Int J Clin Exp Med 2015;8(8):13937-13945
www.ijcem.com /ISSN:1940-5901/IJCEM0009709

Original Article

Early enteral nutrition in combination with parenteral nutrition in elderly patients after surgery due to gastrointestinal cancer

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Received April 29, 2015; Accepted June 23, 2015; Epub August 15, 2015; Published August 30, 2015

Abstract: Objective: To evaluate the therapeutic effects of nutritional support via different routes in elderly patients after surgery for gastrointestinal (GI) cancer. Methods: 105 patients with GI cancer were randomly divided into early enteral nutrition (EEN) group (n = 35), total parenteral nutrition (TPN) group (n = 35) and EN+PN group (n = 35). Results: The nutrition status and immunity were significantly compromised in all patients, while the liver function was improved at 3 days after surgery as compared to those before surgery. At 7 days after surgery, they returned to preoperative level. The nutrition status was comparable among 3 groups at 3 and 7 days after surgery ($P > 0.05$). ALT, AST, ALP and GGT in TNP group were significantly higher than those in EEN group and EN+PN group ($P < 0.05$), whereas there was no significant difference in the liver function between EEN group and EN+PN group ($P > 0.05$). The CD3+ cells, CD4+ cells and CD4/CD8 in EEN group and EN+PN group were significantly higher than those in TPN group ($P < 0.05$), but significant difference was not observed between EEN group and EN+PN group ($P > 0.05$). The NK cells in EN+PN group were significantly higher than in TPN group ($P < 0.01$). The incidence of diarrhea in EEN group was significantly higher than in TPN group and EN+PN group ($P < 0.05$). Conclusion: EN+PN is superior to EEN alone and TPN alone in the old patients with GI cancer in reducing the postoperative complications, improving the immunity and decreasing the hospital stay.

Keywords: Gastric cancer, colorectal cancer, enteral nutrition, parenteral nutrition

Introduction

Gastrointestinal (GI) cancer is one of the most common malignancies in China and its incidence is increasing over year. It has been reported that about 70% of patients with GI cancer may develop malnutrition [1], which is more serious in old patients because they have compromised physiology, poor responses to stresses, poor nutrient absorption, insufficient nutrient intake [2, 3]. In addition, surgery may cause stress, resulting in glucose metabolic disorder and negative nitrogen balance. In addition, 3-4 days of postoperative fasting is recommended after GI surgery in Asia and Europe, which is often accompanied by decompression of the stomach and the administration of a large amount of intravenous fluid [4, 5]. However, prolonged postoperative starvation further jeopardizes malnutrition. Of note, it is usually difficult to conduct nutrition support before surgery in patients with GI cancer. Thus, post-operative nutrition support becomes an important strategy to improve the nutrition status of GI cancer patients after surgery.

Traditionally, the post-operative nutrition support is administered by the parenteral route (total parenteral nutrition, TPN). TPN has definite therapeutic efficacy and can be used in a majority of patients, but it may cause some adverse effects such as intestinal mucosal atrophy and intestinal bacterial translocation. In recent years, randomized controlled trials and meta-analyses have concluded that postoperative early enteral nutrition (EEN) reduces postoperative morbidity (especially infectious complications), mortality, and hospital stay without increasing the risk of GI-related complications [6, 7]. Actually, postoperative EEN is

Table 1. General information of patients in different groups before surgery

Group	Age (year)	MNA score	Body weight (kg)	Hb (g/L)	TP (g/L)	ALB (g/L)
EEN	66.7 ± 7.2	15 ± 9	57.7 ± 8.4	90.51 ± 24.87	53.4 ± 4.5	30.5 ± 2.9
TPN	66.1 ± 8.1	16 ± 8	57.2 ± 6.3	91.24 ± 25.11	52.8 ± 5.1	29.4 ± 3.2
EN+PN	67.2 ± 7.9	15 ± 9	56.4 ± 7.9	89.79 ± 23.72	53.1 ± 5.6	29.7 ± 3.7

