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Efficacy of high-intensity interval training and live Bifidobacterium capsules combined with 5-aminosalicylic acid in treating ulcerative colitis

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Abstract: **Objective** To investigate the efficacy of high-intensity interval training (HIIT)and live *Bifidobacterium* capsules combined with 5-aminosalicylic acid in the treatment of ulcerative colitis (UC), and its impact on immune function, intestinal flora, intestinal mucosal function and inflammatory factors. **Methods** A total of 80 patients with mild to moderate active UC who were admitted to Jiangsu Province (Suqian)Hospital from March 2022 to March 2024 were retrospectively enrolled as the research subjects. All patients received standard treatment based on 5-aminosalicylic acid preparations. On this basis, 40 patients treated with live *Bifidobacterium* capsules were assigned to the control group, and 40 patients treated with HIIT combined with live *Bifidobacterium* capsules were assigned to the combination group. Both groups were treated continuously for one month, with colonoscopy performed before and after treatment to evaluate mucosal healing. The curative effect, as well as the levels of peripheral blood T lymphocyte subsets, intestinal flora, intestinal mucosal function indicators [diamine oxidase (DAO), D-lactic acid] and inflammatory factors[interleukin (IL)-1β, tumor necrosis factor (TNF)-α, IL-8]of the two groups were compared. **Results** After one month of treatment, the overall effective rate of the combination group was higher than that of thecontrol group (97.50% *vs* 80.00%, χ^2 =4.507, *P*=0.034). In both groups, the patients' fecal *Escherichia coli* colony counts, peripheral blood $CD8^+$, serum DAO, D-lactic acid, IL-1β, TNF-α, and IL-8 levels decreased compared to before treatment, while CD4+, CD3+, CD4+ /CD8+, and *Bifidobacterium* and *Lactobacillus* colony counts increased compared to before treatment (*P*<0.05), and all indicators in the combination group were better than those in the control group (*P*<0.05). **Conclusion** Based on standard treatment with 5-aminosalicylic acid, combining HIIT with live *Bifidobacterium* capsules can effectively enhance patients' immune function, optimize intestinal microbiota, improve intestinal mucosal function, reduce UC inflammatory response, and significantly increase the efficacy of UC treatment.

Keywords: High-intensity interval training; Live *Bifidobacterium* capsule; Mucosal healing; Immune function; Intestinal mucosal function; Inflammatory factor

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Ulcerative colitis (UC) is a chronic non-specific inflammatory disease of the colorectum, which is associated with immune mechanism disorder, genetic susceptibility, environmental exposure and intestinal microbial imbalance. Among these factors, immunoglobulin levels often show abnormal elevation, and serum testing indicates the presence of a variety of non-specific colon antibodies, suggesting that the accumulation of immune complexes may be one of the key factors promoting local pathological changes in this disease[1]. Studies have reported that the incidence rate of people with a family history of UC is higher than that of the general population, indicating the role of genetic factors in the pathogenesis of UC[2]. For the clinical management of UC, comprehensive schemes including nutritional support, psychological counseling, drug treatment and surgery are usually adopted to ensure that patients receive the most appropriate treatment[3-4]. *Bifidobacterium* capsules can effectively improve the condition of UC by precisely regulating the intestinal microecology, strengthening the natural defense mechanism of the intestine and inhibiting excessive immune response[5]. High-intensity interval training (HIIT), through the alternating arrangement of high-intensity and low-intensity activities, achieves comprehensive stimulation of the body, and helps to

improve the serum pro-inflammatory factor indexes and immune function indexes of patients[6]. At present, there are many studies on the sole application of these two treatment methods in UC[7], but there are limited reports on the treatment of UC with HIIT combined with *Bifidobacterium* capsules. Based on this, this study explored the efficacy of HIIT combined with Bifidobacterium capsules plus 5-aminosalicylic acid in the treatment of UC and its effect on immune function, in order to provide reference for the clinical diagnosis and treatment of this disease. The report is as follows.

1 Materials and Methods

1.1 General Information

A retrospective study method was adopted. A total of 80 patients with mild to moderate active UC admitted to Suqian Hospital of Jiangsu Provincial People's Hospital from March 2022 to March 2024 were selected as the research subjects. All patients received standard treatment based on 5-aminosalicylic acid preparations. On this basis, 40 patients treated with *Bifidobacterium* capsules were included in the control group, and 40 patients treated with HIIT combined with *Bifidobacterium* capsules were included in the combination group. There was no statistically significant difference in general information between the two groups (P>0.05), as shown in **Table 1**. This study was reviewed and approved by the Medical Ethics Committee of Jiangsu Province (Suqian) Hospital (Ethics Review No.: 2024-SL-0100).

Tab.1 Comparison of basic data between the two groups of patients (n=40)

Groups	Age (years, $\bar{x}\pm s$)	Gender (case)		Disease course (years, $\bar{x}\pm s$)	UC severity (case)	
		Female	Male		Mild	Moderate
Combination Group	46.31±4.64	19	21	3.38±0.35	21	19
Control Group	46.28±4.63	21	19	3.31±0.34	23	17
t/χ^2 value	0.029	0.200		0.907	0.202	
P value	0.977	0.655		0.367	0.653	

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Meet the diagnostic criteria for UC [8], with the disease in mild to moderate active stage; (2) Aged between 18 and 60 years old; (3) Patients and their family members signed the informed consent form. **Exclusion criteria:** (1) Patients allergic to live Bifidobacterium capsules; (2) Patients with other infectious colitis, such as schistosomiasis, intestinal tuberculosis, etc.; (3) Intestinal complications caused by radiotherapy for malignant tumors in the pelvis, abdominal cavity, and retroperitoneum; (4) Incomplete clinical data of patients; (5) Patients who used probiotic preparations within the past 3 months.

