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Clinical Study of Probiotic Enteral Nutrition to Improve Intestinal Flora and Chemotherapy-related Complications in Gastric Cancer Patients Undergoing Chemotherapy

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Abstract: **OBJECTIVE:** In the treatment of gastric cancer patients undergoing chemotherapy, it is important to investigate the effect of probiotic enteral nutrition not only to improve intestinal flora, but also to improve chemotherapy-related complications. **METHODS:** From September 2021 to September 2022, 60 patients with gastric cancer combined with nutritional risk who were hospitalized in the Department of Medical Oncology of our hospital were selected and then divided into 3 groups: 1. control group: patients were given dietary guidance while chemotherapy. 2. enteral nutrition group: oral nutrition therapy was given while chemotherapy. 3. combined probiotics group: enteral nutrition combined with probiotics was given while chemotherapy. For all study subjects, the following study indexes were examined at the time of admission and after chemotherapy: 1. intestinal flora 2. hematological indexes: white blood cells, red blood cells, platelets, blood albumin, prealbumin, T-cell subsets, immunoglobulins, etc. 3. physical indexes: body weight, body composition. 4. symptomatic indexes: stool properties and frequency, severity of nausea and vomiting. **RESULTS:** From the results, before treatment, there was basically no difference in intestinal flora among the three groups. After treatment, the intestinal flora of patients in the combined probiotic group was relatively low. It can be seen that probiotics can contribute to the reduction of intestinal flora, $P < 0.05$; before treatment, there was basically no difference in the hematological indexes of patients in the three groups. After treatment, the hematological indexes of patients in the combined probiotic group were relatively normal. It can be seen that probiotics can contribute to the normalization of hematological indexes, $p < 0.05$; before treatment, there was basically no difference in either the weight of the patients in the three groups or their body composition. After treatment, the body indexes of patients in the combined probiotic group returned to normal. It can be seen that probiotics can promote the return of body indexes to normal; before treatment, there was basically no difference in the stool properties and frequency, or the severity of nausea and vomiting among the three groups of patients. After treatment, the patients in the combined probiotic group had normalized their symptoms. It can be seen that probiotics can contribute to the normalization of symptom indexes. **CONCLUSION:** When treating patients with gastric cancer chemotherapy, applying probiotics to them can effectively improve both the number of intestinal flora and hematological indicators, as well as physical indicators and symptom indicators, which in turn can promote patients' remission and recovery from symptoms.

Keywords: gastric cancer chemotherapy patients; probiotic enteral nutrition; improvement; intestinal flora; chemotherapy-related complications; clinical study

As people's living standard is getting higher and higher, stomach cancer is gradually rising due to irregular work and diet. In the 2015 Academic Conference on Early Gastrointestinal Cancer in Jiangsu Province, Prof. Ruihua Shi, director of Jiangsu Gastrointestinal Endoscopy Society and director of the Department of Gastroenterology of CUH, revealed that the incidence of gastrointestinal malignancies in China accounts for 42% of the world, and 400,000 new cases of gastric cancer are added every year, ranking first in the world. According to Prof. Shi Ruihua, China is a country with high incidence of gastrointestinal malignant tumors, with the incidence rate accounting for 42% of the world, and only 400,000 new cases of gastric cancer are added every year, ranking first in the world. Among the top six malignant tumor incidence and mortality rates in China, gastrointestinal tract malignant tumors occupy "half of the mountain", among which gastric cancer, esophageal cancer and colon cancer are ranked 2nd, 5th and 6th. Because of the huge number of patients with gastric cancer, the treatment of gastric cancer is under great pressure. The problem of gastric cancer treatment has become an issue that needs to be taken seriously in clinical research, and there is an urgent need to solve the problems caused by such problems so as not to affect the treatment effect of the disease and lead to an increase in the death rate of the disease, as well as to affect the development of related medical research, which in turn leads to limitations in the treatment of gastric cancer. However, as medical technology continues to advance, gastric cancer treatment methods are being updated to better treat gastric cancer and facilitate the recovery of gastric cancer patients. In particular, the application of probiotics can not only improve the intestinal flora but also adjust the intestinal environment, which can ensure the health of patients when receiving treatment and thus facilitate the treatment of the disease. Through clinical practice, breakthroughs have also been made in gastric cancer treatment, effectively relieving patients' conditions and even saving their lives, thus promoting the development of gastric cancer clinical treatment. Therefore, since the treatment of gastric cancer is relatively long, the application of probiotics in order to improve intestinal flora and reduce related complications can effectively relieve symptoms as well as promote physical health, and provide favorable conditions for the treatment of gastric cancer, which in turn can lead to the proper resolution of gastric cancer.