Table 2. Complications of patients in different groups

Variables	EEN group	TPN group	EN+PN group	$X^2$1 group	$X^2$2 group	$X^2$3 group
Abdominal pain	6	5	7	0.108	0.094	0.402
Abdominal distention	2	1	1	0.348	0.348	0
Diarrhea	10	2	3	6.741**	4.899	0.215*
Vomitting	4	1	2	1.938	0.729	0.348
Nausea	1	0	0	1.014	0.014	-
Infection	4	12	3	5.185*	0.159	6.873**
Anastomotic leakage	0	0	0	-	-	-

Note: $X^2$1: between EEN group and TPN group; $X^2$2: between EEN group and EN+PN group; $X^2$3: between TPN group and EN+PN group; *P < 0.05; **P < 0.01.

Table 3. Time to anal exhaust, duration of fever and duration of hospitalization

Variables	EN group	PN group	EN+PN group	t1	t2	t3
Time to anal exhaust (h)	36 ± 12	62 ± 11	42 ± 15	9.45**	1.85	6.36**
Duration of fever (d)	4.5 ± 1.9	7.3 ± 3.6	4.1 ± 2.0	3.05**	2.35*	4.60**
Duration of hospitalization (d)	13.8 ± 2.4	17.2 ± 3.6	13.1 ± 2.7	4.65**	1.15	5.39**

Note: t1: between EEN group and TPN group; t2: between EEN group and EN+PN group; t3: between TPN group and EN+PN group. *P < 0.05; **P < 0.01.

considered one of the most important multimodal approaches in the context of enhancing postoperative recovery. However, few studies have been conducted to investigate the therapeutic efficacy of EEN in combination with PN in old patients receiving surgery for GI cancer.

In this study, EEN and/or TPN was administered in old patients undergoing surgery for GI cancer and their therapeutic efficacy was compared, aiming to explore an optimal protocol for the post-operative nutrition support for the old patients with GI cancer.

Materials and methods

Subjects

Inclusion criteria: Patients aged 60-85 years and receiving surgery due to GI cancer were recruited into present study. Mini Nutrition Assessment (MNA) scale was employed for the evaluation of nutrition status. *Exclusion criteria*: Patients had pathologically proved non-GI cancer; patients died within 1 week after surgery; patients had severe kidney, liver, heart and lung dysfunction or metabolic diseases (such as diabetes mellitus) before surgery; patients had complete intestinal obstruction or extensive intestinal adhesion; patients had severe abdominal infection, peritonitis or ascites; patients received emergency surgery.

Grouping

A total of 105 hospitalized patients were recruited from the Department of General Surgery between February 2008 to March 2010 They were pathologically diagnosed with GI cancer and received surgical intervention. These patients were randomly assigned into 3 groups: EEN+PN group (n = 35; 23 males and 12 females), EEN group (n = 35; 22 males and 13 females) and TPN group (n = 35; 23 males and 12 females). There were no marked differences in the age, gender, MNA score, and serum protein among three groups (P > 0.05) (**Table 1**).

Pre-operative nutrition support

Oral Peptisorb (Nutricia, Netherlands) was administered at 7.5 g/kg/d (equivalent to 30

