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Review Article

Short bowel syndrome: treatment options

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ABSTRACT

Introduction: Short bowel syndrome (SBS) refers to the malabsorptive state that occurs following extensive intestinal resection and is associated with several complications.
Methods: The research for this review was conducted in the Pubmed database. Relevant scientific articles dated between 1991 and 2015 and written in Portuguese, Spanish or English were selected.
Results: Several therapies, including nutritional support, pharmacological options and surgical procedures have been used in these patients.
Conclusions: Over the last decades new surgical and pharmacological approaches emerged, increasing survival and quality of life (QoL) in patients with SBS. All SBS patients ought to have an individualized and multidisciplinary care that promotes intestinal rehabilitation.

Síndrome Intestino Curto: abordagens terapêuticas

Palavras-chave:
Síndrome Intestino Curto
Adaptação Intestinal
Tratamento cirúrgico

RESUMO

Introdução: A Síndrome do Intestino Curto (SIC) resulta da perda da capacidade de absorção do intestino após resseção intestinal extensa e está associada a diversas complicações.
Métodos: Esta revisão foi realizada com base em artigos científicos originais pesquisados na base de dados MEDLINE via Pubmed, na língua portuguesa, inglesa e espanhola, com o limite temporal de 1991 a 2015.
Resultados: O tratamento instituído pode ser a nível nutricional, farmacológico ou cirúrgico.
Conclusões: Ao longo das últimas décadas surgiram novas abordagens terapêuticas cirúrgicas e não-cirúrgicas que melhoraram a sobrevivência e a qualidade de vida (QoL) destes pacientes. Deve-se estabelecer uma abordagem multidisciplinar e individualizada para garantir a melhor reabilitação.

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Introduction

Definition

Short bowel syndrome (SBS) is characterized by reduced ability of digestion and absorption due to a surgical resection, a congenital defect, or bowel disease.[1–5] This absorption failure results in nutritional and electrolyte imbalances.[1,3,5–7] According to Buschman et al.[8,9] in adults SBS occurs when the anatomical length of the remaining small intestine is <200 cm.

An important aspect is to distinguish between SBS and intestinal failure (IF). IF refers to a condition resulting from obstruction, dysmotility, bowel resection surgery, congenital defect, or a disease associated with loss of absorptive capacity, in which SBS is its most frequent cause.[4]

Epidemiology

The incidence and prevalence of SBS have increased over the past decades.[10] In Europe, the estimated incidence and prevalence is 2-3 per million and 4 per million, respectively.[4,7,8,11] This condition occurs in approximately 15% of adults undergoing intestinal resection (75% in extensive intestinal resection and 25% in sequenced resections).[4,12] However, the actual values are difficult to determine, since this is a condition that includes all forms of length/function reduction of the small intestine associated with malabsorption syndrome, and moreover, its notification is not detailed. The best estimate is based on the number of patients receiving long-term Parenteral Nutrition (PN) and/or intravenous (IV) fluids, given that a significant percentage of patients under PN have SBS (35%). However, patients no longer treated with PN are not included, and thus the number of SBS patients is underestimated.[7]

Etiology

The etiology is multifactorial and covers all age groups.[8] SBS can result from a congenital or acquired pathology requiring an extensive resection of the small intestine (Table 1).[1,2,6,7,13]

Materials and methods

This review was based on original scientific articles searched in MEDLINE via PubMed, in Portuguese, English, and Spanish idiom, with a time limit from 1991 to 2015. The survey was conducted using the terminology “short bowel syndrome”; “Adaptation AND SBS”; “Nutrition AND SBS”; “Pharmacological Management AND SBS”; “Surgical Treatment AND SBS”; “New approaches AND SBS”; “Quality of life AND SBS”. Papers of interest found through the references were searched. In total, 96 publications were included.

Table 1 – Etiology of SBS.[1,2,6,7,13]

Babies	Children	Adults
Necrotizing enterocolitis	Postsurgical complications	Inflammatory bowel disease
Intestinal congenital anomalies	Malignancies	Mesenteric ischemia
	Trauma	Malignancies
		Postsurgical complications

Results

Pathophysiology

The small intestine has a high adaptive capacity in the face of a substantial reduction of its length; thus, in most cases, resections up to half its size are well-tolerated in the long term. However, a small intestine with less than 200 cm presents an increased risk for the occurrence of a scenario of malabsorption, and hence malnutrition.[14–17]

The manifestations of intestinal resection and SBS are a result of[15,17]:

1. the loss of intestinal absorption surface;
2. the loss of specific sites of absorption;
3. a decrease in production of intestinal hormones;
4. the loss of the ileocecal valve.

