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Original Article

Effects of Bifidobacterium Quadruple Viable Tablets Combined with Immune-Enhancing Enteral Nutritional Adjuvant Therapy on Intestinal Flora, Intestinal Mucosal Barrier and Immune Function in Elderly Patients with Hepatitis B Cirrhosis

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ABSTRACT

Objectives: Hepatitis B cirrhosis is a serious condition caused by the hepatitis B virus, leading to liver fibrosis and vascular proliferation. Current clinical treatments still have limitations, prompting interest in microecological agents and immune-enhancing nutrition. Recent studies indicated the crucial role of intestinal flora imbalance in cirrhosis development, which might be modulated by the "liver-gut" axis. Therefore, this study aimed to investigate the impact of integrating microecological agents and immune-enhanced enteral nutritional support with antiviral therapy on the intestinal flora, mucosal barrier, and immune function in elderly patients with hepatitis B cirrhosis. **Materials and Methods:** Eighty cases of elderly patients diagnosed with hepatitis B cirrhosis in our hospital from January 2020 to December 2022 were included in this retrospective study as study subjects. Both groups received oral tenofovir disoproxil fumarate tablets. The control group underwent basic treatments, including hepatoprotection and a specific diet. The observation group received Bifidobacterium bifidum tetragonum in conjunction with immune-enhanced enteral nutritional support. Nutritional status, gut microbiota, cellular immune status, and intestinal mucosal barrier function were compared before and after intervention in both groups. **Results:** There were no significant differences in baseline characteristics between the groups. After 30 days of treatment, the observation group exhibited significantly increased Enterococci, Enterobacteriaceae, Bifidobacteria, and Lactobacillus abundance compared to pre-treatment and the control group. Inflammatory response indicators and CD8+ expression in the observation group at 7 days postoperatively were markedly lower than control, while CD4+ and CD4+/CD8+ were significantly higher. Nutritional indicators and intestinal mucosal barrier function were also superior in the experimental group after 30 days. **Conclusion:** In conclusion, microecological agents combined with immune-enhancing enteral nutrition support effectively enhance the intestinal mucosal barrier, immune function, and nutritional status in elderly patients with hepatitis B cirrhosis.

Keywords: Microecological agents; Enteral nutrition, Chronic hepatitis B, Liver cirrhosis.

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INTRODUCTION

Hepatitis B cirrhosis refers to the progression of chronic hepatitis caused by Hepatitis B Virus (HBV) infection to a pathological stage characterized by diffuse fibrosis of the liver, pseudofollicular formation, and intra- and extrahepatic vascular proliferation.[1,2] There are no obvious clinical symptoms in the compensated stage of hepatitis B cirrhosis, while the decompensated stage is characterized by portal hypertension and severe impairment of liver function, and patients often die due to complications such as ascites, gastrointestinal hemorrhage, hepatic encephalopathy, hepatorenal syndrome, and carcinoma, leading to multiple organ failure.[3]

With the proposal of "liver-gut axis" theory, it is confirmed that the occurrence and development of cirrhosis of hepatitis B are not only related to HBV infection but also closely related to intestinal flora imbalance.[4] Clinically, patients with cirrhosis show different degrees of loss of appetite, nausea, abdominal distension, diarrhoea and other symptoms, all of which are

