



Revisión

Evidence-based recommendations of the Andalusian Group for Nutrition Reflection and Investigation (GARIN) for the management of adult patients with short bowel syndrome

Recomendaciones basadas en la evidencia del Grupo Andaluz para la Reflexión e Investigación en Nutrición (GARIN) para el manejo del paciente con síndrome de intestino corto

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Abstract

In order to develop evidence-based recommendations and expert consensus for the nutritional management of patients with short bowel syndrome (SBS), we conducted a systematic literature search using the PRISMA methodology plus a critical appraisal following the GRADE scale procedures. Pharmacological treatment with antisecretory drugs, antidiarrheal drugs, and somatostatin contributes to reducing intestinal losses. Nutritional support is based on parenteral nutrition; however, oral intake and/or enteral nutrition should be introduced as soon as possible. In the chronic phase, the diet should have as few restrictions as possible, and be adapted to the SBS type. Home parenteral nutrition (HPN) should be individualized. Single-lumen catheters are recommended and taurolidine should be used for locking the catheter. The HPN's lipid content must be greater than 1 g/kg per week but not exceed 1 g/kg per day, and omega-6 fatty acids (ω 6 FAs) should be reduced. Trace element vials with low doses of manganese should be used. Patients with chronic SBS who require long-term HPN/fluid therapy despite optimized treatment should be considered for teduglutide treatment. All patients require a multidisciplinary approach and specialized follow-up. These recommendations and suggestions regarding nutritional management in SBS patients have direct clinical applicability.

Keywords:

Short bowel syndrome. Home parenteral nutrition. Teduglutide.

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Resumen

Con el fin de desarrollar recomendaciones basadas en la evidencia y el consenso de expertos para el manejo nutricional de los pacientes con síndrome de intestino corto (SIC), realizamos una búsqueda bibliográfica sistemática utilizando la metodología PRISMA junto a una valoración crítica siguiendo los procedimientos de la escala GRADE. El tratamiento farmacológico con fármacos antisecretores, antidiarreicos y somatostatina contribuye a reducir las pérdidas intestinales. El apoyo nutricional se basa en la nutrición parenteral; sin embargo, la ingesta oral y/o la nutrición enteral deben introducirse lo antes posible. En la fase crónica, la dieta debe tener las menores restricciones posibles y adaptarse al tipo de SIC. La nutrición parenteral domiciliaria (NPD) debe individualizarse. Se recomiendan catéteres de un solo lumen y se debe utilizar taurolidina para bloquear el catéter. El contenido de lípidos de la HPN debe ser superior a 1 g/kg por semana, pero no debe exceder 1 g/kg por día, y debe reducirse el ácido graso omega-6 (AG ω 6). Deben utilizarse viales de oligoelementos con dosis bajas de manganeso. Los pacientes con SIC crónico que requieren NPD/fluidoterapia a largo plazo a pesar del tratamiento optimizado deben considerarse para el tratamiento con teduglutida. Todos los pacientes requieren un abordaje multidisciplinar y un seguimiento especializado. Estas recomendaciones y sugerencias con respecto al manejo nutricional de los pacientes con SIC tienen aplicabilidad clínica directa.

Palabras clave:

Síndrome del intestino corto.
Nutrición parenteral domiciliaria.
Teduglutida.

INTRODUCTION

Short bowel syndrome (SBS) is one of the most important causes of acute intestinal failure (IF) and the most frequent cause of chronic IF (75 % of cases). SBS is defined as a reduction in small bowel length, which leaves less than 200 cm or less than 50 % of the initial length. The main causes of SBS are mesenteric ischemia and Crohn's disease. SBS is classified according to the type of anastomoses, i.e., type I (end jejunostomy or ileostomy), type II (jejuno-colic anastomosis), and type III (jejuno-ileal anastomosis) (1,2).

From the clinical point of view, acute SBS frequently develops abdominal sepsis and fluid and electrolyte disorders (3). In chronic SBS, the patient's clinical and metabolic situation will also depend on the intestinal segment affected, the functionality of the remaining intestine, and the presence or absence of terminal ileum, ileocecal valve, and colon (4). Intestinal adaptation is a process that may take up to 24 months after intestinal resection. Different mechanisms are involved, such as the development of compensatory hyperphagia, structural changes that increase the absorption surface, functional changes that slow transit time, and changes in the gut microbiota (4,5). HPN is required indefinitely unless total intestinal adaptation is attained.

SBS is a rare disease and the scientific quality of evidence regarding treatment is generally low, with the exception of specific aspects. Questions about nutritional therapy and pharmacological treatment, among others, still do not have clear answers. The Andalusian Group for Nutrition Reflection and Investigation (GARIN) aims to answer these questions in an attempt to try and improve care for these patients, and standardize routine clinical practice.

MATERIALS AND METHODS

The GARIN group members held a virtual meeting to propose and select questions related to the clinical practice and management of patients with SBS. Nine questions were considered to be of interest either because clinical practice guidelines (CPGs) do not answer them or because the response provided is not clear.

Once selected, on May 1, 2020 a systematic bibliographic search was carried out in PUBMED, which was narrowed down

to published systematic review articles, meta-analyses, controlled clinical trials, case series, and clinical practice guidelines (CPGs) published in the last 10 years. The search formula used was: "Short Bowel Syndrome" AND ("Diagnosis" OR "Therapeutics" OR "Nutrition Therapy" OR "Citrulline" OR "Nutritional Support" OR "Drug Therapy" OR "Diet" OR "Enteral Nutrition" OR "Parenteral Nutrition, Home" OR "Nutrition Assessment" OR "quality of life" OR "Fat Emulsions, Intravenous" OR "Fatty Acids, Omega-3" OR "Probiotics" OR "Bacterial Overgrowth Syndrome" OR "bioelectrical impedance analysis"), with limits: "From 01-01-2010 to 01-05-2020", "Adults over 19 y", "Spanish and English" and "human beings".

The evaluation of the eligibility of the different works was carried out independently by two reviewers (FJVL and LLE). Disagreements between reviewers were resolved by consensus. After the initial reading of the title and Abstract, we excluded case reports, works referred to pediatric populations, and papers not directly related to the topic. The rest of articles required a full reading by both reviewers to assess their eligibility and decide which articles should be included or excluded.

A total of 262 results were obtained, of which 130 articles were reviewed that met the search criteria. Of the 132 articles that were excluded, 15 referred to a pediatric population and 79 were case reports. Another 37 articles were also excluded, since they made reference specifically to the underlying disease of SBS, surgical treatment, etc., rather than aspects related to the diagnosis and medical treatment. Figure 1 specifies the process according to the PRISMA methodology (6).

The quality assessment of each original study was carried out using the grade-pro methodology (<https://gradepro.org/>).

In a second virtual meeting, in which an updated Summary of the literature available on short bowel syndrome was presented, the members of the GARIN group discussed those aspects related to the considered questions that were more controversial, or those in which there was less scientific evidence available. Aspects in which, therefore, our opinion as a group of experts could have added value. The various proposals were debated and agreed. The evaluation of grading the evidence of each proposal was performed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale (7); finally, they were drafted according to the criteria set out in table I.

