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ORIGINAL ARTICLE

The postoperative clinical outcomes and safety of early enteral nutrition in operated gastric cancer patients

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Summary

Purpose: *This study investigated the impact of early enteral nutrition (EEN) on the clinical outcomes of gastric cancer patients after radical gastrectomy.*

Methods: *Four hundred gastric cancer patients undergoing radical gastrectomy of any extend with D2 nodal dissection were randomly divided into an experimental and a control group with 200 cases in each group. Patients in the control group received postoperative parenteral nutrition (PN), while patients in the experimental group received postoperative EEN. After treatment, the clinical outcomes, postoperative immune function, and nutritional status of the two groups were evaluated.*

Results: *The postoperative fever time, intestinal function recovery time, anal exhaust time, and the length of hospital stay for patients in the experimental group were significantly shorter than those of the control group. We did not find significant differences in anastomotic leak, postoperative ileus and regurgitation between the two groups. The activities of multiple immune cell types, including $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, and natural killer (NK) cells, were significantly lower in both groups on postoperative day 1 when compared with the preoperative levels ($p<0.05$). The level of $CD8^+$ was not significantly different between the two groups ($p>0.05$). After treatment, levels of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, and NK cells in the experimental group patients were 35.6±4.2, 42.2±3.0, 1.7±0.3, and 27.3±5.3%, respectively, on postoperative day 7, which were similar to the preoperative levels. The immune cell levels from the control group patients remained significantly lower when compared with preoperative values; in addition, these values were also significantly lower when compared with the EEN patients ($p<0.05$)*

Conclusion: *For gastric cancer patients undergoing radical gastrectomy, the clinical outcome, immune function and nutritional status after EEN were significantly improved. These data suggest the widespread use of EEN in clinical practice.*

Key words: *clinical outcomes, early enteral nutrition, immune function, nutritional status, radical gastrectomy*

Introduction

Patients with gastric cancer show severe protein-caloric malnutrition. Combined with the trauma caused by surgery, patients utilize a large amount of their body fat stores. In addition, it is difficult for these patients to eat after radical gastrectomy, resulting in severe postoperative metabolic disorders [1]. This state of postoperative malnutrition is progressively aggravated because the catabolism of the patient is increased, anabolism is weakened, and immune function is significantly reduced. Postoperative EEN can greatly facilitate the maintenance of the structure and function of the intestinal mucosa, improve the body's defense mechanisms, enhance immunity, and reduce inflammation [2-4]. In our hospital, we investigated the impact of postoperative EEN on the clinical outcomes of patients undergoing radical gastrectomy.

Methods

General information

A total of 400 gastric cancer patients who had un-

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dergone radical gastrectomy from October 2009 to October 2013 were randomly divided into an experimental and a control group with 200 cases in each. Radical gastrectomy was defined as gastrectomy of any extend with D2 nodal dissection. Among these 400 patients, 257 (64.3%) cases had jejunal interposition reconstruction after total gastrostomy, and 143 (35.7%) cases had Roux-en-Y anastomosis. There were not significant differences between these two groups in the methods of digestive tract reconstruction. The control group included 112 (56.0%) males and 88 (44.0%) females (age range 40-79 years, mean 56.0±7.6). The experimental group included 104 (52.0%) males and 96 (48.0%) females (age range 38-78 years, mean 60.8±5.9). All patients underwent preoperative endoscopy and biopsy to confirm the diagnosis. In addition, patients were diagnosed with resectable gastric cancer by abdominopelvic and CT examination. There were no significant differences in gender, age, nutritional status, and surgical methods between the two groups (p>0.05).

Parenteral nutrition

All of the patients had a nasoenteral draining tube for 3-4 days postoperatively. The patients in the control group received PN with a total daily infusion volume of 50 mL/kg. PN contained an energy supply of 105 kJ/mg. The supplementary nitrogen was provided by Novamin (Compound Amino Acid Injection; Huarui Pharmaceutical Co., Ltd, Wuxi, China), 20% of the calories were supplied by fat emulsion, with 60-70% from 10% glucose and 5% glucose/saline solutions; and the vitamins were supplied from Soluvita and Vitalipid (Huarui Pharmaceutical Co., Ltd, Wuxi, China). Addamel was used as a trace element supplement. PN lasted for a total of 7 days.