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related to the imbalance of intestinal flora. The current clinical treatment of hepatitis B cirrhosis includes hepatoprotective therapy and antiviral therapy, which can improve the clinical symptoms of patients to a certain extent, but it is difficult to effectively slow down the progression of cirrhosis. Recent studies show that microecological agents can effectively regulate the intestinal microecological balance disorders in patients with cirrhosis, improve intestinal function, correct endotoxemia, reduce inflammatory cytokines in the blood, and enhance the body's immune defence ability.[5] From a nutritional point of view, supplementation through scientific and rational nutrition has been recognized as an important adjunctive therapy for patients with chronic cirrhosis.[6] Recent studies have shown that the addition of immune-enhancing nutrients, including Arginine (Arg), Glutamine (Gln), nucleotides, and omega-3 fatty acids to Enteral Immunonutrition (EIN), which could modulate the clinical efficacy of inflammation, oxidative stress, and impaired immune function, and has thus gained increasing interest and favour in clinics.[7,8] However, the effects of microecological agents combined with immune-enhancing enteral nutrition adjuvant therapy on intestinal flora, intestinal mucosal barrier and immune function in elderly patients with hepatitis B cirrhosis have rarely been reported at home and abroad. Therefore, the present study was conducted to analyze the clinical comparison in this aspect, aiming to provide a reference for the clinical treatment of elderly patients with hepatitis B cirrhosis, which is now reported as follows.

MATERIALS AND METHODS

Patients

All procedures followed were following with the Declaration of Helsinki and were approved by the Hospital Ethics Committee. Eighty cases of elderly patients diagnosed with hepatitis B cirrhosis in our hospital from January 2020 to December 2022 were included in this retrospective study as study subjects.

The inclusion criteria were as follows: (1) Aged ≥ 60 years; (2) Patients with hepatitis B cirrhosis according to the diagnostic criteria of the Guidelines for the Diagnosis and Treatment of Cirrhosis of the Liver, as revised by the Chinese Medical Association Hepatology Branch (2019 version); (3) None of the patients received any treatment that affected the outcome other than anti-hepatitis B treatment; (4) Patients and their families voluntarily agreed to participate and signed an informed consent form.

The exclusion criteria were as follows: (1) Suffer from serious diseases of the heart, brain, lungs and other important organs;(2) Allergy to the ingredients of the nutritional formula; (3) History of probiotic drug use in the last 1-month period; (4) Gastrointestinal dysfunction and severe malnutrition; (5) Low compliance, inability to read, severe hearing or vision loss, poor Chinese comprehension skills.

Study design

Eighty elderly patients with hepatitis B cirrhosis were divided into experimental and control groups by randomization method. Patients in both groups were orally administered tenofovir disoproxil fumarate tablets (GlaxoSmithKline; specification: 300 mg), 300 mg once a day. In the control group, only basic treatments such as hepatoprotection, low-salt, low-fat and low-sugar diet were used, while in the observation group, Bifidobacterium bifidum tetragonum combined with immune-enhanced enteral nutritional support therapy was used based on the treatment in the control group.

Intestinal microecological agent therapy

Patients in the experimental group were orally administered Bifidobacterium bifidum tetragonum capsule (Hangzhou Yuanda Biological Pharmaceutical Co., Ltd., Batch No.: 201810451, Hangzhou, China) 1.5 g/times, 3 times/day, and the course of treatment was 30 days.

Nutrition Support

All patients' calorie requirements were calculated based on standard body weight [ideal body weight (kg) = height (cm)-105] within 48 hr of admission. The dose and rate are adjusted according to the Simple Gastrointestinal Function Score method. This group used an immune-enhancing enteral nutrition combination (trade name: Ruineng; manufacturer: Fresenius Kabi (China) Company Limited; specification: 500 ml/bottle; registration certificate No. H20040722). All patients were given a slow oral dose of 500 ml per day for 30 days.

Outcome measures

The baseline variables of patients, including age, sex, and clinical data, were collected. All included patients were subject to routine laboratory tests at admission, including routine blood tests, liver function, renal function, electrolytes, blood lipids, and coagulation function. Peripheral venous blood was drawn from all study subjects in the early morning fasting condition at 1d after admission and 30d after treatment. The expression levels of Serum Albumin (ALB), Serum Transferrin (TRF) and serum pre-albumin (PAB), which are indicators of nutrients, were determined by the Hitachi 7060 automatic biochemical analyzer. CD4+, CD8+, and CD4+/CD8+ ratios in the blood circulation were measured by flow cytometry using a BD flow cytometer. Serum Diamine Oxidase (DAO) and endotoxin levels were measured by Enzyme-Linked Immunosorbent Assay (ELISA). The fresh stools of the selected patients were retained in the morning, and the specimens of the stools were put into the culture medium, and put into the 37 °C temperature box for direct incubation for 24 h, and the colonies in the culture medium were observed.

