Comparative analysis of the efficacy of probiotics combined with 5-amino salicylic acid in the treatment of ulcerative colitis

Wang Song Zou Chuanxin(Corresponding author)

Jingzhou Hospital Affiliated to Yangtze University，Jingzhou city Hubei Province，434020；

Abstract: Ulcerative colitis (UC) is a chronic inflammatory bowel disease. While 5-aminosalicylic acid (5-ASA) serves as the first-line treatment, its efficacy remains suboptimal in some patients. This study conducted a systematic review of the clinical efficacy of probiotic combination therapy with 5-ASA in treating acute-onset UC. By comparing the differences between combined therapy and single-ASA treatment in clinical symptom improvement, endoscopic mucosal healing, decreased inflammatory markers, clinical remission rates, and safety profiles, the results demonstrated that the combined therapy group significantly outperformed the single-drug control group across all evaluation metrics, indicating that probiotics can effectively enhance the therapeutic effects of 5-ASA. Comparative analysis of different probiotic preparations revealed that strain specificity was the key factor influencing efficacy, with certain combination preparations and specific strains (e.g., Lactobacillus rhamnosus GG) exhibiting superior synergistic effects. Mechanistically, probiotics exert synergistic effects with 5-ASA through multiple pathways including gut microbiota regulation, intestinal barrier repair, and anti-inflammatory responses. Safety evaluations showed good tolerability of the combined regimen without significant adverse reactions.

Key words: ulcerative colitis; probiotics; 5-amino salicylic acid

DOI:10.69979/3041-0843.25.03.013

Introduction

Ulcerative colitis (UC), a chronic nonspecific inflammatory bowel disease with an unclear etiology, has seen a global increase in incidence. This condition poses significant health risks and compromises patients' quality of life. While 5-aminosalicylic acid (5-ASA) remains the first-line treatment for mild-to-moderate active UC through its anti-inflammatory effects, some patients still experience suboptimal efficacy and frequent relapses. Recent advancements in understanding gut microbiota and inflammatory diseases have highlighted the growing importance of gut microbiota imbalance in UC development, providing theoretical support for probiotic applications. As beneficial microorganisms that regulate host microbial balance, probiotics demonstrate unique therapeutic potential in managing intestinal inflammation through multiple mechanisms: modulating gut immunity, repairing mucosal barriers, and inhibiting pathogen colonization.

1 Efficacy analysis of probiotics combined with 5-ASA in the treatment of initial UC

1.1 Improvement of clinical symptoms

In improving clinical symptoms of ulcerative colitis (UC) patients with initial onset, the combination therapy of probiotics and 5-aminosalicylic acid (5-ASA) demonstrated a synergistic effect superior to using 5-ASA alone. Multiple clinical studies consistently show that the combined treatment group achieved faster and more significant relief in core symptoms such as diarrhea, abdominal pain, bloody stools, and tenesmus. The combined regimen can more rapidly control intestinal inflammation, thereby shortening symptom remission time, with noticeable improvements typically observable within 2-4 weeks of treatment. By comparing changes in the UC Disease Activity Index (UCDAI) or Sutherland Index, the combined treatment group showed significantly greater score reduction at treatment completion compared to the control group, indicating higher overall improvement in clinical symptoms. This advantage may stem from probiotics 'multi-faceted

mechanisms—such as competitively inhibiting harmful bacteria, enhancing intestinal barrier function, and regulating local immunity—working synergistically with 5-ASA's direct anti-inflammatory effects and prostaglandin synthesis inhibition. This comprehensive approach effectively blocks inflammatory cascades, rapidly alleviates patient discomfort, improves quality of life, and establishes a solid foundation for subsequent maintenance therapy.

1.2 Endoscopic mucosal healing

Endoscopic mucosal healing serves as a critical indicator for evaluating the efficacy of ulcerative colitis (UC) treatment, reflecting the depth of disease control. Research data demonstrates that combined probiotic therapy with 5-ASA significantly enhances endoscopic mucosal healing in patients with first-episode UC. The combined treatment group not only more effectively alleviated mucosal congestion and edema but also significantly promoted the repair and healing of erosions and ulcers. Through endoscopic scoring systems (such as UCEIS or Mayo Endoscopic Score), the combined treatment group achieved a significantly higher proportion of endoscopic remission (with mucosa returning to near-normal or showing only mild inflammation) at treatment completion compared to the 5-ASA monotherapy group. This indicates that probiotics, as adjunct therapy, can enhance the direct repair effects of 5-ASA on intestinal mucosa. The mechanism may involve probiotic metabolites (e.g., short-chain fatty acids) providing energy for intestinal epithelial cells to promote their proliferation and repair. Simultaneously, probiotics regulate gut microbiota balance, reducing persistent damage from harmful bacteria and their toxins to the mucosa. This accelerates ulcer healing and reduces the risk of poor mucosal healing, which is crucial for preventing disease recurrence and improving long-term prognosis.

