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A review of the types of diets used in Crohn's disease: the support system for pharmacological treatment

Joanna Śnieżna, Wojciech Florczak, Jakub Dziewic, Karol Dzwonnik, Urszula Zelik, Gabriela Trestka, Wiktoria Domino, Kamila Stępień, Jagienka Włodyka, Sabina Adamczyk, Maria Przygoda

Joanna Śnieżna
Medical University of Lublin: Lublin, Poland
https://orcid.org/0009-0006-2713-0835
asia.sniezna@gmail.com

Wojciech Florczak
Medical University of Lublin: Lublin, Poland
https://orcid.org/0009-0006-8003-0999
florczak.wojciech99@gmail.com

Jakub Dziewic
Medical University of Lublin: Lublin, Poland
https://orcid.org/0009-0008-4338-4573
dziewicjakub@gmail.com

Karol Dzwonnik
Medical University of Lublin: Lublin, Poland
https://orcid.org/0009-0007-1366-3945
karol.dzwonnik@gmail.com

Urszula Zelik
University Teaching Hospital them F. Chopin in Rzeszów, Poland
Fryderyka Szopena 2, 35-055 Rzeszów, Poland
https://orcid.org/0009-0009-3369-7936
ulazelik@gmail.com

Gabriela Trestka
Clinical Provincial Hospital No. 2 in Rzeszów, Poland
Lwowska 60, 35-501 Rzeszów, Poland
https://orcid.org/0009-0009-9504-8923
gabixtre@gmail.com

Wiktoria Domino
Clinical Provincial Hospital No. 2 in Rzeszów, Poland
Lwowska 60, 35-501 Rzeszów, Poland
https://orcid.org/0009-0005-0034-7463
wiktoriadomino1604@gmail.com

Kamila Stępień
Independent Public Health Care Facility of the Ministry of Internal Affairs and Administration in Kielce, Poland
Wojska Polskiego 51, 25-375 Kielce, Poland
https://orcid.org/0009-0000-3579-9308
kamila_stepien@onet.pl

Jagienka Włodyka
University Teaching Hospital them F. Chopin in Rzeszów, Poland
Fryderyka Szopena 2, 35-055 Rzeszów, Poland
https://orcid.org/0009-0000-7243-7023
jagienka.wlodyka@gmail.com

Sabina Adamczyk
Independent Public Healthcare Facility of the Ministry of Internal Affairs and Administration in Opole, Poland
https://orcid.org/0009-0003-9671-6619
adamczyksabinaa@gmail.com

Maria Przygoda
Specialist Hospital named after Stefan Żeromski, Independent Public Healthcare Facility (SP ZOZ), in Kraków
https://orcid.org/0000-0002-6409-7265
maria.przygoda@interia.pl

Abstract
Crohn's disease (CD) is a chronic and progressive disease, that requires a multilateral approach. Its incidence is rising globally, particularly in industrializing regions, correlating with increased consumption of ultra-processed foods. Besides pharmacological and surgical treatment, the diet component plays a crucial role in alleviating symptoms of the disease and preventing its progression. This review highlights the evolving role of dietary interventions as supportive treatments in CD management, complementing pharmacological and surgical approaches. This review represents the analysis of some of the most commonly used diets: the low FODMAP diet, Specific Carbohydrate Diet (SCD), Mediterranean diet, Crohn's Disease Exclusion Diet (CDED), and exclusive enteral nutrition (EEN) in Crohn's disease based on studies from PubMed's articles published within the last five years. The aim of this systematic review is to highlight the importance of dietary element in the management of CD and a wide range of new methods of supporting treatment. Dietary interventions provide significant potential to modulate inflammation, support remission, and improve the quality of life in CD patients. Further research in personalized dietary protocols will help incorporate into multidisciplinary approaches for the treatment.

Keywords: Crohn's disease, diet, inflammatory bowel disease, exclusive enteral nutrition, Crohn's disease exclusion diet, low FODMAP diet, Mediterranean diet, low-lactose diet, high-fiber diet

Introduction

Crohn's disease (CD) is an inflammatory bowel disease (IBD), which is characterized by chronic course and remissions periods. Frequency of Crohn's disease is the highest in western countries but its rate is increasing in newly industrialized regions of Asia and Middle East [1, 2]. Rising number of CD is also noticeable in correlation with prevalence and consumption of ultra-processed foods. North America and Europe demonstrate both the highest consumption of processed meats and soft drinks, correlating with increased risks of Crohn's disease and other forms of inflammatory bowel disease. Crohn's disease most commonly develops between the ages of 20 and 30 years, which represents the peak age of onset.