Statistical analyses

Data analysis was performed by Statistic Package for Social Science (SPSS) 27.0 statistical software (IBM, Armonk, NY, USA). Quantitative data conforming to Normal distribution are expressed as mean ± standard deviation ($\bar{x} \pm s$) and a t-test was used for comparison. Qualitative information was expressed as frequency and percentage (%) and the chi-square test was used for count data. All trials were bilateral and p-value < 0.05 was considered statistically significant.

RESULTS

General information

A total of 80 elderly patients with hepatitis B cirrhosis were included in this study. All patients included in the study were randomized into the control group (n = 40) and the experimental group (n = 40). There was no statistically significant difference between the two groups in terms of age, gender composition, BMI, WBC, Hb, ALB, GLB, ALT, AST, BUN, MELD score (p > 0.05) (Table 1).

Comparison of Liver Function Indicators

To determine the effect of integrating microecological agents and immune-enhanced enteral nutritional support with antiviral therapy on liver function, we determined the ALT, AST, and TB in patients. Before treatment, there was no statistically significant difference in the levels of ALT, AST and TB between the two groups (p > 0.05). After 30d of treatment, the levels of ALT, AST and TB in the two groups were lower than those before treatment, and all the liver function indexes in the Experimental group were significantly lower than those in the control group (p< 0.001). More details are shown in Table 2. Results suggested that both therapies improved liver function, with the combined therapy displaying better efficacy.

Comparison of gut microbiota

As shown in Table 3, there was no statistically significant difference in the number of colonies of Enterococci, Enterobacteriaceae, Bifidobacteria, and Lactobacilli between the two groups of patients before intervention (p>0.05). The number of colonies of Enterococci, Enterobacteriaceae, Bifidobacteria and Lactobacillus in the observation group was significantly higher than that of the pre-treatment and control groups after treatment (p < 0.001), suggesting that combined treatments might modify the abundance of gut microbiota.

Comparison of intestinal mucosal barrier function

To evaluate the intestinal mucosal barrier function in patients by testing DAO and endotoxin indicators. At 30 d after treatment, DAO and endotoxin were lower in both groups than at 1 d after admission (p < 0.05). In the experimental group at 30d after treatment, both DAO and endotoxin indexes were lower than those in the control group at the same time point (p < 0.01). More details are shown in Table 4. Results suggested that microecological agents and immune-enhanced enteral nutritional support with antiviral therapy was able to improve intestinal barrier function.

Comparison of immunological indicators

CD4+, CD8+, and CD4+/CD8+ are important immune system markers that help assess the function and balance of T lymphocyte subpopulations in the body. As shown in Table 5, there was no statistically significant difference in the comparison of T-lymphocyte subsets CD4+, CD8+, and CD4+/CD8+ in the circulation of patients in the experimental and control groups at

Table 1: Comparison of general information between the two groups of patients.

Items	Control (n = 40)	Experimental group (n = 40)	t(χ2)	p
Age (year, $\bar{x} \pm s$)	66.05 ± 3.63	66.38 ± 3.89	0.386	0.701
Gender (Male/Female)	35/5	34/6	0.105	0.745
BMI (kg/m2)	20.67 ± 1.39	21.10 ± 1.58	1.277	0.206
WBC (10^9/L)	3.97 ± 0.87	3.87 ± 0.78	0.587	0.559
NLR	2.78 ± 0.70	2.66 ± 0.71	0.718	0.475
Hb (g/L)	102.32 ± 14.35	101.18 ± 14.15	0.358	0.722
ALB (g/L)	28.24 ± 2.34	29.15 ± 2.29	1.761	0.082
GLB (g/L)	30.86 ± 2.23	30.37 ± 3.32	0.775	0.441
ALT (U/L)	72.52 ± 10.65	75.68 ± 10.46	1.338	0.185
AST (U/L)	76.99 ± 10.18	79.14 ± 10.21	0.944	0.348
BUN (mmol/L)	5.60 ± 1.08	5.27 ± 1.16	1.286	0.202
MELD score	11.65 ± 1.96	11.08 ± 2.34	1.197	0.235

