Probiotics in Inflammatory Bowel Disease

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Prebiotics are food substances that the organism does not digest and which, once they reach the colon, favor the growth of bacterial species of the microbiota considered to produce beneficial effects for the human organism. Among the main benefits are improvement in intestinal motility, both in terms of frequency and of volume; reduction in LDL cholesterol and blood triglycerides; contribution to the synthesis of folic acid; improvement in the immunological function; and, thanks to butyric acid, a reduction in the risk of malignant tumors.

Keywords: ulcerative colitis ; Crohn's disease ; inflammatory bowel disease ; efficacy ; probiotics

1. Introduction

Inflammatory bowel diseases (IBDs) are a group of auto-immune pathologies, with Crohn's disease (CD) and ulcerative colitis (UC) among the most well-known. They are both of recurrent clinical course and show a higher incidence in developed countries [1][2].

The etiology of IBDs is unknown—an inappropriate activation is produced of the immune system against the intestinal mucosa in individuals with a genetic predisposition. Environmental factors have been involved, with possible mediators including geo-localization, tobacco, rest disorders, surgical interventions or infections during childhood, and diet—the latter considered a higher risk factor in the development of such pathologies [2][3].

Treatment is focused on the accepted pathogenic mechanisms. The following have been recommended: quitting tobacco use, specific diet and nutrition, anti-inflammatories such as corticoids (temporary use), immuno-suppressors, biological therapy, and surgery [4]. In similar conditions, different types of diet approaches have been developed for IBDs, such as prebiotics/probiotics/postbiotics, to explore their efficacy as possible change agents of the existent inflammatory processes in these diseases [5]. The microbiota is reciprocally related to the human being: it provides various positive effects in the immune system, competing with harmful micro-organisms, or complementing nutrients which are necessary for the human body [6].The change in the microbiota produced by prebiotics in patients with IBDs, that is, those where low levels of *Firmicutes* and *Bifidobacteria* and a high number of bacteria which are pro-inflammatory for the organism (*Escherichia, Fusobacterium*) have been detected, could favor their remission or maintenance [6][7][8].

2. Prebiotics

Prebiotics are found in foods rich in fiber such as whole grains (wheat, oats, and barley derivatives), vegetables (onion, garlic, leek), fruits (apple, banana), and legumes (soya) [9]. Probiotics are live micro-organisms which have demonstrated a synbiotic effect with the host. Their beneficial effects include re-establishing deficient digestion (sugar intolerances), restitution of the microbiota (diarrhea caused by antibiotics), and prevention of mastitis [9]. Postbiotics are products or a fraction of the lysis of bacteria [10][11]. One of the most studied postbiotics is butyrate, the energetic base of the colonocytes that has suppressive effects on pro-inflammatory cytokines of the intestine [7].

3. Background

There are studies which proposed treating UC with foods from germinated barley, a butyrate precursor. These studies turned out to be very promising and guided research in this direction [12]. Another study proposed that the *Escherichia coli Nissle 1917* probiotic was as valid as the usual UC treatment with *Mesalazine (5-ASA)* to maintain remission. A few years later, studies conducted with the *VSL #3* probiotic (a combination of diverse probiotics) and with *Lactobacillus GG* claimed identical results [13][14]. Likewise, an Italian study found that adding butyric acid in patients with a deficient response to treatment with *Mesalazine* showed good results in maintaining remission in patients with moderate UC [15]. Finally, a compound made of fermented oats, *Lactobacillus plantarum (L. Plantarum) 299v*, barley malt, lecithin, and water (*Profermín*) was tested, which performed well for remission patients in UC [16].

The latest studies have been focusing fundamentally on the use of probiotics and postbiotics. Recent studies have noted that Crohn's disease and UC affect 1.4 million people in the United States, 2.5 million people in Europe, and millions more in the rest of the world. Besides, during the second half of the 21st century, the incidence of these diseases has risen in developed countries, reaching numbers of 6–10/100,000 inhabitants/year in Europe [9]. These figures apply to Spain, both in terms of the increasing number of cases and in the cardinal differences, and are evident in the regions of Córdoba and Seville [1].

Considering the chronicity and development of outbreaks of these diseases, and their predominant onset between childhood and the first half of life, it can be asserted that the treatment of IBDs consumes a large quantity of resources, both economic and personal, as well as for the health system (diagnoses tests, drugs, hospital stays, health personnel, etc.) and the work environment due to the length of possible sick leave [17]. As an example, the cost of caring for a patient with Crohn's disease is estimated at approximately EUR 7000 per year [17][18], 57% of which is attributable to hospital admissions, 33% to pharmaceutical expenses, and the remainder to different causes such as consultations, tests, and surgical interventions [18].

4. Objective

As a consequence of this, the following research question arose: In individuals with inflammatory bowel disease (P), is the use of probiotics (with diverse families and strains) (I) efficient for starting/maintaining the remission of these diseases (O) with respect to the use of the placebo or conventional treatment (C)?

In order to answer that question, the following objective was set out: to analyze the efficacy of using probiotics in patients with inflammatory bowel disease in the active or quiescent phase as a coadjuvant therapy at the beginning of remission or maintenance.

5. Conclusions

The use of probiotics and prebiotics appears to have greater clinical relevance in the treatment of UC than CD, being more significant in the remission of active UC than quiescent UC. In addition, the use of a mixture of probiotics appears to be superior to using a simple strain to induce UC remission.

In relation to preventing quiescent UC, more studies are needed to determine if the regulated use of probiotics can reduce relapse rates. Considering the wide array of genotypes and phenotypes of this condition, it is quite conceivable that the studies performed to date have not yet identified the specific probiotics, or the specific dosages, that may be beneficial in the various forms of this inflammatory process.

On the other hand, no evidence of clinical significance in the management of Crohn's disease has been found. The latest studies have focused on the use of probiotics and postbiotics and the regulation of microbiota. Despite this, more research that is not sponsored by the probiotic industry is needed on this regarding how the microbiota is modified in these cases and the effects on patients diagnosed with IBDs. To deepen our understanding in relation to this theme, it is necessary to unify the criteria for the duration of treatments, manage more relevant strains, and use identical criteria for clinical remission.

In conclusion, the complementary use of probiotics might be recommended in patients with UC, although homogeneous studies are still needed to assess the effectiveness of these in patients with IBDs, especially in relation to Crohn's disease. Future studies should be guided in the combined use of probiotics strains, as it appears to show greater clinical efficacy. This is how the dysbiosis of patients with IBDs would be balanced.

The implications for the clinical practice of the results of this research study suggest an advancement in the health and quality of life of patients with IBDs, as well as the promotion of advancements in the treatment of these diseases, which constitute a public health problem affecting millions of patients and that have enormous repercussions at sanitary, working, and social levels, with a great impact on the socio-sanitary costs of each country worldwide.

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