A consensus was reached regarding the responses to the questions previously selected, taking the available evidence into con-

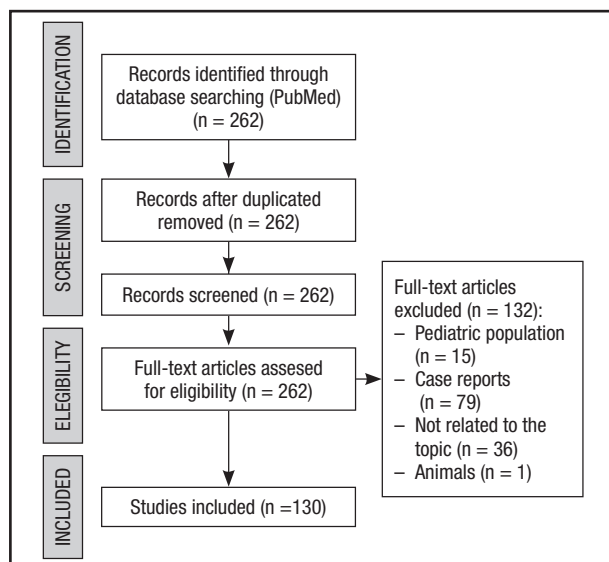


Figure 1. Flow diagram following the PRISMA methodology that reflects the selection and evaluation process of the analyzed papers. Adapted from Liberati et al. (7).

sideration. After the discussion, the group members electronically evaluated the consensus using a Likert-type scale (8). The evaluation form had five possible answers to evaluate each recommendation (“totally disagree” with an assigned value of 1, “disagree” with an assigned value of 2, “neither agree nor disagree” with an assigned value of 3, “agree” with an assigned value of 4, and “totally agree” with an assigned value of 5). The consensus level of each recommendation was calculated by adding the total value resulting from the responses obtained, dividing it by the maximum value, and then multiplying it by 100.

RESULTS

This article includes the responses to 9 questions, obtained from the process described above. After each question, the different proposals suggested by GARIN and the supporting scientific evidence were collected.

All the GARIN group members responded to the surveys. The questions and the level of consensus reached after responding to the Likert scale are specified in table II.

Table I. Grades of recommendation according to the GRADE-ASPEN scale

Quality of evidence	Weighing risks vs benefits	Grade recommendation	Statement
High to very low	Net benefits outweigh the risks	Strong	We recommend
High to very low	Benefits compensate the risks	Weak	We suggest
High to very low	Uncertain if the benefits compensate the risks	Further research needed	We cannot make a recommendation at this time / As expert consensus our proposal is...

Adapted from Druyam et al. (7).

Table II. GARIN group proposals and level of consensus reached after evaluation using the Likert scale

GARIN Group proposals	Consensus level
Which therapeutic measures should be implemented in acute IF secondary to SBS?	
We recommend strict fluid balance in all patients	95.38 %
As a consensus of experts our proposal is to maintain a minimum diuresis of 1 mL/kg/h (or 25/mL/kg/day)	98.46 %
As a consensus of experts our proposal is to determine the concentration of electrolytes in the urine and to maintain Na concentrations above 20 mmol/L or 50 mmol/24 h, together with a Na/K ratio in the urine > 1	87.69 %
As a consensus of experts, our proposal is the use of the bioelectric impedance analysis as an additional method to assess hydration status, in comparison with other pathologies	76.92 %
We recommend the monitoring and replacement of electrolytes (mainly magnesium, sodium, and potassium)	100 %
As a consensus of experts, our proposal is to maintain electrolyte levels at the high limit of normality, in the case of postoperative ileus	75.38 %
What is the optimal symptomatic drug treatment for SBS?	
For SBS patients, especially those with high fecal production, we suggest PPI treatment for the first 6 months, followed by individualized treatment	95.38 %
We are unable to make a recommendation to propose a PPI drug of choice	92.3 %

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Table II (Cont.). GARIN group proposals and level of consensus reached after evaluation using the Likert scale

GARIN Group proposals	Consensus level
What is the optimal symptomatic drug treatment for SBS?	
As a consensus of experts, our proposal is to replace PPI treatment with an H2 receptor antagonist (H2RA) in patients who develop hypomagnesemia when under PPI treatment	96.92 %
We suggest the use of loperamide as a first-line antidiarrheal agent to reduce water and electrolyte loss (after ruling out gastrointestinal tract infection). If losses are not controlled with loperamide, then add codeine	98.56 %
In order to ensure adequate therapeutic adherence, coupled with clinical results, we suggest ease of access to these drugs with this therapeutic indication	96.92 %
As a consensus of experts our proposal is to associate octreotide soon after intestinal resection in patients whose intestinal output is not controlled with the abovementioned drugs, especially if the ostomy is high output	87.69 %
As a consensus of experts our proposal is to associate bile salt chelating resin with antisecretory and antidiarrheal agents in patients with intestinal resection (less than 100 cm of remaining small bowel) and colon in continuity, and non-controlled diarrhea	93.84 %
As a consensus of experts our proposal is use pancreatic enzyme therapy in the case of steatorrhea despite adequate compliance with the dietary recommendations	87.69 %
As a consensus of experts our proposal is to use empirical antibiotic treatment in patients with clinical suspicion of bacterial overgrowth, with rifaximin as the first choice, and in the case of requiring several cycles, different antibiotic regimens should be used in a cyclical way, to avoid the appearance of bacterial resistance	89.23 %
We suggest monitoring the efficacy of other concomitant drugs, mindful that there may be a need for dose increase or alternative route administration	95.38 %
What is the ideal nutritional assessment method for SBS?	
We recommend repeated screening and nutritional assessments for all patients in all the phases of the disease	100 %
As a consensus of experts our proposal is to apply GLIM criteria to establish the diagnosis of malnutrition and grade its severity, with the objective of its validation in the coming years	87.69 %
As a consensus of experts our proposal is to use BIA, in addition to analytical and anthropometric parameters, to detect changes in nutritional status and evaluate the nutritional interventions carried out	84.61 %
What are the recommended nutritional requirements with SBS?	
In the acute phase, we suggest using indirect calorimetry where available	81.53 %
As a consensus of experts our proposal for an alternative is to establish the energy and protein requirements according to the following calculations: – In acute phase: caloric requirements: 25-35 kcal/kg/day; protein requirements: 1.5 g/kg real weight/day – In chronic phase: caloric requirements: 25-35 kcal/kg/day. Use usual weight in case of edema and adjusted weight in case of obesity. As a consensus of experts our proposal is to calculate the caloric requirements using Johnstone's equation if the impedance measurement is available; protein requirements: 1-1.4 g/kg/day	80 %
We recommend adjusting the requirements to the clinical and analytical changes, and to always consider the potential loss of nutrients through the stoma	98.46 %
What recommendations can we establish in oral feeding and enteral nutrition in SBS?	
Acute phase	
We suggest starting an ad libitum oral diet as soon as possible	89.23 %
We suggest reducing the supply of hypotonic fluids (less than 500 mL/day) and administering oral glucosaline solutions with at least 90 mmol/L of Na and 300 mosm/L osmolarity in patients with ostomies	96.62 %
As a consensus of experts our proposal is to supplement with enteral nutrition/enteroclysis if oral intake is not possible or is insufficient	92.3 %
As a consensus of experts our proposal is continuous EN feeding at a low speed, as long as it is a consensual decision made by the therapeutic team and the patient	80.0 %
As a consensus of experts our proposal is the use of polymeric formulations for nasoenteric enteral nutrition, and to resort to oligomeric formulations if there is intolerance	83.07 %

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Table II (Cont.). GARIN group proposals and level of consensus reached after evaluation using the Likert scale

