Clinical Nutrition

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6.1 Introduction

Pediatric patients are particularly vulnerable to the disease-related consequences of malnutrition that may be prevented by clinical nutrition [1]. The clinical nutrition applies in clinical practice the techniques of artificial nutrition (AN) that include enteral nutrition (EN) and parenteral nutrition (PN) [2]. EN consists in administration of complex nutrients into the gastrointestinal tract; PN delivers simple nutrients directly into the blood generally by central venous catheters or in some cases by peripheral veins [3, 4]. The most appropriate nutritional intervention will be determined by assessing patient's age, clinical condition, gastrointestinal function, attitude for oral intake, dietary habits, and costs [2]; however, decisional algorithm starts from the gut function. Following this assessment the patient may receive dietary advice, oral nutritional supplements, enteral nutrition (EN) regimens, or parenteral nutrition (PN) [2].

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According to the ESPGHAN indications, EN support includes both delivery of liquid formulations via tube and provision of specialized oral nutritional supplements (ONSs) [2]. ONSs are suitable to completely replace intake by normal foods and they allow to avoid more invasive AN techniques. They have good taste and are available as liquids or creams. When oral intake is inadequate or intake of normal food is inappropriate to meet the patients' needs, EN by tubes should be approached. It is realized by the use of enteral formulations for the long-term use and subdivided as polymeric, based on cow's milk proteins (PFs); low molecular formulas, containing oligopeptides derived from protein hydrolysates and high amount of medium-chain triglycerides (MCTs) (HFs); and elemental feeds, based on free amino acids (AAs). EN support is the first choice in patients with maintained gut function. PFs are employed in about 50 % of the overall EN candidates; they are inadequate in some digestive diseases, in post-pyloric enteral feeding, and in cow's milk allergy [2, 5, 6].

When gut function is impaired, as in all forms of intestinal failure (IF), PN should be approached [2]. IF refers indeed to all states where the intestine has inadequate absorptive capacity to meet nutritional, fluid, and electrolyte needs to sustain life and growth requirements of a child [7].

The etiology of IF recognizes the short bowel syndrome (SBS) where congenital or acquired lesions have determined extensive loss of intestinal mass, as the most frequent underlying disease

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Fig. 6.1 Summary of clinical nutrition management in pediatric digestive diseases. *PN* parenteral nutrition, * paralytic or mechanical ileus, ° obstruction, *NEC* necrotizing enterocolitis, *EN* enteral nutrition, *ONS* oral nutritional supplements

[8]. Malabsorption due to ineffective mucosal surface (congenital enterocyte disorders, phenotypic diarrhea, and autoimmune enteropathy) and motility disorders with undamaged mucosal surface but wide motility dysfunctions (chronic intestinal pseudo-obstructions, gastroschisis not associated with small bowel resection, and Hirschsprung's diseases) are further categories of IF [7–10].

However, complete enteral starvation should be avoided whenever possible [2]. Therefore, although PN should be firstly considered in IF, EN should be also employed integrating the maximum tolerated amount of enteral intake with the ongoing support of PN. Even minimal quantities of nutrients in the gastrointestinal tract (so-called trophic feeding) may promote intestinal perfusion, initiate release of enteral hormones, and improve gut barrier function [11, 12]. Thus, few clinical conditions are now considered absolute contraindications to EN (see Fig. 6.1). We can ideally represent the nutritional approach to pediatric digestive surgery as a pyramid, in which, proceeding from the base to the tip, increasingly invasive techniques are encountered (see Fig. 6.1).

6.2 Clinical Nutrition and SBS

Nutritional management of SBS is of particular interest because it provides a model of combined PN/EN management. This model may be applied to several digestive diseases at neonatal onset. Following neonatal small bowel resection, IF occurs due to the residual reduced length of the

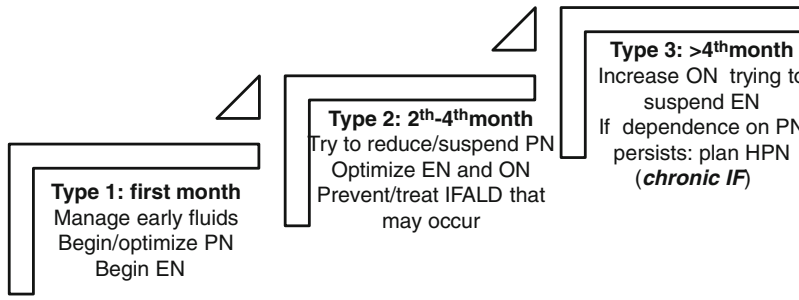

Fig. 6.2 Course of IF after neonatal small bowel resection. *IF* intestinal failure, *PN* parenteral nutrition, *EN* enteral nutrition, *ON* oral nutrition, *IFALD* intestinal failure-associated liver disease, *HPN* home parenteral nutrition

gut, responsible for SBS. The course of IF SBS related can be ideally subdivided into three phases, with distinct clinical characteristics and requiring different nutritional approaches. If long-term dependence on PN is expected (generally more than 3 months), IF can be defined as chronic, and it requires to plan home parenteral nutrition (HPN) programs (see Figs. 6.2 and 6.3) [13, 14].

