Original Article

Role of enteral nutrition in adult short bowel syndrome undergoing intestinal rehabilitation: the long-term outcome

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The objective of this study is to evaluate the long-term clinical significance of enteral nutrition (EN) in weaning adult short bowel patients off parenteral nutrition (PN) undergoing intestinal rehabilitation therapy (IRT). Sixty-one adult patients with small bowel length 47.95 ± 19.37 cm were retrospectively analyzed. After a 3-week IRT program, including recombinant human growth hormone (*rh*GH, 0.05 mg/kg/d), glutamine (30 g/d), and combined EN and PN support, patients were maintained on EN or plus a high-carbohydrate, low fat (HCLF) diet. Continuous tube feeding was used when EN was started. Patients were followed up for 50.34 ± 24.38 months and had an overall survival rate 95.08% (58/61). On last evaluation, 85.24% (52/61) of the patients were free of PN. For 77.42% patients (24/31) with small bowel length <35 cm in jejunoileocolic anastomosis (type III) and <60 cm in jejunocolic anastomosis (type II), weaning off PN was achieved. EN comprised of 52.56 ± 13.47 % of patients' daily calorie requirements on follow-up. Five patients were maintained on home PN (HPN) plus EN. Nutritional and anthropometric parameters, urine 5-hr D-xylose excretion and serum citrulline levels all increased significantly after IRT and on follow-up compared with baseline. In conclusion, with proper EN management during and after IRT, a significant number of SBS patients could be weaned from PN, especially for those who were considered as permanent intestinal failure; continuous tube feeding is recommended for enteral access, and long-term EN support could meet the daily nutritional requirement in majority of SBS patients.

Key Words: short bowel syndrome, enteral nutrition, human growth hormone, nutrition assessment, follow-up studies

INTRODUCTION

In adult patients, short bowel syndrome (SBS) often results from extensive resection of the small bowel because of Crohn's disease (CD), small bowel volvulus or ischemic mesenteric diseases. Patients with SBS often require parenteral nutrition (PN) to maintain adequate nutritional and hydration statuses. Unfortunately, PN is associated with serious complications including catheter infections and sepsis, venous thrombosis, and liver failure.

In recent years, there is increasing awareness of the function of the remnant small bowel and the "gut-oriented" approach has been extensively studied.[1] Strategies to facilitate the adaption of the remnant small bowel were described in literature with promising results.[2,3] Intestinal rehabilitation therapy (IRT), which typically includes recombinant growth hormone (*rh*GH), glutamine, and a modified diet,[4,5] was first described by Byrne *et al* in 1995 and has been proven by prospective randomized studies to be able to wean a substantial percentage of SBS patients off PN.[6,7]

Often, the IRT program incorporates individualized modification of oral diets as a cornerstone of therapy, in addition to optimization of anti-diarrheal medications, particularly as use of PN is weaned. Dietary modifications typically involve smaller, more frequent feedings, use of oral rehydration solutions and soluble fiber, avoidance of simple sugars, oxalate, and, in some cases, lactose and modification of fat intake and consumption of specific foods based on individual tolerance. However, with this approach, studies have revealed that after the period of adaption (2 years), adult SBS patients with post-duodenal remnant small bowel less than 60cm in jejunocolic anastomosis (i.e., SBS type II), and 35cm in jejunoileocolic anastomosis (i.e., SBS type III) are unlikely to avoid home parenteral nutrition (HPN) dependence and maintain hydration and/or nutrient balance.[8,9]

Compared with a regular oral diet, proper management of enteral nutrition (EN) may have a more pronounced potential to promote intestinal adaption and reduce PN dependency. Previous studies have shown that a continuous 24-hour infusion of EN increase the rate of absorption of nutrients compared with oral intake.[10] In patients with ileal resection, continuous EN decreased fecal weight and steatorrhea by about 30% compared with intermittent oral feeding.[11] In addition, continuous supplementation of ent-

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eral nutrients such as L-arginine could promote the adaption of experimental SBS.[12] Levy *et al* also demonstrated that continuous enteral feeding could be attained in the early postoperative period of SBS.[13] The use of elemental and semi-elemental EN, which provides amino-acids or small peptides, and medium chain triglycerides, may also increase the amount of absorbed nutrients through the short intestine. However, although the importance of EN has been recognized in SBS, data on application of EN during IRT process and for long-term usage are insufficient. We hypothesized that proper usage of EN in the IRT program and in the long-term may be helpful in weaning adult SBS patients off PN, especially for those with a shorter residual bowel and poor absorption capacity.

