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Study on the Effect of Traditional Chinese Medicine Regulating Intestinal Microecology on AIDS Prevention and Treatment

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Abstract: ***AIDS is a chronic infectious disease in which the human immunodeficiency virus (HIV) violates human T-lymphocytes and destroys the human immune system, and it has been found that T-cells in the gastrointestinal tract are the primary target and the main site of attack of HIV, and that HIV infection affects the micro-ecological balance of the intestine by influencing the number of intestinal bacterial flora and its distribution, and is closely related to the progress of HIV infection. In this paper, the diversity of intestinal flora, the change of intestinal mucosal barrier permeability and integrity, and intestinal immunity of AIDS patients were studied to further explore the protective effects of Traditional Chinese medicine (TCM) on intestinal mucosal barrier and intestinal immunity by regulating intestinal flora, and to clarify the intrinsic mechanism of the multi-targeted and multi-linked effects of TCM on intestinal microecological regulation.***

Keywords: Traditional Chinese medicine, AIDS, Intestinal microecology, Intestinal flora, Intestinal immunity.

1. Introduction

AIDS is an acquired immunodeficiency syndrome (AIDS) caused by the human immunodeficiency virus (HIV), the main mechanism of disease is caused by the HIV virus in the host target cells (mainly CD4+ T cells). The main mechanism of the disease is that HIV virus replicates in the target cells of the host, causing cellular immune damage, followed by a variety of opportunistic infections and malignant tumors, leading to organ failure and even death. AIDS is mainly caused by HIV infection that destroys the body's immune function and is characterized by immunodeficiency and various opportunistic infections, with the intestinal tract being the main focus of AIDS. Intestinal T cells are the earliest and primary targets of HIV, and the immune status of the gut is the best criterion for judging the progress and healing of patients with HIV/AIDS. The gut and the immune system work together to maintain the stability of intestinal microecology, and Chinese medicine has significant efficacy in improving intestinal microecological homeostasis, but its intrinsic mechanism of action is not clear. In AIDS patients, the intestinal mucosal barrier and function are disrupted, and the structure of intestinal flora is significantly altered, causing intestinal microecological dysregulation, which is the main reason for the depletion of CD4+ T-cells and the disruption of immune function [1]. In this paper, we reviewed the current status of the research on the intestinal microecology of HIV/AIDS and the clinical practice of intestinal microecology in the prevention and treatment of HIV/AIDS in Chinese medicine by reviewing the domestic and foreign literature, and put forward a new idea of the research on the mechanism of the action of Chinese medicine based on the intestinal microecology regulation, so as to provide reference for the further research on the mechanism of the action of Chinese medicine in the prevention and treatment of HIV/AIDS.

2. Relationship between AIDS and Intestinal Microecology

Intestinal microecology is an important immune system of the human body, intestinal epithelial cells, intestinal flora, immune cells interact with each other and influence each other to maintain the balance of the intestinal microecology. HIV infection of the human body, the virus directly attacks the intestinal immune cells, destroying the epithelial cells, causing damage to the intestinal mucosal barrier, the intestinal flora translocation, into the circulatory system, triggering the activation of systemic immune abnormality, and ultimately develops into the systemic immunodeficiency. Deficiency. Intestinal immunity, intestinal flora and HIV are closely related to each other.

2.1 AIDS and Intestinal Immunity

CD4+ T-lymphocytes are the main target cells of HIV, resulting in HIV infection presenting a disease characterized by dysregulation of the number and function of CD4+ T-lymphocytes, T-lymphocyte and other immune cell depletion or functional defects, progressive decline in the body's immune function, and disorders of the immune system function. The gastrointestinal tract and intestinal-associated lymphoid tissues are the largest immune organs in the human body, and they account for a large proportion of the organism's T lymphocytes [2-3]. The activated CD4+ T-lymphocytes mainly exist in the intestinal tissues, which are easily infected by HIV, and close to 80% of HIV is found in the intestinal tissues. The CD4+ T-lymphocytes in the gastrointestinal tract and intestinal lymphoid tissues are damaged or dysfunctional in varying degrees, which, together with inflammatory responses mediated by leukocyte-associated factor releases, cause damage to intestinal mucosal barriers and trigger a persistent intestinal inflammatory response. Inflammatory response, inflammatory factors are released in large quantities, the body's immune system is highly activated, immune dysfunction, and the disease process of AIDS is accelerated [4-6].