Table 4. Nutrition status of patients before and after surgery

Groups		BW (kg)	TSF (mm)	Hb	TP	ALB	PA	TRF
EEN group	1 d before surgery	57.7 ± 8.4	7.9 ± 1.4	90.51 ± 24.87	53.4 ± 4.5	30.5 ± 8.9	212 ± 31.5	1.96 ± 0.46
	3 d after surgery	53.6 ± 7.9*	6.1 ± 1.7**	77.62 ± 23.57*	46.82 ± 9.8**	26.1 ± 5.1*	188 ± 38.7*	1.61 ± 0.53**
	7 d after surgery	55.1 ± 9.2	7.1 ± 1.5*	82.83 ± 22.46	49.51 ± 12.1	28.2 ± 7.5	209 ± 40.1	1.62 ± 0.65*
TPN group	1 d before surgery	57.2 ± 6.3	8.0 ± 2.0	91.24 ± 25.11	52.8 ± 8.1	29.4 ± 6.3	207 ± 32.6	1.91 ± 0.59
	3 d after surgery	52.7 ± 7.5*	6.3 ± 1.9**	78.49 ± 23.59*	47.82 ± 8.9*	26.2 ± 5.2*	190 ± 37.5*	1.55 ± 0.68*
	7 d after surgery	54.4 ± 8.2	7.4 ± 1.6	81.78 ± 24.62	50.63 ± 7.2	28.9 ± 6.9	208.6 ± 30.9	1.59 ± 0.74*
EN+PN group	1 d before surgery	56.9 ± 7.9	8.1 ± 1.5	89.79 ± 23.72	53.1 ± 10.6	29.7 ± 6.7	214 ± 36.7	1.88 ± 0.31
	3 d after surgery	53.2 ± 6.1*	6.4 ± 2.2**	76.29 ± 25.83*	46.91 ± 8.2**	25.9 ± 7.1*	192 ± 32.8*	1.59 ± 0.42**
	7 d after surgery	55.2 ± 8.6	7.2 ± 1.7*	79.78 ± 24.81	50.24 ± 6.9	29.4 ± 5.8	210 ± 41.6	1.62 ± 0.63*

Note: *P < 0.05, **P < 0.01: 3 and 7 days after surgery vs 1 day before surgery.

kcal/kg/d) for 3 days before surgery, which was stopped on the day of surgery.

Post-operative nutrition support

In TPN group, TPN was administered for 7 days via the central or peripheral venous tube. Non-protein calories administered were 30 kcal/kg/d (glucose to lipid ratio: 60%: 40%). The insulin was given at 1 U per 4 g glucose on the first day and thereafter its dose was adjusted according to the urine glucose. The nitrogen amount was 0.2 g/kg/d, and long-chain fatty emulsion (20% Intralipid) and Compound Amino Acid Injection were administered. The fluid (30 ml/kg.d), electrolytes and vitamins were supplemented according to the body weight (SINO-SWED Pharmaceutical Corp. Ltd).

In EEN group, Peptisorb (100 kcal/100 ml) was administered via the nasal tube, and oral Peptisorb was given once anal exhaust was confirmed. In brief, 1/4 of energy was administered on the first day via EN route, 1/2 of energy on the second day via EN route and total energy on days 3-7 via EN route. During the nutrition support, the remaining energy required was given via PN route.

In EEN+PN group, normal saline (500 ml) was administered on the post-operative day 1 via nasal tube and energy given via PN route; 1/8, 1/4 and 1/2 of energy was given via EN route on days 2, 3 and 4, respectively; total energy was administered via EN route on days 5-7. During the nutrition support, the remaining energy required was given via PN route.

Clinical observations

Abdominal pain, abdominal distension, diarrhea, nausea, vomiting, time of anal exhaust, duration of hospitalization, wound infection, pulmonary infection, anastomotic leakage and duration of fever were recorded.

Evaluation of nutrition status

Blood was collected before surgery and at 3 and 7 days after surgery. Hemoglobin (Hb), total protein (TP), albumin (ALB), prealbumin (PA) and transferring (TRF) were measured. Moreover, body weight (BW) and triceps skin fold (TSF) were also detected before and at 7 days after surgery.

Biochemical examination

Before and at 3 and 7 days after surgery, blood was collected, and alanine aminotransferase (ALT), aspartate aminotransferase (ALP), glutamyl endopeptidase (GGT), total bilirubin (TBIL), direct bilirubin (DBIL) and creatinine (Cr) were measured.

