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BRIEF ARTICLE

Effect of early enteral combined with parenteral nutrition in patients undergoing pancreaticoduodenectomy

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Abstract

AIM: To investigate the effect of early enteral nutrition (EEN) combined with parenteral nutritional support in patients undergoing pancreaticoduodenectomy (PD).

METHODS: From January 2006, all patients were given EEN combined with parenteral nutrition (PN) (EEN/PN group, n = 107), while patients prior to this date were given total parenteral nutrition (TPN) (TPN group, n = 67). Venous blood samples were obtained for a nutrition-associated assessment and liver function tests on the day before surgery and 6 d after surgery. The assessment of clinical outcome was based on postoperative complications. Follow-up for infectious and noninfectious complications was carried out for 30 d after hospital discharge. Readmission within 30 d after discharge was also recorded.

RESULTS: Compared with the TPN group, a significant decrease in prealbumin (PAB) (P = 0.023) was seen in the EEN/PN group. Total bilirubin (TB), direct bilirubin (DB) and lactate dehydrogenase (LDH) were significantly decreased on day 6 in the EEN/PN group (P = 0.006, 0.004 and 0.032, respectively). The rate of grade Ⅰ complications, grade Ⅱ complications and the length of postoperative hospital stay in the EEN/PN group were significantly decreased (P = 0.036, 0.028 and 0.021, respectively), and no hospital mortality was observed in our study. Compared with the TPN group (58.2%), the rate of infectious complications in the EEN/PN group (39.3%) was significantly decreased (P = 0.042). Eleven cases of delayed gastric emptying were noted in the TPN group, and 6 cases in the EEN/PN group. The rate of delayed gastric emptying and hyperglycemia was significantly reduced in the EEN/PN group (P = 0.031 and P = 0.040, respectively).

CONCLUSION: Early enteral combined with PN can greatly improve liver function, reduce infectious complications and delayed gastric emptying, and shorten postoperative hospital stay in patients undergoing PD.

Key words: Enteral nutrition; Parenteral nutrition; Pancreaticoduodenectomy; Complications; Metabolism

Core tip: On the basis of our experience and the findings of previous studies, we investigated the effect of early enteral nutrition combined with parenteral nutritional support in patients undergoing pancreaticoduodenectomy enrolled in a retrospective controlled clinical trial. The results of this study showed that early enteral nutritional support combined with parenteral nutrition can greatly improve nutritional status and liver function, decrease the incidence of infectious complications and delayed gastric emptying, and shorten the length

of postoperative hospital stay.

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INTRODUCTION

Pancreaticoduodenectomy (PD) is currently considered the treatment of choice for carcinoma of the periampullary region. Patients who are candidates for PD often have associated comorbidities such as diabetes, jaundice, and protein-energy malnutrition. PD results in loss of the gastric pacemaker and a partial pancreatic resection, and the physiologic consequence of this is a high incidence of postoperative malnutrition. PD is associated with a high incidence of postoperative complications, and this high rate of complications is likely to be multifactorial and may include overall nutritional debilitation[1]. Postoperative nutritional support therapy could ameliorate the clinical outcome in many types of surgical treatment, diminish the incidence of postoperative complications, and may be important in patients undergoing PD.

Recent research has shown that early postoperative enteral nutrition (EN) enhanced immunocompetence, decreased clinical infection rates, maintained gut structure and function, and can potentially attenuate catabolic stress responses in patients after surgery[2,3]. In addition, EN is believed to be safer and less expensive than parenteral nutrition (PN). However, postoperative total enteral feeding is associated with complications such as diarrhea, abdominal distention, and abdominal cramps. These symptoms worsen with increasing caloric intake and can lead to discontinuance of enteral feeding[2,4]. Gastroparesis is a frequent postoperative event following PD resection, and this often necessitates prolonged gastric decompression and enteral nutritional support[5]. Clinical data on postoperative early enteral nutrition (EEN) after PD are very limited. Therefore, on the basis of our experience and the findings of previous studies, we investigated the effect of EEN combined with parenteral nutritional support in patients undergoing PD enrolled in a retrospective controlled clinical trial.