GARIN Group proposals	Consensus level
Chronic phase: general measures	
As a consensus of experts our proposal is that the diet be as restriction-free as possible, but adapted to the general and specific recommendations of each type of SBS, according to the patient's clinical condition	91.66 %
As a consensus of experts our proposal is to supply oral nutritional supplements to SBS patients with a low level of parenteral nutrition dependence	90.77 %
As a consensus of experts our proposal is for several small meals to be ingested throughout the day, to avoid drinking liquids with meals and to minimise the consumption of simple sugars	90.76 %
Currently, we are unable to make a recommendation about the addition of glutamine or other specific nutrients	89.23 %
Chronic phase: symptomatic colon patients	
As a consensus of experts our proposal is to reduce lipid intake to 20 % of the total calorie value (TCV), although this percentage may be raised slightly in a stable patient so as to increase the total intake	89.23 %
As a consensus of experts our proposal is to increase the intake of complex carbohydrates (60 % TCV)	89.23 %
As a consensus of experts our proposal is not to add soluble fibre in a systematic way, although it may be considered in selected cases	87.69 %
As a consensus of experts our proposal is not to exclude lactose in a systematic way	92.3 %
As a consensus of experts our proposal is to reduce the intake of oxalate	95.38 %
Currently, we are unable to make a recommendation about the use of probiotics in these patients	93.84 %
Chronic phase: patients without colon in continuity	
We suggest using salt liberally	92.3 %
We suggest oral rehydration formulas, and for hypotonic and hypertonic fluids to be avoided when there is a fluid imbalance	95.38 %
As a consensus of experts our proposal is a hypercaloric diet, with protein supplying 20 % of the TCV. The fat/carbohydrate ratio is less relevant and it can be increased	93.84 %
As a consensus of experts our proposal is not to add soluble fibre in a systematic way, although in selected cases it may have benefits	84.61 %
As a consensus of experts our proposal is not to exclude lactose in a systematic way	96.92 %
Home parenteral nutrition	
What is the catheter of choice for HPN in patients with SBS?	
As a consensus of experts our proposal is to individualise the choice of access based on the patient's characteristics and the site's experience	95.38 %
We recommend using single-lumen catheters or using a lumen exclusively for PN when using multiple-lumen catheters	100 %
What is the ideal catheter lock?	
We recommend locking the catheter with taurolidine in all cases	98.46 %
What method of administration should we use?	
We suggest administering the HPN cyclically	98.46 %
What should be the formulation composition for macro and micronutrients?	
As a consensus of experts our proposal is to distribute non-protein calories between CH 60-70 % and lipids 30-40 %, once the caloric and protein requirements have been calculated	93.84 %
We suggest that the lipid content be greater than 1 g/kg/week but not greater than 1 g/kg/day	87.69 %
We suggest reducing the supply of ω 6 FAs by using the new lipid emulsions (MCT, olive oil, fish oil)	92.3 %
We suggest limiting glucose intake to less than 5-7 mg/kg/min or 3-6 g/kg/day	96.92 %
We suggest a total volume of 25-35 mL/kg/day, individualized according to fluid losses and in cases such as kidney failure or heart failure	93.84 %
We suggest administering electrolytes based on the recommended daily needs, adjusted in order to normalise plasma levels	93.84 %
As a consensus of experts our proposal is a daily intake of intravenous vitamins based on the recommended daily needs, individualised in accordance with regular monitoring to maintain levels within normality	95.38 %
As a consensus of experts our proposal is a supply of intravenous trace elements based on the recommended daily needs, individualised according to regular monitoring	92.31 %
We suggest an extra dose of zinc (12-17 mg/L of intestinal fluid lost) in case of abundant intestinal losses	87.69 %
We suggest using vials of trace elements with low manganese doses	84.61 %

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Table II (Cont.). GARIN group proposals and level of consensus reached after evaluation using the Likert scale

GARIN Group proposals	Consensus level
Teduglutide	
What is the role of teduglutide in the treatment of SBS?	
We suggest initiating treatment with teduglutide in chronic SBS patients who require ongoing HPN/fluid therapy despite optimised treatment, and with an acceptable nutritional status and fluid and electrolyte balance, who meet the following requirements: non-obstructive and non-malignant underlying disease; clinical stability after the intestinal adaptation period after intestinal resection (estimated at 12 months after extensive bowel resection or 6 months after minor reoperation on a long-standing SBS)	81.82 %
We suggest performing colonoscopy in patients with colon prior to starting treatment	96.36 %
What do we need to consider in patients who are candidates for teduglutide treatment?	
We suggest close monitoring of the water balance, weight, physical examination, biochemical parameters, and intake changes, to adjust nutritional and volume requirements	90.91 %
We suggest a colonoscopy every year for the first two years and then every 5 years	89.01 %
We suggest a six-monthly check-up of biliary and pancreatic parameters	92.73 %
We suggest evaluating the effectiveness of the treatment on a regular basis. In the absence of clinical improvement after 12 months, consider if treatment should be stopped	90.91 %

DISCUSSION

INITIAL ACUTE PHASE MANAGEMENT

What are the therapeutic measures to implement in acute IF secondary to SBS?

GARIN proposal:

We recommend strict fluid balance in all patients (consensus level: 95.38 %) (moderate quality of evidence; net benefits outweigh the risks).

As a consensus of experts, our proposal is to maintain a minimum diuresis of 1 mL/kg/h (or 25 mL/kg/day) (consensus level: 98.46 %).

As a consensus of experts, our proposal is to determine the concentration of electrolytes in the urine and to maintain Na concentrations above 20 mmol/L or 50 mmol/24 h, together with a Na/K ratio in urine > 1 (consensus level: 87.69 %).

As a consensus of experts, our proposal is the use of the bioelectric impedance analysis as an additional method to assess the hydration status, in comparison with other pathologies (consensus level: 76.92 %).

We recommend the monitoring and replacement of electrolytes (mainly magnesium, sodium, and potassium) (consensus level: 100 %) (low quality of evidence; net benefits outweigh the risks).

As a consensus of experts, our proposal is to maintain electrolyte levels at the high limit of normality in the case of postoperative ileus (consensus level: 75.38 %).

The management of acute IF secondary to massive intestinal resections should be multidisciplinary and based on the SOWATS approach, proposed by the Maastricht group and endorsed by ESPEN: (S) Sepsis control, (O) Optimization of nutritional care, (W)

Wound care, (A) Assessment of intestine and fistula anatomy, (T) Timing of surgery, and (S) Surgical strategy (3).

Fluid and electrolyte replacement should be started immediately, before any nutritional intervention. Fluid and electrolyte losses are greater in the initial post-resection period, especially in patients with end-jejunostomy or proximal ileostomy. Therefore, hemodynamic stabilization and prevention/treatment of dehydration and electrolyte deficiencies (especially magnesium, potassium, and sodium) is essential. It is essential to monitor the fluid balance (including intestinal or nasogastric tube drainage losses), kidney function, acid-base balance, and electrolyte levels (3).

A minimum diuresis of 1 mL/kg/h (or 25 mL/kg/day) should be maintained. In general, the water requirements tend to exceed 30-40 mL/kg/day. Urine sodium concentration is a gauge of hydration status. Concentrations below 20 mmol/L or 50 mmol/24 h, together with a Na/K ratio in urine < 1, indicate early fluid and sodium depletion and precede any elevation in urea and creatinine (3).

Bioelectrical impedance analysis (BIA) is a simple, non-invasive, and low-cost method that, in addition to evaluating body composition, allows assessing the hydration status in patients with kidney disease or heart failure, although there are currently no studies in patients with SBS. Hyperhydration assessed by BIA has been associated with an increase in mortality (9).

Electrolyte replacement is crucial. Loss depends on the affected intestinal segment, although often it is not predictable. Hypokalemia, hypomagnesemia, and hypophosphatemia are common and associated with paralytic ileus and refeeding syndrome. Restoring levels to high-normal could be beneficial for treating the ileus, but evidence to support this recommendation is lacking (10).

PHARMACOTHERAPY (Table III)

What is the optimal symptomatic drug treatment for SBS?

GARIN proposal:

For SBS patients, especially those with high fecal production, we suggest PPI treatment for the first 6 months, followed by individualized treatment (consensus level: 95.38 %) (low quality of evidence; benefits compensate the risks).

Currently, we are unable to make a recommendation to propose a PPI drug of choice (consensus level: 92.3 %).

As a consensus of experts, our proposal is to replace PPI treatment with an H2 receptor antagonist (H2RA) in patients who develop hypomagnesemia when under PPI treatment (consensus level: 96.92 %).

We suggest the use of loperamide as first-line antidiarrheal agent to reduce water and electrolyte loss (after ruling out gastrointestinal tract infection). If losses are not controlled with loperamide, then add codeine (consensus level: 98.56 %) (low quality of evidence; benefits compensate the risks).

In order to ensure adequate therapeutic adherence, coupled with clinical results, we suggest ease of access to these drugs with this therapeutic indication (consensus level: 96.92 %) (low quality of evidence; benefits compensate the risks).

As a consensus of experts our proposal is to associate octreotide soon after intestinal resection in patients whose intestinal output is not controlled with the above-mentioned drugs, especially if the ostomy is high output (consensus level: 87.69 %).

