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REVIEW ARTICLE

Recent Advances in the Management of Pediatric Intestinal Failure

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Intestinal failure is a chronic condition in which the intestinal tract has lost most of its function. Prognosis depends on the severity and underlying etiologies. Although many patients survive under parenteral nutrition support, they often suffer from fatal complications such as progressive cholestasis and frequent sepsis. In addition, to decide the proper time to refer selected patients to bowel transplantation remains difficult. A noninvasive biomarker developed to evaluate functional enterocyte mass and the extent of intestinal adaptation is plasma citrulline level. It is shown that serum citrulline correlates with small bowel length, oral tolerance, and parenteral nutrition dependency. Recent evidence has revealed that the use of fish oil containing lipid emulsions to substitute traditional soybean-based formula may reverse a patient's cholestasis and improve lipid profiles. A new method used to prevent catheter-related bloodstream infection is ethanol lock therapy. With both antimicrobial and fibrinolytic activities, studies have shown that ethanol locks can effectively decrease catheter infection and replacement rate with no known resistance reported. As part of intestinal rehabilitation, auxiliary surgeries such as longitudinal intestinal lengthening and tailoring, serial transverse enteroplasty, and tapering enteroplasty can be beneficial for selected patients before bridging to bowel transplantation. With the introduction of these new medical and surgical modalities, patients with intestinal failure are having better outcomes than in the past.

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1. Introduction

Intestinal failure (IF) is a chronic condition where the intestinal tract has lost most of its function, either resulting from extensive bowel resection or diseases in which inadequate water and nutrient can be obtained unless parenteral nutrition (PN) is provided. The underlying causes of IF vary in pediatric patients, with short bowel syndrome (SBS) being the primary etiology.[1] Long-term prognosis depends on the etiologies, severity, and related complications. Although utilization of PN has extended the life span of patients, problems such as IF-associated cholestasis and catheter-related infection remain to be resolved. Previously, the function of the remaining intestine could only be assessed indirectly through oral tolerance, making it difficult to predict whether intestinal adaptation could be achieved. Recently, with the introduction of noninvasive clinical assessment such as plasma citrulline concentration, newer formulation of PN, mainly omega-3 lipid emulsions, more effective antiseptic strategy such as the ethanol lock technique, and auxiliary surgical interventions namely autologous gastrointestinal reconstruction (AGIR), patients with IF can achieve a better prognosis than in the past.

2. New assessment tool for patients with IF

The clinical assessment of pediatric patients with IF includes the following steps. Firstly, the underlying causes of IF and the structure/function of the residual bowel are identified. Diseases predisposing to IF can be classified into three categories which consist of SBS resulting from extensive bowel resection, motility disorders such as Hirschsprung disease, and mucosal abnormalities (Table 1). Determining the underlying etiologies may shed light on whether IF would be "reversible" (i.e., intestinal adaptation/autonomy may be achieved) or "permanent" (i.e., dependence on PN unless a bowel transplantation is performed). For patients with suspected permanent IF, early transplantation should be considered and arranged. The residual bowel length and anatomy can be evaluated by detailed history taking, previous surgical records, radiographic examination, GI series, and intestinal transit time.

Table 1 Diseases predisposing to pediatric intestinal failure.

Short bowel syndrome
— Necrotizing enterocolitis (most common)
— Malrotation with midgut volvulus
— Gastroschisis
— Intestinal atresia
— Inflammatory bowel disease
Motility disorders
— Long segment Hirschsprung disease
— Intestinal pseudo-obstruction
Mucosal abnormalities
— Microvillous inclusion disease
— Tufting enteropathy
— Autoimmune enteropathy

Usually clinical features, underlying physiological changes, and even prognosis can be predicted by the remnant GI regions.[2,3] Sondheimer et al[4] reviewed 44 neonates who had small bowel resection and were dependent on PN for at least 3 months. They concluded that the residual small bowel length after the initial surgery and the percentage of daily energy intake through enteral route at 12 weeks' adjusted age were significantly related to PN dependence.

A new noninvasive biomarker recently used to evaluate functional enterocyte mass is plasma citrulline concentration. Citrulline is a nonprotein amino acid produced almost exclusively by enterocytes; thus, patients with SBS and mucosal injury of the bowel may have lower levels of plasma citrulline. A study by Vecino Lopez et al[5] measured the serum citrulline level in 57 pediatric patients with IF and found that those who were totally or partially dependent on PN had significantly lower plasma citrulline levels compared with those who were weaned from PN (7.1 ± 4.1, 15.8 ± 8.9 vs. 20.6 ± 7.5, 28.8 ± 10.1, $p < 0.001$). Fitzgibbons et al[6] concluded that plasma citrulline >15 μmol/L could predict PN wean off. Rhoads et al[7] showed that serum citrulline >19 μmol/L could predict the development of enteral tolerance. Other studies have also correlated serum citrulline level with small bowel length, bowel adaptation, and PN dependence in pediatric patients with SBS.[8–10] As citrulline is excreted by the kidney, patients with renal insufficiency may not have reduced citrulline concentration. Although there is as yet no consistent cut-off value, these studies show promising results and further research is warranted.

Secondly, the nutritional status of patients, including fluid and electrolytes, trace elements, vitamins, triglycerides, and essential fatty acids (FAs), should be thoroughly assessed. In addition, individualized supplement of each nutrient is very important. Thirdly, any complications related to PN and underlying diseases need to be evaluated and managed throughout the whole care. After these initial evaluations, physicians could provide suitable and individualized treatment programs according to the current status of a patient.

3. New modalities in caring for IF patients

Nearly all patients diagnosed with IF rely on long-term PN to maintain their lives. However, intestinal failure-associated liver disease (IFALD) and catheter-related bloodstream infection (CRBSI) are the two main complications associated with long-term PN use.[11] Therefore, how to prevent and manage these two problems has become a key issue in daily practice.

The prevalence of IFALD varies between studies. It is estimated that 40—60% of children, and up to 85% of neonates receiving prolonged periods of PN will develop IFALD.[12–14] Previous reports have shown that IFALD is directly related to the survival and outcome of a patient.[15,16] The clinical scenarios range from steatohepatitis, cholestasis, and hepatic fibrosis to end-stage liver disease. Generally, neonatal patients often suffer from aggressive, cholestatic liver disease, whereas adult patients only have steatosis or steatohepatitis.[17] Although it is sometimes called parenteral nutrition-associated liver disease (PNALD),