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Does Normalizing Gut Microbiota Decrease Exacerbation in IBD

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Abstract

Inflammatory bowel disease (IBD) including Crohn's Disease (CD) and Ulcerative Colitis (UC) has become a more common diagnosis. The number of screenings for IBD has increased, drawing more attention to finding the cause. Researchers are finding that a change in diet, increased stress levels, and overuse of antibiotics may contribute to IBD by changing the gut microbiota (Skrautvol et al., 2011; Bernstein, 2010). Prebiotics and probiotics, an individualized anti-inflammatory diet, and lifestyle modification to decrease stress are all currently undergoing evaluation to discover a possible role in the reversal of IBD insult to the normal flora of the gut. This literature review examined IBD studies within the past eight years, including children and adults age 10-76, male and female who suffer from IBD and address gut microbiota. Articles were reviewed from EBSCO and PubMed. Cammorata et al. (2015) conducted research on fecal samples from patients with IBD (n=330) and healthy control (n=165) using a Dysbiosis Index (DI). Dysbiosis was associated with a score of >2. All healthy controls were <2 and IBD patients >2. This was confirmed with an Illumina MiSeq test with P=<0.001. Kabeerdoss, J. et al. (2013) researched biopsies from colonic mucosa of patients with IBD (n=60) compared with controls (n=30) undergoing screenings. A decreased ratio of Firmicutes to Bacteroidetes was identified in IBD patients with significance of P=0.0014 proving an altered gut flora in IBD patients. The population of patients examined with IBD who are able to restore their gut microbiota will likely decrease symptoms and decrease the need for long-term treatment with anti-inflammatory medications. Further research is needed to identify specific imbalances in microbiota with the application of results to create an individualized plan to restore gut flora as a key treatment to achieve and maintain remission in IBD patients.

Introduction

•Inflammatory Bowel Disease (IBD) has been increasing in incidence over the past decade. The effects of the disease on an individual and the potential life-long cost of medical treatment are rationales to find and treat the cause of IBD. Researchers are evaluating altered gut flora as a cause of IBD. Dysbiosis was identified as a feature of IBD and interventions directed at themicrobiome may be indicated in thetherapy of IBD (Kabeerdoss et al., 201).

Statement of the Problem

•Patients diagnosed with ID are faced with the potential of life-long anti-inflammatory drugs, steroiBds, biological drugs, and even surgery to decrease or control symptoms. Documented side effects of these treatments are decreased immunity, renal failure, hepatotoxicity, exacerbations of the disease, myocarditis, blood dyscrasias, and anemia. The cost of the medication, side effects, hospitalizations and absenteeism from work add to the burden of patients with IBD.

Research Question

In patients with IBD will restoring gut microbiota eliminate or decrease the need for long-term treatment with medications?

Literature Review

•Casen et al. (2015) termed the microbiota in a healthy patient "normobiosis". The purpose of this study was to obtain fecal samples and examine the relationship between dysbiosis and patients with IBD. Adult male and female patients ages 17-76 (n=330) were selected both with IBD and a control group of healthy individuals (n=165). The fecal samples were probed targeting approximately 300 bacteria to identify dysbiosisusing the GA-map Dysbiosis Test (GA-test) to determine a Dysbiosis Index (DI). In this sample, a DI of >2 was associated with dysbiosis. In all samples collected from healthy individuals results were <2 with a mean of 1.72 and in IBD both treatment naïve and in remission were >2 with a mean from 3.15-3.3. Results confirmed dysbiosis in 70-80% of IBS patients, IBD patients untreated, and IBD in remission vs 16% in healthy controls (Casen, et al., 2015). *Firmicutes*, *Proteobacteria*, *Actinobacteria* and *Ruminococcus gnavus* were predominant bacteria found associated with IBD.

•Kaberdoss et al. (2013) studied the colonic mucosa of patients with IBD and healthy controls to determine alteration in microbial communities Biopsies of colonic mucosa was obtained in 32 patients with UC, 28 with CD, and 30 healthy controls during colonoscopy. Results produced a ratio of Firmicutes to Bacteroidetes was significantly decreased in patients with CD and UC compared to healthy controls indicating dysbiosis in IBD patients with P=0.0014 (Kabeerdoss, Jayakanthan, Pugazhendhi, & Ramakrishna, 2015). Dysbiosis was identified as a feature of IBD and interventions directed at the microbiome may be indicated in the therapy of IBD (Kabeerdoss, Jayakanthan, Pugazhendhi, & Ramakrishna, 2015).