As a consensus of experts our proposal is to associate a bile salt-chelating resin with antisecretory and antidiarrheal agents in patients with intestinal resection (less than 100 cm of remaining small bowel) and colon in continuity, and non-controlled diarrhea (consensus level: 93.84 %).

As a consensus of experts our proposal is to use pancreatic enzyme therapy in the case of steatorrhea despite adequate compliance with the dietary recommendations (consensus level: 87.69 %).

As a consensus of experts our proposal is to use empirical antibiotic treatment in patients with clinical suspicion of bacterial overgrowth, with rifaximin as the first choice. In the case of requiring several cycles, different antibiotic regimens should be used in a cyclical way, to avoid the appearance of bacterial resistance (consensus level: 89.23 %).

We suggest monitoring the efficacy of other concomitant drugs, mindful that there may be a need for dose increase or alternative route administration (consensus level: 95.38 %) (low quality of evidence; net benefits outweigh the risks).

Table III. Pharmacological treatment of SBS (3,4,11,12,14,27)

Therapeutic group	Mechanism of action	Active ingredient (via)	Dose (maximum)
Antidiarrheal agents: slowing of intestinal transit	Peripheral opioid agonist	Loperamide (vo)	2-6 mg QID (24 mg/d)
	Central and peripheral opioid agonist	Codeine (vo)	15-30 mg QID (240 mg/d)
Antisecretory agents: inhibition of gastric secretion	Proton pump inhibitors	Omeprazole (vo/iv)	20-40 mg/12 h
		Lansoprazole (vo)	15-30 mg/12 h
		Pantoprazole (vo/iv)	20-40 mg/12 h
		Esomeprazole (vo/iv)	20-40 mg/12 h
		Rabeprazole (vo)	20 mg/12 h
	H2 antagonists	Famotidine (vo/iv)	20-40 mg/12 h
		Cimetidine (vo/iv)	200-400 mg/12 h
Mixed: inhibits gastric secretion, gastric and colonic motility, and intestinal secretion	Alpha-2 adrenergic agonist	Clonidine (vo)	0.1-0.2 mg/12 h
Mixed: inhibits gastric, biliopancreatic and intestinal secretion, and decreases intestinal motility	Somatostatin analogue	Octreotid (sc)	50-250 mcg/6-12 h
Antibiotics: bacterial overgrowth treatment	Microbiota modification	Amoxicillin-clavulanate (vo)	500 mg-125 mg/8 h
		Ciprofloxacin (vo)	500 mg/12 h
		Rifaximin (vo)	550 mg/8 h
		Metronidazole (vo)	500 mg/8 h
		Trimethoprim-sulfamethoxazole (vo)	160-800 mg/12 h
Pancreatic enzymes	Fat malabsorption	Pancreatic lipase (vo)	500 u/kg/meal (2,500 u/kg/meal or 10,000 u/kg/d)

vo: orally; iv: intravenously; sc: subcutaneously; QID: 4 times per day.

Pharmacotherapy is a symptomatic treatment used for the many SBS-associated pathophysiological mechanisms. The indications and proposed doses are based on those published in the literature; however, many of these drugs are prescribed off-label. The low prevalence of SBS means that clinical trials are practically non-existent and, in many cases, the therapeutic plan is based on the drug response witnessed in other pathologies such as chronic diarrhea or malabsorption.

Antisecretory drugs

Hypergastrinemia secondary to intestinal resection is a cause of gastric hypersecretion, which accelerates transit and neutralizes pancreatic enzymes and bile salts, making digestion difficult. Therefore, the use of antisecretory drugs is useful, initially intravenously and later orally/enterally. PPIs are of choice because they contribute to reducing stool wet weight and sodium excretion (up to 25 %), especially during the first 6 months after surgery and when fecal production exceeds 2 L/day. Long-term maintenance may be considered in individual cases. The effects on energy and macronutrient absorption are less pronounced. All (100 %) of the GARIN group experts use omeprazole as a first-line PPI at varying dosages (between 40 and 80 mg per day) (3,4,11,12).

The use of PPIs has been associated with the development of hypomagnesemia, and this is possibly a dose-dependent effect, so it is essential to monitor magnesium and calcium levels, and to exercise greater caution in high-risk patients such as those with high-output ostomies. In the event of PPI-associated hypomagnesemia, the use of H2RAs should be considered (13). Seventy-five percent of the GARIN group experts use famotidine as an alternative to PPIs in hypomagnesemia cases.

Anti-diarrheal agents

An intestinal resection, especially if it affects the distal small bowel, causes a decrease in PYY, GLP1 and GLP2, which accelerates intestinal transit and reduces the contact time of nutrients with the intestinal mucosa. Antidiarrheal agents help to slow down the gastrointestinal transit. Loperamide reduces the loss of water and electrolytes, helps to reduce the need for intravenous fluid therapy, and facilitates stoma management. It has no central effects and, since it participates in the enterohepatic circulation, it can be administered at high doses safely and effectively in patients with terminal ileum resection. Its effectiveness should be evaluated regularly. One hundred percent (100 %) of the GARIN group experts use loperamide at varying dosages as first-choice antidiarrheal agent. If loperamide is not sufficient, codeine should be added, which has a longer lasting effect; however, it crosses the blood-brain barrier and may cause side effects on the central nervous system. Since they have different mechanisms of action, both drugs can be administered together, 30 to 60 minutes before meals (to compensate for the gastrocolic reflex) and before sleeping. Treatment adjustments should be made every 3-5 days, until

either an adequate clinical response is observed, adverse effects appear, or the maximum dose is reached. Diarrhea associated with *Clostridium difficile* or gastrointestinal infection should be excluded before initiating treatment with antidiarrheals (3,4,11,12).

Octreotide

A somatostatin analogue. It reduces digestive secretions, promotes fluid and electrolyte absorption, and slows transit. It is useful in patients with high-output ostomies refractory to conventional treatment, especially in the short term after intestinal resection. Gallstones appear in 20-50 % of treated patients, so this should be monitored. It may delay intestinal adaptation (3,4,11,12).

Resins (cholestyramine and colestipol)

These are useful in patients whose colon is in continuity. In patients with a residual ileum of less than 100 cm and colon in continuity, they can help prevent unabsorbed bile salts in the ileum spilling over into the colon and inducing osmotic diarrhea. However, they should be avoided in patients with more than 100 cm of ileum because they can induce steatorrhea (3,11,12).

Antibiotics

Antibiotics are recommended in patients with SBS and bacterial overgrowth. Although there are no specific diagnostic criteria for its definition, this therapeutic plan in the event of clinical suspicion is justifiable. Different regimens should be administered cyclically, to avoid the appearance of bacterial resistance (4,12,14). They should be handled with caution in patients with colon because they can alter the gut microbiota and, thereby, inhibit the energy salvage achieved by the absorption of short-chain fatty acids, and increase the risk of lactic acidosis. Although there are no conclusive data in favor of a specific drug as the first choice, rifaximin seems to have better efficacy and tolerability (15).

Pancreatic enzymes

These can be useful in patients with steatorrhea despite having complied with dietary recommendations, in relation to the persistence of rapid transit (12).

Concomitant drugs

SBS patients not only need drugs for symptomatic control but they often have concomitant diseases that require pharmacological treatment. This can be compromised by factors such as acid hypersecretion, rapid gastric emptying, reduced absorption

surface area, accelerated intestinal motility, interruption of enterohepatic circulation, and intestinal microbiota disorders. For this reason, it is essential to monitor the efficacy of the concomitant drugs, since they may require dose titration and, on occasions, alternative administration routes (subcutaneous, parenteral, rectal, etc.) (4).

NUTRITIONAL ASSESSMENT AND NUTRITIONAL REQUIREMENTS

What is the ideal nutritional assessment method for SBS?

GARIN proposal:

We recommend repeated screening and nutritional assessments for all patients in all the phases of the disease (consensus level: 100 %) (low quality of evidence; net benefits outweigh the risks).