Most SBS cases occur after extensive resections, and the length of the remaining intestine is the major determinant of prognosis and of clinical consequences.[15,16]

The loss of nutrient and fluid absorption capacities heralds the onset of malnutrition and electrolyte imbalances; absorption of macro-nutrients, mainly carbohydrates (CH) and lipids, are the most affected.[2,5,6,15,18–21]

The presence of a large amount of unabsorbed solutes in the intestinal lumen results in an increased osmotic pressure and in the onset of one of the major symptoms of SBS, diarrhea, usually more intense at an initial stages. Another symptom reported is steatorrhea, resulting from the decreased release and activity of pancreatic enzymes and bile salts, which makes emulsification, digestion and absorption of lipids and fat-soluble vitamins difficult. On the other hand, deficiencies of water-soluble vitamins are less frequent since, in most patients, the duodenum, and proximal jejunum segments are preserved.[2,6,14–16]

In addition, resection of specific locations on the bowel compromises absorption: removing the distal ileum prevents reabsorption of bile salts and absorption of vitamin B12; the absence of an “ileal brake” reduces further the ability to digest and absorb though gastric hypersecretion, increased gastric/intestinal emptying, resulting in worsening of the diarrhea and steatorrhea; the presence of the colon is essential for the intestinal adaptation, by substantially increasing fluid retention capability and, moreover, the capacity of its bacteria to digest CH into absorbable short chain fatty acids (SCFAs).[1,2,5,6,14,17,18–22] It is also important to preserve the ileocecal valve since its loss will allow upstream growth of colonic bacteria.[5,15,19]

Likewise, intestinal resection will compromise the endocrine capacity of the gut, taking into account that important regulators of the digestive process, e.g. cholecystokinin (CCK), secretin, gastric inhibitory polypeptide (GIP) and peptide YY, are produced in the intestinal mucosa and

are critical for the neurohormonal control of the digestive process. Thus, the decreased production will result in a faster gastric emptying, hypergastrinemia and increased intestinal transit.[8,14,17,22]

As for types of small bowel resection, the most common in SBS are[15,16,19,22]:

1. Resection of part of jejunum and sometimes of ileum, with anastomosis of the remaining portions.
2. Resection of the ileum with a jejunal–colic anastomosis.
3. Resection of the ileum, colon and part of jejunum, with a jejunostomy.

For each type of resection, anatomical and physiological changes can lead to different clinical pictures. Typically, the jejunal resection is the best-tolerated option, though less frequent, taking into account that the preservation of the ileum and continuity of the colon (structures with greater adaptive capacity) ensures the maintenance of a suitable digestive process. Accordingly, patients undergoing jejunostomy are those with higher nutritional and fluid deficits.[5,15,19]

Post-intestinal resection adaptation

Adaptation is an individualized process that depends on factors related to the intestine and to the patient.[4,6] This phenomenon takes place in a period of about 2 years, and is divided into three phases: acute, adaptive, and maintenance phases (Fig. 1), during which the remaining intestine compensates for the loss incurred through structural and motility changes.[1,2,4,14,20,23]

The success of this adaptation depends on both the length and the portion of resected bowel, and will determine whether the patient will require a permanent or non-permanent total parenteral nutrition (TPN), a fact with great impact on quality of life (QoL) and prognosis.[2,4,6,7,17,21–23]

Structural changes

After the resection, an increase in the absorptive surface area occurs, along with an increase in wall thickness, length, and diameter of the digestive tract.[2,4,10,17,23]

At microstructural level, there is hypertrophy of villi, increases of microvilli and crypts, and differentiation of specialized mucosal cells. Simultaneously, local angiogenesis is enhanced, resulting in better blood flow and tissue oxigenation.[4,14,21,23–31]

Motility changes

The changes of intestinal motility occur in two phases: an initial phase in which there is greater motility, followed by an adaptation phase, in which the motility is reduced, thus favoring absorption. These changes are less common after a massive resection, being more pronounced in the jejunum versus ileum.[4,21,32,33]

Functional changes

As for functional changes, it should be mentioned:

- An increase in the number of carrier proteins and of their intrinsic activity.[1,2,4,10,13,23,34,35]
- An increase in the levels of peptide YY.[1,2,4,10,16,17,34]
- An increase of the enzyme activity.[4,36]

