to 18 g/kg/day of carbohydrate, daily, are recommended.⁷

A summary of the nutritional delivery for the course of treatment of this patient is summarised in Table III. Owing to the need for fluid restrictions post surgery, nutritional support for this patient was provided at 40–60% of his nutritional requirements. Thereafter, when the fluid restriction was lifted, full requirements were provided. However, his weight gain remained poor. The slower increase of enteral feeds based on tolerance, and titrating enteral nutrition and PN at a higher fluid volume, aided consistent growth thereafter.

Discussion

Prevention of necrotising enterocolitis

The advancement of enteral feeds has been studied as a modifiable risk factor for NEC. The slower advancement of feeds in daily increments of 15–24 ml/kg/day is common practice, and was previously thought to reduce the risk of NEC developing. The slower advancement of feeds was demonstrated to result in increased time to reach full feeds, as well as an increased risk of developing invasive infection, in a recent Cochrane review by Morgan et al.² The absence of an increased risk of the development of NEC or death in very low-birthweight infants, associated with advances in increments of 30–40 ml/kg, was also reported in this review.

Mother's own milk contains immunological properties which promote intestinal maturation and adaptation, improves feeding tolerance and

Table III: Nutrient delivery to the patient during the course of treatment

Days post surgery	PN	EN	Oral feeds	Clinical aspects
1–3	PN provided at 60–80 ml/kg	<i>Nil per os</i>		<ul style="list-style-type: none"> High gastric aspirates Fluid restriction due to oedema IV potassium and calcium
4–14	PN titrated against EN at 100–150 ml/kg	Breast milk expressed by the mother and extensively hydrolysed formula incrementally increased by 20 ml/kg to 80 ml/kg		<ul style="list-style-type: none"> Stoma losses of 15–33 ml/kg Insufficient volumes of breast milk expressed by the mother available
15	PN provided at 50 ml/kg	Breast milk expressed by the mother and extensively hydrolysed formula provided at 100 ml/kg		<ul style="list-style-type: none"> Stoma losses of 80 ml/kg Insufficient volumes of breast milk expressed by the mother available
16	PN provided at 50 ml/kg	Amino-acid based formula at 100 ml/kg		<ul style="list-style-type: none"> Stoma losses of 87 ml/kg No breast milk available Poor growth
18	PN titrated against EN at 160 ml/kg	Amino-acid based formula feeds reduced to 16 ml/kg		<ul style="list-style-type: none"> Stoma losses reduced to ≤ 30 ml/kg
19–31	PN titrated against EN at 160–180 ml/kg	Feeds of amino-acid based formula and breast milk expressed by the mother increased by 16 ml/kg/day	Small oral feeds of breast milk expressed by the mother introduced	<ul style="list-style-type: none"> Stoma losses of 10–25 ml/kg When losses of ≥ 30 ml/kg were reached, the feed was not increased Satisfactory weight gain of 16 g/kg/day

EN: enteral nutrition, IV: intravenous, PN: parenteral nutrition



remains the first feed choice for preterm infants.⁶ When a mother's milk is not available, the alternatives are either artificial formula or donor breast milk. Formula feeding is associated with superior short-term growth rates, but increases the risk of NEC. Therefore, donor milk is used when breast milk is not available.⁸

The routine use of probiotics to prevent NEC remains controversial. While some strongly support the use of probiotics, others criticise the routine use thereof owing to the heterogeneity of pooled data and lack of data on long-term outcomes.⁹ There is a lack of data on adverse effects, especially in extremely low-birthweight ($\leq 1\ 000$ g) infants, and particular caution should be taken with respect to this group. More research is needed to establish effective preparations, the safety of various strains, timing and length of probiotic use.¹ It is important to note that the benefits of probiotics are strain specific, and should be used according to the specific strain's proven therapeutic effect. The ESPGHAN committee on nutrition advises that the safety and clinical effects of one product should not be extrapolated to others.¹⁰ Guidelines were published by Deshpande et al to address some of these concerns and to optimise the use of probiotic supplementation.⁹

An improvement in the prevention of severe NEC and a reduction in all-cause mortality in preterm infants in association with probiotic use was shown in a review of randomised or quasi-randomised controlled trials. The findings also strongly supported the change in clinical practice.¹ The recommendation for probiotics was reviewed in a recent consensus paper. Probiotic strains, *Lactobacillus acidophilus* NCD01748 and *Bifidobacterium bifidum* NCD01453, received a grade B recommendation for the prevention of NEC.¹¹ The probiotic used in the current case consisted of 1×10^9 colony-forming units of *L. rhamnosus* GG and *B. infantis* per day. This has been shown to reduce the incidence of NEC in very low-birthweight infants in a similar setting.¹²

Short bowel syndrome

The main aim of nutritional management of SBS post surgery is to facilitate gut adaptation, ensure normal growth and development, and to prevent electrolyte imbalances.¹³

Three phases of nutritional management after gastrointestinal resection are recognised.¹³ The first phase (acute phase) follows the recovery from postoperative ileus. This phase may last 1–3 weeks, and is characterised by gastric hypersecretion and large electrolyte and stoma fluid losses, for which PN and IV fluid replacement are required. The second phase (recovery phase) may last for weeks to months, and is characterised by an improvement in the stoma losses as the gut adapts. Enteral feeds are slowly increased and titrated against PN to ensure adequate nutritional intake during this period. Full enteral feeds are tolerated because of successful intestinal adaptation during the third phase (maintenance phase). PN can potentially be discontinued during this phase.