As a consensus of experts our proposal is to apply GLIM criteria to establish the diagnosis of malnutrition and grade its severity, with the objective of its validation in the coming years. (Consensus level: 87.69%)

As a consensus of experts our proposal is to use BIA, in addition to analytical and anthropometric parameters, to detect changes in nutritional status and evaluate the nutritional interventions carried out (consensus level: 84.61 %).

A complete nutritional assessment must be performed in all patients. A consensus was recently reached regarding the diagnosis of nutritional status by a group of experts from the main scientific societies (GLIM Criteria: Global Leadership Initiative on Malnutrition) (3,16).

Bioelectrical impedance (BIA) is a non-invasive tool to measure body composition and nutritional status. The phase angle is considered a marker of cell integrity and, in various pathologies, it has been correlated with other nutritional parameters and/or muscle mass. There are no specific studies involving SBS, but it has been proposed as a prognostic marker in different clinical situations including HIV, cancer, surgery, and chronic liver disease (17,18). Bioelectrical impedance vector analysis (BIVA) is a vectorial approach of BIA, which could represent an alternative method that avoids errors derived from the BIA equation, and provides an improved estimation of body compartments. Fassini et al. concluded that BIVA may represent a better predictor of nutritional status for the analysis and interpretation of body composition in patients with short bowel syndrome (19).

What are the recommended nutritional requirements in the SBS?

GARIN proposal:

In the acute phase, we suggest using indirect calorimetry where available (consensus level: 81.53 %) (low quality of evidence; benefits compensate the risks).

As a consensus of experts our proposal for an alternative is to establish the energy and protein requirements according to the following calculations (consensus level: 80 %):

- In the acute phase: caloric requirements: 25-35 kcal/kg/day; protein requirements: 1.5 g/kg real weight/day.
- in the chronic phase: caloric requirements: 25-35 kcal/kg/day. Use usual weight in case of edema and adjusted weight in case of obesity. As a consensus of experts our proposal is to calculate the caloric requirements using Johnstone's equation if the impedance measurement is available. Protein requirements: 1-1.4 g/kg/day.

We recommend adjusting these requirements to clinical and laboratory changes, and to always consider the potential loss of nutrients through the stoma (consensus level: 98.46 %) (low quality of evidence; net benefits outweigh the risks).

Indirect calorimetry is the gold-standard technique for estimating caloric needs, and it should be repeated periodically to detect changes in energy requirements. However, this technique is not always available and, frequently, it is necessary to resort to predictive equations.

The latest ASPEN (2016) and ESPEN (2019) recommendations for acute-phase patients in the intensive care unit are 25-30 kcal/kg/day (providing 70 % of the estimated requirements during the first week, with progressive increases from then on) and 1.2-2 g/kg/day and 1.3 g/kg/day of proteins, respectively (20,21). The ESPEN recommendations for acute IF are 25-35 kcal/kg/day (depending on whether the patient is in the early catabolic phase or in the later anabolic phase), and up to 1.5 g/kg real weight/day of proteins (3).

Most scientific societies recommend 20-35 kcal/kg in chronic IF (4). The usual weight should be used in the presence of edema, and the adjusted weight in the case of obesity (BMI > 30 kg/m²). In a situation of severe malnutrition, the calorie goal can be 30-35 kcal/kg/day (22). Some authors have compared the results of indirect calorimetry with those of various predictive equations (23). Skallerup et al. concluded that the best approximations are obtained with the Harris-Benedict equation (with anthropometric parameters) or with the Johnstone equation (with impedance measurement), despite the fact that the BMR is overestimated or underestimated in approximately 35 % of the patients with both of them (24). This may mean that formulas are necessary that estimate the BMR using body composition parameters such as fat-free mass or muscle mass index. All these recommendations should be adapted to the clinical situation of the patient, the presence of catabolic stress, body composition (if possible), the presence of comorbidities, and the level of physical activity.

The recommended protein requirements in this phase range between 0.8 and 1.4 g/kg/day (4). In patients with normal renal function the goal would be 0.8-1 g/kg/day, increasing this figure to 1.5 g/kg/day in the presence of metabolic stress (22).

Additionally, none of these recommendations takes into account the sometimes significant fecal losses of nutrients, which results in the calculated requirements being frequently underestimated, as suggested by Fassini et al. (25).

NUTRITIONAL SUPPORT

What recommendations can we establish for oral feeding and enteral nutrition in SBS?

GARIN proposal:

Acute phase

We suggest starting an ad libitum oral diet as soon as possible (consensus level: 89.23 %) (low quality of evidence; benefits compensate the risks).

We suggest reducing the supply of hypotonic fluids (less than 500 mL/day) and administering oral glucosaline solutions with at least 90 mmol/L of Na and 300 mosm/L osmolarity in patients with ostomies (consensus level: 96.62 %) (low quality of evidence; benefits compensate the risks).

As a consensus of experts our proposal is to supplement with enteral nutrition/enteroclysis if oral intake is not possible or is insufficient (consensus level: 92.3 %).

As a consensus of experts our proposal is continuous EN feeding at a low speed, as long as it is a consensual decision made by the therapeutic team and the patient (consensus level: 80 %).

As a consensus of experts our proposal is the use of polymeric formulations for nasoenteric enteral nutrition, and to resort to oligomeric formulations if there is intolerance (consensus level: 83.07 %).

Chronic phase

As a consensus of experts our proposal is that the diet be as restriction-free as possible but adapted to the general and specific recommendations of each type of SBS, according to the patient's clinical condition (consensus level: 91.66 %).

As a consensus of experts our proposal is to supply oral nutritional supplements to SBS patients with a low level of parenteral nutrition dependence (consensus level: 90.77 %).

As a consensus of experts our proposal is for several small meals to be ingested throughout the day, to avoid drinking liquids with meals, and to minimize the consumption of simple sugars (consensus level: 90.76 %).

Currently, we are unable to provide a recommendation about the addition of glutamine or other specific nutrients (consensus level: 89.23 %).

– Symptomatic patients with colon in continuity:

- As a consensus of experts our proposal is to reduce the lipid intake to 20 % of the total calorie value (TCV), although this percentage may be raised slightly in a stable patient so as to increase the total intake (consensus level: 89.23 %).
- As a consensus of experts our proposal is to increase the intake of complex carbohydrates (60 % TCV) (consensus level: 89.23 %).
- As a consensus of experts our proposal is not to add soluble fiber in a systematic way, although it may be considered in selected cases (consensus level: 87.69 %).

- As a consensus of experts our proposal is not to exclude lactose in a systematic way (consensus level: 92.3 %).
- As a consensus of experts our proposal is to reduce the intake of oxalate (consensus level: 95.38 %).
- Currently, we are unable to make a recommendation about the use of probiotics in these patients (consensus level: 93.84 %).

– Patients without colon in continuity:

- We suggest using salt liberally (consensus level: 92.3 %) (low quality of evidence; benefits compensate the risks).
- We suggest oral rehydration formulas and that hypotonic and hypertonic fluids be avoided when there is fluid imbalance (consensus level: 95.38 %) (low quality of evidence; benefits compensate the risks).
- As a consensus of experts our proposal is a hypercaloric diet, with protein supplying 20 % of the TCV. The fat/carbohydrate ratio is less relevant and may be increased (consensus level: 93.84 %).
- As a consensus of experts our proposal is not to add soluble fiber in a systematic way, although in selected cases it may have benefits (consensus level: 84.61 %).
- As a consensus of experts our proposal is not to exclude lactose in a systematic way (consensus level: 96.92 %).

In the acute phase, once hemodynamic stabilisation is ensured, parenteral nutrition should be considered if it is believed that the oral/enteral approach will not be possible or sufficient within a week, which is often the case.

Normally, oral ingestion is initially contraindicated (critical patients, risk of aspiration, high-output stoma, etc.). If this is not the case, or as soon as possible when the contraindication is lifted, ad libitum feeding is recommended by oral ingestion and/or oral supplements. In patients with ostomies, the recommendation is to limit the intake of hypotonic fluids (< 500 mL/day) and ingest oral glucosaline solutions with at least 90 mmol/L Na and 300 mosm/kg osmolarity, to aid absorption and avoid an osmotic effect towards the intestinal lumen (3).