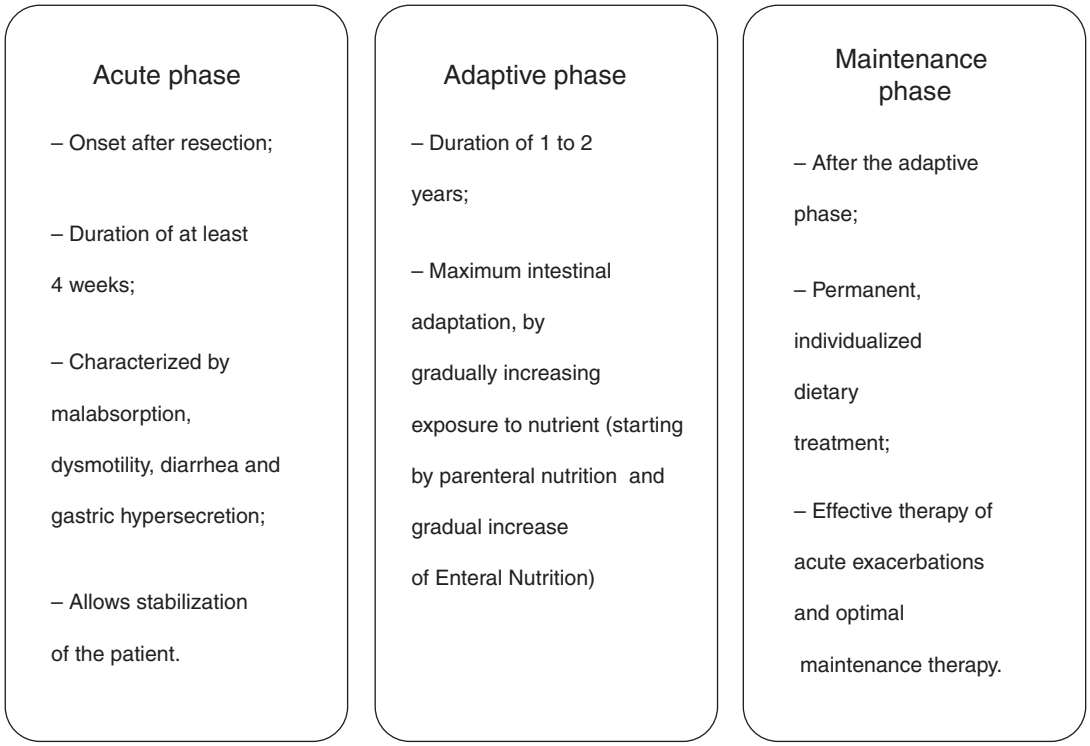

Fig. 1 – Adaptation phases post-intestinal resection.[14]

Treatment

The established treatment occurs at a nutritional, pharmacological or, if necessary, surgical level.[1,19,21,37,38]

Clinical treatment

The patients in the postoperative period begin with PN (at least in the first 7–10 days) as a way to ensure a proper nutrition until there is hemodynamic stabilization with a switch whenever is possible, to enteral nutrition (EN) and later to an oral diet.[4,7,9,10,21,37–40]

The established plan (PN or EN), as well as the composition, volume of the formulation, and number of infusions should be adjusted to individual needs.[4,10,19,29,38–43] However, all patients should ingest small meals several times a day, in order to stimulate the absorption of nutrients.[7,38,39,43–46] The established diet should be rich in complex CH, essential fatty acids (FA), and long-chain triglycerides (TG). Protein should correspond to 20% of the diet.[38,44–47]

Diet in patients with SBS and preservation of the colon

Patients with preservation of the colon can retain up to 1000 extra calories/day by bacterial fermentation.[38,48] As a result, these patients benefit from diets rich in CH, but poor in lipids.[18,38] Among the lipids in the diet, one should prefer medium-chain TGs.[38]

Whenever ileal resection is greater than 100 cm, diets must be low in oxalate and rich in calcium, to reduce the risk of nephrolithiasis.[38,49]

Soluble fiber should be included in the diet, so that the feces are better formed and that there is an increase in intestinal transit. On the other hand, insoluble fibers are less beneficial, by producing the opposite effect.[38,50] In a scenario of diarrhea >3 L/day, diets with high levels of both types of fibers should be avoided.[38,51]

Diet in patients with SBS and with a jejunostomy or ileostomy

In this group of patients, 40–50% of dietary calories should come from complex CHs and 30–40% from lipids.[38,40,52] In contrast to the previous situation, medium-chain TGs should be avoided.[38,48] Soluble fiber in the diet should be included according to the needs.[38,44]