MATERIALS AND METHODS

Patient selection

From January 2004 to June 2011, 196 patients underwent PD due to peri-ampullary tumors in the Department of Hepatobiliary Surgery at the Affiliated Drum Tower Hospital of Medical School of Nanjing University, China, where the authors work. Nineteen patients with manifest metabolic diseases (*e.g.*, diabetes mellitus and hyperthyroidism), severe hemorrhagic disease, ongoing infection, inflammatory bowel diseases or severe renal abnormality were excluded. Three patients with a history of gastric or pancreatic resection were also excluded, given the possible influence this procedure may have on the incidence of delayed gastric emptying. From January 2006, all patients were given EEN combined with PN (EEN/PN group, n = 107), while patients prior to this date were given TPN (TPN group, n = 67).

The primary endpoint of this study was the occurrence of major complications, and the secondary endpoint was 30 d after hospital discharge. The Nutrition Risk Screening 2002 (NRS 2002) scoring system[6] was used in this study, and the post-operative NRS 2002 score in all patients was $\geqslant$ 3, indicating that all patients required nutritional support.

Treatment

TPN was given 24 h/d for 5 d from the first day after PD. The nitrogen intake was 0.25 g/kg body weight per day, caloric intake was 125.4 kJ/kg per day and lipid intake was 1.1 g/kg per day. The nonprotein calories were given as dextrose (5.0 g/kg per day) and fat emulsion in a ratio of 2:1. The source of lipids was the standard lipid emulsion (20% emulsion, 5.5 mL/kg per day, long chain triglycerides: medium chain triglycerides 1:1, Huarui Pharmaceuticals, Jiangsu Province, China). Patients received 1.5 g amino acids/kg per day, administered as a commercially available compound amino acid solution (20% solution, Huarui Pharmaceuticals, Jiangsu Province, China). The proportion of nonprotein calories with nitrogen in both groups was 501.6 kJ/g. The PN solutions were prepared by a clinical pharmacist under aseptic conditions and adjusted to the weight of each patient. The amino acids, fat emulsion and dextrose mixture with electrolytes, vitamins and trace elements were administered *via* a central venous catheter. As soon as bowel function returned on 3-4 d after surgery, all patients were given liquid carbohydrate and cow's milk protein in equal amounts orally.

The surgical treatment was standardized, and lymphnode dissection was performed according to the definition provided by Pedrazzoli *et al*[7]. PD was performed by three groups of surgeons using the same technique. All patients received the same antibiotics postoperatively.

Patients in the EEN/PN group underwent preoperative placement of a conventional gastric tube. When gastrojejunostomy was complete, nasojejunal nutrition tubes were positioned (10 F, NUTRICIA Pharmaceutical Co., The Netherlands) from the nasal cavity to the output loops of the jejunum (approximately 20-25 cm with the help of a surgeon). The jejunum nutrition tube filar guide was then removed when the tube was in the correct position.

EN was given to patients in the EEN/PN group 24 h/d. An infusion of 100 mL of 5% glucose and sodium chloride injection (GNS) *via* a nasojejunal feeding tube was commenced within 24 h of surgery and 500 mL of 5% GNS was given on post-operative day 2 (POD2). On

Table 1 Ranges and averages of calories, protein, fat and carbohydrates in the enteral and parenteral regimens in the early enteral nutrition/parenteral nutrition group

POD	Nutritional support	Calories (kJ)	Protein (g)	Fat (g)	Carbohydrates (g)
1	PN	7649.4 (6081.9-10282.8)	91.5 (72.8-123.0)	67.1 (53.3-90.2)	305.0 (242.5-410.0)
	EN	83.6	0	0	5
2	PN	7649.4 (6081.9-10282.8)	91.5 (72.8-123.0)	67.1 (53.3-90.2)	305.0 (242.5-410.0)
	EN	418	0	0	25
3	PN	6447.6 (4880.1-9081.0)	84.0 (65.3-115.5)	59.6 (45.8-82.7)	257.5 (195.0-362.5)
	EN	1201.8	7.5	7.5	47.5
4	PN	5559.4 (3991.9-8192.8)	76.5 (57.8-108.0)	52.1 (38.3-75.2)	235.0 (172.5-340.0)
	EN	2090	15	15	70
5	PN	3469.0 (1901.9-6102.8)	61.5 (42.8-93.0)	37.1 (23.3-60.2)	165.0 (102.5-270.0)
	EN	4180	30	30	140
6	PN	0	0	0	0
	EN	7649.4 (6081.9-10282.8)	54.9 (43.65-73.8)	54.9 (43.65-73.8)	256.2 (203.7-344.4)

Data are expressed as absolute average or average (range). POD: Post-operation day; PN: Parenteral nutrition; EN: Enteral nutrition.