1.3 Treatment Methods

Both groups of patients received basic medical intervention, including increasing nutrition and protein intake, providing sufficient rest time, taking measures to maintain electrolyte balance in the body, and administration of 5-aminosalicylic acid preparation: oral Mesalazine Sustained-release Granules (Shanghai Ethypharm Pharmaceutical Co., Ltd., National Medicine Approval No. H20143164, specification: 0.5 g/bag), 2 bags each time, 4 times a day. The treatment lasted for 1 month continuously.

The control group was treated with Live Bifidobacterium Capsules (Livzon Group Livzon Pharmaceutical Factory, National Medicine Approval No. S10960040, 0.35 g × 10 capsules/box), orally administered after meals, 2 capsules each time, once in the morning and once in the evening. The treatment lasted for 1 month continuously.

The combination group received the same Live Bifidobacterium Capsules treatment as the control group, combined with HIIT at the same time. All HIIT sessions were guided by the same trained physician team, and a high-intensity cycling interval training program 3 times a week was added. This high-intensity interval training program was divided into three parts: warm-up activation, high-intensity execution, and cool-down recovery. The duration of the first and third parts was set at 5-10 min to ensure the comprehensiveness and effectiveness of the training. In the initial 2 weeks, the training content was set as full-power cycling at 90% of individual maximum oxygen consumption (VO_{2max}) for 30 s, followed by 1 min of complete relaxation. This sequence was repeated 4 times as a training unit, and a total of 3 units were required, with a 4 min buffer time between each unit. In the following 2 weeks, the program entered the intensification stage: the cycling intensity was adjusted to 80% VO_{2max}, the duration was adjusted to 1 min, followed by 1 min of recovery time. This sequence was repeated 4 times to complete one unit, and a total of 5 units were performed, with the rest time between units reduced to 2 min to promote higher-intensity adaptive training. After the exercise, a 5-10 min easy walk was performed to help the heart rate gradually return to normal. The intervention lasted for 1 month. In the actual training, all patients in the combination group completed the entire intervention program, and no one withdrew due to intolerance or other reasons.

1.4 Observation Indicators

The changes of related indicators in the two groups were compared before and after treatment.

1.4.1 Clinical Efficacy

Colonoscopy was performed before and after treatment to evaluate mucosal healing. The scoring criteria were as follows: 0 point for normal mucosa; 1 point for erythema, vanished vascular texture, indicating mild lesions; 2 points for obvious erythema and erosion, indicating moderate lesions; 3 points for spontaneous bleeding and ulcers, indicating severe lesions[8]. After treatment, the efficacy was classified as follows. Markedly effective: Symptoms disappeared, colonoscopy showed no active lesions and normal mucosa; Effective: Symptoms were significantly or mostly relieved, colonoscopy showed vanished erythema and vascular texture, and intestinal mucosal inflammation was improved; Ineffective: The patient's condition did not meet the above criteria. The total effective rate was calculated as: total effective rate = (number of cases with markedly effective + effective) / total number of cases × 100%.

1.4.2 Immune Function

Before and after treatment, the composition of T lymphocyte subsets in the two groups was compared using a FACS CantoII flow cytometer, including the changes in the counts of $CD3^+$, $CD4^+$ and $CD8^+$ cells, as well as the adjustment of the $CD4^+/CD8^+$ ratio.

1.4.3 Fecal Intestinal Flora Levels

Before and after treatment, the composition of intestinal flora of the two groups was compared. A 10 g fecal sample was collected from each patient and sent to the pathology laboratory. *Escherichia coli* were cultured in an aerobic incubator at room temperature for 48 h, while anaerobic Bifidobacterium and *Lactobacillus* were cultured in an anaerobic incubator at room temperature for 24 h. The total number of colonies per gram of sample was counted and recorded, and the result was expressed as log colony forming units per gram (lg CFU/g).

1.4.4 Levels of Intestinal Mucosal Barrier Function-related Indicators

Before and after treatment, fasting venous blood was collected from patients, and the serum concentration of diamine oxidase (DAO) was measured by enzyme-linked immunosorbent assay (ELISA). After collecting peripheral blood, perchloric acid was added and mixed evenly, the supernatant was obtained by centrifugation and stored, and the D-lactic acid level was detected by p-hydroxybiphenyl colorimetry.

1.4.5 Inflammatory Factor Levels

Before and after treatment, fasting venous blood was collected from patients, and serum was separated after centrifugation. The levels of interleukin (IL)-1β, tumor necrosis factor-α (TNF-α) and IL-8 were measured by ELISA.

1.4.6 Adverse Reactions

The occurrence of adverse reactions in the two groups during treatment was observed and recorded.

1.5 Statistical Methods

SPSS 25.0 software was used for data analysis. Count data were expressed as cases (%), and analyzed by χ^2 test and corrected χ^2 test. Measurement data conforming to normal distribution were expressed as $\bar{x}\pm s$, and analyzed by independent samples t-test. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of Clinical Efficacy Between the Two Groups

After 1 month of treatment, the total effective rate of the combination group was 97.50%, which was higher than 80.00% of the control group ($P < 0.05$), as shown in **Table 2**.

