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Mechanism of Action and Clinical Effectiveness of Bacterial Lysates in Preventing Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Abstract. Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide, and its prevalence continues to increase. Acute exacerbation (AECOPD) is a critical step in the progression of the disease, leading to irreversible decline in lung function. Among existing preventive measures, inhaled bronchodilators only alleviate symptoms and fail to reduce the risk of infection-related exacerbations. Vaccines do not cover multiple pathogens, and prophylactic antibiotics are prone to inducing drug resistance, all with obvious limitations. This study reviews the immunomodulatory mechanisms and clinical efficacy of bacterial lysates. High-quality literature from 2020 to 2025 was selected for qualitative and comprehensive analysis. The aim is to clarify the core mechanism of action and clinical efficacy of these lysates in preventing AECOPD, and to provide evidence-based support for clinical practice. The reviewed studies demonstrate that bacterial lysates can significantly reduce the incidence and hospital admission rate of AECOPD by synergistically regulating innate and adaptive immunity and strengthening the respiratory mucosal barrier, thereby reducing antibiotic use. They also have favorable safety and tolerability, providing evidence-based support for clinical practice and are expected to become an important means of AECOPD prevention.

Keywords: Bacterial lysate, Acute exacerbation of chronic obstructive pulmonary disease (AECOPD), Immunomodulation, Clinical efficacy

1. Introduction

The global burden of COPD is increasing due to population aging and persistently high smoking rates, making it a serious chronic respiratory disease threatening public health [1]. AECOPD is a major cause of disease progression and adverse outcomes in patients with COPD, with an average of 2-3 acute exacerbations per patient annually. The in-hospital mortality rate for patients with severe acute exacerbations reaches 10%-20%, and the quality of life of survivors is significantly impaired [2]. From a health economics perspective, AECOPD-related medical expenditures account for 60%-80% of the total medical costs of COPD, covering hospitalization fees, examination fees, drug costs, and rehabilitation costs, exerting enormous pressure on individuals, families, and health insurance funds [3]. Current clinical preventive measures have obvious limitations: inhaled long-

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acting bronchodilators combined with glucocorticoids can only reduce the risk of acute exacerbations by 20%-30%, and have limited effect on infection-related exacerbations [4]; influenza vaccines and pneumococcal vaccines target only specific pathogens, providing no protective effect against exacerbations induced by mixed infections or rare pathogens [5]; long-term use of prophylactic antibiotics easily causes gut microbiota dysbiosis and bacterial resistance, with strictly limited clinical application [6]. Meanwhile, research on immunomodulatory prevention strategies for AECOPD remains insufficient. As broad-spectrum immunomodulators, the specific molecular mechanism of bacterial lysates in regulating respiratory immunity, their applicability to diverse populations, and long-term socioeconomic benefits have not been systematically elucidated [7]. This research gap provides an important direction for this study.

This study, through a systematic literature review, explores the molecular mechanism of action (innate and adaptive immune regulation pathways) of bacterial lysates in preventing AECOPD, evaluates its clinical efficacy (key indicators such as acute exacerbation rate and hospital admission rate) in patients with varying COPD severities, analyzes their safety and tolerability, quantifies their social impact in reducing disease burden and improving patients' quality of life, reviews the limitations of existing research and proposes future research directions, and provides a comprehensive reference for the clinical application and promotion of such preparations.

Theoretically, this study systematically elucidates the immune regulation mechanism of bacterial lysates in preventing AECOPD, contributes to molecular mechanism research in this field, and enriches the theoretical system of COPD immunoprophylaxis. Clinically, it provides an evidence-based basis for the clinical application of bacterial lysates in the prevention of AECOPD, clarifies its applicable population and optimal intervention plan, and provides clinicians with new treatment options.

2. Overview of bacterial lysates

Bacterial lysates are biological agents prepared by culturing and inactivating common respiratory pathogens (such as Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis, etc.) in vitro, and then releasing the active components (antigen proteins, nucleic acids, lipopolysaccharides, peptidoglycans, etc.) through a lysis process. Their core function is to stimulate a broad-spectrum immune response and enhance respiratory immune defense, rather than induce specific immunity against individual pathogens [8].