Parenteral nutrition (PN) and IV fluids

PN should provide about 20–35 kcal/kg/day and should consist of lipids (20–40%, up to 1 g/kg/day), CHs (in the form of glucose, 2.5–6 g/kg/day to 7 g/kg/day) and protein (1.5 g/kg/day). To prevent deficiency in essential FAs, these substances must be provided, 1–2% in the form of linoleic acid and 0.5% as linolenic α-acid. As for essential amino acids, the suplementation should be 186 mg/kg/day.[7,10,38,53–55]

Patients who underwent a terminal jejunostomy require supplementation with IV fluid, as a guarantee of correct hydration and for prevention of renal injury.[4,38] The formulations are administered via subclavian vein with a tunneled or fully implanted catheter, in order to reduce the risk of infection and thrombosis.[7,38]

Home parenteral nutrition (HPN)

In recent decades, a new multidisciplinary approach to the treatment of these patients, HPN, was developed. Initially developed for patients with IF, currently, its use was extended to patients with SBS.[13,30,40,42,56–58]

In the United States, HPN has had a growing interest, with several specialized centers with intestinal rehabilitation programs.[13,53,56] In Europe, HPN still has little impact, and a prevalence of 2–40/million inhabitants is estimated, with large variations among countries.[31] For various reasons, in Portugal HPN is not properly established, with few centers providing this treatment option; thus, there is a need for development in this area, with physicians' awareness and legislative changes.[56]

HPN is indicated in situations where patients require prolonged PN, but without requiring hospitalization.[13,17] Patients should be clinically stable, motivated and aware of the care they should have. Another important point is the guarantee that these patients will have secured a suitable hospital or specialized center support, in addition to receiving information on the formulation and its administration in order to gain autonomy.[13,28,38,57–60]

HPN formulations are standardized mixtures of fluids and electrolytes, CHs, lipids, amino acids, vitamins and minerals, available in commercial preparations, in single or split preparation.[13,56]

In regard to complications, in general they are usually associated with the handling of catheter.[56–59] During HPN, mortality is more closely related to an underlying pathology than with the complications inherent in this technique.[56,58] HPN should be discontinued once it is no longer benefiting the patient, or in the face of the magnitude of associated complications.[58]

Complications of a prolonged PN

Although a risky and, costly therapeutic, low morbidity/mortality prompts its implementation. Table 2 lists the complications behind a prolonged PN.[19,38]

Table 2 – Complications associated to NP.[19,3,8]

Related to catheter	Toxicity	Biliary	Hepatic	Renal	Metabolic bone diseases
Infection associated with the catheter	Aluminum	Mud	Steatosis	Hyperoxaluria	Osteoporosis
Other infections (example: endocarditis)	Chrome	Gallstone	Cholestasis	Gallstones	Osteopenia
Central venous thrombosis	Manganese	Vesicular dysmotility	Fibrosis		Osteomalacia
Loss of venous Access		Non-lithiasic colecistitis	Cirrhosis		
			Terminal liver disease		

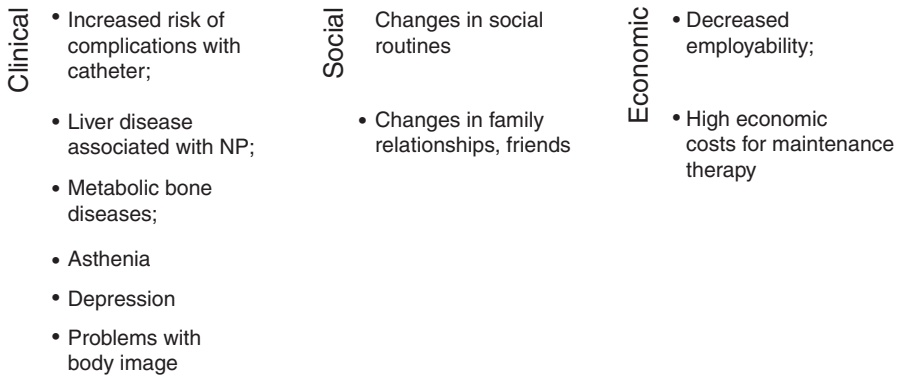

Fig. 2 – Clinical social and economic effects of a prolonged PN.[58]

Within this group, the most common complications are:

Complications related to the catheter
In this group, infection, thrombosis, occlusion, and pneumothorax are included. The reported incidence is 3.6 complications per 1000 catheter-days.[58,59]