Tab.2 Comparison of mucosal healing scores and clinical efficacy between the two groups of patients [n=40, case (%)]

Group	Markedly Effective	Effective	Ineffective	Total Effective
Combination group	30 (75.00)	9 (22.50)	1 (2.50)	39 (97.50)
Control group	24 (60.00)	8 (20.00)	8 (20.00)	32 (80.00)
χ^2 value				4.507
P value				0.034

2.2 Comparison of Changes in T Lymphocyte Subsets Between the Two Groups

After treatment, the levels of $CD4^+$, $CD3^+$ and $CD4^+/CD8^+$ ratio increased, while the CD8+ level decreased in both groups, and the changes in the combination group were more significant than those in the control group ($P < 0.05$), as shown in **Table 3**.

2.3 Comparison of Fecal Intestinal Flora Levels Between the Two Groups

After treatment, the colony count of *Escherichia coli* decreased in both groups, and the count in the combination group was lower than that in the control group ($P < 0.05$); the colony counts of *Lactobacillus* and *Bifidobacterium* increased in both groups, and the counts in the combination group were higher than those in the control group ($P < 0.05$), as shown in **Table 4**.

2.4 Comparison of Intestinal Mucosal Barrier Function-Related Index Levels Between the Two Groups of Patients

After treatment, the levels of DAO and D-lactic acid in both groups decreased, and the levels in the combination group were lower than those in the control group ($P < 0.05$), as shown in **Table 5**.

2.5 Comparison of Inflammatory Factor Levels Between the Two Groups of Patients

After treatment, the levels of interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and interleukin-8 (IL-8) in both groups of patients decreased, and the levels in the combination group were lower than those in the control group ($P < 0.05$), as shown in **Table 6**.

2.6 Comparison of Total Adverse Reactions Between the Two Groups of Patients

During the treatment period, 1 case of rash, 2 cases of diarrhea, and 1 case of vomiting occurred in the combination group; 2 cases of rash and 1 case of diarrhea occurred in the control group. There was no statistically significant difference in the total incidence of adverse reactions between the combination group and the control group (10.00% *vs* 7.50%, $P > 0.05$).

Tab.3 Comparison of changes of T lymphocyte subsets between two groups before and after treatment (n=40, $\bar{x} \pm s$)

Group	$CD4^+$（%）		$CD3^+$（%）		$CD8^+$（%）		$CD4^+/CD8^+$	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Combination group	33.35±3.37	43.56±4.39[a]	62.69±6.27	69.83±7.12[a]	30.69±3.11	26.01±2.64[a]	1.09±0.17	1.67±0.24[a]
Control group	33.24±3.39	37.13±3.75[a]	62.74±6.30	65.04±6.66[a]	30.81±3.09	27.97±2.86[a]	1.08±0.16	1.33±0.22[a]
t value	0.146	7.044	0.036	3.107	0.173	3.185	0.271	6.605
P value	0.885	＜0.001	0.972	0.003	0.863	0.002	0.787	＜0.001

Note: compared with the pre-treatment level in the same group, [a]$P < 0.05$.

Tab.4 Comparison of gut microbiota levels between two groups of patients (n=40, lgCFU/g, $\bar{x} \pm s$)

Group	*Escherichia coli*		*Lactobacillus*		*Bifidobacterium*	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Combination group	12.16±1.36	7.43±0.79[a]	4.13±0.45	8.81±0.94[a]	8.10±0.86	10.10±1.14[a]
Control group	12.09±1.34	8.89±0.92[a]	4.20±0.49	7.47±0.80[a]	8.05±0.82	8.84±0.96[a]
t value	0.232	7.615	0.665	6.866	0.266	5.347
P value	0.817	＜0.001	0.508	＜0.001	0.791	＜0.001

Note: compared with the pre-treatment level in the same group, [a]$P < 0.05$.

Tab. 5 Comparison of indexes related to intestinal mucosal barrier function between two groups of patients before and after treatment (n=40, $\bar{x} \pm s$)

Group	DAO（U/L）		D-lactic acid（mg/L）	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Combination group	3.44±0.35	1.47±0.16 [a]	38.76±4.03	28.24±2.97 [a]
Control group	3.52±0.37	2.12±0.24 [a]	38.84±4.08	33.18±3.36 [a]
t value	0.993	14.252	0.088	6.967
P value	0.324	＜0.001	0.930	＜0.001

Note: compared with the pre-treatment level in the same group, [a]$P < 0.05$.

Tab. 6 Comparison of inflammatory factor levels between two groups of patients (n=40, $\bar{x} \pm s$)

Group	IL-1β(ng/L)		TNF-α(ng/L)		IL-8 (ng/L)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Combination group	57.10±5.81	31.23±3.14 [a]	37.13±3.72	9.84±1.03 [a]	77.13±7.76	55.12±5.53 [a]
Control group	56.99±5.73	37.16±3.75 [a]	37.22±3.73	15.46±1.57 [a]	77.18±7.78	59.87±6.05 [a]
t value	0.085	7.668	0.108	18.929	0.029	3.665
P value	0.932	＜0.001	0.914	＜0.001	0.977	＜0.001

Note: compared with the pre-treatment level in the same group, [a]$P < 0.05$.