1.3 Improvement of inflammatory indicators

The combination therapy of probiotics and 5-ASA demonstrated superior efficacy in improving laboratory inflammatory markers in patients with primary ulcerative colitis (UC), reflecting its effectiveness in controlling systemic inflammatory responses. Patients receiving the combined treatment showed significantly faster and greater reductions in peripheral blood inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) compared to monotherapy groups. As a sensitive indicator of acute inflammation, the rapid decline in CRP levels suggested effective control of intestinal inflammation and alleviation of associated systemic inflammatory reactions. Additionally, the combined treatment group exhibited remarkable improvement in fecal calprotectin levels. Fecal calprotectin, a specific marker for assessing intestinal mucosal inflammation activity and severity, showed significant reduction directly reflecting the alleviation of mucosal inflammation. These multi-level improvements in inflammatory markers not only confirmed the effectiveness of the combined therapy but also provided clinicians with objective quantitative evidence to evaluate treatment outcomes and guide subsequent therapeutic decisions.

1.4 Mucosal histological repair

Mucosal histological repair represents a higher-level objective in UC treatment, indicating not only macroscopic symptom relief but also reversal of microscopic pathological damage. Studies demonstrate that the combination of probiotics and 5-ASA therapy shows superior efficacy in promoting mucosal histological repair in first-episode UC patients. Pathological evaluation of biopsy specimens reveals that the combined treatment group excels in improving histological indices (such as Geboes index and Nancy index). This approach not only significantly reduces inflammatory cell infiltration in the lamina propria (including neutrophils, lymphocytes, and plasma cells) but also effectively promotes crypt structure restoration, reducing crypt deformation, branching, and atrophy, with even visible epithelial regeneration observed. Probiotics provide primary energy for colonic epithelial cells through their metabolites (e.g., butyrate), facilitating cell proliferation and differentiation. Simultaneously, probiotics enhance the expression of tight junction proteins, repairing damaged intestinal epithelial barriers. By fundamentally blocking antigen invasion and chronic inflammation, this mechanism achieves deeper histological healing, which is crucial for reducing recurrence rates and achieving long-term remission.

1.5 Comparison of clinical remission rate and response rate

In evaluating the ultimate clinical outcomes of treatment, the probiotic combined with 5-ASA regimen demonstrated significant advantages in improving clinical remission rates and response rates among patients with first-episode ulcerative colitis (UC). Clinical remission rate, defined as the proportion of patients achieving complete symptom resolution and marked improvement in endoscopic motility post-treatment, serves as the gold standard for measuring treatment success. Multiple meta-analyses revealed that the combined treatment group showed significantly higher clinical remission rates compared to the 5-ASA monotherapy group, with an absolute difference reaching 10%-20%. Concurrently, the clinical response rate (proportion of patients achieving symptom reduction meeting predefined criteria) was also notably higher in the combined treatment group. These differences indicate that the combined therapy not only enables more patients to achieve symptom-free ideal states but also ensures substantial symptom improvement through treatment benefits. This elevated remission and response rate allows more first-episode UC patients to attain good control during initial treatment, preventing chronic progression or refractory transformation caused by inadequate therapy. These findings hold significant clinical practical implications for guiding treatment strategies.

1.6 Safety and tolerance evaluation

The combination of probiotics with 5-ASA demonstrates favorable safety and tolerability in treating first-onset ulcerative colitis (UC), with no additional safety risks observed overall. As a first-line UC treatment, 5-ASA has been extensively validated for its safety profile. The most commonly used probiotic strains in current research — including Escherichia coli Nissle 1917, Lactobacillus, and Bifidobacterium—are all normal intestinal symbionts with long-established clinical applications. Current data indicate that under standard dosing regimens, there is no significant difference in adverse event rates between the combined therapy group and the 5-ASA monotherapy group. Common adverse reactions primarily involve mild gastrointestinal symptoms such as bloating, constipation, or mild abdominal pain, which are typically mild and resolve spontaneously without requiring special intervention, thus not affecting treatment progression. No reports of severe infections or systemic adverse reactions associated with probiotics have been documented. Therefore, combining specific probiotics with 5-ASA serves as a safe and well-tolerated adjunctive therapy strategy for first-onset UC patients, effectively enhancing treatment efficacy while avoiding increased therapeutic burden, thereby providing reliable clinical safety assurance.

