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The Effect of Immunotherapy on the Gut Microbiota, Intestinal Barrier, and Immune Function in Patients with Gastric Cancer

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Abstract: *Objective:* To explore the effect of immunotherapy on the gut microbiota, intestinal barrier, and immune function in patients with gastric cancer. *Methods:* From July 2023 to July 2024, 60 patients with gastric cancer from our hospital were randomly divided into two groups, the control group and the study group, with 30 patients in each group. The control group received conventional treatment, while the study group received immunotherapy. A comparative analysis was conducted between the two groups on gut microbiota content (*Bifidobacterium*, *Fusobacterium nucleatum*, *Streptococcus*, *Lactobacillus acidophilus*), intestinal barrier indicators [D-lactate (D-LA), diamine oxidase (DAO), lipopolysaccharide (LPS)], immune function indicators [Immunoglobulin A (IgA), Immunoglobulin G (IgG), Immunoglobulin M (IgM)], adverse reactions, and treatment effects. *Results:* After treatment, the content of *Bifidobacterium* and *Fusobacterium nucleatum* in the study group was higher than in the control group, while the content of *Streptococcus* and *Lactobacillus acidophilus* was lower than in the control group ($P < 0.05$). The levels of D-lactate and DAO in the study group were lower than in the control group, while the LPS level in the study group was higher ($P < 0.05$). The levels of IgA and IgG in the study group were lower than in the control group, and the IgM level was also lower than in the control group ($P < 0.05$). After treatment, the total incidence of adverse reactions in the study group was lower than in the control group ($P < 0.05$). The overall treatment efficacy rate in the study group was higher than in the control group ($P < 0.05$). *Conclusion:* Immunotherapy in patients with gastric cancer can improve gut microbiota, intestinal barrier, and immune function, reduce the occurrence of adverse reactions, and promote better clinical treatment outcomes, making it worthy of clinical recommendation.

Keywords: Immunotherapy; Gastric cancer; Gut microbiota; Intestinal barrier; Immune function

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1. Introduction

As one of the most common malignant tumors worldwide, gastric cancer shows a high incidence and mortality rate. With the continuous evolution of social changes, living environments, and lifestyle transformations in China, the incidence and mortality rates of gastric cancer have been gradually rising [1]. Surgery is a common

treatment for early-stage gastric cancer and has certain therapeutic effects, but postoperative recurrence rates are high. When gastric cancer progresses to the late stage, the significance of surgical treatment declines substantially, making the search for an effective and safe treatment method all the more crucial. Clinical investigations have revealed that immunotherapy has shown favorable effects in antitumor treatment in recent years. The mechanism of immunotherapy lies in its ability to stimulate the patient's immune system, thereby effectively enhancing the body's ability to recognize and eliminate tumor cells. However, its clinical mechanism remains unclear. Some scholars have noted in their research that immunotherapy, as an innovative approach to cancer treatment, has demonstrated remarkable efficacy in the treatment of gastric cancer. However, due to the complexity of the immune system, further in-depth research is required on the interaction between drugs and the immune system to enhance the antitumor effects of immunotherapy in the future [2,3]. Based on this, this study selected gastric cancer patients treated in our hospital, provided immunotherapy, and analyzed its effect on the gut microbiota, intestinal barrier, and immune function of gastric cancer patients, thus providing some reference data for the subsequent clinical treatment of gastric cancer patients.

2. Materials and methods

2.1. General information

From July 2023 to July 2024, 120 gastric cancer patients from The First Affiliated Hospital of Yangtze University were selected and randomly divided into a control group and a study group. The baseline data between the two groups showed no significant difference ($P < 0.05$), as shown in **Table 1**.

Inclusion criteria: Patients diagnosed with gastric cancer through gastroscopic biopsy, pathology, and medical imaging; complete clinical follow-up data; patients and their families agreed to treatment and signed informed consent; and approved by the hospital's ethics committee.

Exclusion criteria: Participants with liver dysfunction; those with cognitive impairments accompanied by mental health issues that hindered their ability to cooperate effectively in the study; patients with unstable vital signs.

Table 1. Comparison of general information (mean ± SD)

General information		Control group (n = 30)	Study group (n = 30)	t / χ^2	P
Gender	Male	16	17	0.162	0.614
	Female	14	13		
Average age		58.50 ± 2.80	60.00 ± 4.00	0.795	0.831
Average BMI		20.00 ± 2.40	20.50 ± 2.80	0.058	0.931

2.2. Methods

Both groups of patients received routine treatment. The control group was given chemotherapy: oral capecitabine (approval number: National Medicine Standard H20143365) at 2,500 mg/m^2 daily for two weeks, followed by a one-week break; intravenous drip of oxaliplatin (batch number: 2009312707) at 130 mg/m^2 on day 1.