The patients in the experimental group received postoperative EEN. After the intraoperative reconstruction of the digestive tract was completed, a Flocare nasoenteral feeding tube was placed approximately 30 cm from the distal anastomosis of the intestine jejunum-jejunal efferent loop, and a slow infusion of warm saline 250-500 mL was administered through the feeding tube at postoperative postoperative day 1. Without the postoperatively indwelling nasoenteral feeding tube, the patients were given an appropriate amount of water on the first postoperative day, followed by EN on the second day. The patients were asked to intake 500 mL of fractionated Jevity (product of Abbott in the Netherlands, containing 2196.6 kJ/525 kcal) orally with an appropriate amount of 300-500ml drinking water. Subsequently, the patients were given 1000 mL of Jevity (1050 kcal) orally every day with an appropriate amount of 300-500ml semi-liquid diet tailored to patient conditions to ensure their daily energy supply. The course of the EEN treatment lasted for 7 days.

Outcome measures

The general postoperative indicators, including anastomotic leak, postoperative ileus and regurgitation, fever time, intestinal function recovery time, anal exhaust time and the length of postoperative hospital stay of all patients were recorded. Multiple indicators of immune function and nutritional status of the patients were evaluated before surgery and at postoperative day 1 and day 7. Immune function was determined based on the levels of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and NK cells detected with flow cytometry methods as previously described. Nutritional status was determined based on the levels of albumin and prealbumin.

Statistics

The obtained data were statistically processed using SPSS15.0 software (SPSS Inc, Chicago, Ill). The acquired data were compared using Student's *t*-test, and the counting data were compared using x^2 test. p<0.05 was considered statistically significant.

Results

Comparison of general postoperative information between treatment groups

The incidence of fever and its duration, intestinal function recovery time, anal exhaust time and length of postoperative hospital stay of the patients in the experimental group were significantly shorter than those in the control group (p<0.05). We did not find significant differences in anastomotic leak, postoperative ileus and regurgitation between the two groups. The results are shown in Table 1.

Comparison of immune function indicators between treatment groups before and after surgery

Table 1. General information of two groups after operation

Group	*N*	*Postoperative fever time (hrs)*	*Postoperative intestinal function recovery time (hrs)*	*Anal exhaust time (hrs)*	*Postoperative hospital stay (days)*
Control group	200	85.4 ± 7.7	86.3 ± 7.9	84.6 ± 8.7	9.3 ± 2.5
Experimental group	200	68.7 ± 5.9	69.4 ± 6.4	67.3 ± 7.9	6.8 ± 1.9
p value	-	<0.05	<0.05	<0.05	<0.05

Table 2. Comparison of immune function indicators between the two groups before and after surgery

Groups	*CD3+*	*CD4+*	*CD8+*	*CD4+/CD8+*	*NK*
Control group					
Preoperative	36.6 ± 4.7	43.5 ± 3.6	24.7 ± 2.8	1.8 ± 0.3	21.7 ± 3.1
Postoperative day 1	22.8 ± 2.6*	30.5 ± 2.5*	22.4 ± 2.8	1.4 ± 0.3*	17.3 ± 2.9*
Postoperative day 7	26.6 ± 4.6	34.4 ± 2.4	24.1 ± 2.6	1.4 ± 0.8	22.5 ± 4.8
Observation group					
Preoperative	36.7 ± 4.6*	43.5 ± 3.8*	24.3 ± 2.6	1.6 ± 0.4*	21.9 ± 3.6*
Postoperative day 1	22.4 ± 2.7	31.5 ± 2.8	23.9 ± 2.5	1.6 ± 0.6	17.4 ± 3.6
Postoperative day 7	35.7 ± 4.1#	42.1 ± 3.6#	24.1 ± 1.0	1.7 ± 0.3#	27.3 ± 5.3#

Values are mean ± standard deviation. * p<0.05, compared to preoperative control group value, #p<0.05, compared to postoperative control group value. NK: natural killer cells

The activities of multiple immune cell types, including $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and NK cells, were significantly lower for all patients on the postoperative day 1 when compared with preoperative levels (p<0.05). $CD8^+$ not significantly different between the two groups (p>0.05) on the postoperative day 1. After nutritional therapy, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and NK cell levels on the postoperative day 7 were similar to preoperative levels in the EEN group. The immune cell levels in the control group remained significantly lower on the postoperative day 7 when compared with the preoperative levels; in addition, these values were significantly lower when compared with the EEN group (p<0.05). The results are shown in Table 2.