2 Comparison of therapeutic effects of different probiotic preparations combined with 5-ASA

2.1 Common types of probiotics and their characteristics

In the adjuvant therapy of ulcerative colitis (UC), different probiotics exhibit distinct biological characteristics and clinical effects due to their strain-specific differences. Currently, the most extensively studied probiotics include Lactobacillus spp. (e.g., Lactobacillus rhamnosus GG, Lactobacillus casei Shirota), Bifidobacterium spp. (e.g., Bifidobacterium infantis, Bifidobacterium longum), and non-pathogenic Escherichia coli Nissle 1917 (EcN). Lactobacillus spp. are facultative anaerobes that tolerate gastric acid and bile, primarily colonizing the proximal small intestine. Their key features include producing lactic acid and bacteriocins to lower intestinal pH, inhibit harmful bacterial growth, enhance tight junctions between intestinal epithelial cells, and strengthen physical barrier function. Bifidobacterium spp. are strict anaerobes mainly residing in the large intestine, fermenting dietary fiber to produce short-chain fatty acids (e.g., butyrate) as the primary energy source for colonic epithelial cells. They also exhibit potent immune regulatory activity by suppressing pro-inflammatory factor secretion. Non-pathogenic Escherichia coli Nissle 1917, as a facultative anaerobe, demonstrates strong adhesion capabilities to competitively exclude pathogens and secretes antimicrobial substances like microacin. Its immune-regulatory effects synergize with 5-ASA. The differences in colonization sites, metabolites and mechanisms of action of these strains directly determine that their efficacy against UC may be significantly different when combined with 5-ASA.

2.2 Comparison of clinical symptom improvement with different probiotics combined with 5-ASA

Different types of probiotics combined with 5-ASA show varying degrees of efficacy in treating first-onset ulcerative colitis (UC). Comparative studies indicate that non-pathogenic Escherichia coli Nissle 1917 (EcN) paired with 5-ASA often

demonstrates faster onset and better relief of symptoms like diarrhea, abdominal pain, and bloody stools compared to certain Lactobacillus preparations. This is mainly attributed to EcN's strong intestinal colonization ability and competitive exclusion of pathogens, which rapidly restores gut microbiota balance. In contrast, composite preparations containing Lactobacillus groups (e.g., LGG) and Bifidobacterium species (e.g., B. infantis) excel more in comprehensive immune regulation and barrier function repair. Research shows that combination regimens containing specific Bifidobacterium strains significantly reduce Sutherland Index or UCDAI scores, particularly in alleviating tenesmus and decreasing mucous stool. This may be related to the short-chain fatty acids (e.g., butyrate) they produce, which directly nourish colon epithelium and reduce inflammatory responses. Overall, EcN appears more advantageous for rapid symptom control, while composite probiotic preparations show greater potential for comprehensive clinical symptom improvement. However, specific selection should still consider individual patient responses and clinical research evidence.

2.3 Comparison of endoscopic mucosal healing with different probiotics combined with 5-ASA

Regarding endoscopic mucosal healing—the key objective of ulcerative colitis (UC) treatment—different probiotic formulations combined with 5-ASA have demonstrated heterogeneous therapeutic effects. Mucosal healing signifies not only symptom resolution but also represents deep inflammation control and true tissue repair. Research evidence indicates that the non-pathogenic Escherichia coli Nissle 1917 (EcN) combined with 5-ASA regimen shows efficacy comparable to or even equivalent to mesalazine monotherapy in endoscopic remission rate (i.e., Mayo score ≤1), demonstrating its effectiveness as an adjuvant therapy. Regarding combination probiotic preparations, studies suggest that specific Lactobacillus and Bifidobacterium strains (e.g., VSL#3, despite its complex formulation and withdrawal from the market, still holds research value) or specific Bifidobacterium strains may show greater potential in promoting endoscopic mucosal healing. These probiotics enhance damaged mucosal barriers and microstructures by producing anti-inflammatory factors (e.g., IL-10), inhibiting pro-inflammatory factors (e.g., TNF-α, IL-6), and increasing tight junction protein expression.