Septicemia
Of all complications this is the most common, with an incidence of 0.5–1.6/1000 catheter-days, and is responsible for most cases of morbidity and hospital readmissions. The occurrence of sepsis is an indicator of the care offered.[7,13,19,38,58,59] As to predisposing factors, one should take into account the type/characteristics of the catheter, its handling,[13,15,28,38,56] potential underlying diseases, the anatomy of the remaining intestine, the use or not of the catheter for blood sampling, and the frequency of drug administration.[28,39] In the case of recurrent infection, one may add an antibiotic (p. ex., taurolidine) through the catheter valve.[19,58–61] In extreme situations and/or in case of resistance, the catheter should be replaced, but only as a last resort, because the conduct should be as conservative as possible.[28,61]

Catheter occlusion and central vein thrombosis
Venous thrombosis is a common occurrence (0.07 episodes/catheter-year),[56,58,61] and the diagnosis is established by ultrasound with doppler.[28,56] This complication occurs more frequently in patients with coagulation disorders, malignancies, and thrombosis of the mesenteric artery/vein; antithrombotic prophylactic measures with warfarin (not with heparin, due to an increased risk of infection and of catheter occlusion) must be introduced.[7,10,13,28,56] In unresolved cases, or in those that may result in superior or inferior vena cava syndrome, the catheter should be removed and placed in a different location.[38]

Liver complications
These patients are subject to hepatobiliary disorders such as steatosis, cholestasis, liver fibrosis, and cirrhosis; liver failure and death are potential complications.[7,19,28,38,56,58] Preclinical and clinical evidence suggest that the components of PN can be hepatotoxic due to excess lipid, particularly with the use of soy oil-based solutions.[19,38,56,58,62]

Bone metabolic diseases
Patients receiving PN are at greater risk of bone metabolic disease (osteoporosis and osteomalacia), whose etiology is multifactorial, with an increase in incidence after bowel transplantation.[7,56,58]

Other complications
In the long term, in addition to the clinical effects, PN has social and economic effects that affect QoL of patients (Fig. 2).[15,58]

Considerations in discontinuation of PN/IV fluid
Although PN is the nutrition started in the postoperative period, it is important that its discontinuation occurs as soon as possible, to safeguard intestinal adaptation. It is estimated that, after 5 years discontinuation occurs in 55% of adults with SBS, and it is critical the presence of a residual intestine with the greatest possible length, intestinal mucosa without inflammation, a colon in continuity and high levels of plasma citrulline.[13,38,63]

However, prior to discontinuation of PN, 80% of the energy demand must be taken orally, with the occurrence of neither weight loss nor changes in the levels of electrolytes.[38,64] In this sense, the physician may choose between two methods with the same underlying principle: gradual reduction of PN/IV. In the first method, the number of administration days is reduced, and in the second method, the volume administered in each session is decreased. This latter method has the advantage of less risk of dehydration. But for both methods, it is important to conduct periodic monitoring and assessments of nutritional status and hydration, as well as of levels of vitamins and minerals, so that, if necessary, supplementation is carried out.[38,64]

Enteral nutrition (EN)

EN must be started gradually, once the hemodynamic stability is obtained, diarrhea <2 L/day, and with the intestinal activity restored, insofar as it allows to increase the absorptive capacity.[10,18,38,47,54,56] In their study, Joly et al.[27] suggested that continuous tube feeding, either alone or in combination with oral feeding, increases the absorption of macronutrients at intestinal level versus oral feeding. This happens because the

continuous administration of nutrients results in persistent luminal stimulation.[18,38]

Regarding the type of enteral diet, elemental or polymeric, these options are similar in terms of nutrient uptake and loss of electrolytes/fluid. However, polymeric diets are cheaper, less hyperosmolar, improve intestinal adaptation, and are generally well-tolerated, being the most frequently administered.[10,38,42]

Nutritional supplements

Due to malabsorption, SBS patients require supplementation of certain nutrients and minerals such as:

- Calcium (preferably citrate, thanks to increased solubility/absorption).[7,17,30,38,44,65]
- Magnesium.[7,38,54,66]
- Iron.[7]
- Zinc.[38,54,67]
- Vitamin A, B12, C, D, E and K.[19,38,54,68,69]

Adjuvant medication

The absorption of drugs is also altered; but whenever it is necessary to intervene pharmacologically, the drug should be administrated orally.[7]

