



# Effects of preoperative and postoperative enteral nutrition on postoperative nutritional status and immune function of gastric cancer patients

## NUTRITION

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### ABSTRACT

**Background/Aims:** Effects of preoperative one week enteral nutrition (EN) support on the postoperative nutritional status, immune function and inflammatory response of gastric cancer patients were investigated.

**Materials and Methods:** 106 cases of gastric cancer patients were randomly divided into preoperative one week EN group (trial group) and early postoperative EN group (control group), which were continuously treated with EN support until the postoperative 9th day according to different treatment protocols. All the patients were checked for their body weight, skinfold thickness, upper arm circumference, white blood cell count (WBC), albumin (ALB), prealbumin (PA), C-reactive protein (CRP), humoral immunity (IgA, IgG), T cell subsets (CD4, CD8 and CD4/CD8), interleukin-6 (IL-6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), etc. on the preoperative and the postoperative 1<sup>st</sup> and 10<sup>th</sup> day, respectively.

**Results:** PA and IgG levels of the experimental group were higher than those of the control group on the postoperative 10<sup>th</sup> day, whereas IL-6 level of the experimental group was lower than that of the control group.

**Conclusion:** EN support for preoperative gastric cancer patients will improve the postoperative nutritional status and immune function, alleviate inflammatory response, and facilitate the recovery of patients.

**Keywords:** Enteral nutrition, gastric cancer, preoperation and postoperation, immunity

### INTRODUCTION

Gastric cancer patients commonly suffer from severe malnutrition owing to the nature of gastric cancer and adverse effects such as operative trauma and perioperative diet control and low-calorie intake, etc. (1). In the fields of nutrition and surgery, early enteral nutrition (EN) support especially preoperative bowel preparation has been demonstrated to play an important role in postoperative recovery. At present, EN has been verified to be crucial in preoperative bowel preparation (2,3). Although preoperative and postoperative EN support of gastric cancer patients can improve nutritional status, its effects on immune function are still controversial. Osada et al. (4) reported that early postoperative EN support boosted the postoperative immune function of gastric cancer patients. However, postoperative nutritional status and immune function of gastric cancer patients have seldom been accessed. Thereby motivated, this study aims to observe the nutritional status, immune function and inflammatory response indicators by administering differ-

ent nutritional agents in different postoperative stages. Besides, the effects of appropriate preoperative on the nutritional status and immune function of gastric cancer patients have also been investigated.

### MATERIALS AND METHODS

#### General information

106 cases of patients with gastric cancers requiring radical gastrectomy from January 2010 to December 2011 in the Department of Digestive Surgery were selected (70 cases were male, 36 cases were female, aging from 42-75, weighing from 46.8-72.1 kg). The patients were randomly divided into the trial group (preoperative EN Group) and the control group (early postoperative EN Group) equally.

#### Random grouping

Patients were randomly grouped by SAS9.0 program according to the ratio of the trial group and the control group at 1:1.

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**Received:** July 29, 2012

**Accepted:** December 02, 2012

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### Allocation concealment

The resulting random allocation sequences were orderly coded and sealed in opaque envelopes. After the eligibility of trial subjects were determined, patients in the same batch were matched according to their tumor staging, and were finally allocated to the corresponding groups after unfolding the envelopes orderly. No serious organ damages and metabolism and endocrine diseases were diagnosed in the preoperative examinations of patients. Tumor staging, operative methods and operative time of the patients in the two groups did not differ significantly (5).

