

Fecal microbiota transplantation as a possible treatment of irritable bowel syndrome

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The human gut is composed of trillions of microbial organisms making up the microbiome. As our understanding of the composition of the human microbiome has advanced through developments in gene sequencing, its association with human physiologic function and disease has evolved. Alterations in the abundance of certain bacterial families have been noted in a number of intestinal diseases, and interventions to alter microbial ecology have impacted animal models of some diseases (1). In particular, the disruption of an individual's microbiome through fecal microbiota transplantation (FMT) has provided insights into the role of bacterial families in specific human disease processes (2).

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder affecting 5–15% of the general population (3). IBS is often associated with comorbid psychosocial disorders, such as anxiety or depression (4). Although the pathogenesis of IBS is poorly understood, several studies have shown that the fecal microbiota of IBS patients differs significantly from that of healthy subjects and it may contribute to the onset and maintenance of the disorder (5–7). This has consequently generated interest in the potential therapeutic role of FMT in the management of IBS.

The existing data on FMT and IBS is still quite limited. A systematic review of the available literature on FMT and IBS showed improvement in IBS symptoms in 58% of patients after FMT (8). Although studies have shown

an association between altered gut microbiota and several disease processes, including IBS, the data establishing a clear effect or causality is lacking.

In this context, De Palma *et al.* aimed to evaluate the impact of fecal microbiota from patients with IBS in a murine model (9). They colonized germ-free mice with the fecal content of healthy control individuals or IBS patients with diarrhea (IBS-D) with or without anxiety. At baseline, the fecal bacterial constituents of both healthy controls and IBS-D patients were similar at the phylum and genera level, but did exhibit some species-level differences. The mice that received fecal content from patients with IBS-D exhibited faster gastrointestinal transit time and higher colonic paracellular permeability than mice administered fecal content from healthy controls. In addition, differences in lymphocyte numbers, defensins, serum metabolites and chemokines were noted in the colonic tissue of these mice. Interestingly, mice who received fecal matter from patients with IBS-D and anxiety also demonstrated greater levels of anxiety-like behavior in the laboratory setting.

What are the implications of this study for our understanding of IBS-D? This study succeeds in showing an effect of disease-derived fecal content on measures of both IBS and intestinal function in a convincing manner. What is not provided is the mechanism that mediates these changes. Fecal samples contain a heterogeneous mix of bacteria, viruses, fungi, peptides, and miRNA amongst other content. Since only the relative abundance of bacterial

families was quantified in patient samples, any assumption that colonization of the mice colon by particular bacterial species led to these differences is unfounded. Studies of FMT in other settings have shown that the metabolic consequences in the colon of successful FMT may be more important than bacterial abundance (10). An additional useful experiment would be the effect of FMT from healthy patients on physiologic processes in a murine model of IBS. IBS-C and IBS-D are two distinct subgroups of IBS with very different treatments. This data is limited to IBS-D and cannot be extrapolated to the wide spectrum of IBS patients. The study is also limited by a small number of subjects and short-term follow-up of only 3 weeks. In our opinion, FMT as a possible treatment of IBS is an interesting hypothesis. Nonetheless, the existing data of FMT and IBS is too limited to draw significant conclusions regarding its efficacy and further clinical studies are needed.

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Footnote

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