Diarrhea is one of the symptoms described and is more intense if the resections are carried out distally. It has been found that patients undergoing terminal jejunostomy have a faster intestinal transit for liquids versus patients with a preserved colon, due to reduced levels of peptide YY and glucagon-like peptide (GLP) 1 and/or 2.[70] In order to reduce intestinal motility, patients should receive loperamide or diphenoxylate + atropine as a first-line medication. These agents have similar efficacy; although, some studies have attributed advantage to loperamide. As a second-line medication, codeine and opium can be considered; however, considering that these are CNS-acting agents, they are less prescribed.[38,70,71] These drugs should be administered 30–60 min before meals to ensure greater effectiveness.[6,38,70]

Another reported symptom is gastric hypersecretion, whose underlying mechanism is not yet clear, but some authors believe that this phenomenon may be due to the loss of one or more intestinal hormones of gastric secretion.[4,7,24,72] Typically, the gastric hypersecretion is transitory and disappears in weeks to months after resection.[4,70] As treatment, anti-secretory drugs are administered, and the first line consists of proton pump inhibitors. But despite the good tolerability, these agents are associated with an increased risk of community-acquired pneumonia, osteoporosis, and a deficit of vitamin B12.[70,72–74] Among second-line agents, histamine type 2 receptor antagonists can be used.[6,70,72] With regard to α2-adrenergic agonists and analogs of somatostatin, these drugs are prescribed when there is failure of above agents, or because of their high cost, route of administration, increased risk of lithiasic cholecystitis and decreased intestinal adaptation.[38,70,72]

Some patients need antibiotics to control bacterial growth.[15,17,39] Some preclinical studies have shown benefit in the use of prebiotics or probiotics as these agents increased intestinal adaptation, reduced bacterial translocation, and restored the intestinal bacterial flora.[39,70,75,76]

Optimization of oral fluids

Patients who have undergone resections of ileum or colon are at greater risk of diarrhea and dehydration, thus, it is critical an appropriate adjustment of fluids, particularly in patients undergoing terminal jejunostomy or an ileostomy, where the electrolyte needs are greater (1.5–2 L/day).[38,49] However, there are restrictions with respect to what fluids the patient can consume: hypertonic and hypotonic solutions, diuretic drinks, caffeine, and alcohol should be avoided, with preference given to oral rehydration solutions (ORS), as these are formulations containing balanced amounts of electrolytes.[4,38,52]

Emergency treatment

Several mediators are considered as potential intestinotrophic factors, two of which, somatotropin and teduglutide, are currently approved for clinical use in adult patients with SBS.[41,61,77]

Growth hormone (GH)

GH, a pituitary hormone, has been identified as a potential mediator in intestinal adaptation in conjunction with insulin-like growth factor-1.[23,38,78,79]

Somatotropin, the recombinant form of GH, was approved in 2003 by FDA for the treatment of SBS in patients with nutritional support. However, to date, EMA has not yet approved its use for this purpose.[48] The recommended dose is 0.1 mg/kg, 1×/day for 4 weeks.

In a study by Byrne et al. on PN/IV-dependent SBS patients, the effect of somatotropin and of the optimized oral diet supplemented with glutamine in PN/IV requirements were investigated. After 4 weeks, PN decreases in volume were observed in all groups, with greater impact on the volume of the diet supplemented with glutamine and somatotropin. There was also an increase in the consumption of oral fluids, to offset the PN volume reduction.[63,77] In this study, the most common adverse effects of somatotropin were identified: peripheral edema, musculoskeletal disorders, GI complaints, acute pancreatitis, impaired glucose tolerance, diabetes mellitus type 2 and carpal tunnel syndrome, as well as its contraindications: cancer patients, or with acute critical illness in intensive care units.[63,77]

Analog of glucagon-like peptide-2 (GLP-2)-teduglutide

GLP-2 is a hormone produced by intestinal L cells in response to intestinal stimulation, with intestinotrophic effect; this hormone is important in the growth and maintenance of the intestinal epithelium. Moreover, GLP-2 is associated with an increased intestinal absorption as well as the inhibition of motility and gastric secretion.[23,78,80,81]

Teduglutide, the recombinant human analog of GLP-2, increases the intestinal barrier function and the ability of intestinal absorption, and since 2012 this agent has been approved by the FDA and EMA for the treatment of PN-dependent adult patients with SBS.[23,77,78] The recommended dose is 0.05 mg/kg 1×/day.[78]

A study conducted by Jeppesen et al.[82] found that patients treated with teduglutide demonstrated increases in the size of villi, depth of crypts, and of plasma levels of citrulline. Moreover, decreases in the excretion of lipids, nitrogen, sodium, potassium, and fluids via feces were noted, and consequently, a higher absorption capacity.[77,82] Even in patients undergoing resection of the terminal ileum and colon, an improvement in intestinal absorption capacity and nutritional status was found.[83]