1 Materials and Methods

1.1 General Information

Since the period from 09/2021 to 09/2022, 60 patients with gastric cancer combined with nutritional risk who were hospitalized in the Department of Medical Oncology of our hospital were selected and then divided into three groups: control group, enteral nutrition group, and combined probiotic group. Inclusion criteria: (1) patients had lung cancer; (2) patients did not have accompanying symptoms that affected this study; (3) patients were willing to cooperate with clinical work; (4) patients had not suffered from any major diseases other than gastric cancer; (5) patients' immunity was relatively good. Exclusion criteria: (1) patients interfered with this study because of the presence of mental illness; (2) patients were either pregnant or breastfeeding; (3) patients had problems with other internal organ functions that were impaired, such as problems with the heart, kidneys, and liver; (4) patients had other diseases that interfered with this study; and (5) patients had relatively poor immunity. Regarding the control group, the number of patients was 60% of the total number of males (12 cases) and 40% of the total number of females (8 cases); their age basically ranged from 20 to 72 years old, with an average age close to $(40.18+1.24)$ years; the average duration of the disease was approximately $(1.11+0.26)$ years; the number of patients who were usually treated in our hospital was 18, and the number of patients who were occasionally treated in our hospital was 2. In the enteral nutrition group, the number of patients was 40% male (8 cases) and 60% female (12 cases); their age was almost between 20 and 72 years, with a mean age of $(42.12+1.06)$ years; the mean duration of the disease was approximately $(1.16+0.22)$; the number of patients who were usually treated in our hospital was 19, and the number of patients who were occasionally treated in our hospital was 1. . Regarding the combined probiotic group, the number of patients was 50% male (10 cases) and 50% female (10 cases); their ages were almost between 22 and 72 years, with a mean age concentration of $(42.26+1.16)$ years; the mean duration of the disease was approximately $(1.18+0.12)$ times; the number of patients who were usually treated in our hospital was 19 and the number of patients who were occasionally treated in our hospital was 1 case. The hospital ethics committee approved the study and also allowed the patients to sign the informed consent form.

1.2 Method

According to the inclusion and exclusion criteria, 60 patients with gastric cancer combined with nutritional risk who were hospitalized in the Department of Medical Oncology of our hospital were selected and then divided into 3 groups: (1) Control group: patients were given dietary guidance while chemotherapy. (2) Enteral nutrition group: oral nutrition therapy was given while chemotherapy. (3) Combined probiotic group: enteral nutrition combined with probiotic therapy was given while chemotherapy. (Probiotics 60 billion, 1 time/day.) During the intervention period, intake of fermented foods such as yogurt is prohibited.

1.3 Observed indicators

For all subjects, the following study indicators were examined on admission and after chemotherapy: (1) intestinal flora (2) hematological indicators: white blood cells, red blood cells, platelets, blood albumin, prealbumin, T-cell subsets, immunoglobulins, etc. (3) physical indicators: body weight, body composition. (4) symptomatic indicators: stool properties and frequency, severity of nausea and vomiting.

1.4 Statistical methods

Statistics were performed using spss software, % indicates percentage, x2 indicates difference between groups, x+s indicates variance between groups, t indicates difference between groups, P<0.05.

2 Results

2.1 Compare the intestinal flora of the three groups of patients

From the results, before treatment, there was basically no difference in intestinal flora among the three groups of patients. After treatment, the intestinal flora of patients in the combined probiotic group was relatively low. It can be seen that probiotics can contribute to the reduction of intestinal flora, P<0.05. as shown in Table 1

Table 1: Comparison of the intestinal flora of the three groups of patients.

Group	Number of intestinal flora (10n/g) before	Number of intestinal flora (10n/g) after	x ²	P-value
Control group (n=20)	10 ² -10 ¹²	10 ⁶ -10 ¹²	2.211	<0.05
Enteral nutrition group(n=20)	10 ² -10 ¹¹	10 ⁴ -10 ⁹	1.986	<0.05
Combined probiotic group (n=20)	10 ³ -10 ¹²	10 ² -10 ⁴	1.222	<0.05

2.2 Comparison of the hematological indices of the three groups of patients

From the results, before treatment, there was basically no difference in the hematological indices of the three groups of patients. After treatment, the hematological indexes of patients in the combined probiotic group were relatively normal. It can be seen that probiotics can contribute to the normalization of hematological indexes, p<0.05. as shown in Figure 1

