A Systematic Review of Probiotics as a Potential Intervention to Restore Gut Health in HIV Infection

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Probiotics have beneficial effects on the gut in numerous conditions. The purpose of this paper is to present a review of the current literature on probiotics used in chronic illnesses exhibiting similar pathology seen in HIV gut dysfunction, in order to make recommendations for their use to promote and restore healing of the gut with subsequent reduction of ongoing inflammation caused by microbial translocation. A review of the literature was performed, focusing on probiotics as an intervention to improve gut health. Key words were searched in PubMed and the Cumulative Index to Nursing and Allied Health Literature. The literature reviewed was limited to clinical trials, meta-analyses, and practice guidelines. The review provided evidence that probiotics were supportive in modulating aspects of gut physiology, barrier integrity, and immune function. Probiotic use is a supportive adjunct therapy, worthy of consideration and further research in persons infected with HIV.

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Common complaints from patients infected with HIV include diarrhea, bloating, abdominal discomfort, and changes in body weight. In addition, providers and patients are frustrated with regard to patients failing to achieve immune reconstitution despite viral suppression with antiretroviral therapy (ART) (Kelley et al., 2009; Torti et al., 2004). There is growing recognition that this immunologic failure may be due to changes in the gut mucosa. These changes have been attributed to HIV-associated inflammation in the gut (Paiardini, Frank, Pandrea, Apetrei, & Silvestri, 2008; Pandrea, Sodora, Silvestri, & Apetrei, 2008) and significant loss of Th17 cells, a certain type of CD4+ T cell exhibiting the CCR5 receptor that secretes a pro-inflammatory cytokine IL-17 (Brenchley et al., 2008). Probiotics have been effective in managing similar symptoms in other conditions with gut inflammatory etiology. Anecdotally, some providers are beginning to recommend probiotics to alleviate and manage these gastrointestinal (GI) symptoms. However, there is little empirical evidence supporting the effectiveness of probiotics with respect to populations infected with HIV.

There has been growing interest in examining microbial translocation caused by HIV immune activation within the gut-associated lymph tissue (GALT). Microbial translocation is associated with the failure of reconstitution of CD4+ T cells even in the presence of viral suppression with ART (Jiang et al., 2009; Marchetti et al., 2008). Translocation of bacterial products into peripheral circulation is partly a consequence of the degradation of protective

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mechanisms of epithelial components forming the gut barrier (Dandekar, George, & Baumler, 2010). Outcomes associated with this process include ongoing inflammation in the gut and periphery. Serological markers and irritable bowel serological patterns have been studied and found to be present in HIV-infected patients with high levels of detectable translocated microbial products (Kamat, Ancuta, Blumberg, & Gabuzda, 2010). Patients with HIV infection experience a subsequent loss of CD4+ T cells and GI enteropathy with symptoms such as discomfort, diarrhea, bloating, and nutritional deficits described histologically by mucosal epithelial degeneration, intestinal microvilli loss, and inflammation (Bhaijee, Subramony, Tang, & Pepper, 2011). GI dysfunction has been a common companion to all stages of HIV disease (Knox, Spiegelman, Skinner, & Gorbach, 2000).

Complaints of GI discomfort, bloating, constipation, oral and esophageal candidiasis, and ailments such as diarrhea commonly seen in HIV might be well addressed by probiotic therapy. In addition, diarrhea is a side effect of antiretroviral medications and antibiotic use. Furthermore, patients with low albumin levels and CD4+ T cell counts below 50 cells/mm^3 are likely to develop a pathogenic cause of diarrhea (Bonacini, Skodras, Quiason, & Kragel, 1999). Chronic diarrhea increases the risk for mortality (Dillingham et al., 2009), and, in some cases, even after starting ART, survival is limited.

According to Gordon and colleagues (2010), HIV enteropathy affects absorption of ART leading to virologic failure and failure of immune reconstitution, leading to death. The immunopathogenesis of HIV is strongly associated with marked destruction of intestinal CD4+ T cell homeostasis, subsequent microbial translocation, and chronic immune activation (Gordon et al., 2010).

Probiotics have been effectively used as a preventive and therapeutic approach in the arena of inflammatory bowel diseases. Probiotics inhibit pathogenic bacteria and toxins by adhering to the intestinal epithelium, induce anti-inflammatory cytokines, and promote intestinal epithelial cell homeostasis (Vanderpool, Yan, & Polk, 2008). The molecular mechanism of probiotics has provided support for their application as an adjunct and alternative treatment of gut inflammation.

Probiotics are commensal bacteria that have the beneficial effect of sustaining immune mediation and repair of the gut mucosa (Mazmanian & Kasper, 2006; Verhoeven, Sankaran, Silvey, & Dandekar, 2008). The gastroenteropathy seen in HIV is similar in pathology to that seen in inflammatory gut disease, and thus it may be responsive to interventions used to treat inflammatory gut disease. Therefore, probiotics may be a cost-effective adjunct therapy to reduce chronic GI symptoms seen in HIV-infected patients.

The purpose of this paper is to present a review of the current literature on probiotics used in chronic illnesses that exhibit similar pathology to that seen in HIV gut dysfunction in order to make recommendations for their use in promoting and restoring healing of the gut, with subsequent reduction of ongoing inflammation caused by microbial translocation. The overall aim of this paper is to examine the evidence of the effect of probiotic therapy on epithelial function, symptoms, and gut immune response reported in other GI conditions. This is an important first step in identifying interventions that may be efficacious in treating GI symptoms in HIV disease and that warrant further investigation.

Background

The success of HIV treatment is based on effective combination ART with evidence of decreases in peripheral viral loads and increases in CD4+ T cell counts (Verhoeven et al., 2008). However, ART may have little effect on the HIV-associated inflammation that has been linked to HIV-associated comorbidities and abnormalities that occur despite the use of ART (Baker et al., 2011; Deeks, 2011; Harezlak et al., 2011; Mangili, Polak, Quach, Gerrior, & Wanke, 2011). The effects of inflammation on the cardiovascular, renal, neurologic, and gastroenterological systems are unchanged by the suppression of HIV by ART. Therefore, there is a need to clinically address the effects of such inflammation on the body to support health and wellness in addition to treating viral replication. An important research question is whether probiotics demonstrate the same response in HIV infection as they do in other conditions.

There is a complex relationship between the immune system, GI tract, and HIV pathogenesis.