Common preparation methods include alkaline lysis, mechanical lysis, enzymatic hydrolysis, and combined lysis: alkaline lysis employs alkaline solutions such as NaOH to disrupt the bacterial cell wall and cell membrane, followed by neutralization and purification; mechanical lysis uses physical methods such as ultrasonic disruption and high-pressure homogenization to avoid chemical reagent residues; enzymatic hydrolysis uses lysozyme to decompose cell wall peptidoglycans, with high specificity; and combined lysis combines multiple methods to optimize the release efficiency of active components [9]. Clinically used preparations are divided into oral and sublingual types: oral preparations (e.g., OM-85, Ismigen, and Lantigen B) are the most widely used and convenient to administer, with a usual adult dosage of once daily for 1-3 months. Sublingual preparations (such as Luivac) are absorbed through the sublingual mucosa, avoiding the influence of gastrointestinal metabolism. They are suitable for patients with weak gastrointestinal function or poor oral compliance, and are administered 1-2 times a day [10]. Compared with vaccines, which target single or a few pathogen-specific antigens, with high specificity but narrow coverage, bacterial lysates contain complex antigens from multiple bacteria, inducing a broad-spectrum immune response. They also have immunomodulatory and mucosal barrier enhancement functions, making them more

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widely applicable [11]. Compared with probiotics, which indirectly affect systemic immunity by regulating the gut microbiota, with the target site in the gut. Bacterial lysates act directly on the respiratory mucosal immune system, with a more direct target site, independent of the gut microbiota state, and are more targeted for local respiratory defense [12].

3. Mechanism of action

3.1. Effects on innate immunity

Antigenic components in bacterial lysates bind to Toll-like receptors (TLR2, TLR4, etc.) on dendritic cell surfaces, promoting dendritic cell maturation, enhancing their antigen-presenting capacity, and accelerating the initiation of the innate immune response.

Enhancing Mucosal Immunity: Promotes respiratory epithelial cell secretion of mucins (MUC5AC, MUC5B) and tight junction proteins (occluding and claudins), thereby improving the integrity of the respiratory mucosal barrier and reducing pathogen adhesion and invasion.

Stimulating IgA Secretion: Induces B cells in the respiratory mucosa lamina propria to differentiate into plasma cells, which secrete large amounts of secretory immunoglobulin A (sIgA). sIgA binds to pathogens to form immune complexes, preventing their adhesion to mucosal epithelial cells. Additionally, sIgA enhances mucociliary clearance and accelerates pathogen expulsion.

3.2. Regulation of adaptive immunity

At the adaptive immune level, dendritic cell antigen presentation promotes the differentiation of naive T cells, balances the Th1/Th2 response, regulates the secretion of cytokines such as IL-2 and IFN-γ, downregulates the levels of pro-inflammatory factors such as TNF-α and IL-6, avoids excessive inflammatory damage, and prevents excessive inflammatory responses to common respiratory pathogens [7]. Overall, by synergistically enhancing innate and adaptive immune functions, the body's resistance to respiratory viruses and bacteria is improved, and even if a mild infection occurs, it can prevent it from progressing to severe inflammation, thereby reducing the frequency and severity of AECOPD [4].

4. Evidence of clinical efficacy and social impact

4.1. Results of Randomized Controlled Trials (RCTs)

Multiple large-scale RCTs demonstrate that 12 months of intervention with bacterial lysates (such as OM-85), reduces the annual incidence of AECOPD in patients with moderate to severe COPD by 22%-35% compared with the control group, and the benefit was more pronounced in patients with recurrent acute exacerbations [13]. A meta-analysis of 5 RCTs and 1724 patients showed that OM-85 reduced the proportion of patients with acute exacerbations to 39.2%, significantly higher than the 30.3% in the placebo group [14].

Regarding hospitalization outcomes, the intervention group had an 18%-28% reduction in AECOPD-related hospital admission rates, a 20%-30% reduction in hospital stay duration, and a reduction of more than 35% in the incidence of severe acute exacerbations [15]. Regarding antibiotic use, the intervention group showed a significantly lower usage rate, with no significant difference in the incidence of adverse reactions compared with the placebo group, and a 20%-28% reduction in the cumulative course of treatment [14].

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4.2. Systematic review and meta-analysis conclusions

The results of the aforementioned RCT were further validated by systematic reviews. Three meta-analyses published since 2020 confirm that bacterial lysates significantly reduce the incidence of AECOPD (RR=0.72-0.78) and hospital admission rate (RR=0.68-0.75), with statistically significant efficacy [4]. Commercial formulations (e.g., OM-85, Ismigen) exhibit efficacy in managing respiratory infections and COPD in adults, with the OM-85 subgroup showing a 13% reduction in incidence and the Ismigen subgroup a 30% reduction [4].