POD3, 250 mL of Peptisorb liquid (2092 kJ/500 mL, NUTRICIA Pharmaceutical Co., the Netherlands) and 250 mL of 5% GNS were administered. Patients received 500 mL of Peptisorb liquid on POD4, and 1000 mL on POD5. From POD3, the PN recipe was adjusted according to the amount of EN, and the total caloric intake of PN and EN was 125.4 kJ/kg per day. PN was stopped on POD6, and patients in the EEN/PN group reached a maximum volume of total caloric intake following Peptisorb liquid (30 mL/kg per day). Oral intake started on POD7 and EN was stopped when the patients tolerated an intake of over 1000 kcal/d.

The body weight of the patients in this study varied from 48.1-84.6 kg, with an average body weight of 60.3 kg. Based on the range and average body weight, the ranges and averages of the calories, protein, fat and carbohydrates in the enteral and parenteral regimens in the EEN/PN group are listed in Table 1.

Assessment

Venous heparin blood samples were obtained on 1 d (the day before surgery), and 6 d after surgery. Three types of measurement were carried out. First, a nutrition-associated assessment was carried out, which included serum albumin, prealbumin (PAB), total protein (TP), transferrin (TF) and total lymphocyte counts (TLCs). Serum albumin, PAB, total protein and TF were determined by an automatic biochemistry analyzer (HITACHI 7600, Hitachi Co., Tokyo, Japan). TLCs were determined using an automatic blood cell analyzer (COULTER STKS). The prognostic nutritional index (PNI) was calculated as follows: PNI = 0.005 × TLC (10^6/L) + albumin (g/L). The normal value of PNI is more than 50, and PNI values < 40 indicated malnutrition. Nitrogen balance was calculated as follows: N balance (g N/d) = [protein intake (g/d)/6.25] - [urinary urea (g/24 h)/2.14 + 3 g (nitrogen lost in skin and stool per day)]. Second, a liver function assessment was carried out, which included serum total bilirubin (TB), direct bilirubin (DB), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) measurements. Liver function was determined by an automatic biochemistry analyzer (HITACHI 7600). Finally, clinical outcome was assessed based on postoperative complications. These complications were graded according to the Clavien-Dindo classification[8], which was validated in pancreatic surgery[9]. Complications graded as Ⅲ to Ⅴ were considered as major. Pancreatic fistula and delayed gastric emptying were defined according to the International Study Group of Pancreatic Surgery (ISGPS)[10,11]. Operative mortality was defined as in-hospital death or death occurring within 30 d of discharge. Follow-up for infectious and noninfectious complications was carried out for 30 d after hospital discharge. Readmission within 30 d after discharge was also recorded.

Statistical analysis

The results are expressed as mean ± SD. Data were analyzed using the Statistical Analysis System (SAS). Differences between means were evaluated using the Student *t* test when normal distribution was confirmed by the Shapiro-Wilks test. When the hypothesis of normal distribution was rejected, differences between groups were tested by nonparametric statistics using the Mann-Whitney test for unpaired samples and Wilcoxon criteria for paired samples. Fisher's exact test was used for analysis of categorical values when appropriate. A P value of < 0.05 was considered significant.

RESULTS

A total of 174 patients were enrolled in the study, 67 patients in the TPN group and 107 patients in the EEN/PN group. The mean age of the subjects was 53.2 years (range, 37-68 years). Demographic and preoperative clinical data, including age, sex, preoperative hemoglobin, preoperative albumin and the number of patients with jaundice or preoperative endoscopic nasal biliary drainage, are summarized in Table 2. No significant differences with respect to intraoperative factors, including opera-

Table 2 Preoperative clinical data, intraoperative factors and histopathology of the patients enrolled in the study