In the current study, we report our experience with 61 adult SBS patients managed with EN during and after the IRT program. Patients' general condition, surviving time, nutritional and anthropometric parameters, and intestinal absorption function were assessed during follow-up period. The purpose of this study was to assess the value of EN support during IRT and after the adaptive phase (>2 years) of SBS.

MATERIALS AND METHODS

Subjects

From July 1997 to July 2008, 61 adult SBS patients (46 males, 15 females) were retrospectively analyzed. All patients have been followed up for at least 24 months. Their ages ranged from 18 to 74 years (mean, 37.56 ± 14.30 years). Of them, 37 were dependent upon PN on admission and 24 were referred with the intent of preventing the initiation or resumption of it. Criteria for eligibility were: adults aged 18 to 75 years; small bowel length < 100 cm; acceptable liver and kidney function on admission; normal or stable cardiovascular status. Before the study, patients may receive medical therapy for underlying disease (such as prophylactic anti-coagulants for thrombosis) or nutritional therapy (such as PN oral rehydration therapy, anti-diarrhea and anti-secretory agents), but no previous exposure to *rh*GH.

Exclusion criteria included patients with jejunostomy or ileostomy (type I SBS); operation on the stomach, duodenum, or pancreas; pathological lesions in the remnant small bowel such as recurrent CD, fistula, stenosis/obstruction, or ischemia and villous atrophy; history of malignancy; major comorbidities such as diabetes mellitus; ceasing usage of EN or lost to follow-up in 2 years; and secretory diarrhea (defined as stool output >800ml while taking nothing by month over the corresponding 24-hr period).

Post-duodenal small bowel length was documented at the time of operation or estimated from radiograph film of a barium meal follow-through with an opisometer.[14] As defined by Messing *et al*,[15,16] type II SBS means jejunocolic anastomosis and some part of the colon in continuity, while type III SBS means jejunoileocolilc anastomosis and full colon in continuity.

Demographic features of SBS patients were shown in Table 1. Serum biochemical index, including minerals such as iron (reference range, 6.6-32.0 μmol/L), zinc (reference range, 10.8-19.5 μmol/L), and copper (reference range, 11.0-24.4μmol/L) were all determined by a biochemical analyzer. Serum vitamin B12 (VB12, reference range, 200-900 pg/ml) level was determined by radioimmunoassay (RIA).[17]

Table 1. Demographic Characteristics of 61 Patients with Non-malignant Short Bowel Syndrome

Characteristics	No. of Patients (%)
Gender	
Male	46 (75.41)
Female	15 (24.59)
Age at the time of short bowel constitution (yr)	
18-40	35 (57.38)
40-59	20 (32.79)
≥59	6 (9.83)
Underlying diseases for small bowel resection	
Small bowel volvulus	27 (44.26)
Intestinal adhesion/obstruction	13 (21.31)
SMA infarction	8 (13.11)
Mesenteric thrombosis	6 (9.84)
Crohn's disease	3 (4.92)
Radiation enteritis	2 (3.28)
Others	2 (3.28)

SMA: Superior Mesenteric Artery

Table 2. Anatomic Features of 61 Adult Patients with Non-malignant Short Bowel Syndrome

Characteristics	
Digestive circuit type of anastomosis	
Jejunocolic anastomosis (type II)	N=30
Jejunoileocolic anastomosis (type III)	N=31
Remnant small bowel length (cm)	47.95 ± 19.37 (15-100)
Type II SBS (n=30)	51.00 ± 19.67
< 60cm	N=19
60-100cm	N=11
Type III SBS (n=31)	45.00 ± 18.93
< 35cm	N=12
35-100cm	N=19

Type II SBS: Jejunocolic anastomosis, with some part of the colon in continuity; Type III SBS: Jejunoileocolic anastomosis, with the full colon in continuity.

