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• CLINICAL RESEARCH •

Effects of bowel rehabilitation and combined trophic therapy on intestinal adaptation in short bowel patients

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Abstract

AIM: To evaluate the effects of bowel rehabilitation and combined trophic therapy on intestinal adaptation in short bowel patients.

METHODS: Thirty-eight patients with severe short-bowel syndrome (SBS) were employed in the present study, whose average length of jejunum-ileum was 35.8±21.2 cm. The TPN treatment was initiated early to attain positive nitrogen balance and prevent severe weight loss. The TPN composition was designated to be individualized and altered when necessary. Enteral feeding was given as soon as possible after resection and increased gradually. Meals were distributed throughout the day. Eight patients received treatment of growth hormone (0.14 mg/kg.day) and glutamine (0.3 g/kg.day) for 3 weeks. D-xylose test, ^{15}N-Gly trace test and ^{13}C-palmitic acid breath test were done to determine the patients' absorption capability.

RESULTS: Thirty-three patients maintained well body weight and serum albumin concentration. The average time of follow-up for 33 survival patients was 5.9±4.3 years. Twenty-two patients weaned from TPN with an average TPN time of 9.5±6.6 months. Two patients, whose whole small bowel, ascending and transverse colon were resected received home TPN. An other 9 patients received parenteral or enteral nutritional support partly as well as oral diet. Three week rhGH+GLN therapy increased nutrients absorption but the effects were transient.

CONCLUSION: By rehabilitation therapy, most short bowel patients could wean from parenteral nutrition. Dietary manipulation is an integral part of the treatment of SBS. Treatment with growth hormone and glutamine may increase nutrients absorption but the effects are not sustained beyond the treatment period.

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INTRODUCTION

Short-bowel syndrome (SBS) is resulted from extensive small bowel resection due to infarction of the mesenteric vessels, intestinal volvulus, trauma, malignancy, or from complications of Crohn's disease, and is defined as the manifestations of signs, symptoms and complications associated with the inadequate absorptive surface area of functional bowel[1]. It is usually characterized by severe diarrhea, malabsorption, dehydration, electrolyte and metabolic disturbances, and progressive malnourishment.

The pathophysiological consequences following extensive intestinal resection depend on the length and site of resection and the extent of adaptation of the remaining intestine[2-4]. Patients often have to be supported with total parenteral nutrition (TPN) until maximal adaptation of the residual small bowel is complete. This process can take place for up to a year and sometimes longer. Certain patients may require lifelong TPN support depending on the length and health of the residual small bowel. TPN is associated with certain complications, which include catheter sepsis and liver failure[5-8]. It is therefore important for dietary management and pharmacological treatment in the short bowel patients hopefully to wean from TPN. Dietary management and some trophic factors are important in promoting intestinal adaptation after resection. The aim of the study was to define the role of bowel rehabilitation, trophic factors in intestinal adaptation in short bowel patients.

MATERIALS AND METHODS

Patients

Thirty-eight patients (28 men, 10 women; mean age 38.0±16.0 years, range 7-68 years) with severe short-bowel syndrome were eligible for this study. All patients had previously undergone extensive bowel resection for intestinal volvulus, mesenteric infarction or inflammatory bowel disease with or without colonic resection. The average length of jejunum-ileum, as determined from operative reports and confirmed by perioperative radiographs, was 35.8±21.2 cm (range, 0-110 cm) in all patients. Two patients had entire jejunum, ileum and right colon resected. The ileocecal valve and a portion of colon were resected in 13 patients, and 25 patients had intact colon (Table 1). The patients were clinically stable, and did not demonstrate evidence of infection, or extradigestive organ failure. In addition, they did not have a history of cancer. The protocol for the present study was approved by the Ethics Committee of Zhongshan Hospital.

