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Review

Management of short bowel syndrome in postoperative very low birth weight infants

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SUMMARY

Short bowel syndrome is a potentially devastating morbidity for the very low birth weight infant and family with a high risk for mortality. Prevention of injury to the intestine is the ideal, but, if and when the problem arises, it is important to have a systematic approach to manage nutrition, use pharmaceutical strategies and tools to maximize the outcome potential. Safely maximizing parenteral nutrition support by providing adequate macronutrients and micronutrients while minimizing its hepatotoxic effects is the initial postoperative strategy. As the infant stabilizes and starts to recover from that initial injury and/or surgery, a slow and closely monitored enteral nutrition approach should be initiated. Enteral feeds can be complemented with medications and supplements emerging as valuable clinical tools. Engaging a multidisciplinary team of neonatologists, gastroenterologists, pharmacists, skilled clinical nutrition support staff including registered dietitians and nutrition support nurses will facilitate optimizing each and every infant's long term result. Promoting intestinal rehabilitation and adaptation through evidence-based practice where it is found, and ongoing pursuit of research in this rare and devastating disease, is paramount in achieving optimal outcomes.

1. Introduction

Infants with a birth weight of ≤1500 g are at high risk for a variety of morbidities including necrotizing enterocolitis (NEC), ischemic injury along the length of the intestine, jejunal or ileal atresias, and gastroschisis. All of these conditions may require surgical intervention. Short bowel syndrome (SBS) in very low birth weight (VLBW) infants, those born at ≤1500 g, continues to be an unfortunate reality and is the leading cause of intestinal failure in infants [1]. Outcomes vary, and are greatly influenced by age of the injury and potential for intestinal growth, the site of the resection, presence of the ileocecal valve (ICV), the development of parenteral nutrition-associated cholestasis [PNAC, also known as parenteral nutrition-associated liver disease (PNALD)], and functionality of the gastrointestinal (GI) tract [2,3]. Management of SBS can be extremely complicated and recovery may be lifelong for some. The medical journey is further confounded by other comorbidities of prematurity such as chronic lung disease, metabolic bone disease of prematurity, extrauterine growth restriction, and congenital cardiac defects such as patent ductus arteriosus. A multidisciplinary team of neonatologists, gastroenterologists, surgeons, registered dietitians, nutrition support nurses, and pharmacists can enhance the prospect of achieving intestinal adaptation, appropriate growth and neurodevelopment [2,4].

Short bowel syndrome (SBS) is a state of malabsorption, and parenteral nutrition (PN) is needed for a prolonged period of time. Amin et al. define the need for PN as a minimum of three months whereas the Canadian Association of Pediatric Surgeons defines the need for PN as >42 days [2,5]. From 2002 to 2005, surgical SBS was recorded in 0.7% of VLBW infants by the National Institute of Child Health and Development neonatal research network centers [6]. It is extremely difficult to accurately estimate the incidence and prevalence of SBS due to the rarity of the condition and the unclear and varied definitions used to describe not only the criteria but the outcomes. Ultra-short bowel has been defined by Diamanti et al. as ≤10 cm; by Gambarara et al. as ≤20 cm; and by De Greef et al. as ≤40 cm [7–9]. SBS is most frequently the result of a surgical resection of the bowel; however, even if adequate length and anatomy of the GI tract remain intact and well perfused, it may not function properly. Function of the bowel is just as, if not more,

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important as the length of the remaining bowel. Critically decreased function below what is needed for adequate absorption of fluids, electrolytes, macro- and micronutrients results in intestinal failure [10]. It is possible for some patients to be discharged on full enteral nutrition; however, for those with intestinal failure, it is highly unlikely.

The leading cause of SBS in VLBW infants is NEC [6]. Other causes include, but are not limited to: spontaneous intestinal perforation, ileal/jejunal atresias, meconium plugs and/or obstruction, gastroschisis or other congenital malformation of the intestine, malrotation, volvulus, and intussusception. Congenital short bowel syndrome is a rare disorder whereby the length of the small intestine is much less than expected for age, and is hypothesized to have a genetic origin [11]. Data gathered from 2012 by Pant et al. highlight the epidemiology and healthcare resource utilization in the USA. The statistics reflect what most of us know from experience and observation. Children with SBS have a much higher rate of mortality, longer length of hospital stay, higher hospital costs, greater post-discharge needs and costs, and demonstrate more severe illness overall [12]. Complications frequently arise and include progressive liver dysfunction and disease, bacterial overgrowth, dysmotility, renal failure, venous access difficulties or loss, and catheter-related bloodstream infections [13]. Intestinal transplantation, with or without a combined liver transplantation, is a potential long-term intervention for those who suffer from chronic critical complications of PN dependence [10].

When an infant has undergone a surgical resection of the intestine, it is imperative to know exactly what parts of the intestine remain. The three most important elements to determine are whether the ICV remains intact, and the length and location of the remaining bowel. The ICV may slow transit time along the intestine and acts as a barrier to prevent bacterial translocation of colonic contents. It has been suggested that the ICV remaining intact reflects the abilities of the remaining terminal ileum [5]. The ileum absorbs fluid, vitamin B12, and bile acids, and if a significant section is removed, the jejunum has limited ability to adapt and develop some of the absorption abilities of the ileum [2]. Significant loss of the jejunum typically results in increased gastric emptying times and is associated with gastrin hypersecretion which may lead to fat malabsorption by inactivating pancreatic enzymes, acid-peptic injury, exacerbation fluid and electrolyte losses, and damage to the mucosa [2] (Fig. 1).

