Pharmacological Reports 68 (2016) 816–826

Contents lists available at ScienceDirect

Pharmacological Reports

journal homepage: www.elsevier.com/locate/pharep

Review article

Food, nutrients and nutraceuticals affecting the course of inflammatory bowel disease

José Antonio Uranga [a,b,c], Visitación López-Miranda [b,c,d,e], Felipe Lombó [f], Raquel Abalo [b,c,d,e,*]

[a] Área de Histología y Anatomía Patológica, Depto. de Ciencias Básicas de la Salud, Facultad de Ciencias de la Salud, Universidad Rey Juan Carlos (URJC), Madrid, Spain
[b] Unidad Asociada I+D+i al Instituto de Investigación en Ciencias de la Alimentación (CIAL) del Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain
[c] Grupo de Excelencia Investigadora URJC-Banco de Santander-Grupo Multidisciplinar de Investigación y Tratamiento del Dolor (i+DOL). Facultad de Ciencias de la Salud, Universidad Rey Juan Carlos (URJC), Madrid, Spain
[d] Área de Farmacología y Nutrición, Depto. de Ciencias Básicas de la Salud, Facultad de Ciencias de la Salud, URJC, Madrid, Spain
[e] Unidad Asociada I+D+i al Instituto de Química Médica (IQM) del CSIC, Madrid, Spain
[f] Grupo de Investigación "Biotecnología de Nutracéuticos y Compuestos Bioactivos-BIONUC", Instituto Universitario de Oncología del Principado de Asturias, Universidad de Oviedo, Oviedo, Spain

ARTICLE INFO

Article history:
Received 10 February 2016
Received in revised form 7 May 2016
Accepted 9 May 2016
Available online 3 June 2016

Keywords:
Inflammatory bowel disease
Ulcerative colitis
Crohn's disease
Nutraceuticals
Functional foods

ABSTRACT

Inflammatory bowel diseases (ulcerative colitis; Crohn's disease) are debilitating relapsing inflammatory disorders affecting the gastrointestinal tract, with deleterious effect on quality of life, and increasing incidence and prevalence. Mucosal inflammation, due to altered microbiota, increased intestinal permeability and immune system dysfunction underlies the symptoms and may be caused in susceptible individuals by different factors (or a combination of them), including dietary habits and components. In this review we describe the influence of the Western diet, obesity, and different nutraceuticals/functional foods (bioactive peptides, phytochemicals, omega 3-polyunsaturated fatty acids, vitamin D, probiotics and prebiotics) on the course of IBD, and provide some hints that could be useful for nutritional guidance. Hopefully, research will soon offer enough reliable data to slow down the spread of the disease and to make diet a cornerstone in IBD therapy.

Contents

* Corresponding author.
E-mail address: raquel.abalo@urjc.es (R. Abalo).

http://dx.doi.org/10.1016/j.pharep.2016.05.002
1734-1140/

Introduction

Inflammatory bowel diseases (IBD) are chronic relapsing inflammatory disorders of the gastrointestinal tract whose incidence and prevalence is alarmingly increasing. The two main kinds of IBD are ulcerative colitis (UC) and Crohn's disease (CD). Although differentiated by their location and behavior (Table 1), both are debilitating conditions, which also carry an increased risk of colorectal cancer (CRC) [1].

Different etiological factors may be involved in IBD development, including environmental factors, infectious diseases, ethnicity, genetic susceptibility and dietary habits. An individual's susceptibility to IBD probably depends on the interaction of all these factors [1,2]. All of them may cause intestinal microbiota modifications, increased intestinal permeability, increased uptake of harmful adjuvants and antigens, and immune system dysregulation through different mechanisms (Table 2), leading to an altered balance between pro-oxidant and anti-oxidant mediators, pro-inflammatory and anti-inflammatory environment, Th1- and Th2-mediated responses. The final result is mucosal inflammation, which is considered to be the main cause of discomfort in IBD patients [3–8]. Approved drugs for IBD treatment and other therapeutic approaches are summarized in Table 3.

IBD is more prevalent in the Northern than the Southern part of the world, particularly among Caucasian populations. The incidence of IBD is highest in westernized nations, with the highest reported incidence rates in North America, Northern Europe, the United Kingdom and Australia (Table 4) [9–11]. However, the rapid increase in IBD incidence and prevalence in recent decades, particularly in countries with previously lower morbidity rates, such as those in South-Eastern Europe, Asia and much of the developing world, strongly suggests an environmental trigger for these diseases, including westernization of lifestyle, and changes in diet [10].