Bowel rehabilitation

Clinical management Massive fluid and electrolyte losses were noted due to transient gastric hypersecretion and profound diarrhea during the initial postoperative periods. So, initial postoperative treatment was designed to maintain adequate fluid and electrolyte balance. TPN began early to attain positive nitrogen balance and to prevent severe weight loss. It should continue until the adaptive processes were complete or indefinitely, if clinically indicated. The composition of TPN was individualized and altered when necessary. Caloric requirements were delivered in accordance with the resting energy expenditure of patients, and it was reassessed often as the patient's clinical condition warranted. As the patient's oral

intake increased, the amount of TPN was reduced, the frequency of TPN was reduced to every other day in the first week, three times in the next week, and twice during the third week. If the patient lost 1 kg/week or more or if diarrhea exceeded 600 g/day or if laboratory abnormalities developed, then the patients were placed back on TPN. If the patient's eventual adaptation was insufficient to allow survival on oral/enteral feeding alone, the patients usually required lifelong TPN support.

Patients with SBS received at least some enteral feeding as soon as possible after resection. Usually this was administered for a postoperative period of 7-10 days. The ideal composition of enteral formulas for patients with SBS was also dependent upon the length of the small bowel and the presence of a colon. Originally, elemental and peptide based enteral formulas were favored for patients with SBS. Gradually, the diet with intact protein nutrient formulas and dietary fiber was given in accordance with the patients' need. Meals were distributed throughout the day.

Combined trophic therapy

Eight patients (4 males, 4 females, mean age 36±8 years) with severe SBS (mean jejunoileal length 44 cm, range 0 to 80 cm)

Table 1 Patient characteristics and status

Patient No.	Gender	Age(a)	Cause of resection	Jejunum-ileum(cm)	Colon	TPN(a)	Current status	Survival time(a)
1	F	28	Small bowel volvulus	0	ACR	17	HPN	17
2	M	7	Small bowel volvulus	0	ACR	7.6	HPN	7.6
3	M	41	Small bowel volvulus	35	All	0.8	Normal oral diet	13.5
4	M	61	SMA thrombosis	30	All	1.6	Died	2.2
5	M	62	SMA thrombosis	30	All	2.0	Died	2.6
6	M	33	Small bowel volvulus	28	All	1.2	Normal oral diet	14.4
7	M	24	Small bowel volvulus	18	All	1.8	PN+EN	1.8
8	M	35	Small bowel volvulus	45	All	0.5	Died	6.2
9	F	52	Small bowel volvulus	55	ICV(-)	0.3	Died	7.4
10	F	68	SMA thrombosis	70	ICV(-)	0.6	Normal oral diet	9.5
11	F	44	Small bowel obstruction	100	All	0.2	Normal oral diet	9.6
12	M	22	Crohn's disease	80	ICV(-)	0.5	Normal oral diet	12.2
13	M	15	Small bowel volvulus	20	ICV(-)	5.2	Died	5.4
14	M	50	Small bowel obstruction	60	ICV(-)	1.2	Normal oral diet	9.0
15	F	42	Small bowel volvulus	28	All	2.2	PN+oral diet	8.5
16	F	44	Small bowel volvulus	35	ICV(-)	1.0	Normal oral diet	10.8
17	M	59	Small bowel volvulus	30	All	1.2	Normal oral diet	6.4
18	F	50	SMA thrombosis	60	ICV(-)	0.4	Normal oral diet	5.4
19	M	55	SMA thrombosis	40	ICV(-)	1.0	Normal oral diet	7.6
20	M	56	Small bowel volvulus	30	All	0.8	PN+oral diet	4.5
21	M	26	Small bowel volvulus	30	All	1.0	Normal oral diet	8.8
22	M	40	Small bowel obstruction	50	ICV(-)	0.6	Normal oral diet	6.0
23	M	16	Small bowel volvulus	30	All	1.5	Normal oral diet	12.5
24	M	28	Small bowel volvulus	30	All	2.0	Normal oral diet	5.5
25	M	57	SMA thrombosis	45	All	0.3	Normal oral diet	6.5
26	M	34	Crohn's disease	60	All	0.5	Normal oral diet	4.0
27	M	41	Crohn's disease	70	All	0.4	Normal oral diet	2.0
28	M	30	Small bowel volvulus	40	All	0.2	Normal oral diet	1.8
29	M	62	SMA thrombosis	50	ICV(-)	0.8	EN+ oral diet	1.6
30	F	45	Small bowel volvulus	30	All	0.5	EN+ oral diet	1.5
31	M	18	Small bowel volvulus	30	All	0.4	Normal oral diet	2.0
32	M	20	Small bowel volvulus	30	All	0.5	Normal oral diet	2.0
33	M	16	Small bowel volvulus	20	All	1.0	EN+ oral diet	1.5
34	M	36	Small bowel volvulus	30	All	0.4	EN+ oral diet	1.2
35	M	18	Small bowel volvulus	18	All	0.6	HPN+ oral diet	2.6
36	F	46	SMA thrombosis	40	ICV(-)	0.5	EN+ oral diet	0.5
37	M	32	Small bowel volvulus	35	All	0.3	Normal oral diet	1.8
38	F	30	Small bowel volvulus	30	All	0.2	Normal oral diet	1.0
Mean		38±16		35.8±21.2		9.5±6.6		5.9±4.3