### EN support method

Trial group: 1 week before operations, patients were administered orally with 1000 kcal/d intact protein EN powders on the base of semi-liquid diets (Germany Milupa GmbH & Co.KG, model: 320g/tank, each packet was prepared into a 500 mL solution with the energy density of 1 kcal/mL); then they were administered with 250 mL isotonic sodium chloride solution 12 h after operations; they were then treated with 250 mL isotonic sodium chloride solution +500 mL EN suspension (SP) (Nutricia company, short peptide, elemental diet, 500 mL/bottle) by the infusion of an EN pump through a nasal-intestinal tube on postoperative 1<sup>st</sup> day; they were infused with 1000 mL SP on the 2<sup>nd</sup> day; they were then infused with 500 mL SP +500 mL Meiji preparation solution (Shandong Megiddo passenger Biological Technology Co., Ltd.) on the 3<sup>rd</sup> day (500 mL Meiji was given from after postoperative 72 h); finally they were continuously treated with 1000 mL Meiji for 24h by the infusion of the EN pump through the nasal-intestinal tube from the 3<sup>rd</sup> to the 9<sup>th</sup> day after operations. Control group: patients were administered with 250 mL isotonic sodium chloride solution on postoperative 1<sup>st</sup> day; they were then continuously treated with 250 mL isotonic sodium chloride solution +500 mL Meiji for 24h by the infusion of the EN pump through the nasal-intestinal tube on the 2<sup>nd</sup> day (500 mL Meiji was infused from the 48<sup>th</sup> hour after operations); finally they were continuously administered with 1000 mL Meiji from the 3<sup>rd</sup> to the 9<sup>th</sup> day after operations.

### Observation contents and methods

#### Clinical observation

Patients were examined daily during treatment, including the symptoms of nausea, vomiting, abdominal distention, abdominal pain, diarrhea and etc., the complications of intestinal obstruction, intestinal fistula and etc. Their recovery time of bowel movement was also recorded. Clinical status information including body weight, skinfold thickness, upper arm circumference of patients were measured on the day one-week before surgery, day 1 after surgery, and day 10 at the end of the study, respectively.

Laboratory determination: blood WBC, albumin, prealbumin and C-reactive protein (CRP) of the patients were determined on the 1<sup>st</sup> and 10<sup>th</sup> day before and after operations. Peripheral

blood immunoglobulin (IgG), immunoglobulin M (IgM) and immunoglobulin A (IgA) were tested by the enzyme linked immunoassay. T cell subsets (CD4 + T cell, CD8 + T cell and CD4 + T cell/CD8 + T cell) were determined by the flow cytometry. Peripheral blood cytokine interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) were determined by ELISA (6).

### Statistical analysis

Statistical analyses were conducted using SAS statistical analysis system (version 9.0). The statistics were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) and analyzed by ANOVA. All the statistical tests, count data and measurement data underwent double-sided test, Chi-squared test and t test, respectively.  $p < 0.05$  was considered as statistically significant.

## RESULTS

### Comparison between the general clinical status of the two patient groups

The two patients groups were treated according to the plan without any complications such as acute intestinal obstruction and intestinal fistula, etc. Bowel movement recovery time of the two groups was similar ( $p > 0.05$ ). The incidence of abdominal distention and abdominal pain in the trial group (6.14%) was similar to that in the control group (9.13%) ( $p > 0.05$ ). Besides, blood sugar, hepatic and renal functions and electrolytes of the two groups were also similar ( $p > 0.05$ ). Adverse reactions occurred in the two groups on the 1<sup>st</sup> and 2<sup>nd</sup> day after operations, which were all alleviated by adjusting the dripping speed (Table 1, 2).

### Comparison between the nutritional indicators of the two patient groups

Body weight, skinfold thickness of triceps and upper arm circumference of the patients were similar before and after the study ( $p > 0.05$ ). Albumin and prealbumin levels of the two patient groups decreased on postoperative 1<sup>st</sup> day ( $p < 0.05$ ), and the two values rose at the end of the study ( $p < 0.05$ ). Prealbumin level of the trial group was higher than that of the control group on postoperative 10<sup>th</sup> day ( $235.2 \pm 40.8$  mg/L versus  $193.6 \pm 19.7$  mg/L,  $p < 0.05$ , Table 3).

### Comparison between the immune function indicators of the two patient groups

Immune function indicators of the two patient groups all decreased on postoperative 1<sup>st</sup> day ( $p < 0.05$ ) and conversely rose at the end of the study ( $p < 0.05$ ). IgG of the trial group was higher than that of the control group on postoperative 10<sup>th</sup> day ( $12.60 \pm 2.33$  g/L versus  $10.45 \pm 1.82$  g/L,  $p < 0.05$ , Table 4).