Dietary components, such as omega-6 polyunsaturated fatty acids (ω6-PUFAs), long-chain saturated fatty acids, protein, and digestible carbohydrates, may contribute to IBD pathogenesis through altering intestinal microbiota, increasing intestinal permeability, and promoting inflammation. In contrast, omega-3 polyunsaturated fatty acids (ω3-PUFAs), medium chain triglycerides, bioactive food-derived peptides, and non-digestible carbohydrates seem to improve these parameters and intestinal health [5]. Other dietary components, particularly those with anti-oxidant and anti-inflammatory properties, as well as probiotics and prebiotics, with potent effects on gut microbiota, may be beneficial to improve symptoms and reduce relapses in IBD patients, and are currently the focus of intense research.

Table 1
Key differences between ulcerative colitis and Crohn's disease, the main kinds of inflammatory bowel diseases (IBD).

	Ulcerative colitis	Crohn's disease
Gut wall layer(s) affected	• Mucosa only (except in toxic megacolon)	• Transmural
Extension of the inflammatory process	• By continuity • Starting from the rectum (distal to proximal)	• Segmentally propagated (patchy) • From the oral cavity to the rectum
Characteristic symptom(s)	• Bloody diarrhea (+/− abdominal pain or fever) • Constipation during exacerbations (if only rectum affected) • Moderate weight loss	• Diarrhea • Abdominal pain • Fever • Loss of body mass • Anemization
Local complications	• Rare stenosis • Toxic megacolon • Malignization	• Stenosis • Fistulae • Abscesses • Relapse after colectomy • Perianal lesions • +/− Malignization

Table 2
Mechanisms of gut mucosa inflammation in inflammatory bowel disease (IBD).

Inflammatory mediators (local and systemic increased levels)	Inflammatory cells (local infiltration) & T-cell response
Lipid-derived mediators: - Prostaglandins (PGs) - Leukotrienes (LTs) - Endocannabinoids - Platelet activating factor (PAF) **Peptides**: - Cytokines - Interleukins (IL) - Chemokines **Amino acid derivatives**: - Histamine - Nitric oxide (NO) **Reactive oxygen species** (ROS) - Superoxide anion - Hydrogen peroxide **Enzymes**: - Matrix proteases	**Crohn's disease** Th1 response with increased production of: - Tumor necrosis factor (TNF)-α - Interferon-γ (IFN-γ) - IL-1β - IL-6 - IL-12 - IL-17 **Ulcerative colitis** Th2 response with increased production of: - IL-5 - IL-10
Reduced anti-inflammatory cytokines	Other inflammatory cells
- Transforming growth factor (TGF)-β - IL-10	- Neutrophils (early stage) - Macrophages (chronic stage)

Table 3
Treatment of inflammatory bowel disease (IBD).

Step-up approach (for mild to moderate IBD):

Step I
- **Aminosalicylates** (for flare-ups and for maintaining remission in UC, for preventing recurrence after surgery in CD; oral, topical): *sulfasalazine, mesalamine, balsalazide, olsalazine*
- **Antibiotics** (for CD if perianal disease or inflammatory mass): *metronidazole, ciprofloxacin*

Step II
- **Corticosteroids** (for acute-flare ups):
  - intravenous *methylprednisolone* or *hydrocortisone*;
  - oral *prednisone* or *budesonide* (or others);
  - topical *hydrocortisone* or *budesonide*

Step III
- **Immune-modifying agents** or **immunomodulators** (for refractory disease, for fistulas, and for maintenance of remission if aminosalicylates are not useful):
  - **Thiopurine agents**: *6-mercaptopurine, azathioprine*
  - **Anti-TNF monoclonal antibodies**: *infliximab, adalimumab, certolizumab, golimumab*
  - **Integrin antagonists**: *natalizumab; vedolizumab*
  - **Other immunosuppresants**: *cyclosporin, tacrolimus, methotrexate*

Step IV
Clinical trial agents (non-approved):
- CD: *thalidomide, IL-11*
- UC: *nicotine patch, butyrate enema, heparin*

Step-down approach (for severe, refractory disease or dependent on corticosteroids):
- **Immune-modifying agents**: *thiopurine agents*
- **Anti-TNF monoclonal antibodies**: *infliximab, adalimumab*

Other treatments:
- **Anti-diarrheal medications**: *fiber supplement (psyllium powder, methylcellulose); loperamide*
- **Pain relievers**: *acetaminophen*
- **Nutritional supplements**: *iron; vitamin B_{12}; calcium, vitamin D*
- **Probiotic agents** (with aminosalicylates)
- **Enteral or parenteral nutrition** (CD)
- **Tobacco cessation** (CD)

Abbreviations: CD, Crohn's disease; UC, ulcerative colitis; TNF, tumor necrosis factor; IL, interleukin.
Sources (accessed 4th May 2016):
- http://emedicine.medscape.com/article/179037-treatment#d10.
- http://www.mayoclinic.org/diseases-conditions/inflammatory-bowel-disease/basics/treatment/con-20034908.