The possibility of enteral nutrition should be considered if oral intake is not possible or is insufficient. If possible, the administration of enteral nutrition or the chyme to the distal intestinal segment by enteroclysis can reduce the need for and offer an alternative to parenteral nutrition, while awaiting the possibility of reconstructive surgery (3,26). In the chronic phase, enteral tube feeding in combination with oral feeding could contribute to the suspension of parenteral support in patients with a low level of HPN dependence, although compliance seems difficult beyond the short term (3,4).

Polymeric formulas (which favor intestinal adaptation) should be used, with an energy density or protein content adjusted to the calculated requirements. In general, it is not necessary to use specific formulas, whereas oligomeric formulas should be reserved for cases of gastrointestinal intolerance to standard formulas (3).

Dietary advice is essential and should be tailored to the type of SBS, although the following measures are recommended more on a conceptual basis than on the basis of solid scientific evidence. Ideally, dietary recommendations should be given by an experienced dietitian.

To favor digestion and intestinal absorption of nutrients, it is generally recommended that several small meals be ingested throughout the day, and not to drink liquids with the meals. Simple sugars should be avoided as they can potentially have an osmotic effect on the intestinal lumen and increase fluid loss.

Specific measures recommended according to the type of SBS (4, 11, 27)

- *In symptomatic colon patients:*
 - Lipid intake should be reduced (20 % of the TCV): unabsorbed lipids make it difficult to absorb calcium, magnesium, and zinc, and can make diarrhea worse when they reach the colon. Consuming medium chain triglycerides may confer a marginal benefit to overall energy absorption, because they do not require the bile-salt action and they are easily absorbed through the intestinal mucosa, although they are usually poorly tolerated as they are not very palatable. Attention should be paid to possible deficiencies of essential fatty acids and fat-soluble vitamins.
 - An increase in the intake of complex carbohydrates (60 % of the TCV) is recommended to help the colonic synthesis of short-chain fatty acids (SCFA) (acetic, propionic, and butyric acid). SCFA absorption is linked to that of water (with potential diarrhea improvement) and contributes to a positive energy balance, as it can mean an increase of up to 1000 kcal/day.
 - The systematic addition of soluble fibre is not recommended. Although there are few studies in this regard. Pectin supplementation did not improve macronutrient absorption or diuresis (28). However, in a different study, the contribution of ispaghulak husk (seed coats of the *Plantago ovata* Forssk plant) improved calcium absorption and stool consistency (4). In our usual clinical practice, 58.33 % of the GARIN group experts add soluble fibre (the remaining 41.67 % do not do so systematically).
 - Lactose should not be systematically excluded.
 - The intake of oxalate in the diet (berries, leafy vegetables, nuts, chocolate, etc.) should be reduced to minimize the risk of kidney stones.
 - ESPEN does not systematically recommend the use of probiotics in patients with colon. In our usual clinical practice, the majority (83.3 %) of the GARIN group experts do not use probiotics in SBS patients.
 - It should be remembered that the long-term maintenance of these low-fat, high-carbohydrate diets can reduce appetite and energy intake, because they are bulkier, less palatable, and can cause bloating. Therefore, to the extent that the clinical condition permits, the diet should be as least restrictive as possible.
- *In patients without colon:*
 - The fat/carbohydrate ratio of the diet is less relevant.
 - The 24-hour urine measurement including sodium concentration is useful. Diuresis below 800-900 cc/24 h or

sodium excretion in urine < 35 mmol/24 h are suggestive of a deficit of water and sodium absorption.

- In patients with high stoma output, salt consumption should be without restrictions and hydration with high sodium rehydration formulas should be recommended. Absorption is optimal at concentrations of 90-120 mmol/L of sodium, 30 mmol/L of glucose, and 300 mOsm/L osmolarity, but tolerance to long-term rehydration formulas is not favorable (29).
- It is advisable to avoid hypotonic fluids (water, tea, coffee, alcohol) or hypertonic fluids (juices, soft drinks) that increase fluid losses through the stoma.
- Although the ESPEN recommendations do not include soluble fiber, in some cases its consumption could help to gelatinize the stools, and reduce the fecal water content.
- Lactose should not be systematically excluded.
- In relation to specific nutrients, the ESPEN does not recommend adding glutamine or other specific supplements to promote the intestinal adaptation process.

What is the catheter of choice for HPN in SBS patients? What is the ideal catheter lock? And what method of administration should we use?

GARIN proposal:

As a consensus of experts our proposal is to individualize the choice of access based on the patient's characteristics and the site's experience (consensus level: 95.38 %).

We recommend using single-lumen catheters or using a lumen exclusively for PN when using multiple-lumen catheters (consensus level: 100 %) (moderate quality of evidence; net benefits outweigh the risks).

We recommend locking the catheter with tauridolide in all cases (consensus level: 98.46 %) (moderate quality of evidence; net benefits outweigh the risks).

We suggest administering the HPN cyclically (consensus level: 98.46 %) (low quality of evidence; benefits compensate the risks).

Parenteral nutrition is essential in the acute phase, in isolation or complementary to oral/enteral nutrition (when feasible). In the chronic phase, HPN represents an essential, complex, and highly specialized therapeutic alternative, which permits the intestinal adaptation process to be continued on an outpatient basis. It is necessary indefinitely or until complete intestinal adaptation.

In April 2020, the ESPEN updated their clinical guidelines on HPN. Scientific evidence remains scant. Of the 71 recommendations, only 3 have grade A evidence, 17 have grade B evidence, 7 have grade O evidence, and 44 are expert consensus recommendations (30).

An indwelling central catheter is required to administer HPN. There are different options available: peripherally inserted central catheters (PICC), tunnelled subcutaneous catheters, and subcutaneous venous reservoirs.

There is controversy in the literature about the ideal catheter for HPN, although the choice largely depends on the patient and the

site's experience. According to the latest Home and Ambulatory Artificial Nutrition (NADYA) group report, in 2017 38.2 % of HPN patients in Spain used a tunneled catheter, and 32.9 % used a reservoir, possibly due to the high percentage of cancer patients included (31). However, PICCs are increasingly used, displacing the tunneled catheter as the first option in both the Canadian and the United States case series (PICC in 52.9 % and 47 %, and tunneled catheter in 38 % and 43 % of patients, respectively) (32,33). Of all GARIN group experts, 72.72 % use PICC as the venous access of choice. The ESPEN recommends PICCs when HPN is necessary for less than 6 months or in certain settings, such as patients with tracheostomy, and it recommends tunneled/implanted catheters if it is estimated that HPN will be necessary for the long term (30). From a practical point of view, PICCs can make patient self-management difficult.

Conflicting data exist on the infection rates seen with the different types of catheters. No clear differences were found between PICCs and tunneled catheters in two recent meta-analyses, although the infection risk rate was lower in PICCs as compared to implanted ports. Nor do there appear to be differences in the risk of thrombosis or other mechanical complications (34,35). More quality studies are needed to clarify this fundamental point.

The recommendations to minimize infection risk include: a well-defined health care protocol; adequate patient and/or caregiver training; and regardless of the type of catheter, a single-lumen catheter should be used; or in the event of a multi-lumen catheter, one lumen should be dedicated exclusively for PN administration. The ESPEN does not recommend the use of filters or routine catheter replacement (4,36). In a recent meta-analysis, which included 162 patients with HPN and 45,695 catheter days, tauridine locking was shown to be superior to saline solution or heparin in reducing the risk of catheter infection (OR: 0.13; 95 % CI: 0.05-0.32), as well as being a cost-effective measure, especially for the most susceptible patients (37). Although it remains to be clarified whether it should be used systematically, the latest published guidelines by the ESPEN recommend a tauridine lock, with grade B evidence (30).

