Original Article

Structural Modulation of Gut Microbiota in Rats with Allergic Bronchial Asthma Treated with Recuperating Lung Decoction*

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Abstract

Objective To investigate whether recuperating lung decoction (RLD) can modulate the composition of gut microbiota in rats during asthma treatment.

Methods Fifteen Sprague-Dawley rats were divided randomly and equally into control group, model group, dexamethasone (DEX) group, RLD medium-dose group, and RLD high-dose group. The asthma model was established in all groups, except for the control group. The rats in the DEX and RLD groups were treated orally with DEX and RLD, respectively. The rats in the control and model groups were treated orally with 0.9% saline. The intestinal bacterial communities were compared among groups using 16S rRNA gene amplification and 454 pyrosequencing.

Results The microbial flora differed between the control and model groups, but the flora in the RLD groups was similar to that in the control group. No significant differences were observed between the RLD high-dose and medium-dose groups. RLD treatment resulted in an increase in the level beneficial bacteria in the gut, such as *Lactobacillus* and *Bifidobacterium* spp.

Conclusion Oral administration of RLD increased the number of intestinal lactic acid-producing bacteria, such as *Lactobacillus* and *Bifidobacterium,* in asthma model rats.

Key words: Asthma; Gut microbiota; Recuperating lung decoction

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INTRODUCTION

Asthma is characterized by airway inflammation and high airway reactivity[1]. The inflammatory state makes the body susceptible to various factors that lead to hyperresponsiveness and constriction of the airways. The associated eosinophil (EOS) infiltration of the airway causes clinical changes related to asthma, leading to inflammation and other pathological changes in the airway[2-3]. Although incurable, asthma can be controlled with appropriate drugs, self-management education, and by avoiding exposure to allergens[4].

The microflora hypothesis, proposed by Noverr and Huffnagle[5] in 2005, has been widely accepted as a potential explanation of the relationship between intestinal flora and asthma. Based on this hypothesis, the intestinal flora keeps the body healthy by metabolizing drugs and harmful exogenous compounds, resisting exogenous pathogens and conditioned pathogens inside the body, and regulating the intestinal immune system and metabolism[6]. Long-term antibiotic usage and dietary modifications can disrupt the balance of intestinal flora, possibly leading to the occurrence of allergic diseases. Therefore, it is possible to prevent or even cure existing allergies by probiotic treatment aimed at restoring the normal intestinal flora[7]. The regulation of asthma via immune mechanisms remains unclear; however, oxidized lipids are potential immunomodulatory molecules, and mucosal tolerance can be controlled.

In addition, commensal bacteria can modulate the host innate immune system. Infants that were born by cesarean delivery or were administered large doses of antibiotics are prone to develop asthma or other allergic diseases. This may be because cesarean delivery can potentially alter the normal balance of the intestinal flora in infants[9]. Additionally, infants often develop asthma when their mothers have an imbalance of intestinal flora[8]. Björkstén[9] cultured fecal bacterial samples, collected from 62 two-year-old Irish and Swedish children, under anaerobic conditions. He found that the samples from allergic children contained fewer *Lactobacilli* and anaerobic bacteria and more aerobic bacteria, such as coliform bacteria and *Staphylococcus aureus*. Bottcher et al.[10] discovered that the bacterial fatty acid profiles differed between allergic and non-allergic Swedish infants, and that allergic infants had higher levels of caproic acid (associated with *Clostridium difficile*). Furthermore, Penders et al.[11] have reported that the presence of *Escherichia coli* or *Clostridium difficile* was associated with an increased risk for eczema and allergic sensitization in two-year-old infants. These data, along with many others, suggest the potential effects of gut microbiota on the adaptive and innate immunity, which could affect the development of asthma.

Currently, glucocorticoids are the most effective drugs for controlling asthma due to their action on multiple aspects of the inflammatory response. Glucocorticoids regulate target gene transcription in the respiratory tract cells, inhibit inflammatory cell activation and inflammatory factor production, and increase airway β-receptor sensitivity; this in turn prevents airway inflammation and respiratory remodeling, and reduces bronchial hyperresponsiveness (BHR). However, long-term use of glucocorticoids may have some side-effects, such as toxicity, dependence, and may lead to financial strain due to the cost of long-term treatment[12-13].

Allergies[14] are considered as the primary pathophysiological basis of development of asthma. In traditional Chinese medicine, it is generally believed that allergies weaken the immune system, and that abnormal functioning of lungs and spleen contribute to the occurrence and development of asthma[15-16]. Clinical practice[17-18] has proven that an efficient approach for recovery from asthma is the restoration of normal functioning of the vital organs.

Our study aimed to investigate the effects of recuperating lung decoction (RLD) treatment on the microflora structure in rats with asthma. RLD is a decoction based on a traditional Chinese medicine that includes *raw Radix Astragalus*, *Ramulus Cinnamomi*, *Suzi*, *Flos Magnoliae*, *Rhizoma Zingiberis*, *Fructus Corni*, *Fructus Schisandrae Chinensis*, *Fructus Mune*, *Flos Inulae*, *Cortex Magnoliae Offcinalis*, *Rhizoma Anemarrhenae*, and *raw Radix Et Rhizoma Glycyrrhizae*. Previous studies have demonstrated[19-20] that the lung function of rats with asthma was improved after RLD treatment. The effects include a decreased number of eosinophils in bronchoalveolar lavage fluid (BALF) and reduced serum IgE levels, and improved elimination of oxygen free radicals[21]. RLD use was found to be closely related to changes in seven metabolites (valine, malic acid, gluconic acid, galactose, pyran glucose, 6-deoxidation mannopyranose and stearic acid) present in asthma rabbit serum[22] and stearic