3 Discussion

UC is characterized by chronic progression and recurrent episodes. Some patients are prone to developing dependence on hormonal drugs, which increases the complexity of treatment[9-10]. Although drug monotherapy can temporarily relieve symptoms, long-term administration may be accompanied by significant adverse reactions and decreased body tolerance, a problem that is particularly prominent in the elderly patient population[11]. Given the complexity of UC, scientific treatment and management systems should be followed to effectively alleviate symptoms and reduce disease risks[12].

Bifidobacterium regulates the pH of the intestinal environment through its unique metabolic activities, such as the production of acetic acid and lactic acid, effectively resisting the invasion of harmful microorganisms, and improving and consolidating the intestinal microecological balance[13]. Although HIIT cannot directly intervene in the pathological process of UC, it can comprehensively improve physical fitness and enhance immune response[14]. Prolonged excessive strenuous exercise may damage gastrointestinal function, while long-term low-intensity aerobic exercise can improve gastrointestinal function. Studies have indicated that HIIT therapy contributes to the rehabilitation of patients with UC in the remission stage, with more significant therapeutic effects[15].

The results of this study show that the therapeutic efficacy of the combination group is superior to that of the control group, indicating that the combination of HIIT and *Bifidobacterium* capsules has advantages in the treatment of UC. In the pathological environment of UC, the $CD4^+$ cell population is significantly affected, while $CD8^+$ cells, as a class of T cells with inhibitory functions, are essential for the precise regulation of immune responses[16]. Changes in the total number of T lymphocytes are often accompanied by corresponding adjustments in the number of $CD3^+$ cells, which is a key window for monitoring the dynamic changes of T cell immune function[17]. The $CD4^+/CD8^+$ ratio is an important indicator of the internal balance of the T lymphocyte population. Under the abnormal immune state of UC patients, this balance is often disrupted, leading to a shift in the ratio[18]. After treatment in this study, the levels of $CD4^+$, $CD3^+$, and $CD4^+/CD8^+$ ratio in the combination group were higher than those in the control group, while the $CD8^+$ level was lower than that in the control group, indicating that the combination of HIIT and *Bifidobacterium* capsules can effectively improve the immune function of UC patients. The possible reason for this is that the combination of HIIT and *Bifidobacterium* capsules can optimize the intestinal environment, promote the proliferation and functional activation of $CD4^+$ helper T cells and $CD3^+$ labeled T lymphocytes through immune stimulation, laying a foundation for enhancing the ability of the immune system to counteract the pathological mechanism of UC.

In the intestinal microecological environment of UC patients, the colonization pattern of *Escherichia coli* often undergoes abnormal adjustment[19-20]. Under the pathological background of UC, the population dynamics of *Lactobacillus* may be adversely affected, leading to a decrease in its quantity and activity, which further affects the stable colonization of *Lactobacillus* in the intestinal tract[21]. *Bifidobacterium*, as a beneficial flora in the intestinal microecology, is essential for maintaining intestinal homeostasis[22]. In this study, after treatment, the number of *Escherichia coli* decreased in both groups, while the number of *Lactobacillus* and *Bifidobacterium* increased. The decrease in *Escherichia coli* and the increase in *Lactobacillus* and *Bifidobacterium* were more significant in the combination group. The possible reasons are that HIIT can promote intestinal peristalsis and blood circulation, and *Bifidobacterium* viable capsules supplement beneficial flora and inhibit the growth of harmful bacteria. The two complement each other and jointly promote the development of intestinal flora towards a more balanced state.

Inflammatory injury of the intestinal mucosa in UC patients may disrupt the normal function of DAO, leading to its massive overflow from cells and causing an abnormal increase in serum DAO levels[23]. Due to the inflammatory reaction and increased permeability of the intestinal mucosa, this balance is disrupted, and metabolites such as D-lactic acid are more likely to enter the blood circulation, leading to an increase in the concentration of D-lactic acid in the serum[24]. In this study, the levels of DAO and D-lactic acid decreased in both groups, and were lower in the combination group than in the control group, indicating that the combination of HIIT and *Bifidobacterium* capsules can effectively improve the intestinal mucosal function of patients. The possible reason is that HIIT exercise and *Bifidobacterium* capsules, as two methods to enhance intestinal mucosal health and promote efficient nutrient absorption, work together to strengthen physical fitness, improve immunity, and promote the recovery of UC symptoms.

The excessive activity of pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-8 is a marker of aggravated inflammation[25]. The results of this study show that the levels of IL-1β, TNF-α, and IL-8 in the combination group were lower than those in the control group, indicating that the combination of HIIT and *Bifidobacterium* capsules can help reduce the inflammatory response in patients. The possible reason is that HIIT effectively inhibits the inflammatory response in the body, and *Bifidobacterium* improves the intestinal barrier and immunity. The synergy between the two helps to reduce inflammation. There was no significant difference in adverse reactions between the two groups, indicating that the combined regimen does not increase the treatment risk and has good safety.

In conclusion, the combination of HIIT and *Bifidobacterium* capsules can effectively improve the immunity of patients, optimize the balance of intestinal flora and intestinal mucosal function, reduce the inflammatory response of UC, and enhance the therapeutic effect of UC. However, this study still has certain limitations. The small sample size may lead to bias in the results. In the follow-up, the sample size will be expanded to further study its mechanism of action in depth.

