Future of Probiotics in HIV Treatment

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Abstract

HIV infected patients who are on Anti-retroviral Therapy, their gut micro biome is very different from those of healthy individuals. In HIV infected persons dysbiosis may lead to a breakdown in the guts immunologic activity, causing systemic bacteria diffusion and inflammation. But the use of probiotics for health improvement in HIV infection leads to long life expectancy. This mini review will focus on the importance of probiotics to prevent and attenuate several gastrointestinal manifestations and improve gut associated lymphoid tissue (GALT) immunity in HIV infection.

Keywords: HIV; Inflammation; GALT; Infection

Introduction

HIV is a virus that damages the immune system. The immune system helps the body to fight against infections. HIV infects and kills CD4 cells; these are type of immune cell called T cells. As time passes, HIV kills more CD4 cells; the body is more likely to get various types of infections and cancers. HIV is a lifelong condition and currently there is no cure. The medical care includes treatment called antiretroviral therapy (ART) which makes HIV management possible and increases the longevity of HIV infected persons for many years. Without treatment, a person with HIV is likely to develop a serious condition called acquired immunodeficiency syndrome (AIDS).

During initial HIV infection, immune system occurs in gut includes 2/3rd of the CD4 cells. Some CD4 cells, which are called TH17 cells, help to protect the integrity of the gastrointestinal wall from a process called microbial translocation. This process occurs in place where the gut mucosal integrity is breached and microbes from the micro biome (communities of bacteria) and some of their products leak through the gut wall, enabling them to circulate within the bloodstream. This causes systemic inflammation that leads to the occurrence of non AIDS-related conditions such as cardiovascular disease and other diseases. Microorganisms are omnipresent, which makes our body also the habitat of microbes. Microbes (bacteria) found in the gut play an important role in HIV disease progression and pathogenesis. Researchers are working on probiotics that can alter the damaging process and lower the HIV disease progression. Microbial translocation occurs in gastrointestinal tract causes dysbiosis or micro biome dysbiosis. To enhance the life of microbiota of gut, probiotics are used nowadays.

Probiotics

Probiotics are live bacteria and yeasts that are good for humans’ health, especially enhancing the activities of digestive system. They are also called good or helpful bacteria's as they keep our gut healthy. Probiotics have been used in the population generally to promote a healthy microbial balance and they are also studied in diseases such as irritable bowel syndrome and inflammatory bowel diseases. Uses of probiotics are as follows:

- Reduces systemic inflammatory markers
- Increase microbe diversity in the gut micro biome
- Improve immune function in the gut maintenance of the epithelial barrier,
- Inhibition of pathogen adhesion to intestinal surfaces, antibiotic related diarrhoea
- And modulation of the immune system [1].

Probiotics help in real disease treatment and management. The most critical points are in understanding of the disease behavior and its causative agents. For examples, diseases which are related to genetic disorders will cause certain sort of deficiencies like lactose intolerance. The role of Probiotics in such types of cases will be in removing such deficiencies by different mechanisms such as

- The missed gene products are supplied by probiotics to human body, the suitable alternative products are also supplied by probiotics.
- Probiotics help to maintain suitable enzymatic pathway [2].
- Probiotics could support a weak or completely defected pathway which might be due to a defect in a single allele rather than the defect in both alleles that could lead to a mutation [2].
- Probiotics will be the best support for human life when persons become old, helps to enable humans to do extra activity, particularly those related to improving the ability to utilize food.

The gut microbiota and proper functioning of homeostatic systems i.e. nervous, endocrine, and immune system needs to work effectively in maintaining proper health in older age. In elderly person, these system undergo modifications which reduces the functional capacity of all the organs in the body, which evolves inflammation, the process which is characterized by a low-grade inflammatory state, involved in the etiologic of several age-related chronic pathological conditions. Many types of bacteria are involved in probiotics which will improve the old conditions, some of them classified as probiotics like Lactobacillus, Bifidobacterium and Saccharomyces boulardii.

