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The enteric microbiota in the pathogenesis and management of constipation

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For centuries, fiber has been recommended on an empirical basis for the management of constipation; it has only been in recent decades that the mechanisms whereby fiber and related products may influence colonic function have begun to be elucidated. The interaction between fiber and the microbiota of the human colon appears to play a major role in generating the beneficial effects of fiber. The microbiota is also the target for the other therapeutic interventions discussed in this chapter: prebiotics and probiotics. While a scientific basis for a role for these approaches in the management of constipation continues to develop, evidence from high-quality clinical trials to support their use in daily practice continues to lag far behind. While benefits for fiber and, perhaps, for certain prebiotic and probiotic preparations in constipation appear to be extant there is a real need for large well-conducted clinical trials in this important area of human medicine.

Introduction

The context: the microbiota and constipation

Given the impact of fiber and fiber supplements on the colonic microbiota and the fact that the use of prebiotics and probiotics is presumed to be based on their ability to modify this population of microorganisms, one would assume that the role of microbiota-host interactions in a disorder as common as constipation is well defined. Nothing could be farther than the truth; very little is known of either quantitative or qualitative changes in bacteria or other organisms in this condition. This gaping hole in our knowledge is based, in part, on the inadequacies of conventional culture-based techniques which are now known to underestimate the diversity of the colonic microbiota by a factor of as much as 50% and on the relative lack of attention that has been given to the microbiota in constipation.

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Zoppi and colleagues reported increased numbers of clostridia and bifidobacteria among children with constipation [1] while Khalif and colleagues noted that populations of lactobacilli and bifidobacteria were reduced among their adult subjects [2]. Interestingly, Zoppi and colleagues, while noting a modest symptomatic improvement with the administration of calcium polycarbophil failed to detect an impact of this fiber analog on the colonic microbiota [1]. In a more indirect piece of evidence, Celik and colleagues found that a course of vancomycin to constipated patients increased stool volume, frequency, consistency and ease of defecation [3]. Needless to say, the aforementioned caveats with respect to the interpretation of culture-based studies apply, as all of these studies used this methodology.

Recently, an impact of the small intestinal microbiota on constipation has been suggested by studies reporting that the excretion of abnormal amounts of methane following the administration of lactulose as part of a lactulose breath test to detect small intestinal bacterial overgrowth (SIBO) among subjects with irritable bowel syndrome (IBS) is associated with a symptomatology dominated by constipation (C-IBS). While the status of SIBO in IBS, in general, remains a controversial issue [4–10], the association between methane excretion and constipation in IBS has been reasonably consistent [4,5,9,11,12]. Most recently, an association between methane excretion and slow-transit constipation has been described by Attaluri and colleagues [13]. In this study methane production was both more prevalent and higher among slow-transit than normal-transit constipation, again, supporting the idea that methane can slow gut transit [12]. It must be stressed that the origin of methane (or for that matter hydrogen) that is excreted in expired air in excess among these and other study subjects with constipation and C-IBS remains to be defined and some would contend that this signal originates from colonic and not small intestinal methanogens. Though qualitative and quantitative changes have been demonstrated in the fecal microbiota in IBS using sensitive molecular biological techniques there is, as yet, insufficient data to make definitive associations between stool pattern and the composition of the microbiota [14,15]. In the most detailed study to date, Kassinen and colleagues noted depletion of lactobacilli in IBS, in general, and some differences were noted between IBS-C and other IBS subgroups [14]; further study in larger patient populations are required.

Therapies that may influence the microbiota

Fiber and fiber supplements

Fiber has been recommended for the treatment of constipation since at least the 16th century [16] and, based on epidemiological studies linking low fiber diets with low stool output, constipation and such apparently related disorders as hemorrhoids, diverticular disease, appendicitis, colon cancer and gallstones which emerged in the 20th century, began to attract considerable scientific interest. Fiber refers to components of grains, vegetables and fruits which are poorly digestible and is comprised largely, but not exclusively, of non-starch polysaccharides. Two types of fibers can be distinguished based on their chemical properties and physiological actions: water soluble fibers such as pectins, gums and mucilages, and insoluble fibers such as cellulose, hemicelluloses and lignins. The former, though highly effective in retaining water to form highly viscous solutions, have a modest effect on stool output and little effect on colon transit; the latter have negligible water retention effects but significantly increase stool output and are potent stimuli of colon transit [17]. The inverse relationship between the water-holding capacity of a given fiber and its effect on stool weight is thought to be explained by the fact that more soluble fibers will be more susceptible to bacterial fermentation in the proximal colon. Several mechanisms of action have been proposed for the laxative effects of fiber and include the simple bulking effect of undigested fiber particles, the aforementioned water-holding effect, an acceleration of colon transit, the pro-motility effects of products of bacterial fermentation, such as short-chain fatty acids, the stimulation of bacterial populations (which normally contribute significantly to stool dry weight) and increased production of gases and other metabolic by-products that increase fecal mass and, thereby, also promote transit [16,17].

Regardless of mechanism of action, fiber and fiber supplements are widely recommended as therapy for constipation; the usual recommendation being to increase fiber intake to 20 to 25 g per day [18]. It should be noted that studies in healthy volunteers have demonstrated that the effects of 25 g of fiber