Conflict of interest None

Reference

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·炎症性肠病专题·论著·

高强度间歇性运动及双歧杆菌活菌胶囊联合5-氨基水杨酸对溃疡性结肠炎的疗效

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摘要：目的 探讨高强度间歇性运动(HIIT)及双歧杆菌活菌胶囊联合5-氨基水杨酸治疗溃疡性结肠炎(UC)的疗效，及对免疫功能、肠道菌群、肠黏膜功能和炎症因子的影响。**方法** 回顾性选取2022年3月至2024年3月江苏省人民医院宿迁医院收治的80例轻、中度活动期UC患者作为研究对象，均接受以5-氨基水杨酸制剂为基础的标准治疗，在此基础上采用双歧杆菌活菌胶囊治疗的40例为对照组，采用HIIT联合双歧杆菌活菌胶囊治疗的40例为联合组，两组均连续治疗1个月。于治疗前后进行结肠镜检查，评估黏膜愈合情况，比较两组患者的疗效和外周血T淋巴细胞亚群、肠道菌群、肠黏膜功能指标[二胺氧化酶(DAO)、D-乳酸]以及炎症因子[白细胞介素(IL)-1β、肿瘤坏死因子(TNF)-α、IL-8]水平。**结果** 治疗1个月后，联合组总有效率高于对照组(97.50% *vs* 80.00%，χ^2=4.507，*P*=0.034)；两组患者粪便肠杆菌菌落数、外周血$CD8^+$、血清DAO、D-乳酸、IL-1β、TNF-α、IL-8水平均比治疗前降低，$CD4^+$、$CD3^+$、$CD4^+/CD8^+$、双歧杆菌、乳杆菌菌落数比治疗前增加(*P*<0.05)，且联合组均优于对照组(*P*<0.05)。**结论** 在5-氨基水杨酸标准治疗的基础上，HIIT联合双歧杆菌活菌胶囊能有效提高患者免疫功能，优化肠道菌群，改善肠黏膜功能，减轻炎症反应，明显改善UC的疗效。

关键词： 高强度间歇性运动；双歧杆菌活菌胶囊；黏膜愈合；免疫功能；肠黏膜功能；炎症因子
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Efficacy of high-intensity interval training and live *Bifidobacterium* capsules combined with 5-aminosalicylic acid in treating ulcerative colitis

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Abstract: Objective To investigate the efficacy of high-intensity interval training (HIIT) and live *Bifidobacterium* capsules combined with 5-aminosalicylic acid in the treatment of ulcerative colitis (UC), and its impact on immune function, intestinal flora, intestinal mucosal function and inflammatory factors. **Methods** A total of 80 patients with mild to moderate active UC who were admitted to Jiangsu Province (Suqian) Hospital from March 2022 to March 2024 were retrospectively enrolled as the research subjects. All patients received standard treatment based on 5-aminosalicylic acid preparations. On this basis, 40 patients treated with live *Bifidobacterium* capsules were assigned to the control group, and 40 patients treated with HIIT combined with live *Bifidobacterium* capsules were assigned to the combination group. Both groups were treated continuously for one month, with colonoscopy performed before and after treatment to evaluate mucosal healing. The curative effect, as well as the levels of peripheral blood T lymphocyte subsets, intestinal flora, intestinal mucosal function indicators [diamine oxidase (DAO), D-lactic acid] and inflammatory factors [interleukin (IL)-1β, tumor necrosis factor (TNF)-α, IL-8] of the two groups were compared. **Results** After one month of treatment, the overall effective rate of the combination group was higher than that of the

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control group (97.50% *vs* 80.00%, χ^2=4.507, *P*=0.034). In both groups, the patients' fecal *Escherichia coli* colony counts, peripheral blood $CD8^+$, serum DAO, D-lactic acid, IL-1β, TNF-α, and IL-8 levels decreased compared to before treatment, while $CD4^+$, $CD3^+$, $CD4^+/CD8^+$, and *Bifidobacterium* and *Lactobacillus* colony counts increased compared to before treatment (*P*<0.05), and all indicators in the combination group were better than those in the control group (*P*<0.05). **Conclusion** Based on standard treatment with 5-aminosalicylic acid, combining HIIT with live *Bifidobacterium* capsules can effectively enhance patients' immune function, optimize intestinal microbiota, improve intestinal mucosal function, reduce UC inflammatory response, and significantly increase the efficacy of UC treatment.

Keywords: High-intensity interval training; Live *Bifidobacterium* capsule; Mucosal healing; Immune function; Intestinal mucosal function; Inflammatory factor

Fund program: Scientific Research Project of Jiangsu Provincial Health Commission (ZD2022052); Project of Suqian Science and Technology Bureau (SY202216)

溃疡性结肠炎(ulcerative colitis,UC)是一种慢性非特异性的结直肠炎症,与免疫机制紊乱、遗传易感性、环境暴露及肠道微生物失衡等因素有关,其中免疫球蛋白水平常出现异常升高,血清检测提示存在多种非特异性结肠抗体,显示免疫复合物的积累可能是促进本病局部病理变化的关键因素之一[1]。研究报道,具有UC家族史者发病率高于普通人群,表明了遗传因素在UC发病中的作用[2]。临床针对UC,常以营养支持、心理疏导、药物治疗及外科手术等综合方案,确保患者获得最适合的治疗[3-4]。双歧杆菌活菌胶囊通过精准调控肠道微生态、强化肠道自然防御机制以及抑制过度的免疫应答,有助于有效改善UC病情[5]。高强度间歇性运动(high-intensity interval training,HIIT)通过高强度与低强度活动的交替安排,实现对身体的全面刺激,有助于改善患者血清促炎因子指标和免疫功能指标[6]。目前这两种治疗手段单独应用于UC的研究较多[7],但HIIT联合双歧杆菌活菌胶囊治疗UC的相关报道有限,基于此,本研究探究HIIT及双歧杆菌活菌胶囊联合5-氨基水杨酸治疗UC的疗效,及对免疫功能的影响,以期为该病临床诊治提供参考,现报道如下。