### Comparison between the inflammatory response indicators of the two patient groups

Inflammatory response indicators and cytokines of the two patient groups all increased on postoperative 1<sup>st</sup> day ( $p < 0.05$ ) and reduced at the end of the study ( $p < 0.05$ ). IL-6 of the trial group

**Table 1.** Comparison between the general clinical status of the two patient groups

Group	Case of complication	Bowel movement recovery time (d)	Venous Blood sugar (fasting) (mmol/L)	Glutamic pyruvic transaminase (u/L)	Glutamic oxaloacetic transaminase (u/L)	Serum creatinine (μmol/L)	Blood urea nitrogen (μmol/L)
Trial	0	1.42±0.22	5.63±1.05	15.87±10.85	17.36±8.52	50.06±33.28	1.28±2.86
Control	0	1.43±0.26	5.84±1.04	15.2±11.03	17.42±8.02	48.97±36.17	1.30±2.77

**Table 2.** Comparison between the blood electrolytes of the two patient groups

Group	Blood sodium (mmol/L)	Blood potassium (mmol/L)	Blood calcium (mmol/L)	Blood phosphorus (mmol/L)	Blood magnesium (mmol/L)
Trial	136.28±2.31	4.29±0.59	2.31±0.19	1.26±0.23	0.88±0.20
Control	137.05±2.66	4.42±0.71	2.28±0.26	1.22±0.25	0.93±0.14

**Table 3.** Comparison between the nutritional indicators of the two patient groups

Group		Body weight (kg)	Skinfold thickness of triceps (mm)	Upper arm circumference (mm)	PA (mg/L)	ALB (g/L)
Trial	Preoperative	46.4±21.2	6.9±0.8	23.2±2.2	236.8±43.6	39.2±7.2
	Postoperative 1 <sup>st</sup> day	-	6.9±0.8	23.0±2.1	184.9±17.9*	31.9±7.6*
	Preoperative and postoperative 10th day	46.5±19.7	6.7±1.1	23.0±2.1	235.2±40.8*	32.6±3.5*
Control	Preoperative	46.7±18.5	6.6±0.9	23.3±2.3	216.3±34.3	38.7±3.0
	Postoperative 1 <sup>st</sup> day	-	6.6±0.9	23.1±2.1	185.5±45.2*	30.8±2.5*
	Preoperative and postoperative 10th day	46.3±19.7	6.7±1.1	22.9±2.2	193.6±19.7**	35.3±5.0*

\*p&lt;0.05, \*\*p&lt;0.01

**Table 4.** Comparison between the immune function indicators of the two patient groups

Group		IgG (g/L)	IgA (g/L)	CD4+T cell (%)	CD8+T cell (%)	(CD4+T cell)/(CD8+T cell)
Trial	Preoperative	11.52±1.68	2.56±1.08	37.25±5.48	24.77±9.13	1.63±0.62
	Postoperative 1 <sup>st</sup> day	10.08±1.85*	2.27±1.14*	31.52±8.17*	22.62±8.74*	1.61±0.97*
	Postoperative 10 <sup>th</sup> day	12.60±2.33*	3.22±1.62*	36.22±2.51*	25.13±9.74*	2.09±0.42*
Control	Preoperative	12.82±3.49	3.47±2.05	36.21±9.21	25.12±7.85	1.46±0.51
	Preoperative 1 <sup>st</sup> day	9.63±2.44*	2.47±1.66*	28.77±4.57*	24.66±9.08*	1.43±0.52*
	Preoperative 10 <sup>th</sup> day	10.45±1.82*	4.12±3.07*	33.14±4.20*	24.52±7.85*	1.71±0.52*

\*p&lt;0.05, \*\*p&lt;0.01

was lower than that of the control group on postoperative 10<sup>th</sup> day (488.15±83.54 ng/L versus 407.52±91.84 ng/L, p<0.05, Table 5).