BMI = Body Mass Index; WBC = white blood cell; NLR = neutrophil-lymphocyte ratio; Hb = Hemoglobin; ALB = albumin; GLB = globulin; ALT = Alanine amino-transferase; AST = Aspartate transaminase; BUN = Blood Urea Nitrogen; MELD = Model for End-Stage Liver Disease

Table 2: Comparison of gut microbiota between two groups of patients.

	Control ($n = 40$)	Experimental group ($n = 40$)	t	p
ALT (U/L)				
1 d after admission	72.52 ± 10.65	75.68 ± 10.46	1.338	0.185
30 d after treatment	54.80 ± 8.25	32.70 ± 6.79	7.483	< 0.001
AST (U/L)				
1 d after admission	76.99 ± 10.18	79.14 ± 10.21	0.944	0.348
30 d after treatment	50.74 ± 7.95	37.64 ± 5.81	6.557	< 0.001
TB (μmol/L)				
1 d after admission	35.95 ± 5.21	34.36 ± 5.38	0.713	0.419
30 d after treatment	24.73 ± 4.55	18.64 ± 3.80	5.572	< 0.001

ALT = Alanine aminotransferase; AST = Aspartate transaminase; TB = Total bilirubin.

Table 3: Comparison of gut microbiota between two groups of patients.

	Control ($n = 40$)	Experimental group ($n = 40$)	t	p
Enterococcus (log N/g)				
1 d after admission	8.12 ± 0.45	8.09 ± 0.39	0.309	0.758
30 d after treatment	8.42 ± 0.28	8.85 ± 0.39	5.693	< 0.001
Enterobacter (log N/g)				
1 d after admission	9.20 ± 0.44	9.10 ± 0.57	0.873	0.385
30 d after treatment	10.30 ± 0.89	11.34 ± 1.31	4.154	< 0.001
Bifidobacterium (log N/g)				
1 d after admission	8.23 ± 0.56	8.13 ± 0.62	0.774	0.441
30 d after treatment	8.77 ± 0.48	9.69 ± 0.73	6.592	< 0.001
Lactobacillus (log N/g)				
1 d after admission	7.05 ± 0.37	7.13 ± 0.47	0.800	0.426
30 d after treatment	7.66 ± 0.38	8.24 ± 0.42	6.432	< 0.001

Table 4: Comparison of intestinal mucosal barrier function between two groups of patients.

	Control ($n = 40$)	Experimental group ($n = 40$)	t	p
DAO(U/mL)				
1 d after admission	83.27 ± 14.06	86.12 ± 14.30	0.898	0.372
30 d after treatment	61.96 ± 13.28	54.50 ± 10.84	2.753	0.007
Endotoxin (EU/mL)				
1 d after admission	0.28 ± 0.03	0.29 ± 0.04	1.299	0.198
30 d after treatment	0.24 ± 0.03	0.21 ± 0.02	5.343	< 0.001

DAO = Diamine oxidase.

1 d after admission ($p > 0.05$). The CD4+ and CD4+/CD8+ were higher and CD8+ lower in both groups at 30d after treatment than pre-treatment ($p < 0.001$). On the 30d after treatment, both CD4+and CD4+/CD8+ in the experimental group were higher than those in the control group at the same time point, while CD8+was lower than those in the control group at the same time point ($p < 0.001$).