Evaluation of immunity

Before and at 3 and 7 days after surgery, blood was collected, lymphocytes were counted with an automatic blood cell analyzer, and CD3+ cells, CD4+ cells, and CD8+ cells were determined by flow cytometry, followed by calculation of CD4+ cells to CD8+ cells ratio.

Statistical analysis

Statistical analysis was performed with SPSS version 13.0. Quantitative data are expressed as means ± standard deviation and compared with t test. Qualitative data are expressed as percentages and compared with chi square test. A value of $P < 0.05$ was considered statistically significant.

Table 5. Biochemical parameters of patients in different groups before and after surgery

Groups	ALT (U/L)	AST (U/L)	ALP (U/L)	GGT (U/L)	TBIL (μmol/L)	DBIL (μmol/L)	CRE (μmol/L)
EEN group							
1 d before surgery	16.35 ± 6.26	24.87 ± 7.62	63.88 ± 17.82	19.53 ± 14.02	11.21 ± 4.58	3.56 ± 1.41	65.91 ± 23.32
3 d after surgery	22.41 ± 14.25*	29.64 ± 10.59*	70.75 ± 36.21	42.85 ± 21.53**	12.35 ± 5.20	4.15 ± 2.12	88.23 ± 24.60**
7 d after surgery	18.37 ± 10.39	25.71 ± 12.78	74.51 ± 36.68	37.29 ± 19.81**	11.95 ± 4.98	4.22 ± 2.87	84.36 ± 25.1**
TPN group							
1 d before surgery	17.15 ± 8.12	23.99 ± 8.69	65.43 ± 18.17	18.92 ± 16.07	10.59 ± 5.08	4.05 ± 1.76	67.14 ± 19.82
3 d after surgery	35.45 ± 20.28**	47.72 ± 20.61**	96.74 ± 40.25**	61.82 ± 38.19**	15.74 ± 9.82**	4.11 ± 2.51	90.25 ± 23.67**
7 d after surgery	38.28 ± 24.61**	44.18 ± 17.96**	89.62 ± 34.58**	67.69 ± 40.27**	14.86 ± 8.67*	3.99 ± 2.04	87.94 ± 26.41**
EN+PN group							
1 d before surgery	16.82 ± 8.52	25.01 ± 7.55	64.29 ± 15.73	20.24 ± 15.91	11.08 ± 5.37	3.87 ± 1.92	63.59 ± 22.54
3 d after surgery	27.19 ± 11.25**	31.28 ± 11.52*	72.51 ± 26.37	45.69 ± 28.52**	13.82 ± 5.94*	3.99 ± 2.11	87.59 ± 23.65**
7 d after surgery	20.64 ± 9.87	27.88 ± 13.75	60.49 ± 24.58	40.61 ± 26.79**	13.57 ± 6.59	3.69 ± 1.82	84.32 ± 20.89**

Note: *P < 0.05, **P < 0.01, 3 and 7 days after surgery vs 1 day before surgery.