The HPN is delivered cyclically, always by infusion pumps and, generally, at night for 10-15 h (depending on the total volume and the patient's tolerance) in order to interfere as little as possible in daily life. Flexibility in the infusion regimen, and the use of portable infusion pumps are factors that improve the quality of life of these patients (38,39).

What should be the formulation composition for macro and micronutrients?

GARIN proposal:

As a consensus of experts our proposal is to distribute non-protein calories between CH 60-70 % and lipids 30-40 %, once the caloric and protein requirements have been calculated (consensus level: 93.84 %).

We suggest that the lipid content be greater than 1 g/kg/week but not greater than 1 g/kg/day (consensus level: 87.69 %) (low quality of evidence; benefits compensate the risks).

We suggest reducing the supply of ω 6 FAs by using the new lipid emulsions (MCT, olive oil, fish oil) (consensus level: 92.3 %) (low quality of evidence; benefits compensate the risks).

We suggest limiting glucose intake to less than 5-7 mg/kg/min or 3-6 g/kg/day (consensus level: 96.92 %) (low quality of evidence; benefits compensate the risks).

We suggest a total volume of 25-35 mL/kg/day, individualized according to fluid losses and in cases such as kidney failure or heart failure (consensus level: 93.84 %) (low quality of evidence; benefits compensate the risks).

We suggest administering electrolytes based on the recommended daily needs, adjusted in order to normalize plasma levels (consensus level: 93.84 %) (very low quality of evidence; net benefits outweigh the risks).

As a consensus of experts our proposal is a daily intake of intravenous vitamins based on the recommended daily needs, individualized in accordance with regular monitoring to maintain levels within normality (consensus level: 95.38 %).

As a consensus of experts our proposal is a supply of intravenous trace elements based on the recommended daily needs, individualized according to regular monitoring (consensus level: 92.31 %).

We suggest an extra dose of zinc (12-17 mg/L of intestinal fluid lost) in case of abundant intestinal losses (consensus level: 87.69 %) (low quality of evidence; benefits compensate the risks).

We suggest using vials of trace elements with low manganese doses (consensus level: 84.61 %) (low quality of evidence; benefits compensate the risks).

Regarding the composition of the formulation (4,22), once the caloric and protein requirements have been calculated, the non-protein calories should be distributed between carbohydrates (60-70 %) and lipids (30-40 %).

Amino acid mixtures should provide at least 50 % of the total in the form of essential amino acids, with special interest in the content of branched-chain amino acids such as leucine, isoleucine, and methionine, to maintain or increase muscle mass in long-term HPN patients (40).

The minimum lipid content should be 1 g/kg/week to avoid essential fatty acid deficiency, and the provision of more than 1 g/kg/day must be avoided to reduce the risk of liver complications. In the American case series, lipids are administered on average for 3.2 days/week in HPN (33). Glucose intake should be limited to less than 5-7 mg/kg/min or 3-6 g/kg/day (which is the equivalent of less than 350 g in 12 hours for a 70-kg adult) (30).

The latest ESPEN guidelines state that, for the acute phase, it is advisable to use lipid emulsions that include omega-3 fatty acids in critical and surgical patients, due to their immunomodulatory and anti-inflammatory properties (3). There are disagreements as to the type and dose of lipid emulsion to be used for the prevention and treatment of IF-associated liver disease in the chronic phase. Lipid emulsions with MCT, olive oil, or fish oil can be used to reduce the intake of ω 6 FAs. Fish oil (ω 3 FAs) has anti-inflammatory effects; it increases the supply of alpha-tocopherol, and decreases that of phytosterols (41,42). Most of the studies evaluating the efficacy of lipid emulsions have been conducted in children. In the few cases published in adults, it has been shown

to improve or resolve cholestasis, steatosis, and inflammation, but with no changes in liver fibrosis (43,44). One hundred (100 %) of the GARIN group experts use lipid emulsions with MCT, olive oil, and/or fish oil. When the liver is damaged, the majority (75 %) are of the opinion that medium chain triglycerides/olive oil/purified soybean oil/fish oil solutions should be used, while additionally some (25 %) use lipid emulsions composed exclusively of omega-3 fatty acids for the most severe cases.

The total volume is usually 25-35 mL/kg/day. Given the great inter- and intra-individual variability among SBS patients, it is difficult to make a general recommendation for fluid requirements, as these depend on multiple factors: diuresis, fecal losses, physical activity, level of intestinal adaptation, the presence of comorbidities such as renal disease or heart failure, etc. Although it is always necessary to individualize the volume of HPN, ideally a diuresis above 800-1000 cc should be maintained.

The amount of electrolytes, vitamins, and trace elements is based on the recommended daily requirements, and is adjusted on a regular basis.

Table IV. Recommended dosages of electrolytes in HPN* (4)

Electrolyte	mmol/kg/day	mmol/day
Sodium	1.0-1.5	60-150
Potassium	1.0-1.5	40-100
Chlorine	1.0-1.5	
Phosphate	0.3-0.5	10-30
Magnesium	0.1-0.15	4-12
Calcium	0.1-0.15	2.5-10

*Should be adjusted according to the underlying disease, oral intake, drugs, etc.

There are no randomized studies that endorse the dose of electrolytes to be administered. Although the recommendations are based on clinical experience (Table IV) the needs must be individualized as they are influenced by several factors such as the length and segment of the remnant bowel, fecal losses, diuresis, renal or hepatic insufficiency, and concomitant drugs that can alter plasma electrolyte levels. Regular electrolyte controls must be done in order to adjust their administration.

According to an ASPEN review in 2012, the daily intravenous dose of fat-soluble vitamins is approximately the same as the Dietary Reference Intakes for Oral Requirements. Although these are the recommended standard doses, there may be specific deficiencies depending on the underlying disease (Table V).

Trace element requirements in patients with prolonged HPN are difficult to establish. The recommendations for trace elements proposed by the ESPEN, and the composition of the presentations available in our country (Spain), are shown in table VI. It must also be taken into account that the various components of PN contain trace elements as contaminants, which in some cases is not a negligible contribution. In general, zinc and selenium should be administered systematically, as some studies have shown their deficiency even with supplementation (45,46). In cases of abundant intestinal losses, the recommendation is an extra dose of zinc of 12-17 mg per liter of intestinal fluid loss. Scientific societies recommend reducing the standard intake of manganese, copper, and chromium to 55 mcg/day, 0.3-0.5 mg/day, and 0.14-0.87 mcg/day, respectively, since it has been shown that the trace element vials available provide doses much higher than the standard requirements (32,47). Substantially elevated serum manganese levels have been found in patients with long-term HPN, especially in those who develop hepatic cholestasis (46,48). Copper and man-

Table V. Daily vitamin requirements via parenteral route (49)

	Dose	Natrovit® Cernevit®	Viant®	Soluvit®	Vitalipid®
Vit. Fat soluble					
Vit A	900-3300 IU	3500 IU	3300 IU	-	3300 IU
Vit D	200 IU	220 IU	200 IU	-	200 IU
Vit E	10 mg	10.2 mg	9.11 mg	-	9.1 mg
Vit K	150 mcg	-	150 mcg	-	150 mcg
Vit. Water soluble					
Vit B1 (thiamine)	6 mg	3.51 mg	6 mg	2.5 mg	-
Vit B2 (riboflavin)	3.6 mg	4.14 mg	3.6 mg	3.6 mg	-
Vit B3 (niacin)	40 mg	46 mg	40 mg	40 mg	-
Vit B5 (pantothenic ac.)	15 mg	17.25 mg	15 mg	15 mg	-
Vit B6 (pyridoxine)	6 mg	4.53 mg	6 mg	4 mg	-
Vit B12 (cyanocobalamin)	5 mcg	6 mcg	5 mcg	5 mcg	-
Vit C (ascorbic ac.)	200 mg	125 mg	200 mg	100 mg	-
Folate	600 mcg	414 mcg	600 mcg	400 mcg	-
Biotin	60 mcg	69 mcg	60 mcg	60 mcg	-

Table VI. Daily trace element requirements via parenteral route (4,49)

	Dose	Oligoplus®	Supliven®	Addamel®
Copper	0.3-0.5 mg	0.76 mg	0.38 mg	1.27 mg
Chrome	10-15 mcg	10 mcg	10 mcg	10 mcg
Iodine	70-150 mcg	127 mcg	130 mcg	130 mcg
Iron	1 mg	2 mg	1.1 mg	1.1 mg
Manganese	0.06-0.1 mg	0.55 mg	0.05 mg	0.28 mg
Selenium	60-100 mcg	24 mcg	79 mcg	31.6 mcg
Zinc	2.5-4 mg	3.3 mg	5 mg	6.5 mg

ganesse supplementation should be lower even in the case of liver dysfunction or cholestasis, and this sometimes makes it necessary to suspend the trace element vial, which adds to the risk of developing deficits of the other trace elements. Therefore, the ASPEN suggests there is a need for manganese-free trace element presentations. An intake of 1 mg/day of iron is recommended, with an extra 0.5 mg/day in the case of women of menstrual age, although iron may present stability problems with the other components of the mixture (4,49).