Comparison of nutritional indicators

In order to evaluate the nutritional status, we determined the levels of ALB, TRF and PA in control or experimental groups of

Table 5: Comparison of immunologic indices between the two groups of patients.

	Control ($n = 40$)	Experimental group ($n = 40$)	t	p
CD4+ (%)				
1 d after admission	35.63 ± 3.01	36.08 ± 3.10	0.668	0.506
30 d after treatment	40.62 ± 4.57	45.82 ± 4.42	5.162	< 0.001
CD8+ (%)				
1 d after admission	32.17 ± 4.76	31.60 ± 5.72	0.482	0.631
30 d after treatment	26.38 ± 5.26	23.29 ± 5.46	2.582	0.012
CD4+/CD8+				
1 d after admission	1.12 ± 0.08	1.15 ± 0.08	1.277	0.205
30 d after treatment	1.33 ± 0.07	1.48 ± 0.16	5.637	< 0.001

Table 6: Comparison of nutritional indicators between the two groups of patients.

	Control ($n = 48$)	Experimental group ($n = 46$)	t	p
ALB(g/L)				
1 d after admission	28.24 ± 2.34	29.15 ± 2.29	1.761	0.082
30 d after treatment	31.33 ± 2.92	36.69 ± 4.03	6.805	< 0.001
TRF				
1 d after admission	1.24 ± 0.10	1.27 ± 0.13	0.870	0.387
30 d after treatment	1.46 ± 0.15	1.67 ± 0.21	5.045	< 0.001
PAB(mg/L)				
1 d after admission	205.26 ± 14.60	202.33 ± 19.79	0.756	0.452
30 d after treatment	281.160 ± 15.15	297.76 ± 19.41	4.277	< 0.001

ALB = Albumin, TRF = Transferrin, PAB = Prealbumin.

Table 7: Comparison of adverse reactions between the two groups.

Items	Control ($n = 40$)	Experimental group ($n = 40$)	χ^2	p
Nausea	3	6	0.501	0.479
Vomit	2	5	0.626	0.429
Abdominal distension	3	8	2.635	0.104
Diarrhea	2	7	2.003	0.157

patients. At 30d after treatment, the expression levels of serum ALB, TRF and PAB in patients in the experimental group were higher than those in the control group at the same time point ($p < 0.001$). More details are shown in Table 6.

Comparison of adverse reactions and complications

No serious adverse reactions occurred during perioperative nutritional management in either group, and the occurrence of nausea, vomiting, abdominal distension, and diarrhea was rare and minor. The incidence of adverse reactions in the experimental group was slightly higher than that in the control group, but the difference was not statistically significant ($p > 0.05$). More details are shown in Table 7.

DISCUSSION

Hepatitis B cirrhosis is one of the more common end-stage liver diseases in clinic, and it is currently believed that in addition to persistent hepatitis B virus infection, immune dysfunction, abnormal oxidative stress injury, hypersecretion of intestinal inflammatory cytokines, and disruption of intestinal micro-ecological balance are all widely involved in the process of disease progression.[9] At present, the relationship between intestinal microecological changes and hepatitis B is a hot spot in clinical research, and studies have pointed out that patients with liver disease have intestinal flora disorders, and put forward the concept of "intestinal - hepatic axis", and found that there is a

close relationship between intestinal flora and the progression of liver disease.[10]

The composition of intestinal flora is affected by genetics and external environment, including the age of the body and diet.[11] Bifidobacterium and Lactobacillus are beneficial bacteria, which can promote intestinal peristalsis, inhibit the growth of pathogenic bacteria, and decompose harmful and toxic substances; Enterobacteriaceae and Enterococci are neutral bacteria, which are beneficial to health under normal conditions, but once their proliferation is out of control, they can cause damage to the organism.[12,13]