Overall the nutritional care of neonatal SBS onset includes (1) early managing of fluid and electrolyte losses before starting PN and EN; (2) providing adequate PN, for growth and normal development; (3) promoting intestinal rehabilitation by optimizing EN; (4) discharging on home parenteral nutrition (HPN) the patients with protracted dependence on PN; and (5) preventing/treating complications related to the patients' underlying disease and their PN.

6.2.1 Early Managing of Fluid and Electrolyte Losses

SBS patients, at the early stages after bowel resection, have increased losses of fluids and electrolytes which can lead to significant electrolyte imbalance and dehydration. Early restoration of fluid and electrolyte homeostasis is therefore required, and it needs aggressive recovery with fluids [15]. Early fluid replacement is usually 1 mL for every mL of fluid loss. This phase is followed by PN beginning.

6.2.2 Providing Adequate PN

Before approaching each PN program, a reliable vascular access should be warranted. The choice of the access is dependent on the predicted length of the PN support. Peripherally inserted central lines are very effective means of providing PN over a short to medium term, while more definitive central venous access is required for prolonged PN. The expertise of a dedicated hospital-based nutritional team is required to tailor PN to the single patient and to manage central catheters; it is supported by official guidelines published by the pertinent societies [15–17].

SBS is at risk for developing intestinal failure-associated liver disease (IFALD) [18] due to IF-related factors, such as lack of enteral feeding, disturbed enterohepatic bile flow, presence of inflammation, oxidative stress, immaturity of the liver, and infections, but also PN-related factors [18]. Therefore, in patients who are predicted to require long-term treatments, PN should be tailored to reduce the risk of liver injury [9, 19]. To prevent/treat IFALD, some aspects of PN management can be modulated and in particular are the following:

A. Choosing lipid emulsions (LEs)
B. Optimizing non-lipid intake

6.2.2.1 Choosing LEs

Historically, a French study delineated IFALD in adult HPN patients as a value of at least 1.5-fold the upper limit of normal on two of three liver