The need for PN and IV fluid replacement depends on the length and quality of residual bowel, the remaining anatomy and the presence or absence of the ileocaecal valve.¹³ The duration of PN dependence in 63 neonates with a short bowel was investigated in

a retrospective study. It was found that the mean duration of PN was 4.8 months when the small bowel intestinal length was ≥ 50 cm, and 33 months when the intestinal length was ≤ 50 cm.¹⁴ Ideally, these patients should be cared for within a specialised multidisciplinary team, consisting of paediatric surgeons, gastroenterologists, a dietician, and nurses and pharmacists with experience in intestinal failure. Outcomes have been demonstrated to improve following management of these patients by a multidisciplinary team.¹⁵

Choice of enteral feed

Breast milk remains the first choice as an enteral feed as it contains immune-enhancing properties, beneficial bacteria and growth factors. Breast milk is associated with good gastrointestinal tolerance and gut adaptation, resulting in a shorter duration of PN dependence.¹⁶ Currently, there is no consensus regarding which formula to use when breast milk is unavailable. Great variation in practice exists because of the lack of randomised controlled trials. An individualised approach may be necessary with respect to choosing an appropriate formula. When focusing on the goals of nutritional therapy in SBS, nutrients with the greatest potential for gut adaptation, such as whole proteins and long-chain fatty acids, should be considered initially. Protein is absorbed in the upper small bowel and is largely unaffected by NEC-associated gut resections.

Extensively hydrolysed formula or amino acid-based formula can be introduced in a stepwise manner when intolerance to a polymeric feed is suspected. Medium-chain triglyceride-containing formulations may be beneficial when it becomes evident that fat absorption is compromised. A lactose-free feed should be used when transient lactose intolerance is evident. Cow's milk protein intolerance and non-immunoglobulin E-mediated allergies have been reported in these infants. A protein hydrolysate may be appropriate in these cases.

When to start enteral feeds

Enteral nutrition can be started as soon as possible after surgery. Early enteral feeding, i.e. 12 hours post surgery, has been associated with the earlier attainment of full enteral feeds.¹⁶ Continuous feeds are generally better tolerated than bolus feeds. Feeds delivered in a continuous fashion improve nutrient absorption and gut adaptation by providing optimum luminal exposure time.¹³

How to increase enteral feeds

There is a paucity of data on the optimal rate with regard to the increase in enteral feeds post surgery for SBS. Therefore, practices are mainly based on expert opinion. According to Vanderhoof and Young, enteral feeds can be slowly increased by 1 ml/hour/day, based on individual tolerance.¹⁷ Tolerance is assessed by volume and the consistency of the ostomy effluent, vomiting and the presence of faecal-reducing substances. Stool output limits are set on a surrogate threshold of 40–50 ml/kg.¹⁸ Because of high levels of electrolyte losses in the effluent (Table IV), which are dependent on the region of the ostomy, the patient may be at increased risk of electrolyte disturbances above this threshold. Higher ostomy output is accepted in some centres. However, frequent electrolyte monitoring is performed, and appropriate fluid and electrolyte



replacement given. Typically, we aim for a stomal output of 30 ml/kg to prevent electrolyte imbalances. Enteral feeding is increased to tolerance, and the volume can be increased incrementally as the bowel adapts.

Table IV: The electrolyte content of gastrointestinal tract secretions in paediatric patients¹⁸

	Sodium (mmol/l)	Potassium (mmol/l)	Chloride (mmol/l)	Bicarbonate (mmol/l)
Gastric	140	15	155	
Ileostomy	80–140	15	115	40
Colostomy	50–80	10–30	40	20–25
Secretory	60–120			
Diarrhoea	30–40	10–80	10–110	30
Normal stool	5	10	10	0

When to start oral feeds

Early oral feeding is recommended to stimulate the suck-swallow reflex and for oral motor development.¹⁶ Other benefits of oral feeds include increased gastrointestinal secretions of trophic factors and the release of salivary epidermal growth factor, which contributes to gut adaptation and protects against PN-associated liver disease (PNALD).¹³

There is no evidence on the ideal time to start oral feeding.¹⁶ Therefore, a pragmatic approach is used in our centre, i.e. providing small oral feeds, in addition to continuous gastric feeding, as soon as the patient is between 34 and 36 weeks' gestation, clinically stable, not dependent on invasive respiratory support and shows readiness to feed.

Parenteral nutrition-associated liver disease

PNALD is a potentially life-threatening complication in children receiving long-term PN. Risk factors for PNALD include prematurity, sepsis, extensive gut resections, and bacterial overgrowth and/or translocation, as well as lack of enteral stimulation.¹⁹ The exact aetiology of PNALD is unknown, but hepatotoxic factors, including the use of soy bean-based lipid emulsions, have been hypothesised as a likely cause. Fish oil-containing lipid emulsions have been investigated with respect to reversing neonatal cholestasis and liver dysfunction. A lipid emulsion containing soy beans, medium-chain triglycerides, olive oil and fish oil was found to be safe and well tolerated in children, and associated with a decreased bilirubin level, in one randomised controlled trial. The resolution of PN-associated jaundice was demonstrated in another study when patients switched from a soy bean-based emulsion to a mixed-lipid emulsion containing soy beans, medium-chain triglycerides, olive oil and fish oil.^{19,20}

Preventing energy and carbohydrate overload, and providing a taurine-containing amino acid solution and intermittent total PN in patients aged ≥ 3 months, are other nutritional strategies that can be used to prevent PNALD.⁷

Many aspects of the management of SBS in premature infants remain based on expert opinion because of the rarity of this syndrome and consequent lack of controlled trials. Future studies are needed to

address some of the practical aspects of nutritional management, i.e. which type of enteral feed to use when breast milk is not available, in order to improve outcomes. The focus of nutritional management should be the facilitation of adequate growth, gut adaptation and fluid and electrolyte balance, as well as the prevention of long-term complications, i.e. PNALD. Management of these infants within a multidisciplinary team with expertise in the field of paediatric SBS should be prioritised.

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