Body composition was determined by bioelectrical impedance analysis with a human body composition analyzer (Inbody 3.0, Biospace Co. Korea). Rest energy expenditure (REE) was determined with indirect calorimetry. For all patients, the "baseline level" referred to the data collected in the first 3 days of admission, and "after first IRT" means the data before patient's first discharge.

All but 6 patients received treatment within 2 years after intestinal resection. The mean interval between intestinal resection and first admission was 18.49 ± 24.59 (range, 3-144) months.

Methods for Nutritional Support

The treatment procedures were illustrated in Figure 1. On admission, bowel rest and TPN were given to all patients. Intravenous albumin, plasma and furosemide were given if necessary to increase blood osmotic pressure and to

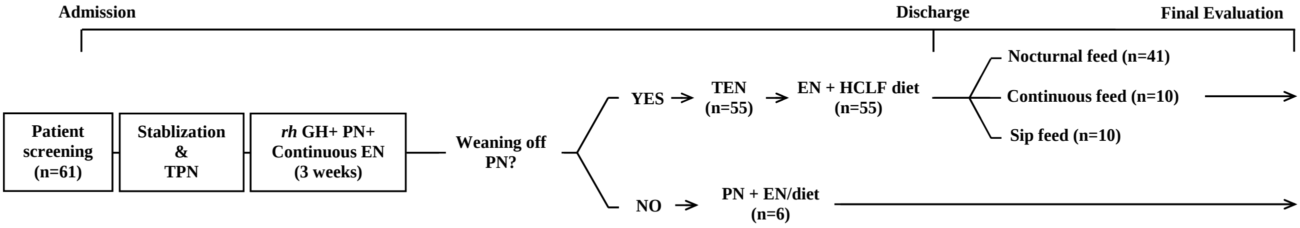

Figure 1. Schematic illustration of treatment procedure of intestinal rehabilitation and follow-up

remove excessive water in the interstitial tissue and intestinal mucosa.

When patients' nutritional status improved and tissue edema regressed, EN was started and combined PN and EN support was given. Typically, EN comprised 33-50 % of patients' nutritional requirements, according patients' remnant small bowel length. After EN was added, there should be a positive enteral balance (defined as enteral fluid intake [ml] minus volume of stool output [ml]).

When patients demonstrated positive nitrogen balance, as determined by Kjedahl's method, IRT was started, *rh*GH (Serono Inc, Switzerland) 0.05mg/kg/d was given subcutaneously for 3 weeks.[18] Oral glutamine powder (Ajinomoto Co., Japan) 30g/d was also given. Before IRT, a written consent was obtained; the therapy was approved by the ethical committee of the hospital.

Peptide-based formula (Peptisorb, Nutricia Co., Nether land) was used in all but one patient (100 cm bowel). For patients with an intact colon, dietary fiber was provided.

Technical Aspects for EN

Continuous nasogastric (NG) tube feeding was given to all patients when EN was started. Care was taken to avoid EN-related intestinal complications: an infusion pump was used to control the starting speed at 25mL/h, if the EN was well tolerated, the speed gradually increased to 80-100mL/h, and the concentration of EN also increased with total calorie from 250-500kcal/d to 1500-2000kcal/d.

Anti-diarrhea agents were given once EN was initiated; commonly used drugs were diphenoxylate-atropine (Lomotil, Pfizer Inc., USA) or loperamide (Imodium, Johnson & Johnson Inc., USA). Other drugs, such as Vitamin D_3, calcium supplements, and anti-acids (omeprazole 40mg/d in two divided dosage), were delivered if necessary.

After patients finished *rh*GH treatment, EN was again increased, and PN was gradually withdrawn. When total enteral nutrition (TEN) was tolerated, a high-carbohydrate, low fat (HCLF) diet was added. The ratio of EN to HCLF diet depended on the absorption capacity and patient's nutritional status.

