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Mechanism of Action and Clinical Intervention Potential of Intestinal Dysbiosis in the Occurrence and Development of Gastric Cancer

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Abstract: *Objective*: To explore the mechanism of action of intestinal dysbiosis in the occurrence and development of gastric cancer and analyze its potential for clinical intervention. *Methods*: Eighty patients with gastric cancer admitted to our hospital from January 2024 to November 2025 were selected as the study group, and another 40 healthy individuals undergoing physical examinations during the same period were selected as the control group. The fecal bacterial and fungal culture method was employed to quantify the primary intestinal flora, including Bifidobacteria, Lactobacilli, Escherichia coli, Enterococci, and Bacteroides, in both groups of study subjects, and the bacilli-to-cocci ratio was calculated. Additionally, serum levels of inflammatory cytokines (IL-6, TNF-α) and immune-related factors (PD-L1, IL-10) were measured. Gastric cancer patients were randomly divided into an intervention group (40 cases) and an observation group (40 cases). The observation group received a conventional chemotherapy regimen, while the intervention group received probiotic intervention in addition to chemotherapy. The incidence of chemotherapy-related adverse reactions and changes in intestinal flora were compared between the two groups. *Results*: The quantities of Bifidobacteria and Lactobacilli, as well as the bacilli-to-cocci ratio, were significantly lower in the study group compared to the control group, whereas the quantities of Escherichia coli and Enterococci were significantly higher, with all differences being statistically significant (all $P < 0.001$). Serum levels of IL-6, TNF-α, PD-L1, and IL-10 were significantly higher in the study group than in the control group ($P < 0.01$). After intervention, the quantities of Bifidobacteria and Lactobacilli, as well as the bacilli-to-cocci ratio, were significantly lower in the observation group than before intervention, while the quantities of Escherichia coli and Enterococci were significantly higher (all $P < 0.01$). Serum levels of IL-6, TNF-α, PD-L1, and IL-10 in the study group remained significantly higher than those in the control group ($P < 0.01$). In the intervention group, the quantities of Bifidobacteria and Lactobacilli, as well as the bacilli-to-cocci ratio, were significantly higher after intervention than before, while the quantities of Escherichia coli and Enterococci were significantly lower (all $P < 0.001$). Furthermore, after intervention, the quantities of Bifidobacteria and Lactobacilli, as well as the bacilli-to-cocci ratio, were significantly higher in the intervention group than in the observation group, while the quantities of Escherichia coli and Enterococci were significantly lower (all $P < 0.01$). The incidence of adverse reactions was significantly lower in the intervention group than in the observation group ($P < 0.001$). *Conclusion*: Dysbiosis of intestinal flora may promote the occurrence and development of gastric cancer through mechanisms such as inducing chronic inflammation and inhibiting anti-tumor

immunity; probiotic intervention can effectively regulate the balance of intestinal flora in gastric cancer patients, reduce adverse reactions to chemotherapy, and hold significant potential for clinical intervention.

Keywords: Dysbiosis of intestinal flora; Gastric cancer; Mechanism of action; Inflammatory response; Immunosuppression; Probiotics

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1. Introduction

Gastric cancer is one of the most common malignant tumors worldwide, and its occurrence and development are the result of the combined effects of genetic factors, environmental factors, and microbial factors [1]. In recent years, the intestinal flora, as the "second genome" of the human body, has garnered widespread attention for its association with tumor occurrence and development. The intestinal flora influences host health by participating in nutrient metabolism, regulating immune system function, maintaining intestinal mucosal barrier integrity, and other processes, while dysbiosis may disrupt the body's homeostasis, induce chronic inflammation, and promote tumor progression [2]. *Helicobacter pylori* has been clearly identified as an important pathogenic microorganism in gastric cancer, but a growing body of research indicates that, in addition to Helicobacter pylori, dysbiosis of the intestinal flora also plays a crucial role in the occurrence and development of gastric cancer [3,4]. Currently, the specific molecular mechanisms by which dysbiosis of intestinal flora promotes the occurrence and development of gastric cancer have not been fully elucidated, and relevant clinical intervention strategies are still in the exploratory stage. This study analyzes the differences in intestinal flora between gastric cancer patients and healthy individuals, explores the mechanism of action of dysbiosis of intestinal flora in the occurrence and development of gastric cancer, and evaluates the clinical effects of probiotic intervention, providing new ideas and experimental evidence for the prevention and treatment of gastric cancer.

