Are Nutrition Interventions to Augment Treatment Plans the Most Personalized Approach to Inflammatory Bowel Disease Therapy?

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Given that diet represents one of the more readily modifiable environmental factors, it is reasonable for patients to expect that dietary manipulation might result in significant changes to inflammatory bowel disease (IBD)-related symptoms, risk of flares, or ultimately a change in the disease course. Furthermore, many patients may initially view dietary changes as a safer approach to disease management when compared to standard medical therapy in terms of adverse effects such as infectious risks or malignancy. Multiple recent studies have highlighted the complex interplay between the microbiome and dietary intake,[1,2] supporting the role that each of these factors may play in the course of Crohn's disease (CD) and ulcerative colitis (UC). Epidemiologic studies have also identified several critical patterns that may influence the risk of development of IBD, including a lower risk of IBD among individuals who consume more fruits and vegetables and increased risk among people who consume more animal fats and sugar.[3–6] Whether dietary interventions can be used to effectively treat patients with IBD, or even to prevent disease among an identified high-risk population, remains an area of active research.

In this issue of *Crohn's Colitis 360*, Collins and Roche[7] review the potential role for personalized nutrition within a larger treatment paradigm for patients with CD and UC. In addition to reviewing the current state of the literature, including successful interventions in the treatment of patients with IBD, the authors provide an excellent perspective on future areas of research including the potential for nutrition to augment existing IBD-related therapy. As highlighted by the authors, a combination strategy focused on not only modulating intestinal inflammation but also potentiating IBD-specific therapy through dietary intervention may allow for substantial improvements in our approach to the treatment of patients with CD and UC. Traditionally, much of our understanding regarding the relationship between dietary factors and the development of IBD or disease outcomes among patients with CD or UC has been studied through large epidemiologic studies.[3–6] Although these studies have informed much of our knowledge and our practice to a large degree, designing studies around patterns identified in population-based evaluations has been more difficult.

As noted by the authors, this is a particularly exciting time to consider the clinical implications of diet in the disease course of patients in IBD and how diet may be utilized as an intervention. The concept of diet as it relates to IBD can be represented in multiple ways, including as micro- and macronutrients, food additives, individual foods, or food groups representing dietary patterns.[8] Despite these complexities, recent studies have demonstrated that dietary intervention in patients with CD such as the Crohn's disease exclusion diet (CDED) with partial enteral nutrition can lead to both sustained remission and changes in the fecal microbiome that are associated with remission.[9] Several other studies focusing on treating IBD via dietary manipulation have also recently been published including the Food and Crohn's disease Exacerbation Study (FACES),[10] the Crohn's disease treatment with eating diet (CD-TREAT),[11] the Specific Carbohydrate Diet (SCD),[12] and the low-fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (low FODMAP) diet.[13] Additionally, the results of several ongoing trials are highly anticipated including those of a Trial of Specific Carbohydrate and Mediterranean Diets to Induce Remission of Crohn's Disease [DINE-CD, comparing the SCD diet with the Mediterranean diet (NCT03058679)], the Personalized Research on Diet in Ulcerative Colitis and Crohn's Disease (PRODUCE) trial [a series of N-of-1 trials where patients alternate between the SCD and modified SCD regimens (NCT03301311)], and

Received for publications April 20, 2020; Editorial Decision April 21, 2020.

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Conflicts of Interest: E.L.B. has served as a consultant for AbbVie, Gilead, Takeda, and Target PharmaSolutions.

doi: 10.1093/crocol/otaa043
Published online 26 May 2020

the Diet for Induction and Maintenance of Remission and Re-biosis in Crohn's Disease (DIETOMICS-CD) trial [comparing the CDED with partial enteral nutrition and exclusive enteral nutrition (NCT02843100)].

Precision medicine remains a critical goal within IBD,[14] and thus, extending these precision health concepts to personalized assessments of nutrition is a logical goal. As the ability to perform multi-omic evaluations has expanded in recent years, significant focus has been placed not only on the underlying differences in the gut microbiota (and other -omic profiles) among patients with IBD but also how therapeutic agents that alter the intestinal microbiota might be used to treat CD and UC.[15] As noted by Collins and Roche, incorporating dietary assessments into expanded future investigations of the role of the microbiome in IBD may be an important piece of developing personalized nutrition strategies. Nutrigenomics, a field of examining the relationship between bioactive compounds within a particular diet and the expression of genes,[16, 17] may provide critical information to improve our understanding of the pathways underlying response (or risk) associated with specific dietary interventions.[18] Combining these novel assessments with existing clinical data and disease activity assessments may ultimately yield the necessary data to make precision nutrition a reality.

As models of precision nutrition within IBD are developed, we must not view dietary decisions within the concept of "IBD" as a whole but must adopt a rigorous approach to defining the population where a particular intervention may be most effective. The role that differences in phenotype, disease location, and disease severity play in a patient's prognosis and ultimate response to therapy have been emphasized in recent years.[19, 20] These differences in prognosis by disease location may exist even among subtypes of IBD, as patients with CD may demonstrate markedly different responses to therapy based on disease location.[21] Defining the correct population for each dietary intervention study will be critical in both guiding approaches to precision nutrition and ultimately assessing the effectiveness of individual strategies, either as an initial solitary intervention or in conjunction with other IBD-specific treatments.

In addition to studying the role of diet in well-defined populations, we must also continue to utilize structured study designs. Although challenges specific to dietary studies such as dietary quality control and the selection of appropriate comparator groups for each dietary intervention being tested may require significant planning and creativity,[8, 18] critical components of any study design will apply. These include the need for strict assessment of adherence to a particular dietary intervention and objective outcome assessments to determine the relative efficacy and effectiveness of dietary interventions. Additionally, the potential to combine dietary assessments within the infrastructure of larger pharmacologic trials may exist. In the DREAM study, where we investigated the relationship between dietary risk factors and disease relapse among patients with UC,[22] a significant number of the included population were originally recruited for a study of mesalamine efficacy in UC.[23]

In the future, if significant gains are made in the area of personalized nutrition and the inclusion of nutrition in precision health assessments in IBD, there is a hope that these strategies might also improve the durability and longevity of dietary interventions. Even if short-term benefits are demonstrated by exclusion diets or even prospective interventions in the context of a clinical trial, understanding how to tailor individual diets to the right patient profile within IBD may ultimately lead to long-term benefits in the management of IBD and improved dietary compliance. Personalized medicine is often described as finding the right treatments for the right patient at the right time. Inserting personalized nutrition into a larger model of precision health-based treatment decisions may ultimately yield important advances in our attempts to optimize our therapeutic approaches.

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