Indicators for the success of EN management

During the PN weaning process, patients were monitored for enteral balance, urine volume, body composition, and serum electrolytes. The main indicator for the success of EN management and PN-weaning is that after TEN, the patient maintained stable electrolytes, remained adequately hydrated as assessed by urine output and positive enteral balance (≥500ml/d), and kept a stable body weight and body composition. After the patient was given TEN, nitrogen balance was again determined to ensure positive nitrogen retention. Patients who could not tolerate TEN were considered as HPN-dependent.

Intestinal absorption test and serum citrulline assay

Intestinal absorption was determined using a 5-hr urine D-xylose excretion and enteral nitrogen balance test as described previously.[5] D-xylose concentration was measured with high performance liquid chromatography (HPLC). For enteral nitrogen balance test, patients were fed with standard enteral formula (Peptisorb, with calorie 1.5 fold of REE) for 3 days. For each 24-hr period, stool volume was recorded. A sample of 2ml was taken for nitrogen determination. Enteral nitrogen balance was calculated as nitrogen in enteral intake not recovered in stool output. Serum citrulline concentrations were determined using HPLC.[5]

Home enteral nutrition and follow-up

When patients tolerated EN and the HCLF diet, they were discharged. On discharge, patients were taught to place the NG tube by themselves. For HEN administration, nocturnal continuous tube feeding were chosen by majority of the patients (n=41), during daytime they were orally supplemented with the peptide-based formula and small frequent HCLF diets; continuous tube feeding were chosen by 10 patients, while the other 10 chose sip feeding. One female patient with CD was given percutaneous endoscopic gastrotomy (PEG) on her 6^{th} admission.

Dietary and nutritional instructions were given to patients to avoid EN and SBS-associated complications. Oral glutamine (30g/d) was taken daily by all patients for at least 2 years.

Patients' survival time, daily usage of EN, nutritional status, and their general conditions were documented during follow-up. Nutrition assessments were evaluated during outpatient visits including anthropometric measurements, blood test, and intestinal absorption test. All the data from the last evaluation was collected within 6 months before the end of the study.

Tube-related complications, such as tube clotting, tube leakage, aspiration pneumonia, and SBS related complications, such as VB12 and mineral deficiency (defined as serum VB12, iron, copper, and zinc levels below normal range),[19] gallstones, kidney stones or renal insufficiency (defined as serum creatinine >133μmol/L),[20,21] end-stage renal disease (ESRD, defined by the need for long-term dialysis or renal transplantation),[13] and metabolic bone diseases (defined as osteopenia and decreased bone mineralization),[22] were all documented. The diagnosis of metabolic bone disease is made mainly on patient's clini-

Table 3. Clinical data of patients who could not be weaned off PN after intestinal rehabilitation therapy

Patient No.	Sex/age	Remnant Small Bowel (cm)	Type of SBS	Diagnosis	EN requirement (kcal/d)	History of SBS (m)	Follow-up period (m)	Current Status
1	M/74	40	II	SMI	500	8	32	Dead
2	M/56	15	III	Vovulus	750	18	56	Alive
3	F/45	15	III	Vovulus	500	12	25	Alive
4	M/52	25	II	SMI	500	37	47	Alive
5	M/54	30	II	SMI	500	6	28	Alive
6	F/61	20	II	SMI	750	7	34	Alive

SMI=superior mesenteric artery infarction.
History of SBS=months between extensive small bowel resection and first admission.

cal symptoms, as bone pain and tenderness, proximal myopathy, and the X-ray shows translucent bands in the medical femoral cortex, pubic ramus and scapula.[23]

Indications for repeated IRT

On follow-up, the patient should be re-admitted for IRT if one of the following symptoms developed: aggravation of diarrhea with a negative enteral balance, weight loss over 10% in recent 3 months, chronic fatigue or emaciation, or malnutrition related complications such as anemia or hypoalbuminemia.

Statistical Analysis

All data were analyzed by SPSS 13.0 statistical software (SPSS Inc). Quantitative data were analyzed with paired t-test. The chi-square test was used to compare differences for qualitative data between groups. A *p* value of <0.05 was considered as statistically significant.