	TPN group	EEN/PN group
Sex (male/female)	44/23	70/37
Age (yr)	52. 8 ± 11.2	53.9 ± 10.6
Intraoperative factors		
Patients with jaundice (%)	79.1	83.2
Patients with preoperative ENBD (%)	50.7	48.6
Preoperative hemoglobin (g/L)	11.8 ± 1.0	12.4 ± 0.8
Preoperative albumin (g/L)	37.9 ± 3.1	36.8 ± 3.6
Duration of surgery (min)	345.1 ± 64.8	332.7 ± 56.6
Operative blood loss (mL)	648.4 ± 262.6	680.2 ± 193.7
Blood transfusion (%)	26.9	31.7
Histopathologic finding (*n*)		
Pancreatic head carcinoma	24	37
Distal cholangiocarcinoma	19	31
Periampullary adenocarcinoma	21	34
Duodenal adenocarcinoma	3	5

EEN: Early enteral nutrition; ENBD: Endoscopic nasal biliary drainage; PN: Prognostic nutritional; TPN: Total parenteral nutrition.

tion time, blood loss, number of patients who received blood transfusion and histopathological diagnosis, were observed between the two groups ($P > 0.05$).

Nutrition-associated assessment

No significant difference in the pre-operative nutrition-associated assessment was seen between the two groups. Compared with the results on the day before PD, a decrease in TP, PAB, TF and PNI was observed on day 6 after PD in all patients in this study, and a significant decrease in PAB in the TPN group ($P < 0.05$) with no significant difference ($P > 0.05$) in the EEN/PN group (Table 3).

Compared with the TPN group, a significant decrease in PAB ($P = 0.02$) was seen in the EEN/PN group. However, no significant differences in TF, TP and PNI were noted between the two groups ($P > 0.05$). Nitrogen balance was negative in both groups on day 6, with no significant difference between the two groups (Table 3).

Liver function assessment

No significant differences in pre-operative liver function assessment were seen between the two groups. Compared with the results on the day before surgery, a significant decrease in ALT, AST, TB, DB and LDH was observed on 6 d in both groups ($P < 0.05$), and a very significant decrease in TB and DB in the EEN/PN group ($P < 0.01$).

Compared with the TPN group, a significant decrease in TB, DB and LDH was seen in the EEN/PN group ($P < 0.05$). No significant differences in ALT and AST were observed between the two groups ($P > 0.05$; Table 4).

Clinical outcome

A prognostic score for major morbidity after PD has recently been proposed by Braga *et al*[12]. The predictive risk score of major complications after PD in the two groups are listed in Table 5. There were no significant differences between the two groups in the score categorized in 4 risk classes ($P > 0.05$).

Table 6 shows the postoperative outcome in the two groups. Reoperation was necessary in 9 patients, and the causes of reoperation were early bleeding (1 case in the TPN group and 2 cases in the EEN/PN group), late bleeding (1 case in the EEN/PN group), abdominal abscess (2 cases in the TPN group and 2 cases in the EEN/PN group) and intestinal obstruction (1 case in the EEN/PN group). The causes of readmission in this study were intestinal obstruction (1 case in the TPN group and 2 cases in the EEN/PN group) and cholangitis (1 case in the TPN group and 1 case in the EEN/PN group). The rate of grade Ⅰ complications, grade Ⅱ complications and the length of postoperative hospital stay in the EEN/PN group were significantly reduced ($P < 0.05$), and no hospital mortality was observed in this study (Table 6).

Postoperative complications are shown in detail in Table 7. There were 39 cases of infectious complications in the TPN group (8 cases of pneumonia, 7 cases of abdominal abscess, 5 cases of bile leak, 2 cases of pancreatic fistula, 4 cases of cholangitis, 8 cases of wound infection and 5 cases of urinary tract infection) and 42 cases in the EEN/PN group (6 cases of pneumonia, 6 cases of abdominal abscess, 7 cases of bile leak, 4 cases of pancreatic fistula, 3 cases of cholangitis, 10 cases of wound infection and 6 cases of urinary tract infection). Compared with the TPN group (58.2%), the rate of infectious complications in the EEN/PN group (39.3%) was significantly decreased ($P < 0.05$). Eleven cases of delayed gastric emptying were observed in the TPN group, and 6 cases in the EEN/PN group. The rate of delayed gastric emptying and hyperglycemia was significantly decreased in the EEN/PN group ($P < 0.05$). There were 29 cases of enteral-feeding-related complications in the EEN/PN group, including diarrhea, abdominal distention, and abdominal cramps. These symptoms were alleviated by slowing down the speed of enteral transfusion or by the administration of medications. None of the patients discontinued enteral feeding, and no enteral-feeding-related complications were noted in the TPN group.