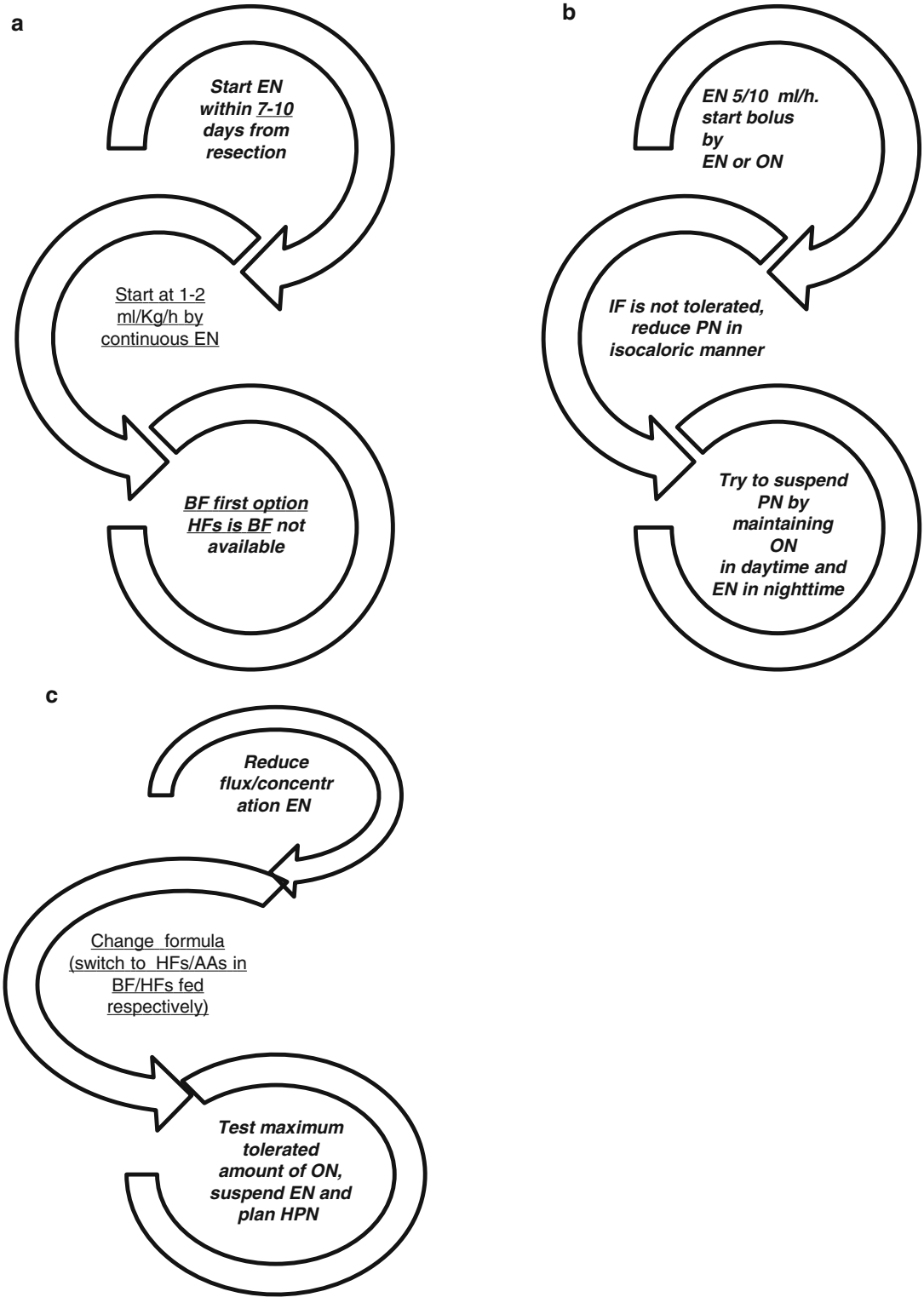

Fig. 6.3 Patterns of combined management of PN and EN after small bowel resection. *PN* parenteral nutrition, *EN* enteral nutrition. (**a**) Pattern of EN beginning. (**b**) Pattern of tolerance to advancing EN. (**c**) Pattern of intolerance to advancing EN. *BF* breastfeeding, *HFs* hydrolyzed formulas, *ON* oral nutrition, *AAs* amino acid-based formulas, *HPN* home parenteral nutrition

function measures for cholestasis that persists for more than 6 months [20]. This study also showed that chronic cholestasis predicts serious liver problems and is associated with the use of soybean oil-based lipids (SO) at doses >1 g/kg/day [20]. Several factors may explicate how LEs can impact on the development of IFALD:

(a) Activation of hepatic macrophages (Kupffer cells) by excess of ω–6 polyunsaturated fatty acids (PUFAs) in SO that leads to the production of proinflammatory cytokines derived from linoleic and arachidonic acids [21].
(b) High intake of phytosterols (e.g., stigmasterol and campesterol, equivalents of cholesterol in vegetable oils) derived from SO; they have structural similarity to bile acids and may act as antagonists to nuclear bile receptors that are protective against cholestasis [21].
(c) Overall content of vitamin E, especially of its most bioactive isoform α-tocopherol, which protects PUFAs from oxidative damage due to lipid peroxidation. The addition of this component to SO has been shown to reduce liver damage in a piglet model of IFALD [21].

Published surveys report that the use of a fish oil-based LEs (FO) is able to reverse IFALD [22, 23]. These surveys, nevertheless, are used at a markedly decreased dosage of FO (1 g/kg/d) if compared to that of SO in the control historic group (3 g/kg/day) [22]. That supports the hypothesis that the overall decreased fat intake rather than FO supplementation is important in reversing IFALD [21]. Interestingly a recently published paper reports two cases of reverted cholestasis by switching from SMOF lipid (Fresenius Kabi, Bad Homburg, Germany), an emulsion containing a mixture of 30 % of SO, 30 % of coconut oil, 25 % of olive oil, and 15 % of FO at 2.0–3.0 g/kg/day, to FO at 1 g/kg/day [24]. That supports the hypothesis that the reduced amount rather than the type of LEs may be hepatotoxic.

Anyway FO monotherapy has now been widely employed in clinical practice. FO alone may not be able to provide enough energy to sustain growth. A mixed LE containing soybean oil (SMOFlipid) compared with SO in a blinded randomized controlled trial in pediatric HPN patients resulted in mild changes in total bilirubin when administered four to five times per week at 2 g/kg/day and in normal growth pattern [25].

In North America, FO alone (Omegaven, Fresenius Kabi, Bad Homburg, Germany) is available on the market, whereas in Europe, it is possible to use LEs containing the mixture (SMOFlipid, Fresenius Kabi, Bad Homburg, Germany). That led to develop two different approaches to optimize LE use in the United States and Canada as compared with Europe.

Many institutions generally combine the use of novel lipid preparations and reduced rates of administration of SO to prevent the development of liver disease [21]; e.g., if bilirubin exceeds 34 μg/L, lipid intake is reduced at 1 g/k/day, while if it goes over 50 μg/L, the lipid source is changed to FO alone at 1 g/kg/day.

