Promoting intestinal adaptation by nutrition and medication

Best Pract Res Clin Gastroenterol. 2016 Apr;30(2):249-61.

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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.

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 hy-

drolysate 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 beneficial to the overall absorption.[13] Another RCT demonstrated that a high fat diet did not influence the volume of jejunostomy output compared to a high carbohydrate diet.[14] In addition, experts suggest that a high load of carbohydrates (mainly monosaccharides and disaccharides) might cause diarrhoea.[15] They argue that restriction of the overall enteral carbohydrate load helps reduce the osmotic load and the substrate for bacterial overgrowth.[15] As far as we know, this theory is not supported by other studies. However, when bacterial overgrowth is present, a carbohydrate reduced diet is sometimes used.

A specific carbohydrate that deserves attention is lactose. Lactose intolerance may occur in after proximal jejunum resection. A cross-over study in adults with SBS demonstrated similar tolerance of a lactose-free diet and a diet containing 20 grams lactose a day.[16] Since there is not enough evidence, a lactose free diet is not recommended for routine use in patients with SBS.

Dietary fiber

Dietary fiber can be divided into soluble and insoluble forms. Insoluble forms (e.g. cellulose found in cereals) bind to water and cause bulking and softening of the stool, shortening the whole gut transit time. Soluble fiber (e.g. pectin, guar gum found in fruits

and vegetables) slow gastric emptying and the overall gut transit time, resulting in a mild anti-diarrheal effect.[17,18] Bacterial fermentation of soluble fiber in the colon produces short chain fatty acids (SCFAs), which account for 5-10% of the total energy intake.[19] A recent study showed that starch is the primary carbohydrate substrate for colonic bacterial fermentation in patients with SBS, although pectin also enhances SCFA production and fluid absorption.[20] Animal studies showed that pectin enhanced bowel adaptation.[21,22] Only one case study reported that pectin supplementation in a single patient caused a prolonged transit time and higher nitrogen absorption.[23] In clinical practice, dietary fiber supplementation is only recommended if the colon is present.[24]

Lipids

Long chain triglycerides (LCTs) undergo bile dependent hydrolysis within the enterocyte, before export into the lymphatic system as chylomicrons. It is thought that LCTs enhance bowel adaptation.[25] In response to the presence of LCTs, the secretion of PYY and glucagon-like peptide 2 is stimulated, which process mediate the ileal and jejunal brake phenomenon[26] resulting in slower transit time. LCTs contain n-3 long chain polyunsaturated fatty acids (LCPs), which might be useful in feeds for SBS patients, although more convincing data are needed.[5] They are known to have anti-inflammatory effects and were shown to improve the splanchnic circulation.[5] Two case-series reported that enteral n-3 LCPs might also improve cholestasis in infants with SBS.[27,28] In contrast, medium-chain triglycerides (MCTs) are absorbed directly across the enterocyte into the portal circulation. This starts in the stomach. An RCT in patients with jejuno- or ileostomy demonstrated that a diet containing high concentrations of MCTs can cause osmotic diarrhoea as a result of rapid hydrolysis of MCTs.[29] In contrast, MCTs improved fat absorption in patients with an intact colon and therefore might be beneficial for patients with bile acid or pancreatic insufficiency.[29] MCTs however do not contain essential fatty acids. In terms of optimizing intestinal adaptation, EN containing LCTs should be used.

Composition enteral nutrition

The composition of EN in patients with IF is much debated. It should take into account the patient's age, underlying diagnosis, length and type of the remaining small bowel and presence of the ileocecal valve and colon. Moreover, different overlapping goals, such as optimal stimulation of adaptation versus rapid weaning off PN, might influence the composition.

High quality RCTs on EN in adults and children are scarce, however, and most data are derived from outcomes of retrospective observational studies and/or case reports.[24]

Human milk

It has been postulated that human milk, which contains glutamine and other growth factors, enhances bowel adaptation.[5] A few cohort studies demonstrated that human milk contains high amounts of nucleotides, immunoglobulin A and leucocytes, which support the immune system of the neonate.[30] It is therefore hypothesised that the immunoglobulins and antimicrobial peptides of human milk enhance mucosal barrier function and prevent bacterial overgrowth.[31] Human milk also promotes intestinal colonisation with appropriate lactobacilli and related bacteria, which are important elements of the healthy microbiome.[32] Animal studies indicated that bovine colostrum is beneficial to bowel adaptation.[33] Two studies in humans, however, could not confirm this.[34,35] Another human study found that breastfed infants with SBS were weaned off PN earlier than non-breastfed SBS infants.[9] RCTs in infants are needed to elucidate the role of human milk on bowel adaptation and the possible advantages of human milk over formula feeding.

