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Diet a	and nutrition against inflammatory bowel diseases: trick or treat(ment)?
Diet a	nd nutrition against inflammatory bowel diseases
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Abstract

Even if the relationships between nutrition and inflammatory bowel diseases (IBDs) remain underexplored, the current literature is providing, day by day, much more evidence on the effects of various diets in both prevention and treatment of such illnesses. Wrong dietary habits, together with other environmental factors such as pollution, breastfeeding, smoke and/or antibiotics, are among the theoretical pathogenetic causes of the IBDs, whose the multifactorial aetiology has been already confirmed. While some of these risk factors are potentially reversible, some others cannot be avoided, and efficient treatments become necessary to prevent IBDs' spread or recurrence. Furthermore, the drugs currently available for treatment of such diseases provide low-to-no effect against the symptoms, making the illnesses still strongly disabling.

Whether nutrition and specific diets will prove to effectively interrupt the course of the IBDs has still to be clarified and, in this sense, further research concerning the applications of such dietary interventions is still needed.

Key Words: Crohn's disease; Ulcerative colitis; Inflammatory bowel disease; Diet; Nutrition; Treatment

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Core Tip: The incidence of inflammatory bowel diseases (IBDs) is alarmingly growing worldwide, and there is still no efficient drug able to induce complete remission since IBDs spread. We read with great interest the article by de Castro *et al.* concerning the role of diet and nutrition in inflammatory bowel disease: as the authors reported, there is currently no consensus in the medical community about nutritional guidelines for adult patients with IBD, as the role of diet in the course of IBD itself is often underestimated¹. In fact, as the incidence of inflammatory bowel diseases (IBDs) is

reaching prevalence rates of 250 cases per 100,000 inhabitantsⁱ, diet and nutrition seem to gain a key role, not only in preventing the onset of the disease, but also in inducing and keeping temporary remission. Whether specific diets have potential to definitively cure the disease while this is already in progress, is still uncertain and much research is still needed to clarify the role of food towards this aspect of IBDs, including Crohn's disease (CD) and Ulcerative Colitis (UC). Moreover, even if these two diseases (which are not the only two members of IBDs) share some of the presenting symptoms, such as abdominal pain, mucosal inflammation, diarrhoea and gastrointestinal bleeding, many of the aspects of their presentation differ significantly, even in the course of the single illness. In our opinion, diet and nutrition have to be classified as pure treatments against IBDs, as it happens for steroids, azathiopirine, mesalazine or others and their administration should be indicated by nutrition specialists, with the greatest degree of customization of dosages and dietary plans.

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TO THE EDITOR

IBDs are generally multifactorial and usually characterised by exacerbated immune response and epithelial barrier disfunction; the intestinal epithelium is appointed to defend the host from bacterial and other micro-organisms' invasion and to control the passage of water and electrolytes; in the case of IBDs, the integrity of the epithelial barrier gets severely compromised, with consequent destabilization of intercellular junctions (tight and adherens junctionsⁱ).

Pharmacological treatments include anti-inflammatory drugs, such as steroids, mesalazine, biological anti-TNF- α or immunomodulators such as azathiopirineⁱⁱ, but they are usually not sufficient to keep disease remission or show low-to-no effects against temporary symptoms; moreover, the high incidence of side effects has to be considered too. Substantially, there is still no efficient drug able to induce complete remission since an IBD spreads. In this sense, the development of alternative and "safer" treatments for preventing the disease or controlling its course, has taken hold

over the last decade; diet itself, together with smoke, pollution, breastfeeding and/or antibiotics, are among the most important environmental factors predisposing to IBDs. The beneficial effect of diet on both development and duration of the remitting phases is already knowniii, even if nutritional supplements and macro-micro-nutrients should be always adapted to patients, as they have different roles in preventing or inducing remission in CD or UC. Furthermore, we would like to stress another aspect of the pathogenesis of such diseases, which is represented by intestinal dysbiosis (the altered composition of the gut microbiota), historically linked to numerous gastrointestinal diseases (including malignancies and chronic hepatits Biv) and often precipitated by the constant and increasing use of antibiotics in our society. The current literature is full of examples of how intestinal dysbiosis can potentially affect the epithelial integrity, progressively leading to the development of chronic inflammatory diseases, but the exact mechanism of such damage is still far from being fully understood and deserves some more attention.

The gut microbiota of the individuals with IBD is characterized by low microbial diversity in general^y and a higher concentration of pathobionts such as adherent/invasive E.Coli and C.difficile, Proteobacteria and Actinobacteria^{yi-yii}, even if patients with CD have greater microbiota dysbiosis than those with UC^{yiii}. Compared to the Mediterranean diet, the Western-style Diet (WSD) contains significantly higher amounts of simple refined carbohydrates, saturated fat, red meat, dairy and industrialized foods. Although the relationship between WSD and IBD has only been partially studied^{ix-x}, WSD involves the use of nutrients capable of eliciting a direct or indirect pro-inflammatory effect on the intestine through alterations in the equilibrium among immune system, microbiota and intestinal barrier.

Food-induced changes in the microbiota have not yet been fully studied, but it is known that higher intakes of fibers, while favouring the production of small chain fatty acids (SCFAs) by the microbiota, can exacerbate the symptoms in patients with IBD, especially during the acute phases. Furthermore, the excess of refined carbohydrates and dairy products and proteins has been shown to alter the gut microbiota by reducing

the abundance of bacteria such as Roseburia and E.Rectale, considered beneficial to health due to their ability to produce butyratexi-xii-xiii. However, the most compelling studies on IBDs have focused on the risk of high-saturation polyunsaturated fatty acids (PUFAs) as a consequence of high meat consumption (especially red meat).

Another possible causative factor is represented by gluten: its digestion gives rise to toxic and antigenic peptides (especially alpha-gliadin peptides), which can interfere not only with the tight junctions between enterocytes but also with enterocyte survival by affecting the whole intestinal barrier. High-fat diets, in general, can lead to higher storage of secondary bile acids, such as deoxycholic acid, which can inhibit the growth of specific bacterial phyla such as Bacteroidetes and Firmicutes Phyla, thus resulting in intestinal dysbiosis similar to that found in IBDsxiv. Also, the negative effect of non-caloric artificial sweeteners on the composition and functioning of the microbiome has been clearly highlighted by several studies, resulting in an increased risk of obesity, insulin resistance and inflammationxx-xvi.

Enteral nutrition (EN), either elemental or nonelemental is considered a plausible alternative to drugs for inducing IBD remission, and it is able to fight the nutritional gap induced by intestinal malabsorption during the acute phase of the disease. EN has been shown to have an anti-inflammatory effect in children with CDxvii, and it seems to have a significant impact in the cascade of pathogenesis, even if the underlying mechanisms of action are not fully understoodxviii-xix. Basically, although conducted on small sized samples of patients, most studies seem to suggest that IBDs-dedicated-diets should reduce the overall quantity of meat, eliminate red and processed meat, and eliminate or strongly reduce gluten and dairy products (i.e. caseins), with the only exceptions of yogurt and kefir.

According to de Castro *et al* and after a quick review of the literature dedicated to this topic and with current knowledge, we can state that it is fundamental to customize the choice of micro-macro-nutrients and supplemental nutrition for each patient; at the same time, it would be excessively superficial to consider the administration of such aids as tricks, only able to delay the spread of the IBDs or the recurrence of their acute

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