TEDUGLUTIDE

What is the role of the GLP2 analogue teduglutide in the treatment of SBS?

GARIN proposal:

We suggest initiating treatment with teduglutide in chronic SBS patients who require ongoing HPN/fluid therapy despite optimized treatment, and who have an acceptable nutritional status and fluid-electrolyte balance, and meet the following requirements: non-obstructive and non-malignant underlying disease; clinical stability after the intestinal adaptation period following intestinal resection (estimated at 12 months after extensive intestinal resection or 6 months after minor reoperation on a long-standing SBS) (consensus level: 81.82 %) (moderate quality of evidence; benefits compensate the risks).

We suggest performing colonoscopy in patients with colon prior to starting treatment (consensus level: 96.36 %) (moderate quality of evidence; benefits compensate the risks).

Teduglutide is an analogue of the native peptide GLP2 (synthesized in L-cells of the terminal ileum and colon) but with a longer half-life. Teduglutide helps the intestinal adaptation process by means of various gastrointestinal effects, but the effects of treatment revert after it is discontinued (50,51).

In the phase-III clinical trials teduglutide was superior to placebo in decreasing the weekly parenteral volume administered by 20 % or more, and in reducing HPN support by at least one day per week (in 70 % of patients treated at 2 years) (52-54). In the initial statistical analysis, no predictive factors associated with

parenteral support independence were identified (55), but the post hoc analysis of these studies (56-58) suggested the existence of 2 response profiles:

1. Enterostomy patients (SBS type I) with high baseline volume requirements, inflammatory bowel disease and absence of vascular disease are characterized by a rapid response to treatment (under 3 months, generally), with a high probability of reducing the parenteral volume administered, but with a low probability of achieving independence from parenteral support.
2. Patients with colon in continuity (SBS type II and III) with low baseline volume requirements, with hyperphagia, and absence of inflammatory bowel disease are characterized by a slow response (over 6 months treatment, generally), but are more likely to achieve complete oral autonomy.

Candidate patients for teduglutide treatment must have the following characteristics: non-obstructive and non-malignant underlying disease; clinical stability after the intestinal adaptation period following intestinal resection (estimated at 12 months after extensive intestinal resection or 6 months after minor reoperation on a long-standing SBS), requiring ongoing HPN/fluid therapy despite optimized treatment, and with an acceptable nutritional status and fluid-electrolyte balance. Contraindications to its use are hypersensitivity to the active ingredient or its excipients, possible malignancy or active malignancy, and a history of malignancy in the gastrointestinal tract in the last 5 years. Therefore, before starting treatment, a colonoscopy should be performed in patients with colon, and if any polyps are identified these should be removed. In the case of malignant polyps, the treatment is contraindicated.

What do we need to consider in patients who are candidates for teduglutide treatment?

GARIN proposal:

We suggest close monitoring of water balance, weight, physical examination, biochemical parameters, and intake changes to adjust nutritional and volume requirements (consensus level: 90.91 %) (low quality of evidence; benefits compensate the risks).

We suggest a colonoscopy every year for the first two years, and then every 5 years (consensus level: 89.01 %) (low quality of evidence; benefits compensate the risks).

We suggest a six-monthly check-up of biliary and pancreatic parameters (consensus level: 92.73 %) (low quality of evidence; benefits compensate the risks).

We suggest evaluating the effectiveness of the treatment on a regular basis. In the absence of clinical improvement after 12 months, consider if treatment should be stopped (consensus level: 90.91 %) (low quality of evidence; benefits compensate the risks).

Teduglutide should be used at a dose of 0.05 mg/kg/day, reducing it to 50 % in patients with a glomerular filtration rate of less than 50 mL/min. It does not require any dose adjustments in case of moderate liver failure.

The most common side effects are those related to the stoma (42 %), abdominal pain (38 %), upper respiratory infection (26 %), nausea (25 %), abdominal distension (20 %), vomiting (12 %), and volume overload (12 %) (59). As it is a gut trophic factor, there is controversy about its oncogenic role. So far, no increased risk of intestinal neoplasia has been observed in patients without a history of cancer, but given the small number of patients treated, and the limited length of follow-up (5 years), it is premature to reach a definitive conclusion and one should be alert to this possibility (60).

The fluid balance (including diuresis and losses through the stoma or the feces), weight, physical examination (data on fluid overload), biochemical parameters, and changes in intake should be closely monitored. All these data together will be the basis for reducing the volume and, if possible, the number of days of administration of fluid therapy or HPN. It is advisable to monitor potential complications: a) perform an annual colonoscopy during the first 2 years, then every 5 years, and individualize according to the findings; and b) perform a six-monthly evaluation of the biliary and pancreatic parameters (bilirubin, alkaline phosphatase, lipase, and amylase) and, depending on the result, consider performing an imaging test.

It is necessary to evaluate treatment efficacy, with patients being considered as responders when there is a reduction of at least 20 % of the HPN/fluid therapy weekly volume. Factors that characterize slow responders should be identified before determining an insufficient response. Even so, if overall improvement is not achieved after 12 months, the need for continuing the treatment must be reconsidered.

CONCLUSIONS

The GARIN group, after reviewing the available evidence, recommends that the diagnosis of SBS be fundamentally based on the clinical condition. Initial management during the acute phase should focus mainly on sepsis control and fluid and electrolyte replacement. Pharmacological treatment with antisecretory drugs, antidiarrheal drugs, and somatostatin contributes to reducing intestinal losses. Treatment with PPIs should be prescribed in patients with SBS, especially when fecal production is greater

than 2 liters/day in the first 6 months after surgical resection. Loperamide should be added as a first-line antidiarrheal agent to reduce the loss of water and electrolytes. Nutritional screening and assessment should be repeated regularly in all patients during the different phases of the disease. Patient requirements should be adjusted in accordance with clinical and laboratory outcomes, not forgetting the potential loss of nutrients through the stoma. Nutritional support is based on parenteral nutrition; however, oral intake and/or enteral nutrition (by tube or enteroclysis) should be introduced as soon as possible. In the chronic phase, the diet should involve as few restrictions as possible and, if the clinical condition requires it, it should be adapted according to the type of SBS. For HPN administration, the choice of access should be individualized based on the patient's characteristics and the site's experience, using single-lumen catheters, or using a lumen exclusively for PN when using multiple-lumen catheters. Taurolidine should be used as catheter lock in all cases. Lipid content in HPN should be greater than 1 g/kg/week but not greater than 1 g/kg/day. The contribution of ω 6 fatty acids should be reduced by using the newer lipid emulsions. Trace element vials with a low manganese dose should be used. Patients with chronic SBS who require long-term HPN/fluid therapy despite optimized treatment, and who have an adequate nutritional status and fluid and electrolyte balance, should be considered for teduglutide treatment after colonoscopy. These recommendations and suggestions regarding nutritional management in SBS patients have direct clinical applicability. However, new studies are needed to increase the quality of the evidence, and to provide concrete answers to pending questions.

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