ACR=ascending colon resection, ICV(-)=without ileal cecal valve, HPN=home parenteral nutrition, PN=parenteral nutrition, EN=enteral nutrition, a=year.

Table 2 Absorption capability of patients before and after treatment with GH+GLN

	Baseline	End of therapy	One week after therapy
D-xylose test (%)	5.4±2.1	7.6±1.8[a]	6.0±2.0[b]
^{15}N-Gly trace test (%)	62.4±14.2	73.2±15.3[a]	58.4±11.8[b]
^{13}C-palmitic acid breath test (%)	55.3±8.8	64.5±11.2[a]	62.6±10.4[b]

Values are mean ±SEM, [a]$P<0.05$ *vs* baseline, [b]$P>0.05$ *vs* baseline.

who previously adapted to the provision of TPN and enteral feedings were admitted for 0.8±0.5 years in the study after surgical resection. The first week served as a control period when nutritional (parenteral and enteral) and medical managements were delivered as the routine therapy. Thereafter, the patients who received treatment of subcutaneous recombinant human growth hormone (rhGH) (0.14 mg/kg.day; Saizen, Serono Co., Switzerland) were divided into two daily injections, intravenous alanyl-glutamine solution (0.3 g/kg.day, Dipeptiven, Fresenius Co., Germany) was delivered daily for 3 weeks. D-xylose test, ^{15}N-Gly trace test and ^{13}C-palmitic acid breath test were done respectively before, at the end of therapy and one week after treatment to determine the patients' absorption capability.

Statistical analysis

Data were analyzed using standard statistical software (SPSS 10.0). For normally distributed data, a paired Student' s *t* test was used for statistical analysis. A probability value less than or equal to 0.05 was considered statistically significant. Data are expressed as mean ±SEM.

RESULTS

Thirty-eight patients were admitted and received nutritional support and rehabilitation therapy, among them 2 died of severe malnutrition 2 years after treatment because they failed to receive nutritional therapy, 2 died of accidental event, 1 died of liver failure 5 years later. Thirty-three patients maintained well body weight and serum albumin concentration. The average time of follow-up for 33 survival patients was 5.9±4.3 years (range, 0.5-17 years). Twenty-two patients weaned from TPN, their average TPN time was 9.5±6.6 months. They maintained their nutritional status well on normal oral diet. Two patients, whose whole small bowel, ascending and transverse colon were resected received home TPN. An other 9 patients received parenteral or enteral nutritional support partly as well as oral diet (Table 1). Eight patients developed gall bladder stones. Cholecystectomy was performed for three patients.

For the eight patients, the 3 week rhGH+GLN therapy resulted in weight gain, and stool output dramatically decreased. Three patients weaned from TPN completely after the treatment period, 3 patients reduced TPN requirements, and 2 patients failed the therapy. The absorption capability of D-xylose, ^{15}N-Gly and ^{13}C-palmitic acid in these SBS patients was much lower than normal level. After 3 week rhGH+GLN therapy, the absorption capability of D-xylose, ^{15}N-Gly and ^{13}C-palmitic acid improved. However, it dropped to the level of baseline at one week after treatment (Table 2).