Table 6.1 summarizes the composition of available LEs employed in PN.

6.2.2.2 Optimizing Non-lipid Intake

Excessive glucose intake causes increased lipogenesis and fat tissue deposition together with subsequent liver steatosis and enhanced production of triglycerides by the liver [3]. The American Society for Parenteral and Enteral Nutrition (ASPEN) [26], the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition [18], and the American Academy of Pediatrics guidelines (ESPGHAN) [27] recommend limiting the glucose infusion rate (GIR) at 12–14 mg/kg/min (18 g/kg per day) in infants and young children up to 2 years. Glucose intake should usually cover 60–75 % of nonprotein calories [3]. As reported above reduced LEs intake as strategy to prevent/treat IFALD may be required; in such cases increased glucose intake, to better satisfy the nutritional needs, resulted as well tolerated [28].

Furthermore, prophylactic cycling of PN may reduce the incidence of IFALD [21]. Cyclical PN is well tolerated and may be 3–6 months of age. In cyclical PN the maximal rate of glucose infu-

Table 6.1 Composition of lipid emulsions available for parenteral nutrition

Emulsion (% fat) (manufacturer)	Lipid source (%)	ω6:ω3 ratio	Phytosterols (mg/L)	α-Tocopherol (μmol/L)
Intralipid 20% (Fresenius Kabi)	SO 100%	7:1	348 ± 33	87
Lipofundin 20% (B. Braun)	SO 50% MCT 50%	7:1	No data	502
ClinOleic-Clinolipid 20% (Baxter)	SO 20% OO 100%	9:1	327 ± 8	75
Lipoplus 20% (B. Braun)	SO 40% MCT 50% FO 10%	2.7:1	No data	562
SMOF lipid 20% (Fresenius Kabi)	SO 30% MCT 30% OO 25% FO 15%	2.5:1	47.6	500
Omegaven 10% (Fresenius Kabi)	FO 100%	1:8	0	505

SO soybean oil, *MCT* medium-chain triglycerides, *OO* olive oil, *FO* fish oil

sion may exceed the advised GIR. The maximal infusion rate should not exceed 1.2 g/kg per hour (20 mg/kg per min). A stepwise increase and decrease of glucose infusion rate at onset and at discontinuation of the infusion should be considered to avoid hyper- and hypoglycemia, respectively. A reliable method for tapering is to halve the rate for 30 minutes and then to halve this again for an additional 30 minutes. Glucose tolerance should be monitored during the first phases of the cycling PN [3].

With regard to the choice of amino acid solution, there is evidence that supplementation of TrophAmine may reduce the incidence of IFALD in certain high-risk populations such as those with NEC [19].

Furthermore, copper and manganese serum levels from PN solutions should be monitored closely in patients who have developed IFALD because they may exacerbate it [19].

6.2.3 Promoting EN

The provision of enteral nutrients is a critical component of the therapy of IF; in SBS patients it represents the fundamental driver of adaptation [15]. Early attempts of oral nutrition confer the critical window of opportunity for establishing normal suck and swallow patterns; if this is not attended, the child is at risk for oral aversion, which has many long-term negative consequences [29]. The most pragmatic way to address EN handling in IF should be to account that all patients regardless of the etiology of their IF may recover to a variable degree and that the strategies to promote EN should be reconsidered on a day-to-day basis. The overall care of IF is based on the judicious integration of two overlapped goals: progressive advancement of enteral calories and gradual weaning from the ongoing support of PN, maintaining a weight gain [15]. If tube feeding is used, the practice of inserting a gastrostomy early allows a more controlled method of delivering feed with an opportunity to preserve and promote voluntary feeding without the negative effects of the long-term presence of a nasal tube [29]. If patients with motility disorders but also with SBS show poor tolerance to gastric feeding, the post-pyloric EN approach should be tried [6]. Main aspects concerning EN management in SBS are:

A. Choosing the formula
B. Assessing methods of feeding
C. Assessing tolerance to EN
D. Using enteral supplements
E. Starting and handling complementary foods

6.2.3.1 Choosing the Formula

There is a paucity of evidence in favoring one type of feed over the other in this setting; however, breastfeeding (BF) should be used when tolerated as it helps and promotes adaptation [30]. The

full advantages of BF include the optimal macronutrient composition for human infant growth, with a full complement of macro- and micronutrients [31, 32]. In addition, it contains trophic factors such as epidermal growth factor, which likely augment the adaptive process [7]. Furthermore, BF contains immunoglobulins and natural antimicrobial properties which both enhance mucosal barrier function and prevent dangerous overgrowth of bacteria within the intestinal lumen. Finally it promotes intestinal colonization by appropriate lactobacilli and related bacteria which are important elements of healthy microbiome [33, 34]. Bovine colostrum also seems to confer beneficial effects on IF [35].