Table 3. Comparison of nutritional status indicators of patients before and after surgery

Groups	*Albumin ($g{\cdot}L^{-1}$)*	*Prealbumin ($g{\cdot}L^{-1}$)*
Control group		
Preoperative	30.5 ± 6.7	174.3 ± 20.3
Postoperative day 1	25.8 ± 5.9*	136.4 ± 16.8*
Postoperative day 7	31.5 ± 7.4	144.5 ± 21.5
Observation group		
Preoperative	30.4 ± 6.7	177.2 ± 23.7
Postoperative day 1	25.3 ± 6.1*	136.3 ± 17.8*
Postoperative day 7	37.5 ± 7.8#	175.5 ± 22.6#

Values are mean ± standard deviation: *p<0.05, compared to preoperative control group value, #p<0.05, compared to postoperative control group value

Comparison of nutritional status between treatment groups before and after surgery

On the postoperative day 1, the levels of serum albumin and prealbumin of all patients were significantly decreased. On the postoperative day 7, the levels of albumin and prealbumin in the experimental group improved and statistically higher when compared with the control group (p<0.05). The results are shown in Table 3.

Discussion

Based on previous reports, the postoperative nutritional status and immune function of patients after radical gastrectomy is significantly reduced [5,6], and the incidence of postoperative complications and mortality is significantly increased [7]. The significantly low immune function and decreased appetite of patients with gastric cancer before surgery and the postoperative stress due to the surgical trauma causes a significant decrease in the patient body weight. After a gastric cancer surgery, the conventional treatment typically consists of PN therapy with gradually supplemented diet after anal exhaust. With the progress of general surgery and the postoperative nutritional science, an increased number of studies have shown that EEN helps restore the gut function.

Immune function can be evaluated based on the activities of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and NK cells [8]. $CD4^+$ and $CD8^+$ cells exhibit synergistic functions in humoral and cellular immunity. $CD4^+$ promotes the differentiation of B cells to produce antibodies, whereas $CD8^+$ inhibits the production of antibodies and the proliferation and differentiation of T cells. The coordinating roles of $CD4^+$ and $CD8^+$ can effectively maintain cellular immune function [9,10]. Experimental examination revealed that the ratio of *in vivo* $CD4^+$ and $CD8^+$ in gastric cancer patients was significantly reduced, suggesting a markedly reduced immune function in patients. Currently, two forms of postoperative nutritional support therapy are clinically applied to gastric cancer patients, including parenteral and enteral nutrition [11,12]. Based on the continuous advances in basic research and clinical studies, EN therapy should be considered superior to parenteral nutrition.

In this study, EEN therapy was given to gastric cancer patients after surgery with positive clinical outcomes. The postoperative intestinal function recovery time of the patients with EN was significantly shorter when compared with patients receiving parenteral treatment. On the postoperative day 1, the counts of multiple immune cell types, including $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and NK cells, were significantly lower in both groups when compared with the preoperative levels. $CD8^+$ was not significantly decreased. On the postoperative day 7, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and NK cell levels of patients in the experimental group were similar to the preoperative level, whereas levels in the control group remained significantly lower when compared with preoperative levels and with the EEN group. In terms of nutritional status, the levels of serum albumin and prealbumin on the postoperative day 1 were significantly decreased in all patients. These levels were improved and significantly higher in EEN patients when compared with the PN group on the postoperative day 7.

Studies have shown that EEN produces a more robust increase in $CD4^+$ activity and decrease in $CD8^+$ activity when compared with PN therapy. The observed changes in these immune indicators promote the *in vivo* production and secretion of the antibodies and the proliferation and differentiation of T lymphocytes, thereby strengthening the anti-tumor effect of the immune system [11,12]. The results of this study show that intestinal function recovery, immune function and nutritional status of EEN patients were superior to patients who received PN therapy. This effect is primarily related to the rapid absorption of the nutritional formulation. Enteral nutrition can quickly provide high amounts of fatty acids and amino acids for patients after surgery and influence gastrointestinal motility by inhibiting the vagus nerve and inducing the secretion of gastrointestinal hormones. In this aspect, PN therapy is slower and less effective. In addition, EEN can increase the secretion of intestinal digestive juices and endocrine hormones, promote the growth of the intestinal mucosa and aid in the recovery of intestinal peristalsis with a greater efficiency when compared with PN. Also, we did not find significant difference between the EEN and PN group in the incidence of complications.