HIV and probiotics vs. micro biota

HIV infection significantly alters total microbial colonization as well as the micro biota composition in the oral cavity, and decreased CD4 cell counts have been associated with the presence of oral lesions [3]. HIV progression is characterized by the deregulations of intestinal immunity that may also persist during highly-active antiretroviral therapy, which affect the gut and oral microbiota dysbiosis and correlates with markers of disease progression [4,5]. The interventions in HIV-positive patients are necessary to restore the integrity of the immune system of gut-associated lymphoid tissue (GALT), and the use of probiotics may recover gut barrier functions, remodel the micro biome, which able tp decrease in bacterial translocation and pro-inflammatory cytokine production, that improves the immune
functions of HIV-infected subjects, which are on short-term antiretroviral therapy (ART) [6-8]. The host's microbiota is very important in improvement of mucosal barrier functions, and modulation of the immune system [9,10].

Approximately 99% of the microbiota is present in the GI, achieving a major impact on the health of their host [11]. This is the reason why the gastrointestinal micro biome is the best-investigated microbiome and they serves as a model for understanding host–microbiota interactions and disease. It is known that a healthy gut flora is largely responsible for the overall health of the host, while gut microbiota alteration is associated with several human diseases, such as bowel diseases, metabolic and allergic diseases, or neurodevelopmental illnesses [11-13]. The intake of probiotics can reduce the risk of diseases associated with intestinal barrier dysfunction by increasing mucus, antimicrobial peptides, and secretory IgA production, as well as increasing competitive adherence for pathogens, and the tight junctions (TJ) integrity of epithelial cells [14-16]. It is known that certain lactobacilli adhere to mucosal surfaces, inhibiting the attachment of pathogenic bacteria and enhancing the secretion of mucus.

The gastrointestinal (GI) tract is a major site of HIV replication, and its disorders are among the most frequent complaints in patients with HIV infection. Patients with HIV infection are susceptible to gastric hypoacidity, which may be responsible for a greater risk of opportunistic infection. HIV infection has an unfavorable effect on the interaction between the commensal microbiota and the immune system, with progressive immune decline associated with inefficient epithelial repair and enhanced epithelial permeability responsible for GI disorders [17]. In people with acquired immune deficiency syndrome (AIDS), the wall of the small intestine is impaired, the crypts are enlarged, and the atrophy of the microvilli decreases their surface area. These modifications are responsible for malabsorption, digestive discomfort, or decreased intake of nutrients. Pseudomonas aeruginosa and Candida albicans, and the reduction of Bifidobacteria levels and Lactobacillus species are associated with damage and loss of mucosal barrier functions [18,19] that are correlated with immune status [5,20,21].

As the initial stage of HIV infection progress, the immune system is unprepared for the attack of the virus, therefore spreading HIV throughout the body. HIV causes a disruption of gut microbiota and massive depletion of lamina propria CD4 cells in early and acute HIV infection because there is no data that it is 50% [22], as these cells may be more susceptible to HIV infection due to high levels of activation and expression of C-C chemokine receptor (CCR5) receptors [22] in particular the CD4 cells that produce IL-17 and IL-22. This depletion leads to apoptosis as well as by bystander cells via pyroptosis and the direct killing of infected cells by natural killer (NK) cells or cytotoxic T-cells [23,24]. These mechanisms may contribute to CD4+ T-cells loss, mucosal barrier damage, and chronic systemic inflammation. The consequences of reduced CD4 cells is the failure of gut mucosal barrier to protect against invading pathogens as well as the loss of cytokines necessary to support normal barrier function. In HIV-infected persons with poor CD4 recovery, intestinal barrier dysfunction and mortality has been linked to elevated plasma kynurenine/tryptophan ratio [25].

Th17 and Th22 cells could play a role in amplifying the innate responses to HIV infection by enhancing the production of IL-22, a critical cytokine for epithelial barrier maintenance, improves epithelial regeneration inducing stem cell–mediated epithelial cell proliferation [26], and the expression of anti-microbial peptides. In inflammatory state of HIV, high levels of tumor necrosis factor (TNF), Tumor necrosis factor Receptors (TNFs)1 and 2, IL-6, IL-1 interferon (IFN)α are observed.