RESULTS

General Outcome

The mean duration of TPN before EN was added was 18.14 ± 6.67 (7-30) days. Six patients could not be weaned off PN after IRT and were maintained on HPN and EN; their data were shown in table 3. The mean follow-up period was 50.34 ± 24.38 (24-130) months.

There were 3 deaths on follow-up, with an overall survival rate of 95.08% (58/61). Of the fatalities, a PN-dependent patient died of catheter-related sepsis (Table 3), one PN-free patient died of heart failure and pneumonia on the 5th year of follow-up, while the 4th patient had dietary abuse, his nutritional status quickly deteriorated and died of cachexia 3 years after discharge.

On last evaluation, 52 patients (85.24%) were weaned off PN. Among them, 47 patients depended on EN supplemented with a HCLF diet; their daily EN prescription was 821.0 ± 352.2 kcal/d, and EN comprised 52.56 ± 13.47% (range, 32.47-87.53%) of patients' daily calorie requirements.

Six patients were maintained on HPN plus EN. Besides the HPN-dependent 5 patients listed on table 3, the other is a 30-year male with 30cm small intestine (type III SBS) who received the first IRT 12 years after operation. At that time TEN could meet his nutritional requirement. Unfortunately, 3 years later he got end stage renal disease (ESRD) due to diffuse renal stone formation and received kidney transplantation, thereafter he could not be weaned off PN even after two episodes of aggressive IRT. Until now, he has been maintained on a combination of PN and EN for 6 years, and no intestinal failure associated liver disease (IFALD) developed.[24-26]

The minimal small bowel length for adult patients to be weaned from PN and maintained on EN was 25cm in type II and 15cm in type III SBS, respectively. Among the 19 patients with <60 cm small intestine in type II SBS and 12 patients with <35cm small intestine in type III SBS, TEN (or plus oral feeding) could be achieved in 77.42% (24/31) patients. A 25-year female with only 25cm jejunum (type II SBS) was weaned off PN and lived on EN plus oral feeding after IRT, and she delivered a daughter on the 7th year of follow-up.

Biomedical and anthropometric parameters

Patients' biochemical index, such as blood hemoglobin, plasma protein (including total protein, albumin, and pre-albumin) and lymphocytes counts, all increased markedly

Table 4. Biochemical parameters of patients at baseline, first discharge and last revision (n=57)

	Baseline	After First IRT	¶ p-Value	Last Evaluation	¶ p-Value
Hemoglobin (g/L)	100.30 ± 22.11	108.12 ± 15.43	0.009	107.33 ± 17.15	0.049
Total Protein (g/L)	58.32 ± 7.52	65.33 ± 5.31	0.004	63.23 ± 6.83	0.013
Albumin (g/l)	35.97 ± 8.23	39.12 ± 5.23	0.008	37.73 ± 5.33	0.033
Pre-albumin (mg/L)	147.53 ± 58.23	223.59 ± 58.15	0.001	196.12 ± 43.53	0.008
Transferrin (g/L)	2.13 ± 0.52	2.33 ± 0.41	0.468	2.22 ± 0.34	0.620
Fibronectin (mg/L)	143.12 ± 32.12	162.29 ± 45.58	0.037	145.12 ± 38.61	0.582
Lymphocytes (cells/mm3)	1896 ± 853	2256 ± 998	0.036	2216 ± 1034	0.048

Data are mean ± S.D. ¶.Compared with baseline
Baseline: Data acquired on the first 3 days after admission.
After First IRT: Data acquired before patients were discharged.

Table 5. Body mass index and bioelectric impedance analysis of SBS patients on baseline, after first IRT and on last evaluation

	Baseline	After First IRT	¶ p-Value	Last Evaluation	¶ p-Value
BMI (kg/m2) (n=58)	17.25 ± 1.70	18.24 ± 1.48	0.001	17.82 ± 1.45	0.001
Body weight (kg) (n=29)	49.38 ± 4.82	51.12 ± 4.51	0.003	50.74 ± 4.50	0.015
Lean Body Mass (kg) (n=29)	40.84 ± 3.91	42.54 ± 3.67	0.008	42.00 ± 3.44	0.012
Fat Free Mass (kg) (n=29)	8.53 ± 1.44	8.58 ± 1.51	0.358	8.74 ± 1.70	0.507
Total Body Water (kg) (n=29)	32.03 ± 3.06	33.23 ± 3.31	0.004	32.70 ± 3.14	0.048

Data are mean ± S.D. ¶.Compared with baseline.