2. Materials and methods

2.1. Study subjects

Eighty patients with gastric cancer admitted to the Department of Gastroenterology and the Department of Gastrointestinal Surgery of our hospital from January 2024 to November 2025 were selected as the study group. Inclusion criteria: (1) Diagnosed with gastric cancer through histopathological examination; (2) No prior radiotherapy, chemotherapy, immunotherapy, or probiotic treatment; (3) No severe liver or kidney dysfunction, intestinal infectious diseases, or autoimmune diseases; (4) Informed consent obtained from patients and their families, with signed informed consent forms.

Exclusion criteria: (1) Presence of other malignancies; (2) Recent use of medications affecting the gut microbiota, such as antibiotics or glucocorticoids; (3) History of intestinal surgery; (4) Pregnant or lactating women. Among them, there were 48 males and 32 females, aged between 45 and 78 years, with an average age of (62.35 ± 8.76) years old.

Pathological staging: 25 cases in stage II, 38 cases in stage III, and 17 cases in stage IV. Additionally, 40 healthy individuals who underwent health check-ups at the health examination center of our hospital during the same period were selected as the control group, including 23 males and 17 females, aged between 42 and 75 years

old, with an average age of (60.12 ± 7.98) years old. There were no statistically significant differences in general characteristics such as gender and age between the two study groups ($P > 0.05$), indicating comparability.

Eighty gastric cancer patients were randomly divided into an observation group and an intervention group using a random number table method, with 40 patients in each group. In the observation group, there were 25 males and 15 females, with an average age of (63.12 ± 8.54) years. The pathological staging was as follows: 13 cases in stage II, 19 cases in stage III, and 8 cases in stage IV. In the intervention group, there were 23 males and 17 females, with an average age of (61.58 ± 8.96) years. The pathological staging was as follows: 12 cases in stage II, 19 cases in stage III, and 9 cases in stage IV. There were no statistically significant differences in general data, such as gender, age, and pathological staging, between the two groups ($P > 0.05$), indicating comparability.

2.2. Research methods

2.2.1. Intestinal flora detection

Fresh fecal samples (5g) were collected from the subjects on an empty stomach in the morning, placed in sterile sampling tubes, and immediately sent for testing. The number of major bacterial groups was detected using the culture method: Bifidobacteria, Lactobacilli, and Bacteroides were anaerobically cultured for 48 hours using BS, MRS, and BBL media, respectively; Escherichia coli and Enterococci were aerobically cultured for 24 hours using MacConkey and Azide Bile Esculin media, respectively. The colony count results were expressed as l g CFU/g, and the rod/coccus ratio [(Bifidobacteria + Lactobacilli)/(*Escherichia coli* + Enterococci)] was calculated.

2.2.2. Serum factor detection

Venous blood samples (5 mL) were collected from the subjects on an empty stomach in the morning, and the serum was separated by centrifugation and stored at -80℃ for testing. Enzyme-linked immunosorbent assay (ELISA) was used to detect the levels of serum inflammatory factors IL-6 and TNF-α, as well as immune factors PD-L1 and IL-10.

2.2.3. Intervention protocol

The observation group received a combined chemotherapy regimen of oxaliplatin and capecitabine: oxaliplatin at a dose of 130 mg/m², administered intravenously on day 1; capecitabine at a dose of 1000 mg/m², taken orally twice daily from days 1 to 14. Each cycle lasted 21 days, and a total of two cycles were administered. In addition to the chemotherapy regimen given to the observation group, the intervention group received oral administration of live combined Bifidobacterium, Lactobacillus, and Enterococcus tablets, with three tablets taken three times a day. The probiotic treatment commenced simultaneously with chemotherapy and continued for the duration of the two chemotherapy cycles.

2.2.4. Adverse reaction observation

Adverse reactions during chemotherapy in both groups were observed and recorded, including diarrhea, nausea and vomiting, decreased appetite, leukopenia, decreased hemoglobin, thrombocytopenia, and liver function impairment. These reactions were graded according to the WHO criteria for grading adverse reactions to anticancer drugs, and the incidence of adverse reactions was calculated.

2.3. Statistical methods

Data analysis was performed using SPSS 26.0 statistical software. Measurement data were expressed as mean ± standard deviation (SD), and comparisons between groups were made using the t-test. Count data were expressed as rates (%), and comparisons between groups were made using the χ^2 test. A P-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of gut microbiota quantity between the study group and the control group

The number of bifidobacteria and lactobacilli, as well as the rod/coccus ratio, in the study group were significantly lower than those in the control group, while the number of Escherichia coli and Enterococcus was significantly higher than that in the control group, with statistically significant differences (all $P < 0.001$). There was no statistically significant difference in the number of Bacteroides between the two groups ($P = 0.609$). See **Table 1**.