Patients with hepatitis B cirrhosis may experience alterations in intestinal wall structure, leading to heightened intestinal permeability. This can trigger pathological bacterial translocation, fostering excessive growth of intestinal bacteria. Furthermore, impaired liver function may disrupt detoxification processes, resulting in intestinal bacterial imbalances. Additionally, reduced gastric acid secretion, restricted intestinal motility, decreased defensins' antimicrobial activity, and diminished bile acid secretion can collectively weaken the antibacterial defence mechanisms in these patients.[14] Compared with healthy people, the intestinal flora of cirrhotic patients has significant disorders in terms of bacterial species and proportions, and the intestinal flora of cirrhotic patients is characterized by an increase in aerobic bacteria and a decrease in anaerobic bacteria. That is, the decrease in the content of beneficial bacteria makes the proportion of harmful bacteria increase, and the damage to the intestinal barrier promotes the release of inflammatory factors, destroys the body's immune function, and leads to the impairment of the liver function of the patient.

Hepatitis B cirrhosis not only suppresses the function of the immune system, but also the patient's nutritional deficiencies can affect the effectiveness of anti-hepatitis B virus therapy. Therefore, nutritional support strategies have become a popular and essential adjunctive treatment modality for patients with hepatitis B cirrhosis.[15] It is increasingly recognized that certain essential nutrients can modulate a range of metabolic, inflammatory and immune processes when intake exceeds normal daily requirements. Immune-enhanced enteral nutrition support is the addition of immunonutrients to standard nutrition, which helps to enhance the patient's systemic and intestinal immune response, counteract postoperative immune damage, and improve inflammation control and tissue regeneration.[16] Currently, immune-enhanced enteral nutrition support consists of four main immunomodulatory substrates: Gln, Arg, omega-3 fatty acids, and nucleotides. Nitric oxide becomes an essential amino acid during recovery and growth of the organism after injury, and Arg is a precursor for nitric oxide synthesis.[17] In addition, Arg has been associated with increased lymphocyte mitosis, allogeneic response and natural killer cell-mediated cytotoxicity. Gln is an essential nutrient for the metabolism of intestinal mucosal cells, and more importantly, it is central to antioxidant defence. Under severe stressful pressures, such as surgery and infection, the intestinal mucosal epithelium is rapidly depleted of Gln, leading to impaired intestinal immune function Omega-3 fatty acids have been shown to play a role in immunomodulatory, vasodilatory, and anti-inflammatory effects, and are able to regulate the synthesis of various eicosanoids which are involved in the regulation of microcirculatory disturbances and nonspecific inflammatory responses in shock, which can lead to pathological damage and dysfunction of vital organs.[18] Previous studies have shown that RNA nucleotide-deficient diets lead to diminished T-cell responses and reduced IL-2 production, so nucleotides are thought to play an important role in the immune response.[19] Immune-enhanced enteral nutrition has demonstrated good clinical prospects in clinical critical care and surgical patients, which is also increasingly widely used in clinical adjuvant therapy, and a series of relevant studies have been carried out in targeted clinical settings. A medical team conducted a parallel, randomized, double-blind, clinically controlled study of patients undergoing tubectomy and found that immunonutrition is a safe and viable nutritional therapy that positively modulates immune responses after esophagectomy.[20]

In the present study, we used microecological agents combined with immune-enhancing enteral nutrition adjuvant therapy on intestinal flora, intestinal mucosal barrier and immune function in elderly patients with hepatitis B cirrhosis. After 30 days of treatment, the number of colonies of Enterococci, Enterobacteriaceae, Bifidobacteria and Lactobacillus in the observation group was significantly higher than that of the pre-treatment and control groups after treatment ($p< 0.05$). The Bifidobacterium quadruple viable tablets used in this study contain diverse bacterial flora, which can be tightly bound to the intestinal mucosal epithelial cells, and not only promote the body's digestion and absorption of nutrients, but also adjust the intestinal flora, help stabilize the intestinal tract and achieve the balance of the intestinal flora. Our study also showed that after 30 days of treatment, peripheral blood T-lymphocyte subsets CD4+, CD8+ and CD4+/CD8+ ratios were higher in the experimental group than in the control group. In many studies, patients with hepatitis B cirrhosis have reduced immune cells, which represents a state of suppressed immune function in patients. Increasing evidence suggests a positive correlation between low immune function and disease progression and prognosis in patients with hepatitis B cirrhosis.[21] The upregulation of CD4+/CD8+ enhances cellular immunity and promotes the activation and differentiation of B-lymphocytes. Activation of B-lymphocytes leads to an increased secretion of IgM, IgG, and IgA, which enhances humoral immunity.[20]