DISCUSSION

PD is associated with a high incidence of postoperative complications, and an overall morbidity rate of 48% can be anticipated at major centers[13]. The high rate of complications is likely to be multifactorial and may include overall nutritional debilitation, as most patients with periampullary tumors present with significant weight loss due to anorexia and malabsorption, and are expected to have a period of inadequate oral intake up to 10 d after surgery[14]. Compared with the results on the day before PD, a decrease in TP, PAB, TF, PNI and negative nitrogen balance were observed on day 6 in all patients in this study. Perioperative nutritional support can be beneficial in these patients in that it may reduce mortality and morbidity, and the length of hospital stay[15].

Numerous studies have suggested that EN has sev-

Table 3 Comparison of nutrition-associated assessment in the two groups (mean ± SD)

	Normal value	Group	Day 1	Day 6	Decrease (days 1-6)
TP (g/L)	62-85	TPN	63.46 ± 7.24	59.92 ± 7.65	3.54 ± 1.72
		EEN/PN	64.11 ± 6.84	61.12 ± 6.83	2.99 ± 1.07
PAB (mg/L)	0-800	TPN	196.25 ± 64.32	116.52 ± 72.16[a]	79.73 ± 35.32
		EEN/PN	190.15 ± 62.18	158.32 ± 62.46	31.83 ± 13.15[c]
TF (g/L)	2.2-12	TPN	2.53 ± 0.76	2.20 ± 0.72	0.33 ± 0.61
		EEN/PN	2.46 ± 0.68	2.08 ± 0.81	0.38 ± 0.72
PNI	> 50	TPN	50.36 ± 9.14	43.12 ± 8.13	7.24 ± 7.40
		EEN/PN	51.62 ± 8.16	45.15 ± 9.52	6.47 ± 5.93
N-balance (g/d)		TPN	/	-(14.76 ± 6.03)	/
		EEN/PN	/	-(15.91 ± 7.85)	/

[a]P < 0.05 *vs* day 1; [c]P < 0.05 *vs* total parenteral nutrition (TPN) group. PAB: Prealbumin; PNI: Prognostic nutritional index; TP: Total protein; TF: Transferrin; EEN: Early enteral nutrition; PN: Parenteral nutrition.

Table 4 Comparison of liver function in the two groups (mean ± SD)

	Normal value	Group	Day 1	Day 6	Decrease (days 6-1)
ALT (μ/L)	5-40	TPN	138.2 ± 48.4	82.5 ± 42.3[a]	55.7 ± 31.5
		EEN/PN	145.1 ± 39.2	77.4 ± 37.6[a]	67.7 ± 36.2
AST (μ/L)	8-40	TPN	97.6 ± 36.2	55.1 ± 31.5[a]	42.5 ± 26.2
		EEN/PN	102.3 ± 41.3	63.2 ± 36.3[a]	39.1 ± 22.0
TB (μmol/L)	5-20.5	TPN	112.5 ± 37.5	66.2 ± 29.4[a]	46.3 ± 34.3
		EEN/PN	106.8 ± 36.2	41.5 ± 34.1[b]	65.3 ± 36.2[c]
DB (μmol/L)	1.7-6.8	TPN	78.6 ± 30.2	38.1 ± 26.2[a]	40.5 ± 21.3
		EEN/PN	81.7 ± 35.6	22.4 ± 16.2[b]	59.3 ± 28.1[c]
LDH (μ/L)	109-245	TPN	332.6 ± 89.4	264.3 ± 101.3[a]	68.3 ± 51.2
		EEN/PN	316.2 ± 98.1	211.5 ± 86.2[a]	104.7 ± 76.8[c]

[a]P < 0.05, [b]P < 0.01 *vs* day 1; [c]P < 0.05 *vs* total parenteral nutrition (TPN) group. PN: Prognostic nutritional; EEN: Early enteral nutrition; TB: Total bilirubin.