2.2 AIDS and Intestinal Flora

The gut flora of AIDS patients is closely related to their immune system function and disease progression. Reduced diversity of bacterial species, which is involved in the maintenance of host immune function, is positively correlated with CD4+ T-lymphocyte counts, and is strongly associated with the incidence of tumors, osteoporosis, circulatory and neuropsychiatric disorders [7]. The number and proportion of commensal bacteria that maintain nutrition and energy metabolism in AIDS patients change, which is mainly manifested in the decrease of the content of Mycobacterium anisopliae, the increase of the content of Mycobacterium anisopliae, Mycobacterium thick-walled and Mycobacterium puerariae, the destruction of the resistance to colonization, the weakening of biological antagonist occupancy and protection, the transformation of intermediate bacteria and conditionally pathogenic bacteria into pathogenic bacteria, the large number of pathogenic bacteria colonization, proliferation, and the suppression of the normal nutritional and absorption function of intestinal bacteria, which gradually lead to AIDS patients' wasting and even malnutrition. In addition, the pathogenic bacteria colonization, intestinal motility dysfunction, bacterial toxins, spoilage substances and other harmful substances are released in large quantities, prompting intestinal inflammation to continue to occur, and complicate a variety of chronic intestinal inflammation, the patient manifests diarrhea or constipation occurs [8-12].

Intestinal flora displacement, a variety of factors lead to intestinal flora dysbiosis, disrupting the integrity of the intestinal mucosal barrier, the various bacterial species, occupancy ratio and normal physiological function of the abnormal changes in the intestinal flora displacement into the tissue then opportunistic infections occur [13]. HIV invades the intestinal tract and related lymphoid tissues, the intestinal mucosal barrier is damaged, and its permeability shows varying degrees of increase is the main mechanism of AIDS intestinal flora translocation, intestinal flora translocation, host immune status is low, and the disease is in the clinical stage of the joint role of each other, interacting with each other, and progressively accelerate the clinical progression of AIDS, the intestinal flora translocation to the circulatory system, the immune system abnormally Activation of the intestinal flora to the circulatory system, abnormalities in the immune system, release of inflammatory factors, further damage to the intestinal mucosal barrier, and deterioration of the metabolic function of the body accelerate the progression of AIDS disease [14-15].

2.3 Intestinal Flora and Intestinal Immunity

Intestinal flora and intestinal immunity interact with each other and participate in the immune response of the organism. The effect of HIV on intestinal flora is closely related to the immune status of the organism [16], and intestinal flora also plays an indispensable role in immunity.

2.3.1 Influence of intestinal flora on body immune cells

Intestinal flora is closely related to the development of Th17 and has an indispensable role in maintaining intestinal mucosal integrity and intestinal mucosal barrier function [17]. Intestinal flora can promote the development of intestinal B cells and protect the intestinal mucosa from attack and invasion by exogenous pathogens [18]. It is involved in inducing the differentiation of immunosuppressive cells Treg [19], down-regulating the immune response of the body, it can also regulate the immune function of NK cells. Most importantly, intestinal flora can enhance intestinal mucosal immune tolerance by promoting tolerogenic differentiation of T cells.

2.3.2 Influence of gut flora on immunity and inflammation production

The intestinal flora influences the physiological and pathological state of the gut [20], and alterations in its composition can have an impact in terms of immunity as well as inflammation. Several studies have shown that the intestinal flora of HIV-infected patients has an increased abundance of Prevotella spp. and a decreased abundance of Mycobacterium avium spp. [21], and the former promotes an inflammatory response through Th17 [22], which promotes the activation of immune cells and makes HIV more susceptible [23], and the latter has an anti-inflammatory effect, suppresses immunity, and maintains immune homeostasis [24]. HIV infection leads to an increased Aspergillus phylum, which disrupts the mucosal barrier and defenses, thereby inducing inflammation [25].

2.3.3 Impact of metabolites of gut flora on immunity

The metabolites of intestinal flora not only affect the digestive ability of the organism, but also influence the immune response of the host. For example, Rochesteria spp, produce butyrate, which not only maintains the integrity of the epithelium, but also regulates the intestinal immune cell response to protect the intestinal barrier. Some scholars believe that gastrointestinal flora can activate immunity through short-chain fatty acids, tryptophan-kynurenine, and trimethylamine production pathways. Relevant experiments have found that the metabolites of the intestinal flora of people with a slow process of HIV infection are favorable to fatty acid metabolism, while the rate-limiting enzymes produced by the intestinal flora of people with a fast process can induce kynurenine production, inhibit Th17 differentiation, induce inflammation, damage intestinal mucosal barriers, and cause intestinal immune dysregulation [26-27].