Treatment method for the study group: Sintilimab (approval number: National Medicine Standard S20180016) at 200 mg every three weeks, or Tislelizumab (batch number: 2018112618) at 200 mg every three weeks, for a total of 6 cycles.

2.3. Observation indicators

2.3.1. Comparison of intestinal flora content between the two groups

Before treatment, 3–5 g of fecal samples were collected, processed under sterile conditions, and cultured on appropriate media plates for bacterial growth. The bacterial content in fecal dilutions (expressed as $\log_{10n}$) was calculated to assess levels of *Bifidobacterium*, *Fusobacterium nucleatum*, *Streptococcus*, and *Lactobacillus acidophilus*.

2.3.2. Comparison of intestinal barrier function between the two groups

Four milliliters of fasting venous blood were collected from the patient's elbows, and centrifuged to remove the supernatant, and the double-antibody sandwich method was used to detect diamine oxidase (DAO). The enzyme colorimetric method was used to detect D-lactate and lipopolysaccharides (LPS), assessing intestinal barrier function.

2.3.3. Comparison of immune function between the two groups

The levels of immunoglobulin A (IgA), immunoglobulin G (IgG), and immunoglobulin M (IgM) in the supernatant were detected using the immunoturbidimetric assay.

2.3.4. Comparison of adverse reactions between the two groups

The incidence of bone marrow suppression, gastrointestinal reactions, and other adverse events in the two groups was compared.

2.3.5. Comparison of clinical efficacy between the two groups

CT scans were used to evaluate tumor size in the tumor area before and after treatment. The overall response rate was calculated as (complete response + partial response) / total cases × 100%.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 26.0 software. Measurement data were expressed as mean ± standard deviation (SD), and the *t*-test was used for analysis. Count data were expressed as percentages (%) and analyzed using the χ^2 test. A *P*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of intestinal flora content between the two groups

Before treatment, there was no statistically significant difference in the levels of *Bifidobacterium*, *Fusobacterium nucleatum*, *Streptococcus*, and *Lactobacillus acidophilus* between the two groups ($P > 0.05$). After treatment, the levels of *Bifidobacterium* and *Fusobacterium nucleatum* increased, while *Streptococcus* and *Lactobacillus acidophilus* decreased in both groups. The levels of *Bifidobacterium* and *Fusobacterium nucleatum* were significantly higher in the study group than in the control group, while the levels of *Streptococcus* and *Lactobacillus acidophilus* were significantly lower in the study group compared to the control group, with a statistically significant difference ($P < 0.05$). See **Table 2**.

Table 2. Comparison of intestinal flora content before and after treatment (mean ± SD)

Groups	Bifidobacterium		Fusobacterium nucleatum		Streptococcus		Lactobacillus acidophilus	
	Before	After	Before	After	Before	After	Before	After
Control group (n = 30)	7.89 ± 0.88	8.12 ± 0.62	7.66 ± 0.66	8.05 ± 0.44	9.33 ± 0.85	8.94 ± 0.65	8.14 ± 0.66	7.94 ± 0.54
Study group (n = 30)	8.01 ± 0.72	9.52 ± 0.77	7.85 ± 0.74	8.76 ± 0.85	9.21 ± 0.75	8.44 ± 0.51	8.26 ± 0.64	7.55 ± 0.62
t	0.667	8.957	1.212	4.692	0.669	3.186	0.825	3.000
P	0.506	0.001	0.229	0.001	0.505	0.002	0.411	0.003

3.2. Comparison of intestinal barrier function indicators between the two groups

Before treatment, there was no statistically significant difference in the intestinal barrier function indicators between the two groups ($P > 0.05$). After treatment, the levels of D-lactate and DAO in both groups significantly decreased, while the levels of LPS significantly increased. The study group had lower levels of D-lactate and DAO compared to the control group, and higher LPS levels compared to the control group, with a statistically significant difference ($P < 0.05$). See **Table 3**.