Premature infants have the greatest potential for intestinal growth and adaptation postoperatively. Intestinal adaptation can begin shortly after resection and lead to improved absorption of nutrients, fluids, and electrolytes. Intestinal adaptation drives overall intestinal rehabilitation by progressively attaining the ability to absorb and utilize all nutrition via an enteral route, without the need for PN support [5]. The length of the small bowel at 35 weeks of gestation is twice the length of the small bowel of a 19–27 week gestation [5]. Intestinal length can increase from 142 ± 22 cm at 19–27 weeks to 217 ± 24 cm at 27–35 weeks and to 304 ± 44 cm at term age [14,15]. Over time, the intestine continues to grow up to 600–700 cm which may be reached by adulthood. There have been various findings and general observations of the bowel length and outcomes. It is generally postulated that, with $\geq$15 cm of remaining small intestine with an intact ICV, or 40 cm of small intestine without an ICV, a successful outcome is likely [16]. Demehri et al. found that presence of $\geq$10% expected small bowel length, an ICV, original diagnosis of NEC or atresia predicted weaning from PN [17]. To calculate the percent of expected bowel length, the authors measured the absolute length of remaining small bowel divided by the predicted length of small bowel based on the child's postconceptual age $\times$100 [17]. Intestinal proliferation, or lengthening of the villi, and to some degree dilatation of the small-bowel lumen, may result in increased mucosal surface area following massive resection and facilitate adaptation [10].

The clinical course of SBS patients has been described in three clinical stages: acute, recovery or intermediate, and a late phase in which PN is maintained with minimal metabolic effects and/or weaning from PN is possible [2,18]. The acute phase is the immediate time following the intestinal surgery. This phase can last up to 2–3 weeks post surgery and is focussed on managing the anticipated fluid, metabolic, and electrolyte fluctuations. The goal of the acute phase is to stabilize the infant, and nutrition is provided solely via PN. Concern for infection is great and the potential compounding effects on the liver from both PN and infection are prevalent. The recovery, or intermediate stage, is the time when enteral feedings are initiated and trialed, while PN continues to be the primary mode of nutrition. If an ostomy is present, the volume of output should to be <40 mL/kg/day [2,19]. Promoting age-appropriate growth, neurodevelopment, and bone mineralization are the ideal goals for premature infant nutrition; however, these goals may be relegated to a secondary role for a period of time if calories and lipids are restricted to minimize the deleterious effects of PN on the liver. The late clinical stage of SBS is when PN volume can be weaned down as the volume of enteral nutrition (EN) is advanced. The ultimate goal for these infants is to wean off PN completely. This late stage is to maximize EN volume, absorption, and overall tolerance, while minimizing PN volume, time, and hepatotoxic effects to promote growth, neurodevelopment, and prevent nutrient deficiencies.

2. Parenteral nutrition strategies

Bypassing the GI tract to provide nutrition and fluids is life-saving in the management of SBS. Parenteral nutrition (PN) standards for VLBW infants promote growth, bone mineralization, and neurodevelopment. Infants dependent on prolonged PN are also at risk for macronutrient and micronutrient deficiencies. Balancing the need for good nutrition with the risks of prolonged PN is delicate and may be limited by vascular access issues, volume restrictions, product availability and manufacturing practices.

Ideal PN macronutrient needs for VLBW provides 90–100 kcal/kg/day, 4 g amino acids/kg/day, and 2.5–3 g fat/kg/day [20]. Frequent, standardized biochemical monitoring may be needed daily postoperatively as the infant is in the acute phase, for the first 2–5 days, but when greater metabolic stability has been achieved it may be monitored 1–2 days each week. Electrolyte and micronutrient imbalances often occur, and may need more frequent adjustment in the PN.

Prolonged duration of PN and lack of enteral feeds increases the infant's risk of developing cholestasis due to the hepatotoxic components used in PN solutions, overfeeding, soy-based intravenous (IV) lipid solutions, chronic infections, and decreased bile flow [21,22]. Delivering excessive macronutrients further exacerbates PNAC. High doses of intravenous dextrose have been shown to worsen PNAC more than IV lipids [21]. Gupta et al. found that limiting IV dextrose to a glucose infusion rate of $\leq$9.3 mg carbohydrate/kg/min in premature infants may be helpful in decreasing the incidence of PNAC [21]. Methionine excess from PN amino acids is also implicated in the development and exacerbation of PNAC [23]. IV lipids derived from soybean oil emulsions are frequently considered as the primary reason for cholestasis due to the effect of raising serum phytosterol concentrations which suppress bile flow, and providing ω-6 fatty acids, which are pro-inflammatory [21,23–25]. For more than a decade, newer intravenous fat emulsions (IVFEs) have been produced that have been

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