Polymeric, oligomeric or monomeric nutrition

Paediatric and adult studies report contradictive findings concerning the type of nutrition. An RCT in children found no difference in absorption between polymeric (containing whole protein, complex carbohydrates and LCT's) and oligomeric formulas (containing protein hydrolysates, complex carbohydrates and MCT's).[10] Small case series, however, found that a monomeric formula (containing amino acids, complex carbohydrates and LCT's) improved feeding tolerance.[36] In seven adults with a high jejunostomy no difference in absorption between polymeric and oligomeric formulas was found.[37] On the other hand, a small RCT in adults with high jejunostomy demonstrated that nitrogen absorption improved with an oligomeric diet.[38] In terms of promoting intestinal adaptation, human milk or a polymeric formula should be used, depending on the age of the patient.

Feeding mode

It is hypothesized that continuous administration of EN enhances enteral absorption by maximizing saturation of the carrier proteins and thereby increasing intestinal function. Case series in adults with SBS showed that when continuous EN was started early, enteral autonomy could be attained after only a mean of 36 days after surgery.[39] A study in children showed that continuous EN promoted nutrient retention and weight gain.[40] However in children with SBS, developing and preserving oral skills is always a priority.[5]

Conclusion

In conclusion, when aimed at promoting intestinal adaptation, EN should consist of complex nutrients i.e. whole proteins, complex carbohydrates and LCT's. However, on individual indication, such as the absence of specific parts of the bowel, adjustments in

the composition of EN might be necessary. While at least a part of EN should be given continuously, small amounts should be given orally to preserve oral skills.

PHARMACOLOGIC TREATMENT

Medication used during the adaptation process can be divided into different subgroups based on their actions: antisecretory, antidiarrheal/antimotility, prokinetic, drugs to treat small intestinal bacterial overgrowth and growth factors (**Table 1**).[26,41,42]

Table 1. Medication used in the treatment of patients with SBS to reduce factors that complicate the adaptation or stimulate intestinal adaptation

Aetiology	Medication
Gastric acid hypersecretion	Histamine receptor antagonist (e.g. ranitidine)
	Proton pomp inhibitor (e.g. omeprazole)
	α2-Adrenergic receptor agonist (e.g. clonidine)
	Somatostatin analogue (e.g. octreotide)
Rapid intestinal transit	Antidiarrheal/antimotility agents (e.g. cholestyramine)
Intestinal dysmotility	Prokinetic agents (e.g. erythromycin)
Small intestinal bacterial overgrowth	Antibiotics (e.g. metronidazole)
	Probiotics (e.g. Lactobacillus rhamnosus (LGG))
Promoting intestinal adaptation	Growth factors (e.g. GLP-2 analogue teduglutide)

Antisecretory medication

A large fluid volume (up to 10 L) is produced and presented daily to the gastrointestinal tract. In healthy adults the small bowel absorbs all but 2 L of fluid, and the colon absorbs 90% of the remaining fluid volume. In patients with SBS fluid losses are a challenging problem. Agents that either inhibit active secretion or stimulate fluid absorption can tackle this problem and alleviate symptoms.

H2 receptor antagonist & Proton pomp inhibitors

After a large small bowel resection, hypergastrinemia occurs which in turn leads to transient gastric hypersecretion that can last up to one year.[43] This is most likely due to inadequate gastrin catabolism in the gut lumen or to decreased secretion of inhibitory hormones. H2 blockers (e.g. ranitidine, famotidine, and cimetidine) inhibit histamine at the histamine H2 receptors of the gastric parietal cells, thus reducing gastric acid secretion, whereas PPIs (such as omeprazole and esomeprazole) stop acid secretion by directly inhibiting the H+/K+-ATPase pump of parietal cells.

For infants with SBS, no safety or efficacy studies on the use of PPIs have been performed. In one case report on a child with SBS[44], ranitidine was found effective in suppressing gastric acid hypersecretion. Omeprazole significantly reduced stool output and sodium losses in adult patients more than 6 months after bowel resection, whereas ranitidine had no effect.[45,46]

For clinical practice, H2 blockers and PPIs can be useful early after bowel resection. H2 antagonists, which have less efficacy than PPIs, are generally considered second-line treatment.