Table 6. Immune parameters of patients in 3 groups before and after surgery

Groups	Lymphocytes ($\times 10^9$/L)	CD3 (%)	CD4 (%)	CD8 (%)	CD4/CD8	NK cells (%)
EEN group						
1 d before surgery	1.58 ± 0.61	59.6 ± 8.5	39.5 ± 4.8	23.7 ± 6.7	1.67 ± 0.57	15.8 ± 3.9
3 d after surgery	1.24 ± 0.33**	52.1 ± 6.4**	25.6 ± 7.2**	17.6 ± 5.8**	1.45 ± 0.67	12.3 ± 3.2**
7 d after surgery	1.41 ± 0.36	57.4 ± 5.2	38.9 ± 5.1	22.6 ± 3.1	1.72 ± 0.20	13.9 ± 4.7
TPN group						
1 d before surgery	1.60 ± 0.72	60.4 ± 7.9	40.1 ± 5.2	24.2 ± 7.1	1.66 ± 0.63	15.1 ± 5.2
3 d after surgery	1.22 ± 0.41**	51.9 ± 8.1**	27.1 ± 6.6**	18.9 ± 6.9**	1.43 ± 0.64	11.3 ± 4.7**
7 d after surgery	1.33 ± 0.38	54.2 ± 6.3**	32.3 ± 4.7**	20.2 ± 5.3	1.60 ± 0.25	12.6 ± 3.6*
EN+PN group						
1 d before surgery	1.59 ± 0.58	58.4 ± 6.9	39.8 ± 4.9	23.5 ± 6.4	1.69 ± 0.58	14.9 ± 3.8
3 d after surgery	1.23 ± 0.36**	52.7 ± 6.8**	26.4 ± 5.3**	18.3 ± 8.0**	1.44 ± 0.77	11.9 ± 4.5**
7 d after surgery	1.61 ± 0.21	59.1 ± 7.3	40.3 ± 6.1	24.5 ± 6.7	1.79 ± 0.39	15.9 ± 3.3

Note: *P < 0.05, **P < 0.01: 3 and 7 days after surgery vs 1 day before surgery.

Results

Clinical observations

All the patients completed this study, and severe complications such as acute intestinal obstruction and anastomotic leakage were not present in these patients. Diarrhea of different extents was observed in 10 patients of EEN group, 2 patients of TPN group and 3 patients of EN+PN group. The incidence of diarrhea was significantly higher in EEN group than that in TPN group and EN+PN group ($P < 0.05$), but comparable between TPN group and EN+PN group ($P > 0.05$). In addition, mild abdominal pain, abdominal distension, nausea and vomiting were found in some patients at 1 and 2 days after surgery in three groups, and there were no marked differences in these symptoms among three groups ($P > 0.05$). In TPN group, 12 patients developed infection which occurred at 3-8 days after surgery; all of them had respiratory infection, and concomitant wound infection was found in 1 patient. In EEN group, 4 patients developed infection including 3 with respiratory infection and 1 with wound infection, which occurred at 3-5 days after surgery. In EN+PN group, all the 3 patients had respiratory infection. The incidence of infection in TPN group was significantly higher than in EEN group and EN+PN group ($P < 0.05$). Three patients developed fever of different extents, and the duration of fever in EEN group and EN+PN group was markedly shorter than in TPN group ($P < 0.05$), and the duration of fever in EN+PN group was also significantly shorter

than in EEN group (P < 0.05). Furthermore, the time to recovery of intestinal function in EEN group and EN+PN group dramatically reduced when compared with TPN group (P < 0.01). The hospital stay in EEN group and EN+PN group was also markedly shorter than in TPN group (P < 0.01), but there was no significant difference between EEN group and EN+PN group (P > 0.05) (**Tables 2** and **3**).

Nutrition status

Intragroup comparisons: The BW, TSF, Hb, TP, ALB, PA and TRF reduced significantly at 3 days after surgery as compared to those before surgery (P < 0.05). At 8 days after surgery, they increased slightly, but were still lower than those before surgery, and significant differences were observed in TSF and TRF (P < 0.05 vs before surgery), but BW, Hb, TP, ALB and PA were comparable to those before surgery (P > 0.05) (**Table 4**).

Intergroup comparisons: The nutrition status was comparable among three groups before surgery (P > 0.05). The highest and lowest reduction was found in EEN group and TPN group, respectively, at 3 days after surgery, but there were no marked differences in the nutrition status (P > 0.05). At 7 days after surgery, the nutrition status returned to pre-operative level (P > 0.05).