With regard to adverse effects, the most common have GI origin, being most intense in the initial period of treatment.[77] An important aspect is that teduglutide carries the risk of providing an accelerated neoplastic growth; thus, a prior colonoscopy and discontinuation of their use in patients with active intestinal malignancy is recommended. In patients with intestinal obstruction, biliary, pancreatic, or cardiovascular disease with an increased cardiac output, teduglutide should be used with caution. The same caution should prevail in patients using pharmaceuticals with narrow therapeutic margins; such patients should be monitored for the risk of increased absorption.[83]

Given the differences between these two drugs, the decision of treatment should be individualized, based on the anatomy, functional status of the remaining intestine, and the reported symptoms.[83]

Surgical treatment

In patients with SBS, surgery plays an important role in preventing, mitigating or even reversing IF, and one should always choose the most conservative approach possible.[84,85]

Surgical options are based on three categories: (1) correction of the intestinal transit,[7,84] (2) improvement of intestinal motility with bowel dilation,[84] and (3) delaying the intestinal transit without dilatation of the intestine.[84]

Surgery to correct intestinal transit

Rarely these patients are presented with a slow/decreased intestinal transit; where this occurs, it is important to investigate possible partial obstructions, blind loops, and entero-enteric fistulae.[85]

Surgeries to improve intestinal motility in cases of intestinal dilatation

In the small intestine of these patients, often bacterial colonization occurs, due to dilated segments and to a rapid intestinal transit. If these patients are refractory to medical treatment, the physician may choose to perform surgery, which consists of a "narrowing/bottleneck enteroplasty" in which the dilated portion of the intestine is removed through the extension of the anti-mesenteric edge. This procedure is applied when length of the bowel is suitable and when the surface area that is lost allows a better progression of peristaltism.[85]

In situations where the length is critical, the Longitudinal Intestinal Lengthening and Tailoring (LILT) technique, first described by Bianchi,[86] is used. In this procedure, a bottlenecking of the intestine is made without loss of surface area, with the creation of a longitudinal, 5-cm avascular space along the mesenteric side of the expanded loop. The intestine is then longitudinally divided, taking care to perform revascularization at each side. Each side of the bowel is then tubularized, forming two hemi-loops that connect in the terminal regions in an isoperistaltic mode. Thus, the operation generates an intestinal loop with half the width and twice the length.[85] This is the most used procedure to increase the surface area, but it is important to use it with caution in situations where the intestine is very short and/or when the patient suffers from a concomitant liver disease.[17,84–86]

Another procedure is the serial transverse enteroplasty (STEP), described by Kim et al.[87] in 2003. In this procedure, the lumen becomes narrower by applying metallic clamps perpendicular to the greater axis of the intestine in a zigzag pattern.[84,87,88] The end result is an increase in the length and a decrease of the diameter of the intestine. This is a process less complex than that previously described.[24,88]

The foremost procedure remains unclear and varies with the surgeon's preference. However, recent studies have shown better long-term results with the LILT technique in terms of survival, PN autonomy, and avoidance of intestinal transplantation. However, the use of the STEP technique is more widespread, thanks to its simplicity. Regarding the inherent complications, these are more significant in the cases treated with LILT.[84,89]

Although an encouraging step, the long-term results show that only half of the treated patients have sustained beneficial results for more than 10 years.[17]

Surgeries to prolong intestinal transit in the absence of intestinal dilatation

- **Reversal of segments of the small intestine (RSSI)**: This surgery consists in the creation of antiperistalsis segments, with the ideal length of 10–12 cm and most distally possible (~10 cm from the terminal stoma or from the junction of the small intestine-colon) to allow a retrograde peristalsis distally and the cessation of motility of the proximal intestine. Additionally, there is the cessation of activity of the intrinsic nerve plexus that will delay the myoelectric activity of the distal segment. With this procedure one can reduce or even discontinue PN.[84,89] It is important a short interval time between the enterectomy and RSSI, and that RSSI >10 cm, in order to allow enteral autonomy.[17,84]
- **Colon interposition**: In the interposition of a colon segment in the remaining small intestine (in an iso- or antiperistalsis mode), intestinal transit is retarded, being the isoperistaltic traffic is the most beneficial.[17,84]
- **Valves and sphincters**: These structures can be designed by an external constriction of the intestine, a segmental denervation, or an intussusception of intestinal segments (the most commonly used procedure). The valves create a partial obstruction which interrupts the normal functional pattern of the small intestine and prevent retrograde reflux.[17,84]