Table 3. Comparison of intestinal barrier function indicators before and after treatment (mean ± SD)

Groups	D-lactate (mg/L)		DAO (U/L)		LPS (EU/L)	
	Before	After	Before	After	Before	After
Control group (n = 30)	5.92 ± 0.54	3.45 ± 0.66	5.59 ± 0.62	2.55 ± 0.96	0.52 ± 0.11	1.45 ± 0.36
Study group (n = 30)	5.96 ± 0.63	2.55 ± 0.74	5.65 ± 0.61	1.65 ± 0.45	0.56 ± 0.18	0.86 ± 0.21
t	0.304	5.741	0.436	5.369	1.199	8.953
P	0.761	0.001	0.663	0.001	0.234	0.001

3.3. Comparison of immune function between the two groups

Before treatment, there was no statistically significant difference in immune function between the two groups ($P > 0.05$). After treatment, the levels of IgA and IgG decreased, and IgM levels increased in both groups. The study group had lower levels of IgA and IgG compared to the control group, and higher levels of IgM compared to the control group, with a statistically significant difference ($P < 0.05$). See **Table 4**.

Table 4. Comparison of immune function before and after treatment (mean ± SD)

Groups	IgA (ng/L)		IgG (ng/L)		IgM (ng/L)	
	Before	After	Before	After	Before	After
Control group (n = 30)	4.45 ± 1.02	3.02 ± 0.96	20.45 ± 2.56	14.77 ± 2.23	3.36 ± 0.68	3.76 ± 0.66
Study group (n = 30)	4.33 ± 1.05	3.84 ± 0.88	19.85 ± 2.46	17.48 ± 2.84	3.23 ± 0.42	2.74 ± 0.54
t	0.518	3.982	1.402	4.666	1.029	7.565
P	0.605	0.001	0.164	0.001	0.306	0.001

3.4. Comparison of adverse reactions between the two groups

Table 5 shows that after treatment, the overall incidence of adverse reactions in the study group was lower than that in the control group, with a statistically significant difference ($P < 0.05$).

Table 5. Comparison of adverse reactions [*n* (%)]

Groups	Chest tightness	Dyspnea	Gastrointestinal reactions	Total incidence
Control group (*n* = 30)	4 (13.33)	3 (10.00)	2 (6.67)	9 (30.00)
Study group (*n* = 30)	1 (3.33)	0 (0.00)	1 (3.33)	2 (6.67)
χ^2				5.164
P				0.023

3.5. Comparison of treatment efficacy between the two groups

Table 6 shows that after treatment, the overall efficacy rate in the study group was higher than that in the control group, with a statistically significant difference ($P < 0.05$).

Table 6. Comparison of treatment efficacy [*n* (%)]

Groups	Significantly effective	Effective	Ineffective	Overall effective rate
Control group (*n* = 30)	12 (40.00)	10 (33.33)	8 (26.67)	22 (73.33)
Study group (*n* = 30)	15 (50.00)	13 (43.33)	2 (6.67)	28 (93.33)
χ^2				4.904
P				0.027

4. Discussion

As a global disease, gastric cancer ranks among the most serious malignant tumors of the digestive tract. The main clinical treatments for gastric cancer include surgery and chemotherapy. However, due to the non-specific symptoms of early-stage gastric cancer, such as abdominal discomfort and morning acid reflux, diagnosis is often difficult. As a result, most patients are diagnosed in the middle or late stages, leading to limitations in clinical treatment [4,5].

In recent years, immunotherapy has emerged as a research hotspot with promising prospects in the field of cancer treatment, showing great potential [6,7]. Clinical investigations have found that the immune system in the body has the ability to identify and eliminate antigenic foreign substances. Since malignant tumors are masses formed by the mutation of normal cells, the immune system can recognize and eliminate them. Therefore, targeting the immune system for treatment holds tremendous research potential [8,9].

The results of this study showed that in the study group, *Bifidobacterium* and *Fusobacterium nucleatum* increased, while *Streptococcus* and *Lactobacillus acidophilus* decreased. After treatment, the intestinal barrier indicators D-lactate and DAO levels decreased, with the study group showing lower levels than the control group, and LPS levels increased, with the study group showing higher levels than the control group. Immunotherapy effectively altered the structure and metabolic function of the intestinal flora, improved the diversity of gut microbiota, and enhanced the thickness of the intestinal mucosal layer, significantly improving the mucosal defense capability. Furthermore, this study found that patients' immune functions improved, and adverse reactions were lower, indicating good clinical value.

In conclusion, immunotherapy for gastric cancer patients results in significant improvements in intestinal flora and immune function, demonstrating effective treatment outcomes and warranting further clinical promotion.

Disclosure statement

The authors declare no conflict of interest.

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