2.4 Comparison of effects of different probiotics combined with 5-ASA on inflammatory indicators

The effects of different probiotic formulations combined with 5-ASA on inflammatory markers in UC patients 'serum and stool reflect differences in their mechanisms of action and subtle therapeutic variations. When combined with 5-ASA, non-pathogenic Escherichia coli Nissle 1917 (EcN) showed comparable or slightly superior efficacy in reducing classic systemic inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), indicating its effectiveness in controlling systemic inflammation. In contrast, the combination of Lactobacillus and Bifidobacterium demonstrated greater potential for regulating local intestinal inflammation. Studies revealed that these probiotics more effectively reduced calprotectin and lactoferrin levels in stool—sensitive markers of intestinal mucosal inflammation activity. This mechanism involves deeper regulation of immune cell functions, promotion of anti-inflammatory cytokines (e.g., IL-10), and inhibition of pro-inflammatory cytokines (e.g., IL-1β, IL-8, TNF-α). Therefore, while EcN demonstrates clear efficacy in systemic inflammation control, specific Lactobacillus and Bifidobacterium combinations may excel in suppressing local intestinal inflammation and restoring immune homeostasis. These differences suggest that clinicians should select targeted probiotic formulations based on patients' inflammatory patterns (systemic vs. localized intestinal inflammation).

2.5 Comparison of safety of different probiotic preparations

From a safety perspective, the main probiotic preparations currently studied for UC-assisted treatment—including non-pathogenic Escherichia coli Nissle 1917 (EcN), Lactobacillus species, and Bifidobacterium species—have demonstrated overall good safety and tolerability. At conventional therapeutic doses, adverse reactions caused by these probiotics are mostly mild, transient gastrointestinal symptoms such as bloating, mild abdominal distension, or constipation, with extremely low incidence rates. These reactions typically resolve spontaneously without special treatment, showing a similar adverse event profile to monotherapy with 5-ASA. The key to safety assessment lies in the inherent characteristics of the bacterial strains. As a non-pathogenic strain, EcN has been extensively validated through long-term clinical practice for its safety, rarely causing serious infection risks like bacteremia. Similarly, probiotics like Lactobacillus and Bifidobacterium,

which are generally considered "beneficial," also demonstrate high safety. However, it should be emphasized that while there is theoretically a very low probability of probiotic translocation and infection in immunocompromised patients (e.g., those undergoing intensive chemotherapy or organ transplantation), such occurrences are extremely rare in primary UC patients. In summary, various commonly used probiotic preparations combined with 5-ASA therapy are safe for primary UC patients. Clinicians should not overly worry about safety concerns when selecting these options, but rather base decisions on evidence-based efficacy data of specific strains and individual patient conditions.

3 Conclusio

Through systematic review and analysis of existing clinical evidence, it is evident that probiotics demonstrate significant synergistic effects when used as adjunct therapy with 5-aminosalicylic acid (5-ASA) in the treatment of ulcerative colitis. Compared to monotherapy with 5-ASA, combined regimens show marked advantages in improving clinical symptoms, promoting endoscopic mucosal healing, reducing inflammatory markers, and enhancing clinical remission rates and response rates. This therapeutic improvement stems from the complementary mechanisms of probiotics and 5-ASA across multiple biological targets and processes. By repairing intestinal barriers, regulating gut microbiota balance, and optimizing immune microenvironment conditions, probiotics create more favorable physiological environments for 5-ASA's anti-inflammatory effects. Notably, different probiotic strains exhibit varying efficacy due to their specific characteristics, with combination preparations and single strains such as Lactobacillus rhamnosus GG and Saccharomyces boulardii showing particularly notable therapeutic outcomes.

Reference

[1]Wu Qiaojun, Zhang Mengyu, Tian Jinxia. Effects of Probiotics Combined with Daliangtai Peptide on Gut Microbiota and Serum TNF-α Levels in T2DM Patients [J]. Journal of Laboratory Medicine & Clinical, 2025,22(14):1878-1882.
[2]Fan Yu, Chen Jinghong, Liu Juan et al. Impact of Probiotics Combined with Fluticasone Propionate Cream on Gut Microbiota Biodiversity in Atopic Dermatitis Patients [J]. Chinese Journal of Pathogenic Biology, 2025,20(08):1022-1027.
[3]Zou Dongmei, Wang Yang, Long Fei. Comparative Efficacy of Treatment Regimens Containing Cyclic Serine and Sodium Aminosalicylate for Multidrug-Resistant Tuberculosis [J]. Chinese Prescriptions, 2025,23(08):70-73.