Our results were in line with the Barlow et al. report [13]. These authors performed an open, prospective multicentre randomised controlled trial within a regional UK Cancer Network. In their study, 121 patients with suspected operable upper gastrointestinal cancer were studied. The authors found EEN was associated with significantly shortened length of hospital stay and improved clinical outcomes. Ghafouri et al. [14] also suggested the EEN can be an effective method of feeding patients in postoperative days of resection of gastrointestinal malignancies. The authors found postoperative hospital stay was shorter, the level of laboratory parameters was improved and postoperative complications such as wound infection and enterocutaneous fistula were reduced in EEN patients. These findings reinforce the potential benefit of EEN in principle and as championed within enhanced recovery after surgery programmes, and such strategies deserve further research in the arena of upper gastrointestinal surgery.

In summary, postoperative EEN for patients with gastric cancer was superior to PN therapy with regards to intestinal function recovery, improvement of immune function and overall nutritional status. EEN is safe, effective, produces functional recovery of the intestinal mucosa, and allows for a thorough recovery of patients with no increased complications.

References

1. Li H, Han X, Su L et al. Laparoscopic radical gastrectomy versus traditional open surgery in elderly patients with gastric cancer: Benefits and complications. Mol Clin Oncol 2014;2:530-534.
2. Hur H, Si Y, Kang WK, Kim W, Jeon HM. Effects of early oral feeding on surgical outcomes and recovery after curative surgery for gastric cancer: pilot study results. World J Surg 2009;33:1454-1458.
3. Heidegger CP, Darmon P, Pichard C. Enteral vs. parenteral nutrition for the critically ill patient: a combined support should be preferred. Curr Opin Crit Care 2008;14:408-414.
4. Gabor S, Renner H, Matzi V et al. Early enteral feeding compared with parenteral nutrition after oesophageal or oesophagogastric resection and reconstruction. Br J Nutr 2005;93:509-513.
5. Chen ZX, Liu AH, Cen Y. Fast-track program vs traditional care in surgery for gastric cancer. World J Gastroenterol 2014;20:578-583.
6. Yu Z, Zhuang CL, Ye XZ, Zhang CJ, Dong QT, Chen BC. Fast-track surgery in gastrectomy for gastric cancer: a systematic review and meta-analysis. Langenbecks Arch Surg 2014;399:85-92.
7. Yang DJ, He WL, Zhang S et al. Fast track surgery accelerates the postoperative rehabilitation and recovery of insulin sensitivity in elective operation for colorectal carcinoma: a randomized controlled clinical trial. Zhonghua Wai Ke Za Zhi 2012;50:870-874 (in Chinese with Engl abstr).
8. Feng F, Ji G, Li JP et al. Fast-track surgery could improve postoperative recovery in radical total gastrectomy patients. World J Gastroenterol 2013;19:3642-3648.
9. Elliott JA, Patel VM, Kirresh A et al. Fast-track laparoscopic bariatric surgery: a systematic review. Updates Surg 2013;65:85-94.
10. Jones NE, Hayland DK. Implementing nutrition guidelines in the critical care setting: a worthwhile and achievable goal. JAMA 2008;300:2798-2799.
11. Zhao Y, Wand Q. Three kinds of nutrition support method in the application of postoperative gastric cancer. Shan dong Medical J 2008;48:91-93.
12. Barlow R, Price P, Reid TD et al. Prospective multicentre randomised controlled trial of early enteral nutrition for patients undergoing major upper gastrointestinal surgical resection. Clin Nutr 2011;30:560-566.
13. Ghafouri A, Salehi OA, Keshavarz SA, Hosseini S, Shojaifard A, Khorgami Z. Evaluation of supporting role of early enteral feeding via tube jejunostomy following resection of upper gastrointestinal tract. Med J Islam Repub Iran 2012;26:7-11.