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# Best Practice & Research Clinical Gastroenterology



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# Promoting intestinal adaptation by nutrition and medication



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Keywords: Enteral nutrition Growth factors Intestinal adaptation Intestinal failure Parenteral nutrition Short bowel syndrome

#### ABSTRACT

The ultimate goal in the treatment of short bowel syndrome is to wean patients off parenteral nutrition, by promoting intestinal adaptation. Intestinal adaptation is the natural compensatory process that occurs after small bowel resection. Stimulating the remaining bowel with enteral nutrition can enhance this process. Additionally, medication can be used to either reduce factors that complicate the adaptation process or to stimulate intestinal adaptation, such as antisecretory drugs and several growth factors. The aim of this review was to provide an overview of the best nutritional strategies and medication that best promote intestinal adaptation.

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Abbreviations: EN, Enteral nutrition; GH, Growth hormone; GLP-1, Glucagon-like peptide-1; GLP-2, Glucagon-like peptide-2; HGF, Hepatocyte growth factor; IGF, Insulin-like growth factor; IF, Intestinal failure; LCPs, Long chain polyunsaturated fatty acids; LCTs, Long chain triglycerides; MCTs, Medium chain triglycerides; PN, Parenteral nutrition; PPIs, Proton pomp inhibitors; SBS, Short bowel syndrome; SCFAs, Short chain fatty acids; SIBO, Small intestinal bacterial overgrowth.

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The main cause of intestinal failure (IF) in both adults and children is short bowel syndrome (SBS), which occurs after an extensive small bowel resection. Intestinal adaptation is the natural compensatory process that occurs after bowel resection. By effecting structural and functional changes this process improves nutrient and fluid absorption in the remnant small bowel [1]. Although not possible in all patients, the ultimate goal is to wean patients off parenteral nutrition (PN) by stimulating the intestinal adaptation, while ensuring adequate nutritional status and preventing complications. Many factors affect the process of adaptation, such as age of the patient, remaining small bowel length, presence of the ileocecal valve and colon and the underlying disease. Stimulating the remaining bowel with enteral nutrition (EN) can enhance adaptation. Additionally, medication can be used to either reduce factors that complicate the adaptation process or to stimulate intestinal adaptation, such as antisecretory drugs and growth factors. The aim of this review was to provide an overview about the nutritional strategies and medication that best promote intestinal adaptation.

This review is evidence-based wherever possible; meta-analysis data, systematic reviews and RCTs are described where available. However, in general, no large trials regarding nutrition and medication in patients with SBS have been performed and therefore also other studies and clinical practice guidelines are described.

#### **Nutritional strategies**

It is generally accepted that EN enhances intestinal adaptation in patients with SBS. The complex mechanism of action can be broken down into three major categories: 1) stimulation of mucosal hyperplasia by direct contact with epithelial cells; 2) stimulation of trophic gastrointestinal hormone secretion; and 3) stimulation of the production of trophic pancreatobiliary secretions [2,3]. In addition, it is known that the higher the complexity of a nutrient, the higher the workload of the digestive mechanisms involved. Thus, the more digestion a nutrient needs (e.g. whole protein), the more hyperplasia it will cause. In the next section, we will discuss what is known about the different nutrients in relation with intestinal adaptation in patients with SBS. In addition, the composition of EN and feeding mode will briefly be discussed.

#### **Nutrients**

#### Proteins

Dietary proteins are either digested into amino acids and directly absorbed, or digested into polypeptides, which are first absorbed inside the enterocytes before they are hydrolysed to amino acids [4]. Dietary protein hydrolysates have been developed to optimize both absorption pathways [5]. A study has shown that the peptide chain length of the hydrolysate affects the absorption of nitrogen and other amino acids residues; the nitrogen absorption rate from hydrolysates containing di- and tripeptides was higher than that from hydrolysates with longer peptide chain length (>pentapeptides) [6]. In addition, a few other studies have shown found that protein hydrolysate solutions appeared to empty from the stomach faster than whole protein solutions and elicited a more rapid increase in plasma amino acid, glucagon and insulin concentrations in enterally fed surgical patients [7,8]. Whole protein is preferred in terms of optimizing intestinal adaptation. When whole protein is not tolerated, hydrolysates can be used [9,10]. Since it is hypothesized that whole protein optimizes intestinal adaptation, the use of hydrolysates is not recommended.

### Carbohydrates

Studies on the effect of carbohydrates in patients with SBS reported conflicting results. In a descriptive case-series, adults with SBS and intact colon absorbed no more than 52% of 50 gram ingested carbohydrates, while 48% were fermented in the colon [11]. Another study found that adults with SBS and intact colon receiving a diet high in carbohydrates had significantly less faecal energy loss than those on a diet high in fat. This difference, however, was not observed in patients without a colon [12].

This beneficial effect of a diet high in carbohydrates was not supported by other studies. For instance an RCT in adults showed that neither a high fat diet nor a high carbohydrate diet was

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