•Olendski, B. et al. (2014) utilized an Anti-Inflammatory Diet (IBD-AID) to help treat symptoms of IBD. Dysbiosis is the theory behind this diet theorizing certain carbohydrates contribute to the proliferation of pathogenic bacteria (Olendzki, Silverstein, Cave, & Baldwin,2014). Eleven of 40 patients chose to remain on the diet and were reviewed by the Harvey Bradshaw Index (HBI) or the Modified Truelove and Witts Severity Index (MTLWSI) before and after the diet (Olendzki, Silverstein, Cave, & Baldwin, 2014). The MTLWSI mean was 7 (range 6-8) and the follow-up mean was 0. The average decrease in the HBI was 9.5 and MTLWSI 7. The sample group was fairly small and only approximately 25% were compliant for four weeks (Olendzki, Silverstein, Cave, & Baldwin, 2014).

Discussion

- Patients with IBD are in a state of gut dysbiosis (Ballal, Gallini, Segata, Huttenhower, & Garrett, 2011). Evidence supports the theory that microbiota is altered in IBD patients (Kabeerdoss, Jayakanthan, Pugazhendhi, & Ramakrishna, 2015). See Figure 1. Eventually, due to disruption of homeostasis in the gut flora, an inflammatory response occurs resulting in erosion of the mucosa of the gastrointestinal tract. Malabsorption of essential vitamins, minerals and nutrients is the result, leaving the body in a suboptimal state.

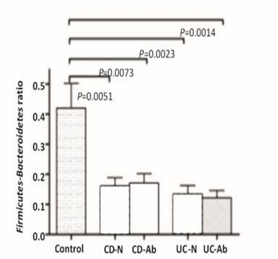

Figure 1. Ratio of Firmicutes (*C. coccoides* plus *C. leptum*) to Bacteroidetes in the mucosal microbiota. The Figure shows the ratio in patients with CD and UC. CD-N and CD-Ab refer to Crohn's disease normal and abnormal mucosa. UC-N and UC-Ab refer to ulcerative colitis normal and abnormal mucosa. Significant *P* values are shown above the bars in the Figure. None of the other differences was significant. IBD biopsies showed a significantly lower ratio compared with controls. (Kabeerdoss, Jayakanthan, Pugazhendhi, & Ramakrishna, 2015)

- Research has found genetic alterations of genes such as the NOD2 risking the development of IBD (Leone, Chang, & Devkota, 2013). Atg16L1, IRGM, and IL-23R were other altered genes associated with patients with IBD (Ballal, Gallini, Segata, Huttenhower, & Garrett, 2011). Testing for genetic components is not routinely performed in IBD but may have potential to prevent onset. A study of using this testing as a predictor may be useful.
- Study of fecal samples are proving helpful in identifying specific bacteria involvement and dysbiosis in IBD (Casen, et al., 2015). Fecal and mucosal sampling to identify dysbiosis would prove beneficial and establish a foundation from which to treat the patient as an individual. The causative imbalance of microbiota could potentially be replaced if properly identified.
- The theory that if diet is a causative component of IBD then diet should be a therapeutic treatment in IBD is of growing interest. Restoring the gut microflora through proper nutrition may be a key component in the treatment and prevention of IBD (Olendzki, Silverstein, Cave, & Baldwin, 2014). Nutrition could be a successful adjunct in the treatment of IBD, decreasing the need for medication and preventing the need for surgical intervention in these patientsThe IBD-AID diet was 100% successful in decreasing the symptoms and dosage of medication of the IBD patients who complied with the diet but the study was small. The need for a larger cohort study focusing on an individualized patient nutritional plan is needed as a result (Olendzki, Silverstein, Cave, & Baldwin, 2014).

Applicability to Clinical Practice

Identifying patients at risk for development and exacerbation of IBD is an important role for primary care providers. As genetic testing, fecal testing and microbiota testing becomes more widely used IBD could be prevented in the future. Research has correlated nutrition's impact on the gut microbiota but larger studies are needed. Patients with IBD have an imbalance in their gut organisms that when balanced could create a state of normobiosis. IBD-AID as a nutritional guide is an optimal approach to healing and reestablishig homeostasis of the gut microbiota (Olendzki, Silverstein, Cave, & Baldwin, 2014). The success of the IBD-AID trial warrants a larger study group utilizing the IBD-AID diet vs the currently used anti-inflammatory drugs, steroids, biological drugs, and surgery. Similar results would support the benefit and the promote the use of the IBD-AID diet as a standard of care. Primary care providers and nutritionists can assist IBD patients, or those at risk of developing IBD due to genetic indicators, in staying adherent to an individualized nutrition plan that could decrease the need for the mainstay medications currently used to treat IBD. Encouraging patient compliance and accountability for health is ongoing and imperative for success in the treatment of IBD. Nutrition in the form of an anti-inflammatory diet has the potential to decrease the need for costly anti-inflammatory drugs, steroids, biological drugs and decrease their dangerous side effects but more research is needed to prove this.

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