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EDITORIAL

Probiotics: Not just good for the gut but for the brain too

The gastrointestinal (GI) tract contains a vast ecology of microbes that are necessary for health but also have the potential to lead to the development of diseases in susceptible individuals. Probiotics are microorganisms that have beneficial properties for the host. Most commercial products have been derived from food sources, especially cultured milk products. The list of such microorganisms continues to grow and includes many strains of lactic acid bacilli (e.g. *Lactobacillus* and *Bifidobacterium*), a nonpathogenic strain of *Escherichia coli* (e.g. *E. coli* Nissle 1917), *Clostridium butyricum, Streptococcus salivarius*, and *Saccharomyces boulardii* (a nonpathogenic strain of yeast). For several decades, the therapeutic potential of probiotics have been largely studied in various GI-related diseases. Clinical benefits have been demonstrated in inflammatory bowel diseases (particularly pouchitis) and are suggested in antibiotic-related diarrhea, *Clostridioides difficile* toxin-induced colitis, infectious diarrhea, hepatic encephalopathy, and irritable bowel syndrome.[1]

The GI tract is recognized to communicate with the brain via a network of neuronal, immunological, and metabolic signaling.[2] The brain influences the GI system by regulating motility, secretion, absorption, and blood flow, while the gut can affect brain function and behavior. Interestingly, recent developments in the understanding of the pathophysiology of neurodegenerative diseases such as Alzheimer's Dementia and Parkinson's Disease (PD) have demonstrated increased intestinal permeability and intestinal inflammation in these conditions.[2] Furthermore, alterations in the gut microbiota (aka gut dysbiosis) and their metabolites have been demonstrated in adults with PD compared to non-PD controls.[3] Importantly, gut dysbiosis has also been associated with more severe PD symptoms.[4]

The mechanism for the benefit of probiotics is thought to include suppression of growth or epithelial binding/invasion by pathogenic bacteria, improvement of intestinal barrier function, modulation of the immune system, and modulation of pain perception.[5] In this issue of *JGH Open*, Tan *et al*. have summarized some of the current evidence for the role of probiotics in PD.[6] They reported that probiotics not only led to a reduction in neurotoxic metabolites but was able to improve motor function in studies conducted on mouse models of PD. Probiotics have also been shown to downregulate proinflammatory cytokines and upregulate anti-inflammatory cytokines in cellular model studies using blood samples from PD patients. In human clinical trials, the best evidence for the efficacy of probiotics has been demonstrated in its efficacy for improving constipation symptoms in PD. Constipation is extremely common, causing significant distress to patients with PD, and is notoriously resistant to current laxatives .[7] Two randomized controlled trials have demonstrated the superiority of multistrain probiotics over placebo in improving constipation in PD over a 4-week period.[6]

As constipation is recognized to predate the onset of motor symptoms in PD,[8] it is possible that prolonged or higher doses of probiotics may be able to reduce debilitating motor symptoms, but this is yet to be proven. PD is also known to have a significant number of nonmotor symptoms such as cognitive impairment, anxiety, depression, and psychosis. Probiotics have also been shown to improve anxiety and depression in non-PD adults in human trials,[3] so it is hoped that these benefits may be extrapolated to PD as well.

The association of gut dysbiosis and neurodegenerative diseases like PD provides a new direction for therapy as current treatment is unable to alter their natural history. Apart from probiotics, other options to improve gut dysbiosis include prebiotics and fecal microbiota transplantation, but the current best evidence has been for probiotics.[9]

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