Table 1. Comparison of intestinal flora quantity between the study group and the control group

Group	Bifidobacteria (lg CFU/g)	Lactobacillus (lg CFU/g)	*Escherichia coli* (lg CFU/g)	Enterococcus (lg CFU/g)	Bacteroides (lg CFU/g)	Rod/Coocus Ratio
Control Group (n = 40)	9.65 ± 1.21	9.32 ± 1.08	6.23 ± 1.15	6.18 ± 1.09	8.23 ± 1.16	2.86 ± 0.45
Study Group (n = 80)	6.82 ± 1.05	6.54 ± 1.12	8.96 ± 1.32	8.75 ± 1.26	8.35 ± 1.23	1.23 ± 0.31
t-value	13.220	12.969	11.133	11.000	0.513	23.233
P-value	< 0.001	< 0.001	< 0.001	< 0.001	0.609	< 0.001

Note: Rod/coccus ratio = (bifidobacteria + lactobacilli) / (*Escherichia coli* + Enterococcus)

3.2. Comparison of serum factor levels between the study group and the control group

The serum levels of IL-6, TNF-α, PD-L1, and IL-10 in the study group were significantly higher than those in the control group ($P < 0.01$). See **Table 2**.

Table 2. Comparison of serum factor levels between the study group and the control group

Group	IL-6 (pg/mL)	TNF-α (pg/mL)	PD-L1 (ng/mL)	IL-10 (pg/mL)
Control group (n = 40)	12.34 ± 3.56	10.23 ± 2.87	18.65 ± 4.23	8.96 ± 2.15
Study group (n = 80)	38.65 ± 8.23	29.54 ± 7.16	45.32 ± 9.65	26.87 ± 6.34
t-value	19.304	16.384	16.670	35.209
P-value	< 0.001	< 0.001	< 0.001	< 0.001

3.3. Comparison of intestinal flora quantity before and after intervention between the observation group and the intervention group

After intervention, the number of bifidobacteria and lactobacilli, as well as the rod/coccus ratio, in the observation group was significantly lower than that before intervention, while the number of Escherichia coli and Enterococcus

was significantly higher than that before intervention (all $P < 0.01$). In the intervention group, the number of bifidobacteria and lactobacilli, as well as the rod/coccus ratio, were significantly higher than those before intervention, while the number of Escherichia coli and Enterococcus was significantly lower than that before intervention (all $P < 0.001$). Moreover, after intervention, the number of bifidobacteria and lactobacilli, as well as the rod/coccus ratio, in the intervention group were significantly higher than those in the observation group, while the number of Escherichia coli and Enterococcus was significantly lower than that in the observation group (all $P < 0.01$). See **Table 3**.

Table 3. Comparison of intestinal flora quantity before and after intervention between the observation group and the intervention group

Group	Time Point	Bifidobacteria (lg CFU/g)	Lactobacillus (lg CFU/g)	*Escherichia coli* (lg CFU/g)	Enterococcus (lg CFU/g)	Rod/Coocus Ratio
Observation Group (n = 40)	Pre-intervention	6.78 ± 1.02	6.52 ± 1.08	8.92 ± 1.28	8.72 ± 1.23	1.21 ± 0.29
	Post-intervention	5.98 ± 1.02	5.76 ± 0.98	9.86 ± 1.35	9.65 ± 1.32	0.98 ± 0.26
t-value		3.508	3.296	3.196	3.260	3.735
P-value		0.001	0.002	0.002	0.002	< 0.001
Intervention Group (n = 40)	Pre-intervention	6.86 ± 1.08	6.56 ± 1.15	8.98 ± 1.35	8.78 ± 1.28	1.25 ± 0.32
	Post-intervention	8.23 ± 1.12	7.96 ± 1.05	7.23 ± 1.12	7.15 ± 1.08	2.15 ± 0.38
t-value		5.569	5.686	6.310	6.156	11.458
P-value		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

3.4. Comparison of the incidence of adverse reactions to chemotherapy between the observation group and the intervention group

The incidence of adverse reactions in the intervention group was significantly lower than that in the observation group ($P < 0.001$). See **Table 4** for details.

Table 4. Comparison of the incidence of adverse reactions to chemotherapy between the observation group and the intervention group

Group	Diarrhea	Nausea and Vomiting	Decreased Appetite	Leukopenia	Decreased Hemoglobin	Thrombocytopenia	Hepatic Impairment	Total Incidence (%)
Observation Group (n = 40)	15 (37.50)	18 (45.00)	16 (40.00)	12 (30.00)	10 (25.00)	8 (20.00)	6 (15.00)	26 (65.00)
Intervention Group (n = 40)	3 (7.50)	5 (12.50)	4 (10.00)	2 (5.00)	1 (2.50)	1 (2.50)	0 (0.00)	9 (22.50)
χ^2	—	—	—	—	—	—	—	14.679
P-value	—	—	—	—	—	—	—	< 0.001

4. Discussion

Under normal circumstances, the intestinal microbiota maintains bodily health by participating in digestion and absorption, synthesizing vitamins, regulating immunity, etc. Any disruption to this balance leads to dysbiosis [5].