Finally BF supports physiological and psychological relationship between infant and mother. If the mother's own milk is not available, banked breast milk, even with pasteurization, has nearly identical physiologic benefits [31]. Overall BF should be the first choice in SBS patients.

If BF is not available, formula selection should be based on:

(a) Low allergenicity, because SBS infants are at high risk for allergy [36]
(b) Fat profile based on a combination of medium-chain triglycerides (MCTs) and long-chain triglycerides (LCTs) (ratio of MCTs to LCTs of 30 %/70 %) that seems to favor fat absorption in patients with significant intestinal resection, with or without a colon in continuity [37]
(c) Pre-hydrolyzed protein content that may be more suitable than the whole proteins to give nitrogen source to an inefficient mucosal surface [32]
(d) Low osmolality (less than 310 mOsm/L) to minimize the risk for osmotic diarrhea [38, 39]]
(e) Glucose polymer as main carbohydrate source rather than lactose, due to the possible lactose intolerance, especially in SBS children [16]

Some HFs and AAs meet the above reported criteria. AAs have been shown effective in decreasing PN length in small and uncontrolled series of SBS patients [18, 40].

6.2.3.2 Methods of Feeding

EN should be started as soon as postoperative ileus resolves [16, 41, 42], by the most physiological mode. This ideally should be in the form of oral bolus feeding via the breast or bottle. In infants unable to tolerate oral feeds, nasogastric tube feeding is needed. Continuous tube feeding is associated with increased feed tolerance by improved mucosal contact and decreased transit time within the gut [16]. Bolus tube feeding helps gut motility and adaptation and provides periods of fasting, thus reducing persistent hyperinsulinemia. After establishing an appropriate base of enteral nutrients, the general pattern is to increase the provision of enteral nutrients by a slow but steady increment, beginning at 10–20 mL/kg/day (for the average newborn). After the infant can tolerate continuous feeds of 5 mL/h, it is extremely useful to begin transition to oral feeds, providing in small quantities, three to four bolus oral feedings a day (equal or less than the volume continuously tolerated per hour). After establishing a stable feeding pattern, feeds are steadily increased on a daily basis [16]. In order to maximize overall enteral intake, it is often helpful to have continuous drips overnight. To correctly switch from PN to EN, it needs to consider that the net caloric extraction from EN is not 100 % as from PN and that macronutrient absorption from EN is superior than that of electrolytes and fluids. Therefore, PN should be decreased according to the calories provided by EN and not volume for volume [41].

6.2.3.3 Assessing Tolerance to EN

In SBS infants, increasing stool output, vomiting, and irritability to the advancing EN may suggest poor tolerance to the current EN regimen. If stool output is between 30 and 40 mL/kg body weight, it needs to carefully increase EN. Doubled stool output or outputs >40 mL/kg/day are contraindications to increase enteral feeds and indications to deal with a short-term reduction in feeding volume that will be gradually reintroduced. Stool frequency greater than six times per day should induce to cautiously increase EN [16].

Carbohydrate intolerance, which determines frequent and liquid stools, is frequent in SBS

Table 6.2 Markers of impaired EN tolerance and of evolution toward chronic IF

		Reference (n°)
Anatomical markers	1. Residual small bowel length (≤40 cm) 2. Residual small bowel length assessed by GA (<10 %) 3. Type of the remaining bowel (relevant loss of ileus) 4. ICV and colon loss (?)	[7, 8, 10, 17, 42]
Clinical markers	1. Frequency of stools (>6–8/day) 2. Impaired growth 3. Diaper rash due to liquid feces 4. Fecal or stoma output >30–40 ml/Kg	[17, 42, 43]
Biochemical markers	1. Plasma citrulline concentration (<12–15 μmol/L) 2. pH of feces (values <5 indicates acid and not absorbed stools) 3. Urine electrolytes (sodium <30 mEq/L and urine sodium-to-potassium ratio <1:1)	[7, 42, 43]

GA gestational age, *ICV* ileocecal valve

patients, and it can be suggested by the presence of reducing substances on the stools and by the stool pH <6.

The rise in plasma citrulline concentration frequently accompanies the successful achieving of enteral tolerance. Citrulline is a nonessential amino acid produced by the enterocytes of the small bowel; its serum level has been shown to reflect intestinal mass in various gastrointestinal diseases. Citrulline concentration of 12–15 μmol/L or greater following EN beginning seems to predict a successful PN withdrawal [41]. In Table 6.2 we report the markers of impaired EN tolerance useful in clinical practice. The combinations of several markers are associated with evolution toward chronic IF.

