Study on the Intestinal Microorganisms and Its Immunity

Chunhua Yu, Qingfeng Wang, Lang Ding

Jiangxi medical college, Shangrao, Jiangxi, 334000

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Abstract: Intestinal microbes and the human immune system are symbiotic and interact with each other. Previous studies have shown that the occurrence of autoimmune diseases such as inflammatory bowel disease, rheumatoid arthritis, and systemic lupus erythematosus is related to changes in the intestinal microbiota. Detection and change have a certain diagnostic value and therapeutic effect. The composition of intestinal microbiota in patients with various autoimmune diseases is different from that of healthy people. Through diet and drug regulation, rebuilding the intestinal micro-ecology will help improve the disease. This paper reviews the role of gut microbiota in systemic lupus erythematosus, rheumatoid arthritis, spondylarthritis, and inflammatory bowel disease, as well as current advances in disease diagnosis and treatment.

1. Introduction

The normal number of intestinal micro-organisms in humans ranges from 1012 to 1014. Their average mass is about 1.5 kg [1], and about 6 to 10 groups (3000 species) are composed of microbes. Infants colonize the intestines shortly after birth until the gut microbes reach a stable symbiotic group [2]. Intestinal microorganisms are beneficial to the host. In the past 10 years of research, intestinal microbes have been found in human development, intestinal barrier, immune regulation, metabolism, nutrient absorption, toxin excretion, and the occurrence and development of diseases. Play a huge role. Disruption of the intestinal microflora may lead to various diseases such as obesity, cirrhosis, diabetes, cardiovascular diseases, and autism. The main function of the intestinal microflora is to help the host to metabolize, so that the energy and nutrients are better utilized to provide nutrition for the intestinal epithelial cells, enhance the host immune function, and help the host resist pathogens. Recently, a large number of studies have shown that the metabolic function of the intestinal microflora is very important, and the efficiency far exceeds the metabolic function of the liver. For example, intestinal microflora can not only affect the fatty acid composition of the retina and the density of the eye lens, bone, and the formation of blood vessels in the intestine; but also can provide essential nutrients (biotin, vitamin K, butyric acid, etc.) and digest the dietary fiber Su. Gut microbes have evolved with spine animals for thousands of years, so the implementation of the immune system's normal function (resisting bacterial pathogens) needs to rely on intestinal microbes. At the same time, intestinal microflora is an important factor that stimulates the maturity of the mucosal immune system (mucosalimmune system) and the systemic immune system. Many experimental studies have found that the composition and metabolites of the intestinal microflora have important effects on immune and inflammatory responses. If the internal immune system of the intestine collapses, chronic enteritis diseases such as Crohn's disease and ulcerative colitis can be caused. However, due to the diversity of commensal intestinal microbes and the difficulty of determining which bacteria are commensal or conditional Bacteria, so the immune regulation of intestinal microbial colonization is complex. In recent years, the research on intestinal flora and immunity has received more and more attention.

2. Intestinal Microorganisms and Digestive Diseases

IBD is a chronic, non-specific intestinal inflammatory disease of unknown etiology including ulcerative colitis (UC) and Crohn's disease (CD). The disease is usually repeated and prolonged. Currently, there are still no effective treatments for the disease. In recent years, three aspects of

intestinal microbiology and its metabolites, host gene susceptibility, and host intestinal mucosal natural or acquired immune response imbalance have been jointly involved in the pathogenesis of IBD. Studies based on animal models confirmed that the intestinal tract does not show inflammation in a sterile environment. However, if the normal flora of the intestine is restored, intestinal inflammation may occur, suggesting that the presence of intestinal microflora is not essential for the development of IBD. Or missing [3]. Studies have confirmed that ileal mucosal epithelial mucosa invading Escherichia coli, M. paratuberculosis and CD are closely related; Salmonella, Campylobacter jejuni and other related pathogens may increase the risk of IBD occurrence or recurrence. Intestinal microbial metabolites also play an important role in IBD. For example: butyric acid is not only the main source of energy in the intestinal epithelial cells, but also can prevent the signal transduction pathway of pro-inflammatory cytokine expression; butyric acid-producing bacteria can improve the intestinal inflammation and necrosis in rats, giving rats butyric acid Culture supernatants of bacteria can improve intestinal inflammation. Studies have confirmed that the content of butyric acid bacteria such as Clostridium perfringens and Clostridium sp. in the intestinal tract of IBD patients is reduced, and the utilization rate of butyric acid is reduced.