Among different populations, the preventive effect was weaker in patients with mild COPD (incidence reduction of 15%-20%), while the effect was more significant in patients with moderate to severe COPD (25%-35%). Elderly patients and those with comorbidities still derive significant benefits without increased adverse reaction risk [16].

4.3. Safety and tolerability

After confirming efficacy, safety becomes a key consideration. Common adverse reactions of the biological bacterial lysate are mainly mild gastrointestinal reactions (nausea, diarrhea, abdominal distension), with an incidence of 3%-8%, mostly occurring in the early stages of use and resolving spontaneously; a small number of patients experienced low-grade fever (1%-3%), with no serious adverse reactions reported [14]. Multiple studies confirm that the incidence of adverse reactions is not significantly different from that of the placebo group, and long-term use does not increase the risk of liver and kidney damage. Patient tolerance is favorable, with compliance exceeding 80% [17].

4.4. Social impact

In terms of disease burden, based on an average hospitalization cost of RMB 15,000 per episode of AECOPD in China, intervention with the biological bacterial lysate can reduce 1-2 hospitalization admissions per patient annually, reducing the average annual medical cost per patient by RMB 15,000-30,000, significantly easing the burden on individuals and medical insurance funds [3]. In terms of socio-economic benefits, it reduces patient work absenteeism (an average of 10-15 days per year), alleviates family caregivers' burden, and improves the health level of the workforce [18]. Regarding the patients' quality of life, the St. George's Respiratory Questionnaire (SGRQ) score decreased by 8-12 points in the intervention group, the dyspnea score (mMRC) improved by 0.5-1 grade, and there were significant enhancements in independent living ability and psychological status [19].

In summary, bacterial lysate intervention not only significantly reduces the risk of acute exacerbations in COPD patients but also yields substantial economic benefits for individuals, families, and healthcare systems by decreasing hospitalizations and antibiotic use.

5. Discussion

Mechanism studies are incomplete, primarily focusing on immune cell activity and cytokine changes [7]. However, specific pathways regulating mucosal barriers and synergistic effects of active ingredients remain unclear [7]. Future research should elucidate these mechanisms to inform therapeutic strategies.

Existing studies exhibit significant heterogeneity, with substantial differences in intervention formulations, dosages, treatment durations, and study populations. Some meta-analyses report

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moderate-to-high heterogeneity (I^2=50%-80%), undermining the consistency of interpretation of results [4]. Regional and population differences are prominent. Existing studies are mostly based on European and American populations (accounting for over 70%), with limited data on populations in Asia and other regions. Studies targeting specific populations such as children and end-stage COPD patients are extremely rare [16].

Quantitative studies on social impact are insufficient, with most assessments relying on indirect indicators. Long-term follow-up health economic evaluations and systematic subjective indicator assessments are lacking [18].

Further exploration of mechanisms of action should be pursued to elucidate the specific molecular pathways regulating mucosal barrier and balancing immune responses, and to identify core active ingredients and their targets [7]. Future research should conduct individualized immunoprophylaxis studies, determining optimal formulations, dosages, and treatment courses for different populations based on immune status, COPD phenotypes, and other characteristics [16].

Regarding combined applications, RCT studies should be conducted to evaluate the combined use of bacterial lysates with influenza and pneumococcal vaccines, assessing potential synergistic effects [20]. Strengthen application research in special populations, including prospective studies on children, the elderly (≥80 years old), patients with severe comorbidities, and end-stage COPD patients [16].

6. Conclusion

Bacterial lysates reduce respiratory pathogen infections and trigger acute exacerbations by activating innate immunity and regulating adaptive immunity, thereby lowering the incidence and hospital admission rates of acute exacerbations of AECOPD and reducing antibiotic use. They also exhibit favorable safety and tolerability, with OM-85 emerging as a promising option supported by existing evidence. Furthermore, these formulations play a positive role in reducing the economic burden, improving socioeconomic benefits, and enhancing patient quality of life. However, current research still has limitations such as high heterogeneity, incomplete mechanistic studies, insufficient regional and population coverage, and inadequate quantitative research on social impact. Future research can focus on individualized interventions, combination therapy, studies in special populations, health economics evaluations, and in-depth exploration of mechanisms to enhance the clinical application value and social significance of bacterial lysates.

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