CD can also occur at younger or older ages, including in children and older adults. Age over 60 is consider a second smaller peak of CD occurrence [3]

Crohn's disease develops due to an immune response to luminal bacterial antigens, leading to chronic inflammation. Immune cell infiltration, including CD4+ T-cells, CD8+ T-cells, B-cells, CD14+ monocytes, and natural killer cells, contributes to tissue damage and mucosal inflammation.. Certain genetic factors, such as Muc2 gene variants leading to reduced intestinal mucus production, and FUT2 gene mutations affecting bacterial adhesion, have been linked to increased predispositions to CD [4]. The inflammatory response is further driven by interactions between immune cells and adhesion molecules, which lead to the production of pro-inflammatory cytokines, such as TNF-α, IL-12, and IFN-γ. IL-34 is another key cytokine, increasing in areas of active inflammation and promoting further TNF-α and IL-6 release [4, 5]. This immune activation is also caused by Th1 and Th17 cells, which trigger the inflammatory response seen in CD, as opposed to the Th2 response observed in ulcerative colitis. The dysregulated immune response in CD patients is also characterized by T-cell stimulation with excessive cytokine production leading to sustained mucosal damage. [6]

The intestinal microbiota plays huge component in Crohn's disease pathophysiology. Studies show that CD patients have increased level of Bacteroidetes and *Escherichia coli* presance and lower level of *Firmicutes* and *Faecalibacterium prausnitzii* compared to the microbiome of healthy population [7].

Crohn's disease can occupies the intestinal track in every region, most commonly the ileum and colon. The most frequent manifestation of the disease include abdominal pain, diarrhoea and weight loss [8] This immune imbalance leads to chronic tissue damage, including intestinal strictures, fistulas and intra-abdominal ab [4]. Iron connected anemia, vitamin D deficiency and high levels of inflammatory markers are also signs of CD but the most sensitive screening test is fecal calprotectin. Additionally Crohn's disease is characterize by variety of extra-intestinal manifestations, such as anal skin tags, peripheral arthritis, erythema nodosum and pyoderma gangrenous [9].

Current Crohn's disease treatment focuses on suppressing the overactive intestinal immune system and involves two phases: induction and maintenance. During induction, higher doses of steroid-sparing medications are used to achieve remission quickly, often alongside steroids like budesonide in mild to moderate cases due to its reduced systemic effects. Maintenance therapy relies on lower doses of immune modulators or biologics to sustain remission and prevent flares, as steroids are unsuitable for long-term use due the complications [10]. At least 50% of CD patients will require one or more surgeries over the course of their lives, often due to complications like intestinal strictures, fistulas, or abscesses. Additionally, CD is commonly associated with malnutrition, resulting from the disease's impact on nutrient absorption and limited food intake. Some patients may also require a stoma [11].

Nowadays, a multidisciplinary approach to the treatment of Crohn's disease offers better therapeutic outcomes and significantly improves the quality of life for patients. This review is focused on "the support system" for pharmacology and surgery - diets used in CD. Main subjects of this review include a low FODMAP diet, Specific Carbohydrate Diet, Mediterranean diet, Crohn's disease exclusion diet and exclusive enteral nutrition.

Methods

This article is based on search on PubMed for clinical trials, meta-analyses, systematic reviews and observational studies. The selection criteria focused on articles published within the past five years to ensure the inclusion of up-to-date findings. Additionally, studies reporting on the efficacy, safety, and practical implications of dietary interventions in Crohn's disease were prioritized. The review incorporated both pediatric and adult populations to evaluate the broad applicability of the diets discussed. A multidisciplinary perspective was applied, integrating insights from gastroenterology, nutrition science, and immunology. The aim was to analyse the therapeutic potential of dietary interventions as adjuncts to pharmacological treatments and to evaluate their role in improving patient quality of life.

Discussion and Analysis

Significance of diet used in management of Crohn's disease is increasing over the past view years. This article is analysing and compering some of the most popular nutritional approaches in CD treatment. Individual diets have specific impact. CDED (Crohn's Disease Exclusion Diet) is characterized by a stepwise food reintroduction strategy aimed at modulating the gut microbiota and reducing dietary triggers. Exclusive Enteral Nutrition (EEN) involves the use of nutritionally complete liquid formulas as the sole source of nutrition to induce remission in pediatric Crohn's disease patients. Specific Carbohydrate Diet (SCD) eliminates grains, lactose, sucrose, and most processed foods, focusing on monosaccharides to reduce gut inflammation and bacterial dysbiosis. Mediterranean Diet emphasizes whole grains, vegetables, fruits, nuts, and olive oil, promoting anti-inflammatory effects through a high intake of fiber and antioxidants. Low FODMAP Diet limits fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, aiming to manage symptoms by reducing fermentable substrates in the gut [14].

Exclusive enteral nutrition (EEN) is the safe and least invasive first-line treatment for children with Crohn's disease, being provided via a powdered or liquid formulation containing necessary macro- and micronutrients. Research indicates that the EEN can induce mucosal healing in almost 80% of cases and will also provide enough nutrition for that general growth and development. Implementation of EEN in adult's treatment is wildly discuss and controversial long-term adherence due to flavor monotony and lack of social alignment [15]. EEN is a liquid diet providing complete nutrition but is excluding regular table foods for a specified period. The main formula types used in EEN is elemental, semielemental, and polymeric. Daily intake is based on individual energy requirements and is administered orally or via a nasogastric tube when necessary. The duration of the therapy is around 6-8 weeks. This has been reported to go up to anywhere between 4 and 12 weeks. After such duration, food is slowly resumed to establish a normal diet [16]. Only minimum and temporary side effects are reported and the most frequently describe are nausea, diarrhoea, constipation, abdominal pain, distension and taste fatigue [17].

