Inflammatory Bowel Disease and Diet

Subjects: Nutrition & Dietetics
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Inflammatory bowel diseases (IBD) are chronic relapsing diseases of unknown origin affecting the gastrointestinal tract. Diet is one of the key factors.

Keywords: IBD ; nutrition ; micronutrients

1. Introduction

Diet is one of the key factors in their pathogenesis and outcome, since it could have a pro-inflammatory effect [1]. Notably, the incidence of IBD worldwide has significantly increased in the last decades [2][3], and it could be related to differences in lifestyle, including the adoption of a western diet, characterized by high amounts of proteins and saturated fats, in concomitance with low amounts of vegetables, fibers, and fruits [4].

Patients with IBD are particularly aware of the dietary influence on their disease, since approximately 70% of them think that diet could influence their condition [5], 60% consider diet to play a major role in inducing a relapse [6], and 16% are convinced that diet could initiate the disease [7]. Interestingly, in order to modify their dietary habits, patients frequently tend to avoid certain foods rather than increasing the intake of dietary components with presumably more beneficial properties [8].

Several dietary factors have been suggested to have a potential causative role in IBD [9]. On the other hand, diet components may have therapeutic implications, being able to correct nutritional deficiencies as well as to exert anti-inflammatory properties [10].

However, although in recent years, clinical and experimental research significantly increased the therapeutic armamentarium [11], few data are currently available for dietary suggestions. Some guidelines included specific formula diets as induction or adjunctive therapy for Crohn's disease (CD), while there is no specific recommendation for ulcerative colitis (UC) [12].

2. Nutrition in IBD Pathogenesis

IBD are multifactorial diseases in which genetic predisposition, altered immune system, dysbiosis, and environmental factors contribute to disease onset and recurrence [13].

In the last decades, the incidence of IBD in developing countries, but not in the Western world, increased significantly: Since genetic changes manifest over large time frames, external factors have been called into question [3]. Migrants from low- to high-prevalence regions tend to acquire a "high-prevalence" pattern of IBD onset in two generations [14]. The adoption of a low-fiber diet, rich in saturated fats, refined sugars, processed foods, associated with a diet-induced gut dysbiotic profile, appears to play a major role in the link between environment and inflammation [4][15].

2.1. Fat and IBD

2.1.1. Saturated Fats

Saturated fats are found mainly in animal products, such as meat and dairy products.

In-vivo studies in animal models found that a diet rich in high saturated fats promotes chronic inflammation [16], although the mechanism is still unknown. One explanation is that the amino acid taurine, present in saturated fats, linked to bile acids, seems to increase substrate availability for sulfur-reducing bacteria like *Bilophila Wadsworthia*, highly prevalent in the dysbiotic microbiota of IBD patients. Furthermore, Muhomah et al. [17] found that saturated fats are able to reduce the level of secretory immunoglobulin (sIg) A, altering the immune response to intestinal microbiota.

In addition to the risk of developing IBD, a diet rich in saturated fatty acids seems to increase the relapse risk, particularly in UC [18].

2.1.2. Polyunsaturated Fats (Omega-3)

Omega-3 fats, contained in olive oil, are powerful antioxidants and are associated with a lower risk of IBD, both in UC [19] [20], as well as CD: Children that consume a diet rich in omega-3 fats are at lower risk of CD development [21].

2.2. Red Meat and IBD

The consumption of red meat, due to its high content of saturated fat and cooking method, has been linked to an higher risk of colon cancer and inflammation [22]. Red meat is metabolized by intestinal bacteria with production of branched-chain amino acids and toxic elements like hydrogen sulfide, nitrous compounds, amines, and ammonia that induce DNA damage of eucaryotic cells and promote colon inflammation in murine models [23][24]. Notably, large epidemiological data confirmed the association between high consumption of red meat and risk of IBD development, in particular UC [25], where it was found to affect also the relapse risk [26].