Liver cirrhosis is the pathological end-stage manifestation of chronic liver disease. Intestinal microbes, increased intestinal permeability, bacterial translocation, endotoxemia, and inflammatory cytokine release can all affect the development of cirrhosis and its complications. Early research based on traditional culture methods found that the content of beneficial bacteria such as bifidobacteria in the intestinal tract of patients with liver cirrhosis was reduced [4]. Recently, Chen et al. analyzed the fecal flora in patients with cirrhosis using 16S rDNA pyrosequencing based on the metagenomics strategy and found that the content of Bacteroidetes in the stool of patients with cirrhosis was significantly lower than that of healthy controls. The contents of bacteria and Fusobacteria increased, and the families of Enterobacteriaceae, Veillonococcus, and Streptococcus were significantly higher than the healthy control group at the Familia level, but the incidence of the Fabriaceae was significantly lower. The study also concluded that the contents of potential pathogenic bacteria such as Enterobacteriaceae and Streptococcus in the intestinal tract of patients with cirrhosis increased, and the content of beneficial bacteria such as Fabriaceae decreased, affecting the prognosis of patients with cirrhosis.

3. Intestinal Microbes and Inflammatory Bowel Disease

A number of studies have found that patients with inflammatory bowel disease (IBD) have varying degrees of intestinal microbial abnormalities, the most common of which are the reduction of thick-walled phylum and the increase of Proteobacteria. Most of the reduction in intestinal microbial diversity originated from the reduction of Clostridium in the phylum Clostridium, especially Clostridium perfringens. In contrast, lactobacillus was significantly increased in patients with active IBD. A meta-analysis of 623 patients with IBD including 10 clinical studies proposed that patients with active IBD have lower abundance of Clostridium spp., Clostridium perenne, Clostridium punctae, and Bifidobacterium, among which the above bacteria are in ulcerative The active period and the remission period of colitis are different. In Crohn's disease, only the latter three are different, while the abundance of E. coli and Lactobacillus is not different between the active and remission periods of IBD.[5] The current microecological queue for Crohn's disease, by comparing 447 cases of Crohn's patients and 221 healthy controls, proposed a "dysbiosis index" and found that it is parallel to the severity of the disease. It is considered that intestinal microorganisms can be used as a marker for the diagnosis and early prognosis of Crohn's disease. A prospective cohort study found that after remission of Crohn's disease with infliximab, a low proportion of P. lentae and Bacteroides was an independent predictor of disease recurrence. The onset of IBD has a certain degree of genetic susceptibility and is related to the interaction of various factors such as the environment, immunity, and microorganisms. IBD genomics studies have shown that certain polymorphic gene products are involved in intrinsic mucosal immunity, the role of which includes the identification of intracellular bacteria nucleotide binding oligomerization domain containing 2,