3. Traditional Chinese Medicine and AIDS

3.1 Recognition of AIDS in Traditional Chinese Medicine

Traditional Chinese Medicine (TCM) has been studying AIDS for more than 30 years. During the acute stage of infection, patients mainly suffer from fever, headache, sweating, sore throat, muscle pain, rash and diarrhea, and then enter into an asymptomatic period that lasts for several months to 10 years or longer. TCM has not yet formed a unified viewpoint on AIDS. According to the symptoms of AIDS patients in the natural course of the disease, TCM has classified AIDS into the categories of "epidemic virus", "obscene poison", "ambient temperature disease" and "deficiency labor", etc. Among the five organs, the spleen is

the key invading part of HIV. According to the symptoms of the natural course of AIDS patients, TCM classifies AIDS into the categories of “epidemic virus”, “obscene poison”, “ambient temperature disease”, “deficiency labor” and so on, and the spleen among the five viscera is the key invasive part of HIV.

3.2 Traditional Chinese Medicine and Gut Flora

Intestinal flora is related to the “spleen” in Chinese medicine, and the identification of evidence and holistic concept is the key to the diagnosis and treatment of diseases in Chinese medicine, in the process of Chinese medicine diagnosis and treatment, “looking, smelling, inquiring and checking” is the premise of accurately grasping the symptoms of diseases, AIDS disease process of intestinal flora dysbiosis patients showed Diarrhea, constipation, fatigue, lack of appetite, emaciation and other clinical manifestations, the lesion organs are located in the spleen and stomach, when the treatment from the spleen; intestinal flora and Chinese medicine “spleen” physiology, pathology, diagnosis and treatment related. Intestinal flora and protein, fat, vitamins and other substances metabolism, to ensure adequate energy metabolism of the body supply, and “spleen qi dispersal essence” physiological function of the reference; intestinal flora dysbiosis patients defecation cycle disorders, nutrient absorption and metabolic disorders, external manifestations of diarrhea, constipation and other gastrointestinal manifestations or even malnutrition occurs, and the “spleen qi deficiency evidence”. The pathologic mechanism of “spleen qi deficiency and deficiency syndrome” and the diagnosis and treatment of medication are in line with each other.

TCM treatments based on the basic theoretical system of TCM can play a role in adjusting the ecological balance of intestinal flora, which is manifested in the direct effect on the intestinal flora, balancing the number and proportion of the flora, as well as influencing the metabolism of substances. It was found that the ratio of commensal and pathogenic bacteria in the intestinal flora of rats with constipation in the spleen qi deficiency syndrome was imbalanced, which was manifested by an increase in the number of Escherichia coli and fungi and a decrease in the number of bifidobacteria and other flora [28]. Formulas for strengthening the spleen and transporting the spleen, such as Si Mu Tang, Si Shen Wan, and Ginseng Ling Bai Zhu San, can regulate the balance of intestinal flora in rats with spleen qi deficiency, effectively inhibit the abnormal proliferation of opportunistic pathogens such as Escherichia coli and Lactobacillus, and promote the proliferation and growth of bifidobacteria, so as to improve the gastrointestinal symptoms of rats with the spleen qi deficiency syndrome [29-32]. The Chinese medicine Coptis chinensis is bitter and cold in nature, mainly used for clearing heat and drying dampness, diarrhea and detoxification, and is commonly used in the middle Jiao damp-heat diseases. Modern pharmacological studies have shown that Coptis chinensis’s pharmacological components are mainly flavonoids, and clinical studies have shown that Coptis chinensis and the prescriptions using it as a monarch have a good therapeutic effect on the treatment of intestinal infectious diseases and type 2 diabetes mellitus, which is related to the adjustment of the intestinal flora [33-34].