Clonidine

Clonidine is an alpha-2 adrenergic receptor agonist that has both a central and peripheral mechanism of action, reducing small and large bowel motility and prolonging gastric emptying and intestinal transit times. Clonidine also decreases bicarbonate secretion and increases sodium absorption, which promotes passive water diffusion across the enterocyte and diminishes intestinal fluid losses.[47-49] Only few studies of clonidine use in patients with SBS have been performed; none specifically in children. These studies showed a longer intestinal transit time and decreased faecal weight loss and faecal sodium loss.[47,48,50] Given the potential for adverse effects and the likelihood of limited reductions in output, this medication should be restricted to SBS patients with high-output jejunostomies who cannot be controlled otherwise.

Somatostatin analogue

Octreotide is the long-acting analogue of somatostatin that is primarily produced by the pancreas and along the gastrointestinal tract and inhibits secretion of multiple enteric hormones like CCK, gastrin and motilin.[51] Octreotide has been used in SBS to reduce gastric hypersecretion, salt and water secretion and prolong gastrointestinal transit time.[52] In two infants with IF, stool output and PN dependency improved, although side-effects occurred.[53] Octreotide reduced stoma output by an average of 3.3 L/day in 10 adult patients with end-jejunostomy dependent on PN.[54] It is not considered a first-line drug because of the inconvenience of subcutaneous injection, high costs and side effects.[55,56] Octreotide may benefit those patients with severe diarrhoea insensitive to other medical alternatives.

Antidiarrheal/antimotility medication

Symptoms of SBS such as diarrhoea, dehydration and malabsorption are dependent on the degree and type of bowel segment resected. The ileum, in contrast to the jejunum, is more able to adapt to functional loss of the intestine. It absorbs bile acids and fluids, and slows small bowel motility via the ileal brake. Antidiarrheal/antimotility and antisecretory drugs are the first line therapy.[41] There is a great variability in the application of these

therapeutic strategies; however, none of the used agents is backed by scientific evidence in SBS patients.

Loperamide

Loperamide binds to the opioid receptor, thereby slowing the intestinal motility and increasing the transit time.[57] The faecal volume decreases with increase of consistency. The increased absorption results in depressed secretion of gastric fluid, bile acids and pancreatic enzymes.[58] Loperamide can normally be absorbed and taken up into the enterohepatic circulation, which is especially important after ileum resection.

Cholestyramine

Normally, a considerable proportion of the endogenous bile acid pool is regenerated by enterohepatic circulation in the terminal ileum. In patients with SBS in whom functional bile uptake is significantly reduced and intestinal continuity is re-established, the unabsorbed bile acids enter the colon, causing secretory diarrhoea. Bile acid-binding resins, such as cholestyramine, could alleviate these symptoms. On the other hand, more extensive ileal resections cause a net loss of bile acids because more bile acids are excreted than can be replaced through liver synthesis. For these patients, bile acid-binding drugs can exacerbate steatorrhea and fat malabsorption and should be avoided.[59]

Glucagon-like peptide 1 receptor agonist

In five adult patients suffering from SBS who received exenatide, a glucagon-like peptide 1 (GLP-1) receptor agonist, stool frequency and form improved and three of them patients could be weaned off PN.[60] Further research is necessary before exenatide can be used in clinical practice.

Prokinetics

When intestinal dysmotility of the gastrointestinal tract is present, prokinetic drugs can be prescribed. Erythromycin helps with gastric emptying, whereas domperidone increases gastric and duodenal motility. In addition, specialized IF teams often prescribe amoxicillin/clavulanic acid.[61] The evidence for these agents is heterogeneous, however, and scarce in patients with IF.[62] Usually, these agents are prescribed for a trial period and discontinued if no effect is observed.

Drugs to treat small intestinal bacterial overgrowth

Small intestinal bacterial overgrowth (SIBO) is a common problem in patients with IF. The following definition is most frequently used: microbiological presence of 10^5 or more colony forming units/ml of bacteria grown from a jejunal aspirate.[63] Risk factors are resections including removal of the terminal ileum and/or ileocecal valve, presence of

blind bowel loops, small bowel dilatation, strictures, dysmotility and specific underlying diseases such as chronic intestinal pseudo-obstruction. Furthermore, antisecretory and antimotility agents, as described above, can disturb the normal bacterial flora. Symptoms of SIBO include diarrhoea, abdominal pain, abdominal distension, steatorrhea, cramping, flatulence and weight loss.[64] Besides, SIBO may lead to impaired absorption of nutrients, resulting from maldigestion in the lumen or malabsorption due to enterocyte damage.[65] In rare cases, patients with SIBO develop D-lactic acidosis, due to proliferation of bacteria producing D-lactic acid. The overgrown bacteria may translocate to the bloodstream and cause bacteraemia.[66] Previous studies showed that weaning off PN is more difficult in children with SIBO.[67,68] The diagnosis of SIBO is often empirically made and improvement in symptoms after treatment is seen as confirmation of the diagnosis. The management of SIBO consists of treating risk factors, correcting nutrient deficiencies and suppressing abnormal colonization with antibiotics or probiotics.[64] Reducing dosages of antisecretory and antimotility drugs should be considered.[41]