Second diet we discuss is The Crohn's Disease Exclusion Diet (CDED) which is a whole-food diet structured to limit dietary components that could trigger inflammation by disrupting the gut microbiota, immune system, and intestinal barrier function [12]. This diet was found in 2014 by Professor Arie Levine and his colleagues [13].

The CDED is a structured diet divided into three phases. Phase 1, which is about 0-6 weeks, is highly restrictive, eliminating all potential trigger ingredients while prioritizing high-quality protein and ingredients that support the microbiome. In Phase 2 (weeks 6–12), the diet becomes less restrictive, allowing the gradual reintroduction of previously excluded foods. From week 13 onward, phase 3 focuses on maintenance, continuing for at least 9 months until a personalized dietary plan can be adopted. This phased strategy enhances patient adherence, making the CDED more practical and promoting sustained long-term compliance [12]. Beneficial effect on remission of CD's patients is shown in 2023' systematic review "Effects of Crohn's disease exclusion diet on remission: a systematic review" examined the influence of CDED on achieving remission in CD. Every study included in the review recognized the beneficial effects of CDED, reporting a reduction in disease activity and improvements in CRP and FCP levels [13].

The Specific Carbohydrate Diet (SCD) is one of the most popular of all therapeutic diets in Crohn's disease. This diet has an extremely clear specification of what it allows versus what it forbids with regard to food. Fresh fruits and vegetables are included, with some exceptions pertaining to starchier ones, such as potatoes and yams. Acceptable legumes are lentils and some split peas, whereas certain categories of beans, for example chickpeas and soybeans, have to be avoided. The SCD prohibits all grains. Saccharin and honey are the permitted sweeteners. Canned fruits and vegetables are excluded due to possibility of added sugars and starches. Fresh meats are not specified as they are allowed, while all other meats, including processed, canned, and in most cases smoked meat, are limited as a result of sugars and starches being present in their additives. Milk is excluded on account of lactose but some very low-lactose cheese and homemade yogurt allowed to ferment for 24 hours are acceptable [18].

The Mediterranean diet concentrates on high fruit, vegetable, whole grain, legume, nut, and olive oil intake, with certain amounts of fish and poultry and minimal intake of red meat and processed foods. Study of patients with Crohn's Disease comparing the Mediterranean diet with the Specific Carbohydrate Diet indicated that both improvements in symptoms occurred for patients on either diet [18]. The Mediterranean diet is associated with reduced systemic inflammation and improved gut microbiota composition, factors that may influence the course of Crohn's disease. While evidence specific to Crohn's disease remains limited, its anti-inflammatory and microbiome-modulating effects suggest potential benefits for disease management [21].

Compelling evidence indicates that certain FODMAP carbohydrates produce abdominal symptoms. Acute challenge tests using lactose, fructose, fructo-oligosaccharides (FOS), or sorbitol elicit symptoms such as bloating, abdominal pain, nausea, and altered bowel habits, such as diarrhoea and/or constipation from numerous subjects, especially in people with IBS [19]. Like the diet types that were mentioned earlier, low-FODMAP diet lacks sufficient evidence to confirm its effectiveness in treating IBD. Some reports point toward some possible good results in relieving IBS-like symptoms in patients with IBD [20].

Conclusion

Crohn's disease (CD) is a complex inflammatory condition influenced by genetic, immunological, and environmental factors, including dietary habits. The rising global incidence of CD, especially in the much industrialized regions, has driven the need for effective intervention and comprehensive managing strategies for the disease. Although the pharmacological and surgical approaches dominate the treatment modalities, dietary modifications are now considered as vital supportive therapies. New paths for Crohn's disease opened thanks to more holistic approach in treatment. Many different studies show promising data on the implementation of diet in patients with CD. Such evidence indicates that specific dietary approaches can influence disease progression, improve symptom control, and enhance the quality of life of patients.The low FODMAP diet, Specific Carbohydrate Diet, Mediterranean diet, Crohn's Disease Exclusion Diet, and exclusive enteral nutrition each offer unique benefits adjusted to the diverse needs of CD patients. The diet should be carefully match and adjust to the patient's needs and patient's conditions. A crucial factor in selecting a diet is the patient's age, as there are differences in recommended diets for pediatric and adult patients. Despite these promising observations, further investigations will reveal standardized protocols regarding dietary interventions, as well as their long-term effectiveness in the management of CD. A multidisciplinary approach, integrating dietetics with medical and surgical care would further help in optimizing outcomes.

Disclosure

Author's Contribution:

Conceptualization: JŚ,WF; methodology: JŚ, UZ, JD; software: WF, UZ; check: GT, WF and MP; formal analysis: WF, SA, JD; investigation: JŚ, KS; resources: GT, KD, JW, WF; data curation: JŚ, KS, WF, JW; writing - rough preparation: JŚ, WF, JD; writing - review and editing: JŚ, UZ, KD, MP; visualization: WD, UZ, GT; supervision: JŚ, WF; project administration: JŚ, SA, UZ, KD, WD, JW;

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