3.3 Traditional Chinese Medicine Regulates Intestinal Microecology

TCM and intestinal flora interact and influence each other, Chinese medicine can directly or indirectly affect the composition and metabolism of intestinal flora, while intestinal flora participate in the metabolism and bio-availability of drugs, which directly or indirectly affects the therapeutic efficacy of drugs. TCM can directly promote the growth of beneficial bacteria such as Bifidobacterium bifidum [35], inhibit the growth of pathogenic bacteria such as Escherichia coli [36], regulate the composition and structure of intestinal flora, and improve intestinal homeostasis. Ginseng saponins and Huanglian detoxification soup regulate the diversity of intestinal flora to improve clinical symptoms [37-38], and Chinese external treatment methods such as acupuncture and tuina also have significant efficacy in regulating the structure and homeostasis of intestinal flora [39-40]. Herbal medicines can also indirectly regulate intestinal flora by affecting gastrointestinal pH [41], gastrointestinal motility [42], promoting the induction of the release of certain peptides or proteins [43], and regulating the barrier function of the gastrointestinal mucosa [44]. TCM affects the metabolism of intestinal flora through metabolic enzymes, and intestinal flora can also affect the absorption and metabolism of TCM [45]. TCM can not only regulate the intestinal flora, improve intestinal homeostasis, and promote immune reconstitution, but also indirectly affect the composition and metabolism of the intestinal flora by influencing the immune function of the body, and the two interact with each other, e. g. , the formula for strengthening the spleen and detoxifying the toxin increases the number of Escherichia coli and enterococci in patients with lung, spleen, and qi deficiency and enhances the nonspecific immune function of the body [46].

4. Summary and Outlook

In recent years, there has been a gradual increase in the exploration of the mechanism of TCM in the treatment of AIDS, but most of the studies have focused on the changes in intestinal flora, the damage to the mechanical barrier of the intestinal mucosa, and the changes in the subpopulation of CD4+ T lymphocytes, and the studies on the chemical barrier of the intestinal mucosa are lacking. There are a huge number of immune cells and various immune molecules in the mucosa, and the interaction between immune cells on the surface of the intestinal mucosa is also one of the future research directions, and the related research mainly focuses on animal models and in vitro cellular studies, with fewer studies in human beings. Although existing studies have fully demonstrated the efficacy of TCM in regulating the intestinal microecology, most of them are limited to the improvement of a single intestinal flora or the repair of a single intestinal barrier or intestinal mucous membrane, and they have not integrated the regulation of intestinal microecology of patients with AIDS by TCM, which lacks a systematic evaluation, and the difference between the bacterial genera of patients with AIDS and those of normal people is not a dominant bacterial genus, and it has a small proportion in the total intestinal bacterial flora. The results are not only susceptible to individual differences, sample size, environment, diet, geography and other factors, but also present different results due to different

specimen types, sampling sites, and bacterial detection techniques, and ART drugs themselves also affect the intestinal flora, resulting in a single target and pathway, which makes it difficult to elucidate the complex mechanism of TCM efficacy.

Modern medical research has confirmed that intestinal microecology plays an extremely important role in the pathogenesis and disease progression of AIDS, and under the guidance of the holistic concept of TCM, the development of the overall regulation of intestinal microecology by TCM has a broad application prospect [47]. Based on the intestinal microecological regulation provides a new way of thinking for the study of the mechanism of action of TCM in the prevention and treatment of AIDS. The intestinal flora and the intestinal mucosal barrier interact and influence each other, so we can study the diversity of intestinal flora, the change of permeability and integrity of the intestinal mucosal barrier, and the intestinal immunity of patients with AIDS, and carry out the correlation analysis, so as to understand the complex relationship and influence between intestinal flora, intestinal mucosal barrier and intestinal immunity, and to explore the role mechanism of HIV infection in affecting the intestinal microecology of the patients through the intestinal flora - intestinal immunity axis, which can provide a theoretical basis for the prevention and treatment of the disease. We will explore the mechanism of HIV infection through the intestinal flora - intestinal immune axis, and provide theoretical basis for the prevention and treatment of the disease. The application of TCM intervention and detection of index changes, exploring the protective effect of TCM on intestinal mucosal barrier and intestinal immunity through the regulation of intestinal flora, clarifying the intrinsic mechanism of multi-targets and multi-links of the regulation of intestinal micro-ecology played by TCM, providing evidence of modern medicine for the treatment of AIDS by TCM, promoting the research and development of TCM new drugs, and giving full play to the advantages of TCM in the prevention and treatment of AIDS.

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