2.3. Sugars and IBD

Sugars are part of everyone's diet. The modern diets are rich in sugar; chocolate, cookies, cakes, ice creams, fruit punches, energy drinks, soft drinks, iced tea, and lemonade contribute to the "pandemic" of obesity, diabetes, and steatosis that plagues the western world [27]. Sucrose, a disaccharide composed of monosaccharides fructose and glucose, is the most common sugar found in processed foods. Many studies have linked high sugar intake with IBD incidence [28][29][30][31].

The pathogenic mechanism that links high sugar intake with the onset of IBD is not fully elucidated. A possible explanation is a reduction of intestinal mucus [32]. A sugar-rich diet favors the increase of *Akkermansia muciniphila*, a mucolytic bacterium. The mucus layer separates luminal bacteria from intestinal epithelium: A thinner mucus layer allows bacteria to come in contact with the epithelial cells, eliciting an inflammatory response. In addition, this type of diet increases the percentage of pro-inflammatory *Sutterellaceae* and *Marinilabiliaceae*, which induce bowel inflammation [33], and reduce bacteria with anti-inflammatory properties like *Lachnospiraceae* and *Lactobacillaceae*, able to produce the short-chain fatty acid (SCFA) butyrate, the main anergy source of enterocytes [34].

2.4. Fiber and IBD

In contrast to eastern and African diets, the western diet is low in fiber. Butyrate-producing bacteria, like those belonging to Bacteroidetes and Firmicutes phylum, exert their anti-inflammatory activity metabolizing dietary fibers: A low-fiber diet leads to reduced production of butyrate, which acts as a negative regulator of pro-inflammatory pathways and enhances the intestinal barrier function [35]; this, in turn, increased the risk of IBD onset [36]. When substrate is scarce, intestinal bacteria use the intestinal mucus as a nutrient, which leads to inflammation through close contact between bacteria and the epithelial layer [37]. Long-term intake of fibers from fruit has been shown to be protective against the development of CD, but not of UC [38][39][40][41][42].

The benefit of fibers in IBD remission is uncertain. Brotherton et al. [43] found that a low fiber consumption in CD during remission is associated with a higher risk of clinical relapse, but in the case of stricturing CD, the consumption of dietary fibers could precipitate obstruction.

2.5. Nuts and IBD

A diet rich in nuts and dried fruits, due to their high content of omega-3 fatty acids, fibers, and antioxidants, has been shown to decrease the cardiometabolic and inflammatory risk; the beneficial effects on health include reduced risk of cancer, diabetes, neurological diseases [44]. A diet rich in walnuts protects mice from dextran sulfate sodium (DSS)-induced colitis [45]. The mechanism of action seems to be a decrease of macrophages activation, reduction in the production of pro-inflammatory cytokines like IL-6, IL-8, IL-1α, tumor necrosis factor (TNF), and an increase of anti-inflammatory cytokine IL-10.

2.6. Vitamin D and IBD

The health benefits of vitamin D are pleiotropic and include bone health, modulation of the immune system, antimicrobial protection, and mucosal integrity [46]. Deficiency of vitamin D is common in patients affected by IBD, in particular CD, due to malabsorption, and is worsened by reduced sunlight exposure and steroid treatment [47].

The positive effects of vitamin D are related to the improvement of epithelial barrier function [48] T-cells development, production of anti-inflammatory cytokines, and modulation on both innate and adaptive immunity [49], but even to antimicrobial peptides secretion [50]. In in vivo experiments, inadequate dietary intake of vitamin D promotes colitis development [51]. One possible explanation for this observation is that vitamin D deficiency produces intestinal dysbiosis, with a reduction of bacteria with anti-inflammatory properties (e.g., *Firmicutes*) and an increase in pathobiontic bacteria (e.g., *Bacteroides* and *Proteobacteria*) [52]. Moreover, even clinical observations have frequently found a link between low levels of vitamin D and a more aggressive course of IBD [53][54][55].

2.7. Emulsifiers and IBD

The western diet contains large amounts of emulsifiers, widely used in processed food to improve food appearance, texture, and palatability due to their intrinsic properties. Emulsifiers affect the gut microbiota, disrupt the mucosal barrier, and promote inflammation; in mice models, they induce metabolic syndrome, colitis, and translocation of *Escherichia coli* [56][57].

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