The intestinal mucosa is an important natural barrier for the human body, and surgical stress can damage the intestinal mucosal barrier and severely impair the function of the intestinal

mucosa, which in turn can lead to serious complications and affect the patient's prognosis. DAO is a copper-containing cytoplasmic enzyme found mainly in intestinal epithelial cells that plays an important role in the oxidative deamination of intestinal histamine. Since DAO produced in the intestinal epithelium is metabolized in the liver shortly after release into the bloodstream, changes in serum DAO activity reflect damage to the intestinal barrier.[22] In addition, disruption of the barrier function leads to the entry of endotoxin into the bloodstream. Endotoxin stimulates the secretion of several pro-inflammatory cytokines, such as TNF-α, via Toll-like receptor 4 (TLR4) in immune cells and induces endotoxic shock.[23] Thus, the level of endotoxin in the circulation also reflects the state of intestinal mucosal barrier function. In this study, both DAO and endotoxin levels were lower in the experimental group than in the control group, which suggested that immune-enhanced enteral nutrition support could produce better promotion of intestinal function and improved intestinal mucosal barrier damage. Comparison of nutritional indicators showed that the blood expression levels of ALB, TRF and PAB were higher in the experimental group than in the control group. The reason for analyzing the above results may lie in the fact that microecological agents combined with immune-enhancing enteral nutrition support can better improve the inflammatory response and immune function of patients with hepatitis B cirrhosis and restore the intestinal mucosal barrier function. Therefore, it can effectively reduce the nutritional consumption of patients with hepatitis B cirrhosis and promote the absorption of nutrients. However, the incidence of adverse reactions in the experimental group was not significantly different from that of the control group, which suggests that microecological agents combined with immune-enhancing enteral nutrition support are safe and reliable in the treatment process and do not bring too much physical burden and side effects to patients, and further research is needed to demonstrate.

CONCLUSION

In conclusion, microecological agents combined with immune-enhancing enteral nutrition support can effectively improve the intestinal mucosal barrier, immune function and nutritional status after laparoscopic surgery for elderly patients with hepatitis B cirrhosis, and its clinical application is safe and well tolerated.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the ethics committee of Yantai Qishan Hospital. Signed written informed consents were obtained from the patients and/or guardians.

ABBREVIATIONS

HBV: Hepatitis B virus; **BMI:** Body Mass Index; **WBC:** White blood cell; **NLR:** Neutrophil-lymphocyte ratio; **Hb:** Hemoglobin; **ALB:** Albumin; **GLB:** Globulin; **ALT:** Alanine aminotransferase; **AST:** Aspartate transaminase; **BUN:** Blood Urea Nitrogen; **MELD:** Model for End-Stage Liver Disease; **TB:** Total bilirubin; **DAO:** Diamine oxidase.

SUMMARY

Hepatitis B cirrhosis, a severe condition resulting from hepatitis B virus infection, leads to liver fibrosis and vascular proliferation. Research has highlighted the importance of addressing intestinal flora imbalance through the "liver-gut" axis in cirrhosis management. A study involving elderly patients investigated the effects of microecological agents and immune-enhancing nutrition alongside antiviral therapy. Results showed that this approach improved gut microbiota composition, immune status, and intestinal barrier function compared to standard treatments. Overall, integrating these interventions effectively boosts intestinal health and immune function in elderly hepatitis B cirrhosis patients.

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