6.2.3.4 Use of Enteral Supplements

IF patients can loss bicarbonate and sodium in their stool or stoma which must be closely monitored and replaced, not only intravenously but also via enteral route [10]. It is important to monitor sodium balance, because sodium deficiency can limit growth in infants [7, 41]. The simple spot measurement of the urinary sodium and, in selected cases, the calculation of the fractional excretion of sodium are rapid and effective ways to monitor the sodium loss. If the spot urine sodium is <10 mEq/L, increased sodium intake, both in EN and in PN, is required. The sodium content in PN should be titrated to keep urine sodium >30 mEq/L and to maintain urine sodium-to-potassium ratio at least 1:1. Weekly monitoring of the urinary sodium is a preemptive way of assessing status, rather than waiting for the serum level to drop, and long-term monitoring of this parameter is suggested [7].

When increasing in feeds does not result in appropriate weight gain, it should consider supplementation with additional fat [15]. There is good rationale for using long-chain triglycerides (LCTs) as supplemental vegetable oils, or olive oil, or emulsified preparations. Additionally it may be reasonable to add MCTs because they are absorbed directly across the enterocyte membrane, without requiring lymphatic absorption. This occurs in the proximal small bowel and even the stomach; therefore, to add gradually increasing amounts of MCTs to the formula being used, especially if delivered by tube feeds, may favorably increase the overall caloric intake. MCTs are nevertheless less effective than LCTs in promoting intestinal adaptation [43].

6.2.3.5 Starting and Handling Complementary Foods

The introduction of complementary, age-appropriate foods between 4 and 6 months of age, as well as oral boluses of human milk/formula as soon as tolerated, is helpful to stimulate oral motor development and to prevent feeding aversion [10].

Early weaning (17 weeks) has the advantage of promoting feeding maturation with respect to solids and a reduction in milk fluid volume which may exacerbate a tendency to vomit or induce an increase in osmotically driven stomal losses [10]. Feeding therapy is usually required as these

infants are likely to have some degree of oral aversion due to delayed introduction of oral feeds as a result of prematurity, prolonged intubation, and cardiovascular instability.

Patients without a colon tolerate better diets that are high in fat (30–40 % of caloric intake), whereas those with intact colons experience steatorrhea and magnesium and calcium loss with high-fat intake. With calcium loss, oxalate absorption is enhanced in the colon and kidneys, which can lead to the formation of oxalate renal stones [41, 44]. Hence, it is necessary to restrict oxalate intake in SBS patients with a colon to decrease the risk of oxalate renal stones. Oral calcium supplements can also reduce the formation of oxalate stones.

Soluble dietary fiber (pectin or guar gum) can slow gastrointestinal transit time allowing for improved absorption (see above). The soluble fiber in the colon is fermented to short-chain fatty acids, including butyrate which is an energy source for colonocytes. In addition, the butyrate regulates colonocyte proliferation and improves water and sodium absorption by upregulating the sodium-hydrogen exchangers [7]. However, excess pectin (>3 %) can lead to an osmotic diarrhea which can counteract its benefits.

In SBS children there is a potential for significant malabsorption of carbohydrates, especially lactose. Therefore, feed with a glucose polymer as a main carbohydrate source is likely to be better tolerated [16]. Solids rich in complex carbohydrates, such as cereals and soluble fibers, lean meat, and unsweetened fruits, are well tolerated in patients with little or intact colon. Patients without a colon or with a stoma tolerate foods at high lipid contents and poor of carbohydrates.

6.2.4 Discharging on HPN

HPN represents the best care option in infants who do not need hospitalization but are dependent on long-term PN. It is indicated if the transition from PN to full EN, although possible, is expected over a long period [45]. Patients eligible for HPN should be clinically stable. As soon as sufficient stability is reached, the child should be discharged under continued outpatient care with a team experienced in intestinal rehabilitation. A coordinated multidisciplinary approach is essential throughout, and the early training of parents in the complexity of HPN care is essential. A specialized nurse dedicated to the coordination of the HPN service is essential, and once the funding and provision of a HPN service are put in place, early discharge home benefits the child and family [10]. Transferring care of these children from hospital to home has a positive influence on CVC infections, social circumstances, as well as reducing the cost of treatment. At the same time, it also puts a significant burden on the family who has to spend a lot of time caring for the child and has difficulty in maintaining gainful employment [45].

6.2.5 Preventing/Treating Complications

The complications of IF SBS related [46–54] can be subdivided into two main categories:

A. CVC-related complications
B. IF-/PN-related complications

Main complications and suggested way of prevention are summarized in Fig. 6.4.