1　资料与方法

1.1　*一般资料*　采用回顾性研究方法,选取江苏省人民医院宿迁医院2022年3月至2024年3月收治的80例轻、中度活动期UC患者为研究对象,均接受以5-氨基水杨酸制剂为基础的标准治疗,在此基础上采用双歧杆菌活菌胶囊治疗的40例为对照组,采用HIIT联合双歧杆菌活菌胶囊治疗的40例为联合组,两组一般资料差异无统计学意义(*P*>0.05)。见表1。本研究获江苏省人民医院宿迁医院医学伦理委员会审核批准(伦审号:2024-SL-0100)。

表1　两组患者一般资料比较　(*n*=40)

Tab.1　Comparison of general data between two groups　(*n*=40)

组别	年龄(岁,$\bar{x}\pm s$)	性别(例)		病程(年,$\bar{x}\pm s$)	UC程度(例)	
		女	男		轻度	中度
联合组	46.31±4.64	19	21	3.38±0.35	21	19
对照组	46.28±4.63	21	19	3.31±0.34	23	17
t/χ^2值	0.029	0.200		0.907	0.202	
*P*值	0.977	0.655		0.367	0.653	

1.2　*纳入与排除标准*　纳入标准:(1)符合UC的诊断标准[8],且病情处于轻、中度活动期;(2)患者年龄18~60岁;(3)患者及家属签署知情同意书。排除标准:(1)对双歧杆菌活菌胶囊过敏者;(2)患有其他感染性结肠炎,如血吸虫病、肠结核等;(3)由放射线治疗盆腔、腹腔、腹膜后恶性肿瘤引起的肠道并发症;(4)患者临床资料缺失;(5)近3个月内使用益生菌制剂者。

1.3　*治疗方法*　两组患者均接受基础医疗干预,具体措施包括增加营养与蛋白质摄入,提供充足的休息时间,采取措施维持体内电解质平衡,给予5-氨基水杨酸制剂:口服美沙拉秦缓释颗粒(上海爱的发制药有限公司,国药准字H20143164,规格:0.5 g/袋),2袋/次,4次/d。连续服用1个月。

对照组采用双歧杆菌活菌胶囊(丽珠集团丽珠制药厂,国药准字S10960040,0.35 g×10粒/盒)进行治疗,餐后口服,2粒/次,早晚各1次。连续服用1个月。

联合组接受与对照组相同的双歧杆菌活菌胶囊治疗,同时联合HIIT。HIIT均由经过培训的同一医师团队进行指导,加入每周3次的高强度蹬车间歇训练计划,该高强度间歇训练方案分为准备激活、高强度执行与恢复整理三大部分,第一和第三部分的时长设定在5~10 min,以确保训练的全面性和有效性。初始2周,训练内容设定为以个人最大

氧耗量（maximum oxygen consumption，VO_2max）的90%全力蹬车30 s，随后进行1 min的完全放松，该序列重复4次作为一组训练单元，共需完成三组，每组间设有4 min的缓冲时间。接下来的2周进入深化阶段，蹬车强度调整为80% VO_2max，持续时间调整至1 min，随后是1 min的恢复时间，重复4次完成一组，共进行五组训练，且组间的休息时间缩减至2 min，以促进更高强度的适应性训练，在运动结束后，进行5~10 min的轻松步行，帮助心率逐渐恢复正常。干预1个月。实际训练中，联合组患者均完成全部干预方案，未出现因不耐受或其他原因退出者。

1.4 研究指标 收集治疗1个月后疗效评价结果及各指标变化。

1.4.1 临床疗效 于治疗前后进行结肠镜检查，评估黏膜愈合情况，0分，正常黏膜；1分，红斑、血管纹理消失、轻度病变；2分，明显红斑、糜烂、中度病变；3分，自发性出血、溃疡，重度病变。治疗后，患者症状消失，结肠镜检查结果无活动性病变，黏膜正常，为显效；患者症状得到明显缓解或大部分缓解，结肠镜评估显示红斑、血管纹理消失，肠黏膜炎症状况有所好转，为有效；患者状况不符合上述评判标准，则为无效[8]。总有效率=（显效+有效）例数/总例数×100%。

1.4.2 免疫功能 治疗前后，利用FACS Canto Ⅱ流式细胞仪对比两组T淋巴细胞亚群构成，包括$CD3^+$、$CD4^+$、$CD8^+$细胞的数量变化，以及$CD4^+/CD8^+$比值的调整情况。

1.4.3 粪便肠道菌群水平 治疗前后，对比两组患者的肠道菌群构成，采集每位患者10 g粪便样本，提交至病理学实验室，肠杆菌在有氧培养箱中37 ℃条件下培养48 h，厌氧生长的双歧杆菌与乳杆菌被置于厌氧培养箱中，于37 ℃条件下培养24 h；统计并记录每克样本内含有的菌落总数，结果以对数菌落形成单位（colony forming units，CFU）/克（lg CFU/g）表示。