Probiotics administration

Probiotic administration protects the gut surface and can delay the progression of HIV infection to AIDS. The use of probiotics may be inexpensive and potentially useful to reduce HIV-related morbidity and mortality [27]. There are many possible mechanisms by which probiotics may interfere with HIV. Probiotics can compete for nutrients and epithelial and mucosal adherence, inhibit epithelial invasion, counteract the inflammatory process by stabilizing and strengthening the gut microbiota responsible for the intestinal barrier integrity, prevent microbial translocation, lower mucosal and systemic inflammation, stimulate production of antimicrobial substances [28-30], and promote intestinal immunoglobulin. Responses to improve the immunological barrier function [31-39]. Some of the microbes are correlated with healthy intestinal flora. Their metabolic end products of growth are organic acids (lactic and acetic acids). These acids have a tendency to lower the pH of the intestinal contents, thus creating an atmosphere for harmful bacteria. Probiotics secrete antibacterial peptides which kills harmful bacteria in the gut. Probiotics in the GI tract help to reinforce the barrier function of the intestinal lining, lowering the chance of bacteria in the intestines entering into the blood stream this will lead to decrease infections and immune related reactions, thus supporting the health of the immune system. As the knowledge of intestinal flora is growing, it is becoming evident that the protection of these beneficial bacteria is needed. Probiotics can be obtained from quality supplements, raw fermented and cultured foods [40,41]. This diet supplementation improves antioxidant defenses and promotes the reconstitution of the immune function.

Probiotics by altering intestinal flora may induce epithelial healing, and by preventing the decline in CD4+ cell counts may lower the risk of virus transmission and reduce hospitalization for co-infections. ART-treated patients who fail to have an immunologic response (CD4 <200) have lower levels of lactobacilli, elevated levels of LPS and sCD14, and increased inflammatory markers, results in the improvement of gut microbiota composition, the reduction of sCD14, CD4+ T-cell activation (CD25). A combination of probiotic bacteria upregulates Treg cell activation and suppresses pro-inflammatory immune responses, thus providing a rationale for the use of probiotics in HIV infection.

In addition to the ability of probiotics to improve barrier function and intestinal homeostasis, specific probiotic strains may be able to revert the HIV-induced Th-2 polarization [34]. It was shown that HIV-infected patients on ART were supplemented with probiotics, have significantly reduced inflammation and markers of microbial translocation [28]. In HIV-infected subjects, diet supplementation for four weeks with Lactobacillus casei Shirota were virologically, bacteriologically, and immunologically beneficial, leading to increased levels of CD56+ cells and to a reduction of inflammatory status with significantly increased IL-23 serum levels. In addition, probiotic supplementation could be useful in the reduction of risk factors for cardiovascular diseases, such as hypercholesterolemia, as well as in the improvement of quality of life by improving the nutritional status, alleviating GI manifestations, and stimulating mucosal immune function [35]. Bacterial vaginosis may increase the risk of transmission or acquisition of HIV, increasing proinflammatory cytokines and
disrupting the mucosal barrier function [36], and probiotic intervention may be prophylactic for bacterial vaginosis [37]. Thus, in HIV-affected patients, probiotics may be a low-cost and accessible treatment approach to periodontal diseases that confer benefits upon host well-being that improves the quality of life [38-41].

Conclusion

Healthy microbiota reduces the chances to get infected. Use of probiotics helps the microbiota in increasing their functionality and improves gut immunity. It seems very important in HIV infected persons by increasing the life expectancy. Probiotics are easily available and not costly, reachable to everyone. Beyond the HIV/AIDS stigma it is recommended that Probiotics are a powerful tool that improves the life of diseased person. This will be future therapeutics to HIV/AIDS. Although ART and other pharmacological therapies are life-saving in HIV-positive subjects, due to the suppression of plasma viremia, the number of mucosal CD4 cells does not always fully recover, and microbial translocation is still not under full control and remains associated with systemic immune activation and inflammation, which needs to be understood fully. The elevated pro-inflammatory cytokine levels, as well as T and B cell activation and tight junction dysfunction between the epithelial cells of the mucosal barrier is also part of research.

References


