

Diet in IBD Remission

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Identification of the dietary triggers of inflammatory bowel diseases (IBD) and of a dietary regime which can be followed in the long-term by patients, is of paramount importance. Hence, we performed a comprehensive and detailed review of the literature about the role of diet in the maintenance of clinical remission in Crohn's disease (CD) and Ulcerative colitis (UC), in both adult and paediatric patients. More specifically, we investigated:

- 1) the efficacy of food reintroduction protocols in maintaining clinical remission in patients with CD, following induction of remission with nutritional therapies
- 2.) the efficacy of dietary therapies, including strategies using maintenance enteral nutrition or ordinary food-based diets, on reducing clinical relapse rates in patients with CD and UC
- 3.) the association of dietary components with the risk of developing a clinical relapse in patients with CD and UC

Furthermore, we included specific study-related recommendations, which we believe should form the basis of future research studies investigating the role of diet in maintaining clinical remission in IBD.

Keywords: IBD ; Crohn's disease, diet trigger, relapse

1. Introduction

Inflammatory bowel diseases (IBD) are chronic, relapsing and debilitating inflammatory disorders, of which Crohn's disease (CD) and Ulcerative colitis (UC) are the most common^[1]. While UC involves only superficial inflammation in the colon and rectum, CD can cause transmural, granulomatous inflammation throughout the gastrointestinal tract, anywhere from mouth to anus. Indicative IBD symptoms include diarrhea, abdominal pain, blood in stool, extra-intestinal manifestations, such as arthritis and delays in growth and puberty in children. IBD prevalence is particularly high in North America, central and northern Europe, including Scotland^{[2][3]}. The rising IBD incidence in newly-industrialized countries adopting a Western type lifestyle^[4], serves as a prime example of the significant contribution of environmental factors and especially diet to IBD etiopathogenesis.

2. Diet

Although the complete etiology of IBD remains to be fully understood, the prevailing paradigm suggests a multifaceted interaction between an aberrant immune response and environmental stimuli, mediated through the gut microbiome, in genetically susceptible people. Patients with CD have a distinct, "dysbiotic" gut microbiome profile, compared to healthy people, characterized by lower gut bacterial α diversity, and perhaps lower relative abundance of *Faecalibacterium prausnitzii* and increased abundance of *Escherichia coli*^{[5][6]}. The microbial composition differences which have been observed between patients with CD and UC, potentially suggest that the observed microbial signature is at least partially disease-specific^[7]. So far, there is inconclusive and contradictory evidence on whether changes in disease activity precede or follow shifts in the gut microbiome^{[5][8][9][10]}.

Several epidemiological studies suggest that a Mediterranean-type dietary pattern, comprising mainly fiber-rich sources, such as fruit and vegetables, and ω -3 fatty acid-rich food sources, is associated with reduced risk of IBD development. Conversely, a Western-style diet, consisting mainly of processed food, food additives, red meat and animal fat has been associated with increased risk of IBD onset^{[11][12][13][14]}. However, recent cohort studies have challenged these associations, thus highlighting that epidemiological evidence, surrounding pre-illness dietary intake, and the onset of IBD, is inconclusive^{[15][16]}.

An extensive literature search was undertaken on PubMed (inception to May 2020), including Medical Subject Heading terms ("inflammatory bowel disease" OR IBD OR Crohn OR colitis) AND (diet OR diet* OR nutrition OR nutr* OR food OR "enteral nutrition" OR polymeric OR elemental). 18,924 records were identified. Eligible studies included intervention and cohort studies investigating the role of diet for the maintenance of clinical remission in both adult and pediatric IBD populations in remission. Animal, in vitro and studies not in English were excluded. We also excluded studies assessing

dietary strategies for the induction of remission or perioperative nutritional support, single-nutrient supplement studies, and observational studies associating pre-illness diet with the onset of IBD. After full-text review of 226 articles, 39 studies fulfilled the eligibility criteria. In addition, five studies were identified after cross-checking reference lists from the included papers, subsequently resulting in a final inclusion of 44 studies. Comprehensive evidence tables presenting the included studies and relevant information are displayed in Supplementary file 1.

We first present studies examining the efficacy of food reintroduction protocols in patients with CD, after induction of remission using nutritional therapies. Subsequently, we focus on studies employing enteral nutrition as a maintenance regime in patients with CD, and on studies using ordinary food-based diets for maintenance of clinical remission in both CD and UC. Finally, we present the current evidence on prospective, observational studies exploring the associations with dietary components and risk of relapse in CD and UC.

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