Group	Leukocytes(L)	Erythrocytes(L)	Platelets(L)	Hemoglobin(L)	Pre-albumin(L)	T-cell subpopulation(L)	Immunoglobulin(L)	x ²	P-value
Control group (n=20)	Before (7.1±2.1)×10 ⁹ /L	(4.19±0.40)×10 ⁹ /L	(222±60)×10 ⁹ /L	(115±11)g/L	(112±10)g/L	(7.1±2.1)×10 ⁹ /L	(112±10)g/L	7.408	<0.05
	After (7.5±2.2)×10 ⁹ /L	(4.69±0.41)×10 ⁹ /L	(210±60)×10 ⁹ /L	(125±13)g/L	(125±11)g/L	(7.5±2.1)×10 ⁹ /L	(128±11)g/L		
Enteral nutrition group(n=20)	Before (7.1±2.1)×10 ⁹ /L	(4.19±0.40)×10 ⁹ /L	(222±60)×10 ⁹ /L	(115±11)g/L	(112±11)g/L	(7.1±2.1)×10 ⁹ /L	(112±11)g/L	4.498	<0.05
	After (8.6±2.5)×10 ⁹ /L	(5.82±0.39)×10 ⁹ /L	(202±63)×10 ⁹ /L	(135±19)g/L	(132±16)g/L	(8.8±2.5)×10 ⁹ /L	(138±16)g/L		
Combined probiotic group (n=20)	Before (7.1±2.1)×10 ⁹ /L	(4.19±0.40)×10 ⁹ /L	(222±60)×10 ⁹ /L	(115±11)g/L	(112±11)g/L	(7.1±2.1)×10 ⁹ /L	(112±11)g/L	6.708	<0.05
	After (9.8±2.7)×10 ⁹ /L	(6.82±0.29)×10 ⁹ /L	(176±67)×10 ⁹ /L	(145±13)g/L	(142±13)g/L	(9.6±2.7)×10 ⁹ /L	(148±13)g/L		

Figure 1: Comparison of hematological indices of the three groups of patients.

2.3 Comparing the physical indicators of the three groups of patients

From the results, before treatment, there was basically no difference in either the weight of the three groups of patients or their body composition. After treatment, the body indexes of patients in the combined probiotic group returned to normal. It can be seen that probiotics can promote the return of body indicators to normal. As shown in Table 2

Table 2: compares the physical indicators of the three groups of patients.

Group	Weight (before)	Weight (after)	Body composition (before)	Body composition (after)
Control group (n=20)	Thin	Thin	On the low side	On the low side
Enteral nutrition group(n=20)	Thin	Near normal	On the low side	Near normal
Combined probiotic group (n=20)	Thin	Normal	On the low side	Normal

2.4 Comparing the symptom indicators of the three groups of patients

From the results, before treatment, there was basically no difference in either the stool properties and frequency or the severity of their nausea and vomiting among the three groups. After treatment, the symptom indexes of patients in the combined probiotic group returned to normal. It can be seen that probiotics can contribute to the normalization of symptom indexes. As shown in Table 3

Table 3: Compares the symptom indicators of the three groups of patients.

Group	Stool characteristics and frequency (before)	Stool pattern and frequency (after)	Severity of nausea and vomiting (before)	Severity of nausea and vomiting (after)
Control group (n=20)	Abnormal (0 times/two days)	Abnormal (0 times/two days)	Abnormal(3 times/day)	Abnormal(3 times/day)
Enteral nutrition group(n=20)	Abnormal (0 times/two days)	Normal(1 time/two days)	Abnormal(2 times/day)	Abnormal(1 time/day)
Combined probiotic group (n=20)	Normal (0 times/day)	Normal(1 time/day)	Normal(1 time/day)	Normal (0 times/day)

3 Discussion

Gastric cancer is one of the most common malignant tumors of the digestive system, and its incidence and mortality rate rank second among malignant tumors in China. In recent years, the incidence rate of gastric cancer has been increasing and the mortality rate has also risen, which has aroused the general concern of medical personnel and scientific researchers. As patients with gastric cancer are often accompanied by nausea, vomiting, abdominal pain and weight loss, and weight loss is often the first clinical manifestation of malnutrition, the incidence of weight loss is 31% to 87% depending on the primary lesion, and the incidence of gastrointestinal tumors is higher. With the update of chemotherapy drugs and the continuous improvement of chemotherapy regimen, the remission rate of patients with intermediate and advanced gastric cancer has been significantly improved and the survival period has been prolonged, but chemotherapy drugs also have obvious side effects, such as diarrhea,

constipation, nausea, vomiting, etc., which aggravate the occurrence of malnutrition and make patients' tolerance and compliance to chemotherapy greatly affected. How to improve the nutritional status of patients, improve the tolerance of chemotherapy, reduce complications and improve the therapeutic effect has become the focus of clinicians, including oncologists and nutritionists. The development of gastric cancer is a multifactorial and multi-stage process with complex formation factors, generally related to *H. pylori* infection, dietary structure, alcohol consumption and genetic factors. Probiotics such as bifidobacteria are the most important physiological bacteria in the intestinal tract of humans and some mammals, and also constitute the main component of the intestinal mucosal flora. Probiotics can not only antagonize the growth of many kinds of tumors, but also prevent the development of many kinds of tumors. A large number of studies have proved that there is a link between intestinal flora and colorectal tumors, and probiotics have potential inhibitory function on colorectal cancer. Meanwhile, studies have shown that intestinal flora alteration also exists in patients with esophageal cancer, liver cancer, pancreatic cancer and other tumors. However, so far, there are few studies related to gastric cancer and intestinal flora.