6.2.5.1 CVC-Related Complications

Administration of long-term PN requires placement of indwelling central venous catheter. The problems associated with central lines include infections, mechanical damage, blockages, and thrombosis. Infections are the commonest complication with incidence being around 1–6 per 1000 days of PN [17]. Prevention of infections is based on optimal catheter placement and strict hand hygiene. Taurolidine, a derivative of amino acid taurine, has been shown to have a role in reducing catheter-related sepsis [55]. With advances in the type of catheters used and insertion techniques, there has been a significant reduction in complications [17].

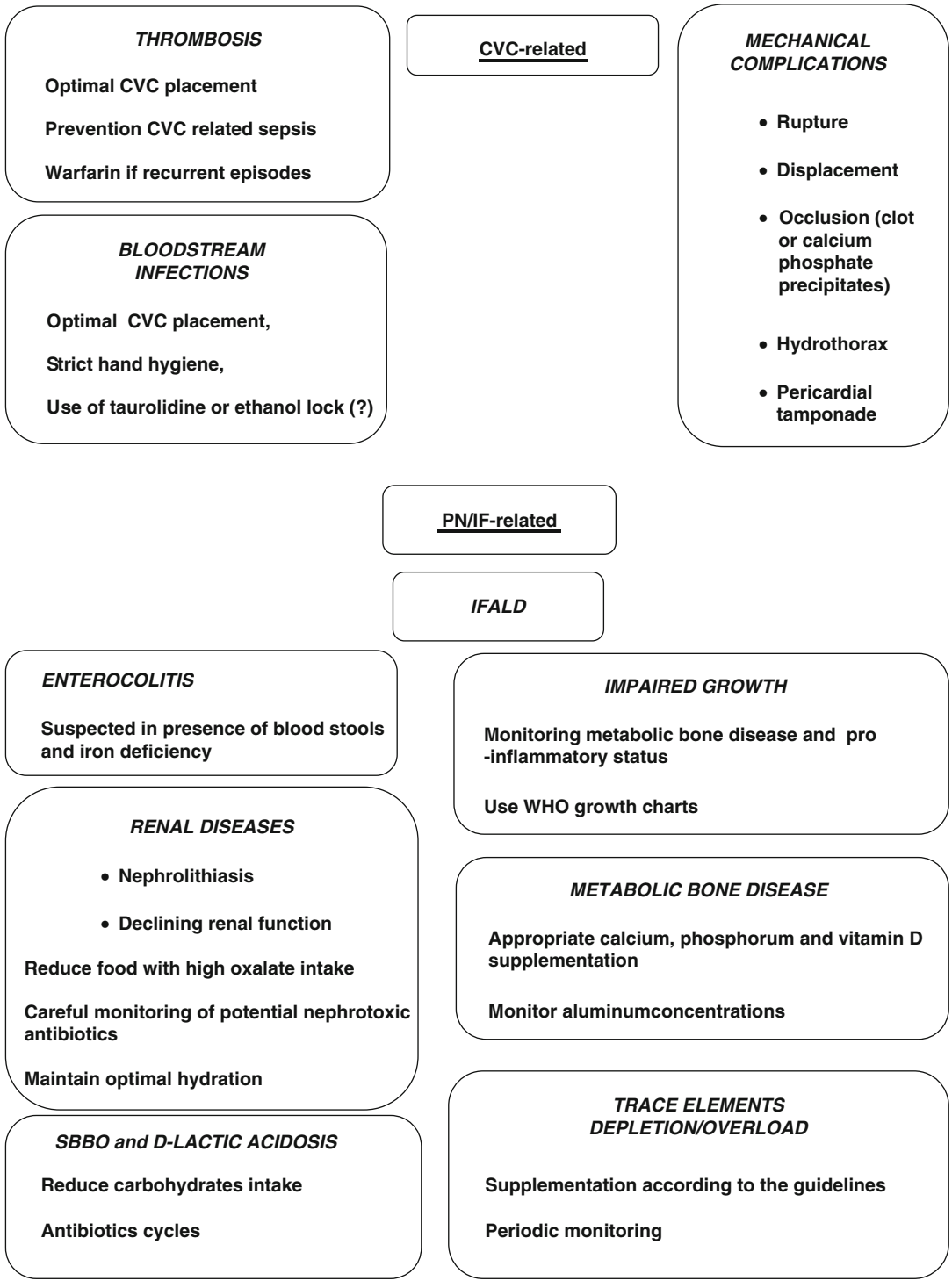

Fig. 6.4 Summary of short bowel syndrome complications. *CVC* central venous catheter, *PN* parenteral nutrition, *IF* intestinal failure, *IFALD* intestinal failure-associated liver disease, *WHO* World Health Organization, *SBBO* small bowel bacterial overgrowth

6.2.5.2 IF-/PN-Related Complications

Trace element depletion is very common among patients with surgical short bowel syndrome if parenteral administration is inadequate. Adequate parenteral zinc supplementation is particularly important; its deficiency is generally associated with high output from the stoma but also with congenital diarrhea. As zinc is a cofactor for alkaline phosphatase synthesis, an excellent surrogate marker for zinc deficiency is the serum alkaline phosphatase level, which is likely decreased in patients at risk for the clinical manifestations of zinc deficiency [7].