DISCUSSION

After extensive resection of the small intestine, the remaining bowel, to some degree, had a significant adaptation response to resection. Bowel adaptation, characterized by epithelial hyperplasia and increase in villus diameter, height, and crypt depth, occurred weeks to months after resection[9-11]. Various nutritional and medical therapies can be tried to improve bowel absorptive capacity. TPN is the most important factor responsible for prolonging the lives of patients with SBS. In the initial stages after massive resection of bowel, TPN should begin early to attain positive nitrogen balance and to prevent severe weight loss[12,13]. TPN has been shown to greatly increase the chances of long-term survival. It should be delivered until the adaptive processes were complete or indefinitely, if clinically indicated[14]. This process can take place for up to a year and sometimes longer. Long-term TPN resulted in small bowel mucosa atrophy and was associated with certain complications, such as catheter sepsis and liver failure[15]. So, oral diet is encouraged, if there is any absorptive capacity of the remaining bowel, bowel adaptation should be promoted. An enteral tube feeding might be used to supplement the diet in an effort to wean patients from TPN[16]. At first, diluted solutions of chemically defined diets containing simple amino acids and short-chain peptides were offered. Gradually, the diet with intact protein nutrient formulas and dietary fiber was given in accordance with the patients' need. The parenteral supply had to be adjusted according to the oral intake. As the patient' s oral intake increased, the amount of TPN was reduced, the frequency of TPN was reduced to every other day for 1 week, three times in the next week, and twice during the third week or weaned from TPN at last[17]. If the patient lost or more 1 kg/week of body weight or more, if diarrhea exceeded 600 g/day or if laboratory abnormalities developed, then the patients were placed back on TPN[18]. In our group, 22 patients weaned from TPN among the 33 survived patients after receiving rehabilitation therapy. They maintained their nutritional status well on normal oral diet. It indicated that rehabilitation therapy for SBS played important roles in the intestinal adaptation.

Combination of glutamine, human recombinant growth hormone has been shown to influence bowel adaptation[19-24]. The study by Byrne *et al*[25,26] indicated that at one year of follow-up 40 % of treated patients were able to reduce or discontinue parenteral nutrition. Patients in the study were also receiving other medical therapy, including medications known to slow down intestinal motility and oral rehydration solutions. It is not clear whether glutamine, growth hormone, diet, or other factors contributed to the favorable outcome. It did not necessarily mean that fluid and nutrients absorption was increased because absorptive studies were not performed. Szkudlarek *et al*[27] reported in a randomized control study of eight short-bowel patients the combination of growth hormone and glutamine for 28 days did not result in a significant increase in fluid or nutrient absorption. In our clinical trial, we used D-xylose test, ^{15}N-Gly trace test and ^{13}C-palmitic acid breath test to determine the patients' nutrient absorption capability. The results showed that the absorption of carbohydrates (from 5.4 % to 7.6 %), protein (from 62.4 % to 73.2 %) and fat (from 55.3 % to 64.5 %) increased. Weight gain was observed and stool output dramatically decreased. Three patients weaned from TPN completely after the treatment period and 3 patients reduced TPN requirements. However, the absorption capability dropped to the level of baseline at one week after treatment. We found that the treatment with growth hormone and glutamine might increase absorption of nutrients but the effect seemed to be transient with no long term improvement in gut function when treatment was discontinued. This has been supported by recent clinical studies[28-30].

In conclusion, by rehabilitation therapy, most short bowel patients could wean from parenteral nutrition. Dietary manipulation is an integral part of the treatment of SBS. Treatment with growth hormone and glutamine may increase nutrients absorption but the effects are not sustained beyond the treatment period. Therapeutic efficacy can be achieved only when the treatment plan is tailored to meet individual need.

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