Antibiotics

Antibiotics commonly used are metronidazole, ciprofloxacin, rifaximin, amoxicillin/clavulanic acid, doxycycline, neomycin and tetracycline, mostly prescribed for 7-14 days.[41] When chronic prescription is necessary, drug-free intervals may be recommended such as 3 weeks on, 1 week off. Drug rotation may prevent the development of resistant bacterial strains. Antibiotics are preferably given enterally. No RCTs on the safety and efficacy of different antibiotics in SBS have been reported.

Probiotics

Limited evidence from studies using different probiotics suggests that probiotics might increase the rate of height and weight gain and improve the faecal microbiota of children with SBS.[69] However, cases of bacteraemia with the prescribed probiotic bacteria in infants with SBS have also been reported.[70] Since the effect of probiotics in patients with SBS has not yet been adequately assessed, the routine use of probiotics is not recommended.[69]

Growth factors

In the past decade, much attention has been paid to the development and use of intestinal growth factors that could stimulate intestinal adaptation.

Growth hormone and glutamine

Growth hormone (GH) is produced in the anterior pituitary gland, binds to GH receptors present throughout the intestine and stimulates the production of insulin like growth

factor (IGF)-1. In 2003, somatropin, a recombinant form of human GH, was approved for short-term treatment of adults with SBS receiving specialized nutrition support.

Human GH and glutamine, the primary fuel for enterocytes, are believed to act synergistically on intestinal adaptation. Several RCTs on the effect of recombinant human GH alone or combined with glutamine in adults with SBS[71-75] reported improved body weight[72-75], lean body mass[72,73] and increased intestinal absorption at the end of treatment.[72-74] The latter, however, was not found when measured five days after GH discontinuation.[75] In a more recent RCT[71], patients receiving somatropin and glutamine and patients receiving somatropin with glutamine placebo had greater reductions of PN volume than patients receiving glutamine alone. However, three months after completion of the study, body weight of all patients was lower than that at baseline.[71]

The effect of somatropin is mainly related to increased wet weight absorption (fluid retention), while the effect on energy absorption is minor. Furthermore, the effect seems especially present when the colon is in continuity. A Cochrane review from 2010 concluded that there is insufficient evidence for recommending GH because the positive effect was only temporary in most trials.[76] The European Society of Parenteral and Enteral Nutrition (ESPEN) Guideline on Parenteral Nutrition does not recommended routine use of GH.[77] Additionally, there is no conclusive evidence that the addition of glutamine enhances the effect of GH.[76] Moreover, the use of glutamine alone to stimulate adaptation is not supported by sufficient evidence.[78]

In children, the effect of GH remains unknown. In a RCT in 14 children with SBS, GH treatment during 8 months versus 4 months did not improve weaning off PN.[79] A non-randomized trial[80] showed that a 12-week recombinant human GH treatment led to a decrease in PN, but only 2/8 children could be definitively weaned from PN.

Glucagon-like peptide 2

Glucagon-like peptide-2 (GLP-2) is produced by the enteroendocrine L cells, predominantly found in the ileum and colon.[81] GLP-2 leads to villous hyperplasia, stimulation of crypt cell growth, reduced enterocyte apoptosis and increased intestinal absorption.[82] Furthermore, it inhibits gastric acid secretion and gastric emptying, stimulates intestinal blood flow, increases intestinal barrier function, has anti-inflammatory characteristics and may decrease bone resorption.[82]

A proof-of-concept study in adults with an end-jejunostomy showed that GLP-2 improved intestinal energy and wet weight absorption and increased body weight (reviewed in [82]). Since GLP-2 is rapidly inactivated, an alternative was developed, the recombinant human GLP-2 analogue teduglutide. This was approved in 2012 for the treatment of adults with SBS dependent on PN despite optimal medical therapy. The recommended dose

is 0.05 mg/kg administered subcutaneously once daily. Two phase III clinical studies with teduglutide have been performed.[83,84] In one, patients receiving teduglutide at the recommended dose had greater PN volume reductions than patients receiving placebo.[83] Although these patients received less PN, their body weight gain was significantly higher than that of patients receiving placebo.[83] Small bowel biopsies showed that teduglutide increased villous height and crypt depth.[82] In a 28-week open-label extension study[85], a mean PN reduction of 52% from baseline levels was shown. In the other phase III clinical study, a placebo-controlled RCT in 68 adults[84], patients treated with teduglutide for 24 weeks had significantly higher PN reductions, associated with improvements in quality of life.[86] The consecutive open-label study showed that teduglutide also reduced PN volume after 2 years (reviewed in [82]).