1.4.4 肠黏膜屏障功能相关指标水平 治疗前后，采集患者空腹静脉血，运用酶联免疫吸附试验测定血清中二胺氧化酶（diamine oxidase，DAO）的浓度；采得患者外周血后，加入高氯酸并混合均匀，通过离心步骤获取上清液储存，之后利用对羟基联苯比色技术检测D-乳酸水平。

1.4.5 炎症因子水平 于治疗前后取患者空腹状态下的静脉血，离心后分离出血清，用酶联免疫吸附试验测定白细胞介素（interleukin，IL）-1β、肿瘤坏死因子-α（tumor necrosis factor-α，TNF-α）及IL-8水平。

1.4.6 不良反应 观察并记录两组患者治疗期间不良反应发生情况。

1.5 统计学方法 采用SPSS 25.0软件分析数据。计数资料以例（%）表示，采用χ^2检验和校正χ^2检验；符合正态分布的计量资料以$\bar{x}\pm s$表示，采用独立样本t检验。$P<0.05$为差异有统计学意义。

2 结 果

2.1 两组患者临床疗效比较 治疗1个月后，联合组总有效率为97.50%，高于对照组的80.00%（$P<0.05$）。见表2。

2.2 两组患者T淋巴细胞亚群变化比较 治疗后，两组的$CD4^+$、$CD3^+$、$CD4^+/CD8^+$增高，$CD8^+$降低，联合组比对照组更优（$P<0.05$）。见表3。

2.3 两组患者粪便肠道菌群水平比较 治疗后，两组患者肠杆菌菌落数降低，联合组低于对照组（$P<0.05$）；两组乳杆菌、双歧杆菌菌落数增高，联合组高于对照组（$P<0.05$）。见表4。

表2 两组患者临床疗效比较 ［n=40，例（%）］

Tab.2 Comparison of clinical efficacy between the two groups of patients ［n=40，case（%）］

组别	显效	有效	无效	总有效
联合组	30（75.00）	9（22.50）	1（2.50）	39（97.50）
对照组	24（60.00）	8（20.00）	8（20.00）	32（80.00）
χ^2值				4.507
P值				0.034

表3 两组患者治疗前后T淋巴细胞亚群变化比较 （n=40，$\bar{x}\pm s$）

Tab.3 Comparison of changes of T lymphocyte subsets between two groups before and after treatment （n=40，$\bar{x}\pm s$）

组别	$CD4^+$（%）		$CD3^+$（%）		$CD8^+$（%）		$CD4^+/CD8^+$	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组	33.35±3.37	43.56±4.39[a]	62.69±6.27	69.83±7.12[a]	30.69±3.11	26.01±2.64[a]	1.09±0.17	1.67±0.24[a]
对照组	33.24±3.39	37.13±3.75[a]	62.74±6.30	65.04±6.66[a]	30.81±3.09	27.97±2.86[a]	1.08±0.16	1.33±0.22[a]
t值	0.146	7.044	0.036	3.107	0.173	3.185	0.271	6.605
P值	0.885	<0.001	0.972	0.003	0.863	0.002	0.787	<0.001

注：与同组治疗前比较，[a]$P<0.05$。

表4　两组患者肠道菌群水平比较　(n=40, lgCFU/g, $\bar{x}\pm s$)

Tab.4　Comparison of gut microbiota levels between two groups　(n=40, lgCFU/g, $\bar{x}\pm s$)

组别	肠杆菌		乳杆菌		双歧杆菌	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组	12.16±1.36	7.43±0.79[a]	4.13±0.45	8.81±0.94[a]	8.10±0.86	10.10±1.14[a]
对照组	12.09±1.34	8.89±0.92[a]	4.20±0.49	7.47±0.80[a]	8.05±0.82	8.84±0.96[a]
t值	0.232	7.615	0.665	6.866	0.266	5.347
P值	0.817	<0.001	0.508	<0.001	0.791	<0.001

注：与同组治疗前比较，[a]P<0.05。

2.4　两组患者肠黏膜屏障功能相关指标水平比较　治疗后，两组DAO、D-乳酸水平均下降，联合组较对照组更低(P<0.05)。见表5。

2.5　两组患者炎症因子水平比较　治疗后，两组患者IL-1β、TNF-α、IL-8水平均降低，联合组较对照组更低(P<0.05)。见表6。

2.6　两组患者总不良反应比较　治疗期间，联合组出现1例皮疹，2例腹泻，1例呕吐；对照组出现2例皮疹，1例腹泻。联合组和对照组不良反应总发生率比较差异无统计学意义(10.00% *vs* 7.50%, P>0.05)。

表5　两组患者治疗前后肠黏膜屏障功能相关指标水平比较　(n=40, $\bar{x}\pm s$)

Tab.5　Comparison of indexes related to intestinal mucosal barrier function between two groups before and after treatment　(n=40, $\bar{x}\pm s$)

组别	DAO(U/L)		D-乳酸(mg/L)	
	治疗前	治疗后	治疗前	治疗后
联合组	3.44±0.35	1.47±0.16[a]	38.76±4.03	28.24±2.97[a]
对照组	3.52±0.37	2.12±0.24[a]	38.84±4.08	33.18±3.36[a]
t值	0.993	14.252	0.088	6.967
P值	0.324	<0.001	0.930	<0.001

注：与同组治疗前比较，[a]P<0.05。

表6　两组患者炎症因子水平比较　(n=40, $\bar{x}\pm s$)