Table 6. Intestinal absorptive capacity on baseline, after first intestinal rehabilitation therapy, and on last evaluation (n=41)

	Baseline	After first IRT	¶ p-Value	Last Evaluation	¶ p-Value
Enteral nitrogen balance (g/d)	+ 6.65 ± 1.74	+ 8.95 ± 1.42	0.008	+ 8.08 ± 1.53	0.008
Stool Frequency (/d)	3.48 ± 1.13	2.61 ± 0.81	0.004	2.52 ± 1.06	0.004
Stool Weight (g/d)	1452 ± 376	1028 ± 340	0.005	1175 ± 372	0.008
Urine D-Xylose excretion (%)	6.49 ± 4.85	8.51 ± 6.15	0.007	7.12 ± 5.83	0.028
Serum Citrulline (μmol/L)†	5.48 ± 2.18	6.23 ± 1.92	0.037	5.72 ± 1.86	0.154

Note: Enteral nitrogen balance represented the average value of three consecutive days.
Data are mean ± S.D. ¶.Compared with baseline. †n=21

after IRT and maintained high after long-term EN (Table 4). The anthropometric parameters, as body mass index (BMI), body weight (BW), lean body mass (LBM) also improved after IRT (Table 5), and remained increased on the last evaluation. Compared with baseline, intestinal absorptive capacity also improved after IRT and maintained at a better condition on last evaluation (Table 6). Serum citrulline, a marker for small intestinal enterocytes mass and absorption function, also increased after IRT (Table 6), but on follow-up, the increase was not significant (p=0.154, Table 6)

EN and Short Bowel Related-Complications

Diarrhea was the main complication in SBS patients receiving EN, and it was the direct reason for readmission in 10 patients for 30 times. Ten patients complained of abdominal bloating/distension, but none stopped EN because of this. No vomiting or nausea was recorded. Twenty patients reported at least one tube-related complication, such as tube clotting, tube leakage or tube displacement, and sinusitis. No aspiration pneumonia was detected. The patient given PEG reported tube leakage 1.5 years after placement and the tube was changed.

Short bowel syndrome related chronic complications were listed in Table 7. In 8 patients with renal calculi, 4 got renal insufficiency, and 2 eventually got ESRD. A male patient presented with several episodes of D-lactic acidosis and was successfully treated with intravenous bicarbonate, rehydration and oral antibiotics.[27]

Table 7. Chronic Complications of Adult Short Bowel Syndrome

Name of Complications	No. of patients
Vitamin and mineral deficiency	7
D-lactic acidosis	1
Gallstones	6
Renal calculi	8
Renal Insufficiency	2
End-stage Renal Disease (ESRD)	2
Metabolic bone disease	9

Note: Some patients have more than one SBS-related complications.

Repeated IRT

Repeated IRT was given to 14 patients for 45 times, among them the mean remnant small bowel length was 35.00 ± 12.90cm (15-80cm). In subgroup analysis, among 29 patients with remnant small bowel length ≥60cm in type II SBS and ≥35cm in type III SBS (group 1), 2 received repeated PN: one was a 68-year-old male with 80cm small intestine (Type II), who received his first IRT 11 years after small bowel resection, and received repeated treatment for 5 times; another is a girl with Crohn's disease and 60cm small intestine (Type III), and she received repeated IRT for 4 times; while for the other 23 patients with remaining small bowel <60cm in type II SBS and <35cm in type III SBS (group 2), repeated PN were given in 12 of them for 36 times. There is a significant difference in times of repeated IRT between 2 groups (p<0.01).