In contrast to adults, studies with teduglutide in children are scarce. A study on the pharmacokinetics and safety of a GLP-2 analogue in children with IF was recently published.[87] Seven children received GLP-2 subcutaneously during 6 weeks. GLP-2 was well tolerated, and the pharmacokinetic profile was similar to that of adults.[87] Furthermore, an open-label study was performed in 42 children with SBS, receiving 0.0125, 0.025 or 0.05 mg/kg/day teduglutide or standard of care.[88] At week 12, the mean prescribed PN volume decreased, with the greatest effect of 0.05 mg/kg/day. Four patients achieved intestinal autonomy (3 with 0.05 mg/kg/day). However, two of them resumed PN 4 weeks thereafter.

One study regarding the combination of GLP-2 and GLP-1 showed that this led to additional beneficial effects on intestinal absorption compared to either drug given alone.[89]

Other growth factors

A number of other growth factors have shown effect in animal studies, including insulin[90], endogenous serine protease dipeptidyl peptidase IV[91], epidermal growth factor (EGF)[92], IGF-1[93] and hepatocyte growth factor.[94] Insulin and EGF have also been tested in humans. In an open-label pilot study in children with SBS, oral or enteral insulin increased EN, though not statistically significant.[95] Two of the ten children were weaned off PN. EGF administration in five children with SBS was associated with a significant improvement in carbohydrate absorption and percentage of calories received enterally.[96] Further research should determine the role of these growth factors in patients.

SUMMARY

Intestinal adaptation is the natural compensatory process that occurs after small bowel resection. The aim of this review was to provide an overview about the nutritional strategies and medication that best promote this process.

In terms of promoting intestinal adaptation, human milk or polymeric nutrition (containing whole protein, complex carbohydrates and long chain triglycerides) is recommended, depending on the age of the patient. However, on individual indication such as absence of specific parts of the bowel, the EN composition should be adjusted if necessary. At least a part of EN should be given continuously, while to preserve oral skills small amounts of oral feeds should be given.

Routinely used medications in SBS patients are antisecretory and antidiarrheal medication, prokinetic drugs and antibiotics to treat bacterial overgrowth. There is, however, a great variability in the application of these drugs and the scientific evidence is limited. Regarding growth factors used to promote intestinal adaptation, the GLP-2 analogue teduglutide is suitable for adults with SBS dependent on PN despite optimal medical therapy. Other growth factors, such as growth hormone, are not recommended for routine use.

Further research is necessary to investigate the best EN composition to promote intestinal adaptation. Additional evidence regarding the effectivity and safety of teduglutide in children needs to be provided before it can be used in clinical practice. Trials on the effectiveness of certain nutrition and medication strategies in patients with SBS are complicated by the fact that it is hard to tell whether the effects on intestinal adaptation are actually due to the intervention or the normal clinical course of intestinal adaptation.

PRACTICE POINTS

- Due to heterogeneity in terms of age of the patient, residual bowel anatomy and nutritional requirements, management of patients with SBS is highly complex and individualized.
- To promote intestinal adaptation, human milk or polymeric formula (containing whole protein, complex carbohydrates and long chain triglycerides) is recommended, depending on the age of the patient.
- On individual indication such as the absence of specific parts of the bowel, the EN composition should be adjusted if necessary.
- At least a part of EN should be given continuously, while to preserve oral skills small amounts should be given orally.
- Routinely used medications to reduce factors that complicate the adaptation process are antisecretory and antidiarrheal medication, prokinetic drugs and antibiotics to treat small intestinal bacterial overgrowth.
- The GLP-2 analogue teduglutide is suitable for adults with SBS dependent on PN despite optimal medical therapy. Recombinant human growth hormone is not recommended for routine use.

RESEARCH AGENDA

- Determining the best composition of enteral nutrition.
- Evaluating the effectivity and safety of antibiotics and probiotics used to treat SIBO.
- Further evidence for the effectivity and safety of GLP-2 analogue in children.
- The value of the promising growth factors arising from animal models for the treatment of patients with SBS.

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