In this study, the changes of intestinal flora of gastric cancer patients before and after chemotherapy were quantitatively analyzed to investigate the changes of intestinal flora of gastric cancer patients and the intervention effect of probiotics on the balance of intestinal flora of gastric cancer patients; meanwhile, the effects of enteral nutrition therapy combined with probiotics on chemotherapy tolerance, complications, gastrointestinal symptoms, inflammatory factors and nutrition-related indexes of gastric cancer chemotherapy patients were observed.

Advances in oncology treatment have, on the one hand, brought encouraging results. On the other hand, it has inevitably increased the loss of nutritional reserves in patients with gastric cancer. A study of patients with gastrointestinal tumors found that the proportion of patients with decreased body mass during concurrent radiotherapy was as high as 75%. A study of patients with gastrointestinal tumors found that the proportion of patients with decreased body mass during the course of concurrent radiotherapy was as high as 75%, which in turn led to suspension of radiotherapy and interruption of chemotherapy and increased unplanned admissions during radiotherapy. Therefore, early detection of patients with nutritional risk and malnutrition, and reasonable nutritional intervention are inevitable requirements to increase the treatment tolerance, improve the efficacy and reduce the adverse effects of gastric cancer patients. The ESPEN guidelines recommend that enteral nutrition should be given during chemotherapy to improve or maintain nutritional status and improve quality of life for non-end-stage cancer patients with weight loss and malnutrition.

In recent years, microecological modulators have been more and more widely used in clinical practice, and have been recognized and used by a wide range of physicians and patients, and have increasingly shown their outstanding advantages. Probiotics such as *Bifidobacterium* can not only antagonize the growth of many kinds of tumors, but also prevent the development of many kinds of tumors. The dysbiosis of intestinal flora is an important factor to induce tumor. At present, the research on intestinal flora is mostly focused on colorectal cancer, and there are also a few studies on the relationship between esophageal cancer, liver cancer, pancreatic cancer and intestinal flora. There are few studies on the relationship between esophageal cancer, liver cancer and pancreatic cancer. The mechanism may be as follows: intestinal flora dysbiosis abnormalizes the signaling mechanism of intestinal mucosal pro-inflammatory response, leading to increased damage of intestinal mucosal epithelium and eventually tumor formation and malignancy; the products of certain intestinal microorganisms in the process of nutrient metabolism have toxic effects on intestinal epithelial cells, and incomplete repair of damaged intestinal mucosal epithelium can lead to its tumorigenic sexualization. The intestinal flora can even affect the treatment of tumors, and anticancer drugs can induce intestinal flora displacement and thus cause potential intestinal mucosal barrier damage and gastrointestinal mucositis, which may reduce the efficacy of the drugs.

Supplementation of probiotics to adjust the intestinal flora of tumor patients, combined with enteral nutrition therapy, may achieve the purpose of improving patients' nutritional status, improving drug efficacy, reducing side effects and prolonging survival through immune enhancement and precise nutrition. Precision nutrition therapy has also become the future trend of tumor nutrition therapy.

In the current study, the results showed that before treatment, there was essentially no difference in the intestinal flora of the three groups of patients. After treatment, the intestinal flora of patients in the combined probiotic group was relatively low. It can be seen that probiotics can contribute to the reduction of intestinal flora, $P < 0.05$; before treatment, there was basically no difference in the hematological indexes of patients in the three groups. After treatment, the hematological indexes of patients in the combined probiotic group were relatively normal. It can be seen that probiotics can contribute to the normalization of hematological indexes, $p < 0.05$; before treatment, there was basically no difference in either the weight of the patients in the three groups or their body composition. After treatment, the body indexes of patients in the combined probiotic group returned to normal. It can be seen that probiotics can promote the return of body indexes to normal; before treatment, there was basically no difference in the stool properties and frequency, or the severity of nausea and vomiting among the three groups of patients. After treatment, the patients in the combined probiotic group had normalized their symptoms. It can be seen that probiotics can contribute to the normalization of symptom indexes. Therefore, when treating patients with gastric cancer chemotherapy, the

application of probiotics can effectively improve the number of intestinal flora and hematological indicators, as well as physical indicators and symptom indicators, which in turn can help patients to alleviate their disease and recover from symptoms.

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The authors declare no conflict of interest.

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