D-lactic acidosis occurs among patients whose gastrointestinal tract is colonized by D-lactate-synthesizing organisms. Humans have the ability to rapidly catabolize L-lactate, which is a product of human anaerobic metabolism, but D-lactate can be catabolized and cleared very slowly, and toxic blood levels can build up when the small intestine is overgrown with anaerobic bacteria. Signs and symptoms of D-lactic acidosis include confusion, somnolence, dementia, ataxia, or even seizures. This condition is characterized by acidosis associated with an anion gap but a normal blood L-lactate level. Lactobacilli and other bacteria, including *Clostridium perfringens* and *Streptococcus bovis*, when present, may ferment non-absorbed carbohydrate to D-lactic acid, which cannot be metabolized by L-lactate dehydrogenase [41]. These microorganisms may proliferate in the acidic environment of the colon that is the result of the metabolism of unabsorbed carbohydrate to SCFAs. D-lactic acidosis presents with encephalopathy (ataxia, blurred speech, decreased consciousness) and should be considered when there is a high anion gap metabolic acidosis with normal serum lactate and high gram + strains in the stools [41]. Preventive measures for D-lactic acidosis include the reduction of carbohydrate intake, followed by antibiotics (such as metronidazole or co-trimoxazole) when dietary changes fail [51].

Vitamin B12 absorption may be impaired among patients who have undergone distal small bowel resections. Serum levels of B12 are sometimes falsely elevated because of the production of biologically inactive B12 analogues among patients with bacterial overgrowth syndrome [43].

Provision of enteral water-soluble vitamins is unnecessary while patients are on parenteral vitamin supplements, but if adaptation occurs and patients are weaned off TPN, enteral provision of most water-soluble vitamins is advisable. Fat-soluble vitamin supplementation is delivered via parenteral vitamins and parenteral lipid generally preventing deficiency, but after weaning of TPN, enteral supplementation is advisable.

Iron deficiency can occur in patients with SBS, but it is frequently correctable with oral iron supplements because the efficiency of enteral iron absorption is maximal in the duodenum which is often maintained after neonatal surgical resections. For patients who cannot tolerate enteral iron or who remain deficient despite enteral supplementation, parenteral iron may be given. Iron deficiency can be also due to chronic gastrointestinal bleeding [41].

Another concern of the long-term PN is the potential exposure to toxic plasma aluminum concentrations. A recent Canadian survey found that in pediatric patients receiving long-term PN, aluminum intake is significantly greater than recommended by the US Food and Drug Administration to prevent aluminum toxicity [54]. In SBS patients on PN, aluminum is stored in the body because the protective gastrointestinal barrier is bypassed and renal function may be impaired. The long-term aluminum exposure can contribute to chronic bone disease (by inhibition of PTH) and to neurotoxicity of PN. In addition it is involved in IFALD (it accumulates in the liver) and in the development of hypochromic, microcytic anemia (binding to transferrin).

Colonic oxalate absorption is increased in patients with SBS, resulting in hyperoxaluria and in calcium oxalate nephrolithiasis. The risk of stone formation is reduced if the colon is partially or fully removed. Renal function can also be compromised by some antibiotics or by uncorrected control of fluids and electrolytes in the first phase of IF.

Growth is usually impaired in SBS at neonatal onset. These infants will be small and to push their weight gain to the 50th percentile or higher

is not physiologic. It is more appropriate to examine the birth record and weight and to use these to guide the decision as to which percentile seems appropriate. There should be careful serial measures of length, head, and weight gain, with plotting of the appropriate normative or "Z" scores. It may be necessary to tolerate a modest growth in weight, so long as growth in height and especially head circumference are maintained. It is likely appropriate to follow the WHO growth curves.

Conclusions

The key concept of nutritional care in digestive pediatric surgery is to give the maximum tolerated EN to meet the nutritional needs for each patient. If the gut function is impaired, the maximum tolerated EN should be combined with the ongoing support of PN. The final objective is to achieve total or partial nutritional rehabilitation. Nutritional workup of neonatal onset SBS is usually complex and requires close attention. It should be tailored to the single case. The outcome is significantly improved if they are managed by a multidisciplinary team that allows for fully integrated care of inpatients and outpatients with IF by favoring coordination of surgical, medical, and nutritional management [7, 10, 15, 41, 56].

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