Biochemical indicators

Intragroup comparisons: At 3 days after surgery, ALT, AST, ALP and GGT increased to different extents in EEN group as compared to those before surgery, and marked differences were observed in ALT, AST and GGT (P < 0.05). At 7 days after surgery, ALT, AST and GGT reduced to different extents as compared to those at 3 days after surgery, ALT and AST returned to pre-operative level (P > 0.05), but GGT was still markedly higher than the pre-operative level (P < 0.01). At 3 and 7 days after surgery, ALP, TBIL and DBIL were comparable to those before surgery (P > 0.05), and serum Cr was still markedly higher than that before surgery (P < 0.01). In TPN group, ALT, AST, ALP, GGT, TBIL and Cr at 3 and 7 days after surgery were dramatically higher than those before surgery (P < 0.05), but they remained unchanged at 3 and 7 days after surgery (P > 0.05). In EN+PN group, TBIL at 3 days after surgery was significantly higher than that before surgery, and the changes in other parameters were similar to those in EEN group (**Table 5**).

Intergroup comparisons: The liver function was comparable among three groups at 1 day before surgery. At 3 and 7 days after surgery, the liver function in TNP group was better than in EEN group and EN+PN group, and ALT, AST, ALP and GGT were significantly improved in TNP group when compared with EEN group and EN+PN group (P < 0.05). The liver function was comparable between EEN group and EN+PN group after surgery (P > 0.05).

Immune parameters

Intragroup comparisons: At 1 day after surgery, CD3+ cells, CD4+ cells, CD8+ cells and NK cells reduced markedly as compared to the pre-operative levels (P < 0.01); at 7 days after surgery, these cells in EEN group and EN+PN group increased markedly, but were comparable to those before surgery (P > 0.05). In TPN group, these cells also increased to different extents, and the total lymphocytes, CD8+ cells and CD4/CD8 were similar to those before surgery (P > 0.05), but CD3+ cells, CD4+ cells and NK cells were still markedly lower than those before surgery (P < 0.01 or P < 0.05). CD4/CD8 in TPN group reduced slightly as compared to the pre-operative level and no significant difference was observed (P > 0.05) (**Table 6**).

Intergroup comparisons: At 1 day before surgery, total lymphocytes and lymphocyte subsets were similar among three groups (P > 0.05). At 1 day after surgery, total lymphocytes, CD3+ cells, CD4+ cells, CD8+ cells, CD4/CD8 and NK cells reduced to different extents, but comparable among three groups (P > 0.05). At 7 days after surgery, total lymphocytes in EEN group and EN+PN group were markedly higher than those in TPN group, and these cells in EN+PN group were also markedly higher than those in EEN group (P < 0.05 and P < 0.01). CD3+ cells, CD4+ cells and CD4/CD8 significantly increased in EEN group when compared with TPN group (P < 0.05), but were comparable between EEN group and EN+PN group (P > 0.05). NK cells in EN+PN group were dramatically higher than those in EEN group and TPN group (P < 0.01).

Discussion

Malnutrition to a degree in patients receiving surgery is associated with changes and impairments in body composition, tissue wasting, muscle strength, wound healing, and immunity

[8]. Generally, patients undergoing GI surgery have a high risk for malnutrition due to anorexia, dietary restriction, malabsorption, increased intestinal losses, or altered nutrient requirement peri-operatively, and preoperative malnutrition of patients with GI malignancies has been found to increase the postoperative complications, infections, and mortality, prolong the duration of hospital stay, and elevate the hospital costs. However, it is generally difficult to improve the malnutrition due to multiple factors.

The nutrition support can be administered via enteral and parenteral routes. The traditional view was that the oral intake of fluids or nutrients be reserved until postoperative ileus has resolved. Nevertheless, studies demonstrate that postoperative oral intake restriction is not based on scientific evidence. In recent years, some clinical studies and guidelines strongly recommend the use of EN in the critically ill and surgical patients due to a lower infection rate or shorter duration of hospital stay with accompanying cost savings. EN is considered to be better than conventional PN because it is less expensive, safer, more physiologic, and maintains the nutritional, metabolic, immunological, and barrier function of the intestines in critically ill and surgical patients [9]. It is recommended that patients with a functioning GI tract are often unable to tolerate oral intake after surgery, EN is recommended within 1-2 days after surgery in severely malnourished patients, 3-5 days in moderately malnourished patients, and 7 days in normally or over-nourished patients. For patients who are unable to receive adequate EN because of GI insufficiency, administration of PN is life-saving [6].