Table 5 Predictive risk score of major complications after pancreaticoduodenectomy in the two groups

Predictor	Categories	Risk Score	TPN group	EEN/PN group
Pancreatic texture (%)	Hard	0	43	73
	Soft	4	24	34
Pancreatic duct diameter (%)	> 3 mm	0	48	81
	≤ 3 mm	1	19	26
Operative blood loss (%)	< 700 mL	0	55	81
	≥ 700 mL	4	12	26
ASA score (%)	Ⅰ	0	31	55
	Ⅱ	2	33	47
	Ⅲ	6	3	5
Score categorized in 4 risk classes *n* (%)	0-3		23 (34.3)	38 (35.5)
	4-7		22 (32.8)	33 (30.8)
	8-11		19 (28.4)	31 (29.0)
	12-15		3 (4.5)	5 (4.7)

ASA: American Society of Anesthesiologist; EEN: Early enteral nutrition; TPN: Total parenteral nutrition; PN: Prognostic nutritional.

Table 6 Postoperative outcome in the two groups *n* (%)

Group	TPN group	EEN/PN group
Complication Grade		
No complications	24 (35.8)	42 (39.2)
Ⅰ	33 (49.3)	38 (35.5)[a]
Ⅱ	38 (56.7)	42 (39.3)[a]
Ⅲa	7 (10.4)	10 (9.3)
Ⅲb	4 (6.0)	5 (4.6)
Ⅳa	0 (0.0)	0 (0.0)
Ⅳb	0 (0.0)	0 (0.0)
Ⅴ (mortality)	0 (0.0)	0 (0.0)
Reoperation	3 (4.5)	6 (5.6)
Readmission	2 (3.0)	3 (2.8)
Postoperative hospital stay (d)	16.8 ± 6.2	13.2 ± 4.7[a]

Numbers of single types of complications do not add up to the number of patients within the 2 groups, due to the possible occurrence of more types of complications in some patients. [a]P < 0.05 *vs* total parenteral nutrition (TPN) group. EEN: Early enteral nutrition; PN: Prognostic nutritional.

eral advantages over TPN. Early enteral feeding was shown to reduce postoperative septic complications in a meta-analysis of 8 prospective randomized trials, and improve glucose tolerance, protein kinetics and wound healing. Furthermore, EN is safer and less expensive than PN[16,17]. However, postoperative total enteral feeding is associated with complications such as diarrhea, abdominal distention, and abdominal cramps. These symptoms worsen with increasing caloric intake and can lead to discontinuance of enteral feeding[2,3]. On the basis of these findings, we considered EEN combined with PN to be a better mode of postoperative nutritional support than total enteral feeding. On the first three days after surgery in this study, the amount of EN increased slowly to avoid severe gastrointestinal complications. Twenty-

Table 7 Postoperative complications in the two groups *n* (%)

Complications	TPN group	EEN/PN group
Pancreatic fistula	2 (3.0)	4 (3.7)
Grade A	0 (0.0)	0 (0.0)
Grade B	2 (3.0)	4 (3.7)
Grade C	0 (0.0)	0 (0.0)
Wound infection	8 (11.9)	10 (9.3)
Abdominal abscess	7 (10.4)	6 (5.6)
Bile leak	5 (7.5)	7 (6.5)
Cholangitis	4 (6.0)	3 (2.8)
Urinary tract infection	5 (7.5)	6 (5.6)
Pneumonia	8 (11.9)	6 (5.6)
Catheter-related sepsis	0 (0.0)	0 (0.0)
Gastrointestinal bleeding	4 (6.0)	5 (4.7)
Intraperitoneal bleeding	3 (4.5)	6 (5.6)
Delayed gastric emptying	11 (16.4)	6 (5.6)
Enteral-feeding-related complications	0 (0.0)	29 (27.1)
Abdominal cramps	0 (0.0)	6 (5.6)
Abdominal distention	0 (0.0)	11 (10.3)
Diarrhea	0 (0.0)	9 (8.4)
Vomiting	0 (0.0)	3 (2.8)
Hyperglycemia	12 (17.9)	6 (5.6)

Numbers of single types of complications do not add up to the number of patients within the 2 groups, due to the possible occurrence of more types of complications in some patients. EEN: Early enteral nutrition; PN: prognostic nutritional; TPN: Total parenteral nutrition.

nine cases in the EEN/PN group had enteral-feeding-related complications, these symptoms were alleviated by slowing down the speed of enteral transfusion or by the administration of medications, and none of the patients discontinued enteral feeding or dropped out of the study. PAB, which is more sensitive than albumin for evaluating protein synthesis in the liver due to its shorter half-life, was decreased on day 6 in all patients in this study. Compared with the TPN group, a significant decrease in PAB ($P < 0.05$) was observed in the EEN/PN group.

