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Gut Microbial Flora, Prebiotics, and Probiotics in Multiple Sclerosis: Their Current Usage and Utility

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Abstract

The gut micro biome is now regarded as a major organ with direct effects on the gastrointestinal system, immunological function, and endocrine system. In recent years, the results of various studies have shown changes in the intestinal micro biome profile in patients with autoimmune diseases. Probiotics have been found to have a great impact on the maintenance of anti-inflammatory responses. This article discusses the latest data available regarding the effect of the gut micro biome, prebiotics, and probiotics on Multiple Sclerosis (MS).

Keywords: Gut micro biome; Probiotic; Multiple sclerosis; Mini review

Introduction

The Gut Micro biome (GM) is the largest one that includes trillions of bacteria, fungi, and viruses that live in the intestinal tract. These bacteria have been identified to influence immunological responses linked with a variety of disorders including Rheumatoid Arthritis (RA), gastrointestinal diseases especially Irritable Bowel Syndrome (IBS), fatty liver, and asthma. Another disease that has been studied in recent years in connection with the intestinal microbiome in autoimmune Central Nervous System (CNS) disease. The global prevalence of autoimmune illnesses is quickly rising. One of the most important diseases of this group is Multiple Sclerosis (MS) with an incidence rate of 2.1 per 100,000 persons/year [1]. The animal model of MS is Experimental Autoimmune Encephalomyelitis (EAE) [2]. Due to the importance of the intestinal microbiome in MS, various animal and human studies have evaluated this relationship. In this mini-review study, we review some of these studies.

Gut microbiome and MS

It has been shown in the pre-clinical studies that an imbalance in the gut microbiota, called “dysbiosis”, is associated with EAE. Disruption of the intestinal microbiome in favor of pathogenic bacteria can damage the Blood-Brain Barrier (BBB) permeability and the function of microglia and myelin [2,3]. Preclinical studies have shown that in EAE -induced mice, dysbiosis induce naive T-cell differentiation to Th1 and Th17 cells (which produce pro-inflammatory cytokine such as interferon (IFN)-γ) and reduce the expression of anti- inflammatory proteins and cytokines specially FoxP3+ Treg cells, IL-10 and IL-13 [2,4]. On the other hand, the process of differentiation of naive T cells into T cells with anti-inflammatory properties is accelerated by polysaccharide A (PSA) produced by some bacterial strains such as B. fragilis [5,6]. In addition, it has been shown that the production of Short-Chain Fatty Acids (SCFA) by intestinal bacteria can improve the naive T-cell differentiation to regulatory T (Treg) and reduce the risk of EAE [7]. Lactobacillus and Turicibacter spp. are among the bacterial strains involved in the production of SCFA [8,9].

Among the human studies, Mirza et al. in a systematic review study showed that there wasn’t any significant difference in gut microbiome alpha-diversity among the patients with MS compared to the control group. However, they found a lower relative abundance of Prevotella, Faecalibacterium prausnitzii, Bacteroides coprophilus, Bacteroides fragilis, and higher Methanobrevibacter and Akkermansia muciniphila in MS cases versus controls [10].

Probiotics and MS

In recent years, several animal and human studies have evaluated the effect of different bacterial strains on human and animal models of MS. Baokun et al. showed that Lactobacillus reuteri DSM administration led to a significant reduction in the EAE severity in animal models. Also, they found that L. reuteri could reduce TH1/TH17 cells ratio and their associated cytokines IFN-γ/IL-17 in EAE mice [11]. Kwon et al. in another study on animal models of MS showed that oral administration of mice with a mixture of five probiotic strains, Streptococcus thermophilus, L. reuteri, Bifidobacterium bifidium, Lactobacillus acidophilus, and Lactobacillus casei delayed the EAE onset [12]. In our previous study which was conducted on patients with MS, it has been shown that multi-strain probiotic supplementation

led to a significant improvement in mental health parameters [13]. Similar findings were reported in another study [14]. Also, a randomized, double-blind, placebo-controlled study revealed that multispecies probiotic supplementation (specific strains: Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, and Lactobacillus fermentum) reduced gene expression of interleukin-8 and tumor necrosis factor-alpha, however, there wasn't a significant difference between probiotic and control group in term of expression of interleukin-1 (IL-1), peroxisome proliferator-activated receptor gamma (PPAR-γ), or oxidized Low-Density Lipoprotein Receptor (LDLR) [15]. Similarly, anti-inflammatory response, with reduced frequency of intermediate monocytes (CD14highCD16low) and impaired levels of Mean Fluorescence Intensity (MFI) of CD80 on classical monocytes and Human Leukocyte Antigen–Antigen D Related (HLA-DR) MFI on dendritic cell also resulted from oral administration of Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus casei, and Lactobacillus delbrueckii subspecies bulgaricus [16]. Finally, in a meta-analysis study obtained from 6 clinical trials, the results showed that probiotic supplementation significantly reduced the score of the Expanded Disability Status Scale (EDSS), Beck Depression Inventory-II (BDI-II), and General Health Questionnaire [17].

Conclusions

Current research efforts, although varied, mostly indicate the importance of gut microbiome favorable effects of probiotics on patients with MS. Long-term studies with different strains of probiotics are thus required to analyze the processes and consequences on MS, particularly in humans.

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