This study reveals that patients with gastric cancer have significantly lower levels of beneficial bacteria, such as Bifidobacterium and Lactobacillus compared to healthy individuals, while the levels of harmful bacteria, such as *Escherichia coli*, are significantly elevated, and the rod/coccus ratio decreases, confirming the prevalence of intestinal dysbiosis in gastric cancer patients [6]. Beneficial bacteria can exert anti-tumor effects by producing short-chain fatty acids that inhibit harmful bacteria and maintain the intestinal mucosal barrier; conversely, excessive proliferation of harmful bacteria produces endotoxins and other substances that damage the barrier and induce chronic inflammation. This study also found that gastric cancer patients have higher serum levels of inflammatory cytokines such as IL-6 and TNF-α, which are associated with dysbiosis, suggesting that dysbiosis may promote the occurrence and progression of gastric cancer through chronic inflammation.

The immune system serves as a crucial defense against tumors, and the intestinal microbiota can influence anti-tumor immunity by regulating the function of immune cells [7]. This study found that the serum levels of PD-L1 and IL-10 in gastric cancer patients are significantly higher than those in healthy individuals. PD-L1 can bind to PD-1 on T cells, inhibiting their activity and leading to tumor immune escape, while IL-10 can suppress the function of antigen-presenting cells, weakening anti-tumor immunity. Dysbiosis of the gut microbiota can promote tumor progression by regulating the expression and secretion of both PD-L1 and IL-10. Additionally, a reduction in beneficial bacteria such as Bifidobacterium can lead to insufficient production of short-chain fatty acids, weakening their ability to enhance immunity through G protein-coupled receptors.

Dysbiosis of the gut microbiota can also promote cancer through metabolic disorders. Harmful bacteria metabolize proteins to produce toxins such as ammonia and hydrogen sulfide, which damage the intestinal mucosa and induce mutations, or reduce nitrates to generate strong carcinogens such as nitroso compounds. Beneficial bacteria, on the other hand, can lower the intestinal pH by producing acids, thereby inhibiting the growth of harmful bacteria and reducing carcinogens [8].

Targeted regulation of the gut microbiota has emerged as a new direction for gastric cancer intervention [9]. This study utilized Bifidobacterium Lactobacillus Triple Viable Tablets to intervene in gastric cancer patients undergoing chemotherapy. The results showed that after intervention, the number of beneficial bacteria in the patients' intestines and the rod/coccus ratio significantly increased, while the number of harmful bacteria decreased, and the microbial balance improved. Moreover, the incidence of chemotherapy-related adverse reactions in the intervention group was significantly lower than that in the observation group. This suggests that probiotics can reduce chemotherapy-related adverse reactions and improve patient tolerance by regulating microbial balance, consistent with previous studies. Additionally, fecal microbiota transplantation, as an emerging intervention technique for the gut microbiota, can rapidly restore microbial balance in patients by transplanting fecal microbiota from healthy individuals. Studies have confirmed that this technique can improve the microbial structure in patients with advanced gastric cancer, enhance anti-tumor immunity, improve the efficacy of radiotherapy, chemotherapy, and immunotherapy, and prolong patient survival [10]. A diet high in dietary fiber can promote the growth of beneficial bacteria, while a diet high in fat and protein is prone to disrupt the balance of the bacterial community and increase the risk of tumors. Reasonable dietary adjustments, combined with approaches such as probiotics and fecal microbiota transplantation, hold promise for opening up new avenues in the treatment of gastric cancer.

5. Conclusion

In summary, intestinal dysbiosis is prevalent among patients with gastric cancer. It may promote the occurrence

and progression of gastric cancer through mechanisms such as inducing chronic inflammatory responses, inhibiting anti-tumor immune function, and increasing the production of carcinogenic substances. Probiotic intervention can effectively regulate the balance of intestinal microbiota in patients with gastric cancer, reduce adverse reactions to chemotherapy, and improve patients' tolerance to chemotherapy, demonstrating significant potential for clinical intervention. In the future, further in-depth research is needed to explore the specific molecular mechanisms underlying intestinal dysbiosis and the occurrence and progression of gastric cancer. In addition, it is also important to investigate more effective targeted intervention strategies for intestinal microbiota, providing new ideas and methods for the prevention and treatment of gastric cancer.

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Disclosure statement

The authors declare no conflict of interest.

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