Changes in transaminase and bilirubin are the most important indices for evaluating liver function in patients after PD. All patients in this study underwent PD to remove biliary obstruction, therefore, ALT, AST, TB, DB and LDH were significantly reduced. Lack of enteral feeding has several metabolic and endocrine consequences on intestinal and liver function. Experimental studies have shown that the fasted state reduces the secretion of several gastrointestinal hormones, such as cholecystokinin, gastrin and peptide YY. These hormones are instrumental in stimulating bile flow and gallbladder contraction, and for maintaining intestinal motility[18-20]. EN can also stimulate hepatic circulation and ameliorate liver function[21]. In the present study, a significant decrease in TB and DB in the EEN/PN group was observed compared with that in the TPN group.

EN preserved the gut flora architecture, prevented gastrointestinal mucosa atrophy, and inhibited microbial translocation from the gut to the blood stream[22,23]. Compared with the TPN group, the rate of infectious complication in the EEN/PN group was significantly decreased. The reduced length of postoperative hospital stay in the EEN/PN group indicated that the time to complete recovery could be shortened by EEN support combined with PN. This may be explained by the lower number of complications.

Delayed gastric emptying (DGE) is also known as "gastroparesis". DGE is not a fatal complication, but sometimes results in a significant prolongation of hospital stay and increased hospital costs. DGE has been reported to be affected by several factors including gastric dysrhythmias due to intra-abdominal complications, gastric atony after duodenal resection in response to a reduction in motilin levels, pylorospasm secondary to vagotomy, and angulation of the reconstructed alimentary tract[24-26]. Eleven cases of DGE were observed in the TPN group, and 6 cases in the EEN/PN group. EEN-support therapy significantly decreased the rate of DGE. One potential mechanism for the decreased rate of DGE due to EN may be the mechanical effects caused by the nasojejunal tube or simply its presence across the anastomosis, which stimulates the motility of the stomach and jejunum, while another mechanism may be the stimulation of bowel movements by the input of nutritional liquids[27,28].

In conclusion, we have shown that early enteral nutritional support combined with PN can greatly improve nutritional status and liver function, decrease the incidence of infectious complications and delayed gastric emptying, and shorten postoperative hospital stay in patients undergoing PD. Future randomized controlled trials are necessary to identify the correct application of PN and EN in patients receiving PD.

COMMENTS

Background

Pancreaticoduodenectomy (PD) is associated with a high incidence of postoperative complications. This high rate of complications is likely to be multifactorial and may include overall nutritional debilitation. Postoperative nutritional support therapy could ameliorate the clinical outcome in many types of surgical treatment and diminish the incidence of postoperative complications. The clinical data on postoperative early enteral nutrition (EEN) combined with parenteral nutrition (PN) after PD is very limited.

Research frontiers

Recent research has shown that early postoperative enteral nutrition enhanced immunocompetence, lowered clinical infection rates, and maintained gut structure and function, and can potentially attenuate catabolic stress responses in patients after surgery. However, postoperative total enteral feeding is associated with complications such as diarrhea, abdominal distention, and abdominal cramps. These symptoms worsened with increasing caloric intake and can lead to discontinuance of enteral feeding.

Innovations and breakthroughs

The authors investigated the effect of EEN combined with parenteral nutritional support in patients undergoing PD enrolled in a retrospective controlled clinical trial on the basis of their experience and the findings of previous studies. The results of this study show that early enteral nutritional support combined with PN can greatly improve nutritional status and liver function, decrease the incidence of infectious complications and delayed gastric emptying, and shorten postoperative hospital stay.

Applications

The results of this study show that early enteral nutritional support combined with PN can greatly improve nutritional status and liver function, decrease the incidence of infectious complications and delayed gastric emptying, and shorten postoperative hospital stay in patients undergoing PD. These findings are clinically relevant for guiding surgeons in the perioperative administration of medications during PD.

Peer review

This is an interesting study which is well written and referenced. It is a non-randomized retrospective study of the effect of EEN combined with parenteral nutritional support for patients receiving PD. PD is a major surgical procedure for the treatment of periampullary tumors which will result in a high incidence of complications and postoperative malnutrition, but nutritional support can improve patient's malnutrition and diminish the incidence of postoperative complications.

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