However, EN may cause some adverse effects such as nausea, abdominal distension, abdominal pain and diarrhea. Especially, in old patients, the functional recovery of gastrointestinal tract is relatively slow and EN alone is insufficient to provide enough energy. Thus, it is imperative to optimize the nutrition support for the old patients after surgery for GI cancer. In the present study, EN and/or PN were administered in old patients who received surgery due to GI cancer, and clinical symptoms, nutrition status, biochemical parameters and immune parameters were employed to compare the therapeutic efficacy of nutrition support via different routes.

Influence of different regimens for nutrition support on the post-operative GI function

Patients may develop gastrointestinal paralysis of different extents soon after surgery due to the anesthesia and surgery induced stress. Traditionally, the recovery of GI function requires 2-3 days for patients receiving abdominal surgery, and oral intake of fluid or nutrients is administered once anal exhaust is present. Especially, in patients undergoing GI surgery, the time to oral intake and the amount of nutrients are strictly controlled considering the anastomotic healing. Available studies confirm that GI function begins to recover at 12 h after surgery and returns to normal at 24-48 h after surgery, but the absorptive function of the intestine may completely recover within several hours after surgery [10]. There is evidence showing that early enteral nutrients may stimulate the secretion of digestives and endocrine hormones, increase the visceral blood flow and promote the intestinal mucosal growth and the recovery of intestinal peristalsis [11]. In the present study, the time to anal exhaust in EEN group and EN+PN group was earlier than in TPN group, and anastomotic leakage was not observed in three groups. This suggests that post-operative EN may not increase the anastomotic complications, but improve the recovery of GI function.

The advantages of EEN after surgery have been confirmed in numerous studies. However, the intestinal absorption and digestion vary at different peri-operative stages in old patients with GI cancer, and EEN alone usually fails to meet the peri-operative requirement for nutrients. Chen et al found 36 out of 120 GI cancer patients receiving EEN (30%) showed intolerance, of whom 6 withdraw from the study [12]. In the present study, results showed some patients developed symptoms such as abdominal distension, abdominal pain and nausea, which had similar incidences among three groups ($P > 0.05$). One patient in EEN group developed vomitting, which was not observed in TPN group and EN+PN group, showing no significant difference ($P > 0.05$). In addition, 10 patients (28.57%) in EEN group developed diarrhea, and this incidence was significantly higher than that in TPN group and EN+PN group ($P < 0.05$). This suggests that the recovery of GI function is slow after surgery in the old patients with GI cancer, the tolerance to EEN varies

among individuals, and EEN alone may not meet the requirement for nutrients of all the patients. The incidence of GI adverse effects in EN+PN group was significantly lower than in EEN group, and the time to recovery of GI function in EN+PN group was also earlier than in TPN group, but similar to that in EEN group. This indicates that EN+PN is better for the post-operative recovery of GI function of old patients with GI cancer.

Influence of nutrition support via different routes on the post-operative liver and kidney function

The metabolic hormones involved in the occurrence and development of GI cancer together with the surgical trauma may increase the protein catabolism, which facilitates the energy consumption, lead to a hypercatabolic status and increase the work load of the liver and kidney. In the present study, results showed ALT, AST, ALP, GGT and CRE increased significantly at 3 days after surgery in 3 groups as compared to those before surgery ($P < 0.05$ or $P < 0.01$), but they reduced to different extents at 7 days after surgery. The reduction in EEN group and EN+PN group was earlier than in TPN group, and the post-operative liver and kidney function was comparable between EEN group and EN+PN group ($P > 0.05$). This may be explained as follows [13-16]: (1) EEN may improve the intestinal blood flow after stress, improve the ischemia/reperfusion injury, promote the recovery of GI function and attenuate the acute inflammation and hypercatabolism; (2) EEN may improve the blood flow of portal vein as well as the enterohepatic circulation; (3) Long term fasting, bacterial translocation, excess energy and nutrients, and insufficiency of some nutrients (such as choline and glutamine) may induce parenteral nutrition associated liver disease (PNALD). Our results demonstrate that both EEN and EN+PN are able to improve the liver and kidney function after surgery induced stress, which is better than TPN alone.