DISCUSSION

An important aspect in the current study is the incorporation of EN in the PN-weaning process during IRT treatment. Our results demonstrated that with proper EN strategy, weaning off PN could be achieved and long-term EN could meet the nutritional requirements in the majority of adult patients with a short bowel, even for ultra-SBS with only 20-30cm small intestine.

As proposed by Joly *et al*, continuous tube feeding of EN in both early and late postoperative period improves intestinal absorption in SBS patients compared with isocaloric normal oral diets.[28] The authors also suggested that tube feeding of EN could be used as a potentially effective medical therapy in IRT programs for SBS adult patients after the postoperative period. However, although this approach is routinely used in pediatric patients to increase enteral tolerance and autonomy,[29] in adults undergoing IRT, experience with tube feeding of EN during the PN-weaning process is scarce. In *Jinling* Hospital, we launched IRT for SBS in 1997. Initially, we used a HCLF diet after PN discontinued, but later found that oral feeding was not sufficient to provide adequate energy supply and wean patients off PN, therefore, continuous EN was used instead. To our knowledge, our study is the first to report the experience of tube feeding of EN in this population. Continuous feeding remained the primary choice for most (51/61) of the patients after discharge to maximize patient's absorptive capacity.

Traditionally, small bowel length at 60cm in type II SBS and 35cm in type III SBS were considered as the cut-off values for transient and permanent intestinal failure,[30,31] and patients with a residual bowel length below that level will require long-term PN nutrition even after aggressive treatment. In this study, over 75% of the patients with <60cm in SBS type II and <35cm in SBS type III remained off PN after the adaptive phase with proper EN management during and after IRT. Undisputedly, their intestinal tracts are more vulnerable compared with those with a longer remnant bowel, as indicated by the need for repeated IRT. Malnutrition could develop in some SBS patients even with TEN. If not treated properly, intestinal wall edema and malabsorption could worsen due to malnutrition, which may result in a "vicious cycle", causing rapid deterioration of the nutritional status. Once enteral nutrient absorption could not meet patient's requirement, the bowel should be rested and IRT was given again for better nitrogen retention. This mode (i.e. long-term EN plus intermittent repeated IRT) may alleviate the financial burden of patients and improve their quality of life.

For long-term usage, the formula of EN should be adjusted to avoid SBS-related chronic complications, especially diffuse kidney stone formation, which is difficult to manage and may eventually lead to kidney dysfunction. We used a high carbohydrate (69% of total energy), low fat (15% of total energy) elemental EN (455mOsmol/L) in this study. Compared with a low-carbohydrate, high-fat EN preparations, this HCLF formula may increase the possibility of osmotic diarrhea and small intestinal bacterial overgrowth (SIBO),[32,33] but for long-term use it would be helpful in decreasing oxalate absorption and subsequent kidney stone formation.[34] Tight dietary control is also important, and a low-fat, low-oxalate diet should be selected. Of 8 patients who got kidney stones, 4 had a "liberal" diet and 2 eventually got ESRD. Compared with polymeric formula, peptide-based preparations could be efficiently absorbed in the 100cm proximal small intestine and is therefore selected.[35]

Five patients could not be weaned off PN after IRT, for these patients, partial EN should be attempted. Because of the compartmentation of nutrients in splanchnic and systemic circulations, PN could not substitute for portohepatic nutrition in the maintenance of hepatic health and may cause IFALD, while even the duodenum is capable to digest and absorb significant quantities of protein and carbohydrate to "feed the liver".[36,37]

Citrulline, an amino acid not included in proteins and produced almost exclusively by small bowel enterocytes, is a candidate quantitative marker for intestinal enterocyte function.[38] Our previous data has demonstrated that increased serum citrulline levels in patients receiving IRT followed a trend of correlating with that of intestinal absorption and urine D-xylose excretion.[9] Other studies also revealed that IRT had a borderline effect on citrulline concentration.[39,40] In the current study, we illustrated that serum citrulline increased after IRT, and after the adaptation phase it is still elevated, although not significantly (p=0.154). Whether serum citrulline could be used as an indicator for intestinal adaption needs further large-scale studies.