NOD2] , autophagy related protein 16 like protein 1 (ATG16L1), immune-related GTPase family M protein (IRGM), epithelial barrier function hepatocyte nuclear factor 4A (hepatocyte nudear) Factor 4A, HNF4A), CHD1, LAMB antigen presentation human leukocyte antigen (HLA) - DQA1] and inflammatory factor production Tumor necrosis factor receptor superfamily 14 Member 14, TNFRSF14), tumor necrosis factor ligand superfamily member 9, TNFSF9, interleukin 1 receptor type II, IL1R2, interleukin 7 receptor (Interleukin 7 receptor,IL7R). Variations in these genes result in downregulation of innate immunity and ineffective clearance of intracellular bacteria. The absence of tolerance to bacterial antigens in the gut is a key link in the occurrence of IBD. As found in animal models, IL-2 knockout mice do not develop severe colitis under sterile conditions, whereas feces from mice with colitis can induce colitis. Under the action of environmental or infectious factors, the barrier function of the intestinal mucosal epithelium is disrupted and the immune system loses immunotolerance to the antigen in the intestinal lumen, activates dendritic cells, and stimulates naïve T lymphocytes at mesenteric lymph nodes to assist Differentiation of T lymphocytes (Th1, Th2, Th17, etc.) and production of inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-12, IL-23, etc.). By changing the population or community of microorganisms, remodeling the structure and function of the intestinal microflora, and then regulating immunity, it is expected to provide new possibilities for the treatment of autoimmune diseases. IBD animal experiments suggest that Bifidobacterium bifidum BGN4 can inhibit IFN-γ and monocyte chemotactic protein-1 (MCP-1) levels by blocking abnormal T cell activation, preventing CD4 + CD45RBhigh T cell-mediated inflammatory bowel disease. The use of certain antibiotics, such as rifampin, metronidazole, and ciprofloxacin, can induce active Crohn's disease and remission of ulcerative colitis. Clinical meta-analysis of 21 randomized controlled trials and recent randomized controlled trials have shown that the use of bifidobacteria, lactobacillus and other probiotics as well as fecal transplantation in healthy people can induce and maintain the remission of ulcerative colitis, and there is no obvious side effect. However, the efficacy of fecal transplantation in the treatment of Crohn's disease is not yet accurate. There is no evidence that prebiotics such as fructooligosaccharides and probiotics such as lactobacillus and yeast are beneficial to the relief of Crohn's disease.

4. Intestinal Microbes and Rheumatoid Arthritis

At present, the "intestine-joint axis" is considered as one of the possible mechanisms of the development of rheumatoid arthritis. Intestinal microecological abnormalities lead to changes in permeability of the intestinal mucosa, breaking the inherent immune tolerance, the intestinal antigens stimulate the activation of the immune response, through deamidation and increased citrullination, resulting in a new immune epitope activation The systemic immune response to disease results in the production of autoantibodies and end-organ damage such as synovium, cartilage, and bone. An animal experiment suggested that serum antibody titer and Th17 cells were significantly reduced in a sterile K/BxN mouse model, while segmented filamentous bacteria could induce the differentiation of Th17 cells and be recruited to the intestinal lamina propria to promote arthritis. happened.

Animal experiments suggest that oral L. casei can reduce proinflammatory cytokines [IL-1β, IL-2, IL-6, IL-12, IL-17, by inhibiting Th1-type cellular immunity and humoral immune response. IFN-γ, TNF-α, cyclooxygenase (COX)-2, inhibit collagen-induced arthritis, reduce joint swelling and reduce lymphocyte infiltration and cartilage destruction. Recent studies have shown that the application of Lactobacillus casei can reduce the symptoms of patients with rheumatoid arthritis, reduce disease activity and improve the body's inflammatory state. In the collagen-induced arthritis model, mice treated with enrofloxacin to deplete the natural intestinal flora were more severe than those in the control group, and serum IFN-γ, IL-17A, and IL-4 were decreased. Some antibiotics can affect the severity of arthritis by changing the intestinal flora.

5. Conclusion

The research on the intestinal micro-ecology has gradually become hot spots. More and more studies have confirmed that the intestinal micro-ecological abnormalities are closely related to a variety of autoimmune diseases. The interaction between intestinal microbes and the intestinal mucosa and immune system affects the occurrence and development of the disease, and the underlying mechanism remains to be further explored. It is believed that through the study of intestinal microbes, new strategies and approaches will be provided for the diagnosis and treatment of various autoimmune diseases including systemic lupus erythematosus.

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