Influence of nutrition support via different routes on the post-operative immunity and nutrition status

The nutrition status is influenced by multiple factors in the old patients with GI cancer. Old patients usually show the degeneration of some organs and have some chronic diseases, which together with cancer invasion and surgical trauma makes the malnutrition more severe. Furthermore, malnutrition further compromise the defense against stress, wound healing and immune function, which are important factors cause post-operative infection and organ dysfunction [17]. Although TPN may improve the nutrition status to a certain extent, long term TPN alone may cause intestinal mucosal atrophy and intestinal bacterial infections, or even inhibit the cellular immunity [18]. Our results showed the nutrition status and immunity were significantly compromised at 3 days after surgery in 3 groups as compared to those before surgery ($P < 0.05$), and there were no significant differences among these groups ($P > 0.05$). On post-operative day 7, the immunity of EEN group and EN+PN group returned to pre-operative level, but the immunity in TPN group was still lower than that before surgery. In EN+PN group, the CD3+ cells, CD4+ cells and CD4/CD8 were markedly higher than in TPN group ($P < 0.05$); in EN+PN group, total lymphocytes and NK cells were dramatically higher than those in EEN group and TPN group ($P < 0.05$). These findings suggest that EEN alone and EN+PN block the surgery induced vicious cycle and the nutrition status returns to normal at 7 days after surgery; EN+PN is better than EEN and TPN in promoting the recovery of immunity, and the recovery of immunity is the slowest if TPN alone is administered.

Clinical efficacy of nutrition support via different routes

The goal of nutrition support is to maintain the metabolism of cells, organs and tissues, assure their normal functions in the regulation of physiological processes, facilitate the tissue repair, promote patients' rehabilitation and reduce medical cost. Braunschweig et al [19] summarized studies on the nutrition support in patients with malnutrition, and they found the mortality of patients without nutrition support was significantly higher than that of patients receiving PN, and the incidence of infection in EN treated patients was markedly lower than in PN treated patients. In the present study, results showed the post-operative incidence of infection in TPN group was dramatically higher than in EEN group and EN+PN group, and the duration of fever in TPN group was also markedly longer than in later two groups. In addition, Chen et al

[12] also revealed that EP treated patients had shorter hospital stay and reduced medical cost as compared to PN treated patients. Our results showed patients in EN+PN group had the shortest hospital stay, but the hospital stay in EN+PN group and EEN group was significantly shorter than that in TPN group ($P < 0.01$), and there was no marked difference between EN+PN group and EEN group ($P > 0.05$). This suggests that EEN alone and EN+PN may reduce the post-operative incidence of complications (including infection), promote the recovery and reduce the medical cost in old patients with GI cancer.

Taken together, our results demonstrate that EEN alone and EN+PN have similar capabilities to improve the post-operative nutrition status and liver and kidney function in old patients with GI cancer, and their efficacy is better than that of EEN alone. In addition, EN+PN is more suitable to the GI tract of old patients, and thus may cause low incidence of GI adverse effects. On the basis of our findings, EN in combination with PN is a better strategy for the nutrition support for old patients receiving surgery for GI cancer.

Acknowledgements

This study was supported by the Innovation Key Project of Health System in Putuo District, Shanghai (PTKW08-B02).

Disclosure of conflict of interest

None.

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