Intestinal transplant

In Portugal, the first simultaneous transplant of liver and intestine was carried out at the Hospital de Coimbra in 1996.[90]

Although promising, this technique is reserved for patients in whom an autologous GI reconstruction failed, or for those who will not be able to discontinue PN.[1,8,56,85,91] In addition,

Table 3 – Contraindications to perform an intestinal transplant.[84]

Absolute	Relative
Active infection	Reduced neurodevelopment
Malignancies	Psychosocial factors

not all patients are able to undergo this procedure, due to contraindications (Table 3).[84]

Some patients with SBS suffer from an associated liver disease, for which certain conditions, for example, a significant portal hypertension, require a combined liver-intestine transplant, and also of the pancreas and stomach in those patients where a multiorgan disorder or complete splenic vein thrombosis exists.[84,92]

Currently, intestinal transplantation is a successful surgery, thanks to advances in immunosuppression. However, this option should be considered at an early stage, in order to prevent the occurrence of hepatic complications, and consequently, liver transplantation, since, given the clinical characteristics necessary for its realization, these patients are at a disadvantage versus patients who only depend on a bowel transplant.[84] The survival rates at 1 year and the percentage of non-rejection of the graft are 89%[42] and 79%, respectively, after an intestinal transplant and 72% and 69% if there was a combined liver-intestine transplant.[89] However, the survival of patients with small bowel transplantation decreases in the long term, since these patients have a higher incidence of chronic rejection versus patients undergoing a combined liver-bowel transplantation. This can be explained by the greater tolerance of hepatic lymphocytes compared to that of intestinal lymphocytes.[84]

Even considering that, currently, patients undergoing intestinal transplant will get the same results to patients subject to a permanent PN. It is important to note that most transplanted patients consist of individuals in whom continuous maintenance of PN would result, in the medium term, in a mortality rate of approximately 100%.[84]

Quality of life (QoL)

In health, quality of life is described as the perspective that the patient has about his/her health status, as well as on the impact of disease and its treatment on a day-to-day basis.[1,93–95]

Patients with SBS report a lower QoL, regardless of the therapy, and QoL is lower when patients receive PN for extended periods.[1] Even patients on HPN or EN refer a major impact, not only at a physical but also at a social level. However, this subjective experience has not been properly evaluated, resulting in an over-estimate of the reported values.[1,56,94] There are few studies reporting measurements with validated QoL measurement instruments. Only in 2010 Baxter et al.[95] devised a specific instrument (a provisional questionnaire and psychometric tests) to evaluate QoL of patients with SBS in HPN.[95]

It is important that the clinician understands what are the goals and expectations that each patient has about the treatment, as well as what are the symptoms related to disease or to treatment that are most upsetting so that the best therapeutic approach can be provided.[1]

Table 4 – Prognostic factors of SBS.[4]

Prognostic factors
√ Remaining intestine (size and location)
√ Underlying/remaining intestinal pathology
√ Resection/non-resection of colon
√ Absence/presence of the ileocecal valve
√ Intestinal adaptation
√ Pharmacological therapy
√ Nutritional support (dependence on PN/EN)
√ Patient (age, BMI)
√ Other affected organs

Prognosis

Patients with SBS have a reduced survival.[19] Overall, the percentage of survival after 6 years from the date of resection is 65% for patients with a remaining small intestine greater than 50 cm; this percentage decreases in patients with a length below 50 cm,[41] due to a greater propensity to the development of renal and liver failure, and of dependence on PN.[4]

Table 4 lists the factors associated with prognosis.[4]

Conclusion

SBS is a condition with a great variability, both in etiology and in its manifestations.[1]

Over the years, various developments have been made in order to ensure the best treatment. Although PN is essential in the postoperative period, its prolongation is associated with risks and complications that cause high morbidity/mortality. In this sense, it is important to ensure enteral autonomy for a better intestinal adaptation, as well as a better QoL.[93–95]

In cases where the treatment is not effective, one must opt for a surgical approach, including a intestinal transplantation.[85]

The last years have witnessed the development of new drug therapies, for instance, teduglutide and somatotropin, which promote intestinal rehabilitation, improve the function of the remaining bowel, and allow a significant reduction in PN needs.[1,77,93]

To improve QoL, the physician should educate and monitor patients appropriately, so that their expectations are fully met.

Conflicts of interest

The authors declare no conflicts of interest.

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