The main limitation of the present study is the lack of a control group. Nonetheless, preliminary observations on clinical efficacy and safety are empirical for designing large, controlled trials. Furthermore, it is appropriate to mention here that the ratio for PN weaning after IRT in the study by Byrne *et al* and Wilmore *et al* was about 40% and 57%, respectively.[6,41,42] Therefore, the 85.24% (52/61) PN-weaning ratio in this study seemed to be higher than that of conventional therapies. The application of EN was the major factor explaining the differences. However, this assertion requires our admission that the effects seen in an uncontrolled trial need to be confirmed in large, randomized controlled studies. The influence of the cause for bowel resection should not be neglected, and it might also affect the outcome. In our study, the leading cause of bowel resection was small bowel volvulus, obstruction, or ischemic mesenteric disease, and a healthy bowel remained; while in previous studies, inflammatory bowel disease (primarily CD) and radiation enteritis comprised the majority of the cause, and the residual small bowel had a relative poor quality.[43] In addition, the mean interval between bowel resection and IRT was 18.49 months, which means that the majority of the patients undergoing IRT was still at the adaptive phase.[44] While this mean interval was 4 years in Byrne's study.[6,42] Actually, the remnant small bowel is still adaptable after PN-weaning in our study. On last evaluation, 5 patients weaned completely off both PN and EN and lived on a HCLF diet, indicating a further compensation of the remaining gut.

In conclusion, the present results suggest that with enteral nutrition management, weaning off parenteral nutrition could be achieved in a substantial percentage of adult short bowel patients after intestinal rehabilitation therapy. Although this is not a prospective randomized study, the outcomes indicates that the strategy may provide an alternative for adult patients who were once thought to have permanent intestinal failure with high probabilities of parenteral nutrition dependence, especially for those having <35cm small intestine with jejunoileocolic anastomosis and <60cm small intestine with jejunocolic anastomosis. Continuous enteral tube feeding is recommended for better enteral nutrition tolerance and enteral nutrient absorption in adult short bowel patients.

AUTHOR DISCLOSURES

GONG Jian-feng, ZHU Wei-ming, YU Wen-kui, LI Ning, LI Jie-shou, no conflicts of interest.

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Original Article

Role of enteral nutrition in adult short bowel syndrome undergoing intestinal rehabilitation: the long-term outcome

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成人短腸綜合症患者腸康復治療時腸道營養的應用和長期療效觀察

本研究目的在於評價成人短腸綜合症(SBS)患者在腸康復治療時應用腸道營養(EN)的價值和長期療效。回顧性分析61例成人SBS患者的資料，平均小腸長度47.95±19.37 cm。所有患者均予3週的腸康復治療(IRT)，包括重組的人生長激素(0.05 mg/kg/d)、穀氨醯胺(30 g/d)和聯合腸道營養和腸外營養(PN)支持，隨後以腸道營養或加上高醣低脂(HCLF)飲食長期維持。腸道營養是以連續性鼻胃管灌的方式給予。平均隨訪50.34±24.38個月，患者總體存活率為95.08%(58/61)。85.24%(52/61)的患者最終擺脫PN。其中小腸長度<35 cm的III型SBS(空腸-迴腸吻合)和<60cm的II型SBS(空腸-結腸吻合)中有77.42%(24/31)患者擺脫腸外營養。腸道營養提供患者52.56±13.47%的每日熱量需求。有5例患者，除腸道營養外同時需予在家PN支持。IRT結束後及最後一次隨訪時，患者營養狀態及體位指標、尿液5小時D-木糖排泄量和血清瓜氨酸水平，均較基礎值顯著改善。本研究的結果表明，在腸康復治療過程中和治療後採用合適的腸道營養支持策略，有相當一部分SBS患者可擺脫腸外營養，尤其是那些曾被認為是永久性腸衰竭的患者。推薦採用連續性管灌餵食作為腸道營養的通路，長期腸道營養支持可滿足多數成人SBS患者的每日營養需要量。

關鍵字：短腸綜合症、腸道營養、人生長激素、營養評價、隨訪研究