Tab.6　Comparison of inflammatory factor levels between two groups　(n=40, $\bar{x}\pm s$)

组别	IL-1β(ng/L)		TNF-α(ng/L)		IL-8(ng/L)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
联合组	57.10±5.81	31.23±3.14[a]	37.13±3.72	9.84±1.03[a]	77.13±7.76	55.12±5.53[a]
对照组	56.99±5.73	37.16±3.75[a]	37.22±3.73	15.46±1.57[a]	77.18±7.78	59.87±6.05[a]
t值	0.085	7.668	0.108	18.929	0.029	3.665
P值	0.932	<0.001	0.914	<0.001	0.977	<0.001

注：与同组治疗前比较，[a]P<0.05。

3　讨　论

UC具有慢性迁延、反复发作的特点，部分患者易对激素类药物产生依赖，增加治疗复杂性[9-10]。单独依靠药物治疗，虽可暂时缓解症状，但长期使用可能伴随显著的不良反应及机体耐受性下降的问题，在老年患者群体中更加突出[11]。鉴于UC的复杂性，应遵循科学的治疗与管理体系，以有效缓解病痛，降低疾病风险[12]。

双歧杆菌通过其独特的代谢活动，如产生醋酸和乳酸，来调节肠道环境的酸碱度，有效抵御有害微生物的侵袭，改善并巩固肠道的微生态平衡[13]。HIIT运动方式虽不能直接干预UC的病理过程，但可全面提升身体素质、增强免疫应答[14]。长时间过度剧烈运动会损伤胃肠道功能，长期低强度有氧运动可以改善胃肠道功能，研究指出HIIT疗法有助于缓解期UC患者的康复，HIIT治疗效果更加显著[15]。

本研究显示，联合组的疗效优于对照组，表明HIIT与双歧杆菌活菌胶囊联合治疗UC具有优势。在UC的病理环境中，$CD4^+$细胞群体受到显著影响，而$CD8^+$细胞，作为一类具有抑制功能的T细胞，对于精细调控免疫反应至关重要[16]。T淋巴细胞总数的变化往往伴随着$CD3^+$细胞数量的相应调整，是监测T细胞免疫功能动态变化的关键窗口[17]。$CD4^+/CD8^+$比值作为T淋巴细胞群体内部平衡的重要指标，在UC患者的免疫异常状态下，这一平衡往往被打破，导致比值发生偏移[18]。本研究治疗后，联合组$CD4^+$、$CD3^+$、$CD4^+/CD8^+$高于对照组，$CD8^+$低于对照组，表明HIIT与双歧杆菌活菌胶囊联合可有效提高UC患者免疫功能。分析原因可能为HIIT联合双歧杆菌活菌胶囊可优化肠道环境，通过免疫刺激作用，促进$CD4^+$辅助性T细胞和$CD3^+$标记T淋巴细胞的增殖与功能活化，为增强免疫系统对抗UC病理机制的能力奠定基础。UC患者的肠道微生态环境中，肠杆菌的形成模式常发生异常调整[19-20]。在UC的病理背景下，

乳杆菌的种群动态可能受到不利影响，导致其数量下降、活性减弱，进而影响乳杆菌在肠道内的稳定定植[21]。双歧杆菌作为肠道微生态中的有益菌群，对于维持肠道稳态至关重要[22]。本研究中，治疗后，两组肠杆菌数目减少，乳杆菌、双歧杆菌数量均增加，而联合组肠杆菌的下降、乳杆菌和双歧杆菌上升的变化都更为显著，分析原因可能为HIIT可促进肠道蠕动与血液循环；双歧杆菌活菌胶囊补充有益菌群并抑制有害菌的滋生。两者相辅相成，共同推动肠道菌群向更加平衡的方向发展。UC患者肠道黏膜的炎症性损伤可能扰乱DAO的正常功能，导致其从细胞内大量溢出，促使血清DAO水平异常升高[23]。由于肠道黏膜的炎症反应和通透性增加，这一平衡被打破，D-乳酸等代谢产物更容易进入血液循环，导致血清中D-乳酸的浓度上升[24]。本研究中，两组DAO、D-乳酸水平均降低，且联合组低于对照组，表明HIIT联合双歧杆菌活菌胶囊可有效改善患者肠黏膜的功能，分析原因可能为HIIT锻炼与双歧杆菌活菌胶囊作为两种增强肠道黏膜健康、促进营养高效吸收的方法，共同作用可强化体质，提升免疫力，促进UC病症的康复。IL-1β、TNF-α、IL-8等促炎细胞因子的过度活跃，是炎症加剧的标志[25]。本研究显示，联合组IL-1β、TNF-α、IL-8水平低于对照组，表明HIIT联合双歧杆菌活菌胶囊可助于降低患者体内炎症反应，分析原因可能为HIIT有效抑制体内的炎症反应，双歧杆菌改善肠道屏障与免疫，二者协同，有助于减轻炎症。两组不良反应无明显差异，表明联合方案未增加治疗风险，安全性良好。

综上所述，HIIT联合双歧杆菌活菌胶囊可有效提升患者免疫力，优化肠道菌群的平衡和肠黏膜的功能，减轻UC的炎症反应，增强UC的治疗效果。但本研究尚存在一定局限性，样本量较小，导致结果可能存在偏倚，后续将扩大样本量进一步深入研究其作用机制。

利益冲突　无

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