## DISCUSSION

Tumor progression is often accompanied by malnutrition and poor immune function. Radical surgeries of gastric cancer will up-regulate the catabolism of patients and lead to immunodepression (7). Besides, surgical stress will result in systemic inflammatory response, decrease the quality of life and even affect prognosis. Therefore, rational and effective nutrition support

will be conducive to malnutrition cancer patients. It has been previously reported that the function of small intestine usually began to recover within 6~12 h after operations (8), indicating the possibility of initiating EN support. Early postoperative EN rather than parenteral nutrition is advocated by researchers when intestines can normally work (9), which thus allows the wide application of EN support in clinical practice. In addition, early postoperative EN support has been reported to be able to reduce the high metabolism induced by surgical trauma, maintain intestinal mucosal barrier function, prevent enterogenic infections and facilitate the recovery of patients (10,11).

**Table 5.** Comparison between the inflammatory response indicators of the two patient groups

Group		IL-6 (ng/L)	TNF- $\alpha$ (ng/L)	WBC (109/L)	CRP (mg/L)
Trial	Preoperative	333.56 $\pm$ 72.58	91.25 $\pm$ 26.52	4.83 $\pm$ 1.05	1.49 $\pm$ 0.43
	Postoperative 1 <sup>st</sup> day	535.74 $\pm$ 127.57*	134.28 $\pm$ 33.60*	11.28 $\pm$ 4.51*	1.43 $\pm$ 0.54*
	Postoperative 10 <sup>th</sup> day	488.15 $\pm$ 83.54*	117.89 $\pm$ 79.95*	7.28 $\pm$ 2.26*	1.69 $\pm$ 0.48*
Control	Preoperative	312.24 $\pm$ 76.65	91.58 $\pm$ 20.03	5.36 $\pm$ 1.24	1.61 $\pm$ 0.62
	Preoperative 1 <sup>st</sup> day	314.05 $\pm$ 152.68*	123.75 $\pm$ 31.04*	12.03 $\pm$ 4.18*	1.61 $\pm$ 0.97*
	Preoperative 10 <sup>th</sup> day	407.52 $\pm$ 91.84*	113.67 $\pm$ 22.41*	6.79 $\pm$ 2.57*	2.08 $\pm$ 0.42*

\*p&lt;0.05, \*\*p&lt;0.01

Enteral nutrition support products are mainly classified into three types: amino acid or short peptide (element type), intact protein (non-element type) and component. Short-peptide type (element type) products can be absorbed after several steps of digestion utilizing protein hydrolysates as the nitrogen sources, which are applicable to the patients right after surgeries (12). Thus, we provided various EN agents for the patients at different perioperative stages according to their gastrointestinal functions. In order to ameliorate the preoperative malnutrition of gastric cancer patients, they were administered with 160 g/d Meijike orally and treated with nutrition intervention right after admission. After surgeries, the patients were first treated with predigestive SP (short peptides) to reduce the burden and adverse reactions of intestines and facilitate the absorption and utilization of diverse nutrients. The gradual transfer into Meijike thereafter recovered intestinal functions owing to the existence of dietary fiber, the benefits of which have been reported previously (13,14). The comparisons between albumin, prealbumin, immune function, IgG, cytokine and IL-6 in both groups suggest that partial EN support during perioperation will not only improve the postoperative nutritional status and immune function, but also moderate the inflammatory response of gastric cancer patients after operative trauma.

Moreover, partial preoperative EN support has been verified to facilitate the postoperative gastrointestinal absorption of nutrients by gastric cancer patients, accelerate the recovery of patients, and enhance the overall clinical outcome (15). It is also noted that previous study reported that nutrition support should be limited to gastric cancer patients who severely malnourished (16), the present study did not address in this regard. Further efforts are still in need to ensure the safe utilization of preoperative and postoperative enteral nutrition to gastric cancer patients.

In conclusion, preoperative and postoperative enteral nutrition support can improve the nutritional status as well as immune function, alleviate inflammatory response, and facilitate the recovery of gastric cancer patients undergoing radical gastrectomy.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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