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Effects of the Crohn's Disease Exclusion Diet on the Clinical Course of Inflammatory Bowel Diseases in Pediatric and Adult Populations

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Abstract

Introduction:

Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract and a major subtype of inflammatory bowel disease (IBD). Its multifactorial etiology involves genetic, immunological, and environmental factors, among which diet plays a key role in modulating gut microbiota and intestinal barrier function.

Aim of the study:

This narrative review aims to evaluate the role of dietary interventions in Crohn's disease, with particular emphasis on the effectiveness of the Crohn's Disease Exclusion Diet (CDED) in inducing and maintaining remission.

Materials and methods:

A comprehensive literature review was conducted using Google Scholar and scientific databases. The analysis included randomized controlled trials, prospective and retrospective studies, and experimental research focusing on the impact of dietary interventions, particularly CDED, on clinical outcomes in patients with Crohn's disease.

Results:

The reviewed studies indicate that CDED, especially when combined with partial enteral nutrition (PEN), is effective in inducing clinical remission and reducing inflammatory markers. Compared to exclusive enteral nutrition (EEN), CDED demonstrates better patient adherence and tolerability. Additionally, the diet positively influences gut microbiota composition and intestinal barrier integrity.

Conclusions:

CDED appears to be a promising dietary strategy in the management of Crohn's disease. However, despite encouraging results, further large-scale and long-term studies are required to confirm its effectiveness and establish its role in standard treatment guidelines.

Keywords:

Crohn's disease, inflammatory bowel disease, CDED, diet therapy, remission, gut microbiota

1. Clinical Picture and Treatment of Crohn's Disease

1.1. Definition and Epidemiology

Crohn's disease (CD) is a chronic, relapsing inflammatory disease of the gastrointestinal tract with a heterogeneous clinical course. It can affect any segment of the gastrointestinal tract – from the oral cavity to the anus – but most commonly involves the distal ileum and colon (Torres et al., 2017). The incidence of CD shows an upward trend worldwide, particularly in industrialized countries, reaching up to 20–25 cases per 100,000 persons annually in Western Europe and North America (Ng et al., 2018). The etiology of CD is multifactorial and involves the interaction of genetic factors (including NOD2/CARD15 gene mutations), immunological, environmental, and gut microbiota composition factors.

1.2. Clinical Presentation

Typical symptoms of CD include: chronic or recurrent abdominal pain (particularly in the right lower quadrant), diarrhea – often without blood, weight loss, fatigue, and fever (Torres et al., 2017). The disease course can take an inflammatory, stricturing, or penetrating character, reflecting the transmural nature of the inflammatory process affecting the entire thickness of the intestinal wall. Intestinal complications, such as fistulas, abscesses, and strictures leading to obstruction, constitute a significant clinical problem, frequently requiring surgical intervention (Rieder et al., 2016).

In 25–40% of CD patients, extraintestinal manifestations (EIM) also occur, affecting the musculoskeletal system (peripheral arthropathy, axial involvement), skin (erythema nodosum, pyoderma gangrenosum), eyes (uveitis, episcleritis), and bile ducts – including primary sclerosing cholangitis (PSC) (Vavricka et al., 2015).

In children and adolescents, growth disturbances and delayed sexual maturation are frequent accompanying problems. Disease activity is assessed using standardized tools: in adults – the Crohn’s Disease Activity Index (CDAI) or Harvey–Bradshaw Index (HBI), and in children – the Pediatric Crohn’s Disease Activity Index (PCDAI). The Montreal classification (for adults) and Paris classification (for children) enable stratification of patients by disease location and phenotype.

In the context of the impact of diet on the clinical course of CD, it should be emphasized that certain dietary components can directly induce or exacerbate symptoms. Highly processed products, rich in emulsifiers, saturated fats, and rapidly fermentable oligosaccharides (FODMAPs) correlate with worsening of abdominal pain, diarrhea, and bloating (Lewis & Abreu, 2017). Particularly clinically significant is protein-calorie malnutrition, occurring in 65–75% of hospitalized CD patients, leading to sarcopenia, impaired immune response, and worse surgical outcomes (Levine et al., 2019). In children, deficiencies of macro- and micronutrients directly translate into growth disturbances recorded in the PCDAI. Dietary interventions therefore constitute not only a supportive element for pharmacotherapy, but also an independent tool for modifying the natural disease course.

1.3. Pharmacological Treatment

The goal of CD treatment is to induce and maintain clinical remission and – in the long term – prevent complications, minimize corticosteroid exposure, and improve quality of life (Torres et al., 2017). Modern pharmacological management is based on a step-up or top-down approach, tailored to the patient's risk profile.

Corticosteroids (prednisone, budesonide) are used exclusively for remission induction, due to lack of efficacy in maintenance therapy and numerous adverse effects with long-term use (Torres et al., 2017). Thiopurines – azathioprine and 6-mercaptopurine – as well as methotrexate are immunosuppressive drugs used in remission maintenance; due to delayed onset of action (approximately 3–6 months) they are often combined with corticosteroids in the early phase of treatment.

A breakthrough in CD treatment came with the introduction of biological agents. TNF-α inhibitors – infliximab and adalimumab – remain the best-studied first-line biological agents, demonstrating efficacy in both induction and maintenance of remission (Colombel et al., 2010). Anti-integrins (vedolizumab) act selectively on the intestinal mucosa, showing a favorable systemic safety profile. Ustekinumab – an IL-12/23 inhibitor – is used in both induction and maintenance of remission, particularly in patients previously treated with anti-TNF therapy (Feagan et al., 2016). The newest class comprises small molecules – JAK kinase inhibitors (upadacitinib), which have received approval for the treatment of moderate-to-severe CD.

1.4. Surgical Treatment and Nutritional Therapy

A separate group of interventions consists of nutritional methods, which – particularly in children – occupy a high position in the therapeutic algorithm. According to ECCO/ESPGHAN guidelines, EEN is recommended as the first line of remission induction in luminal CD in children, demonstrating remission induction efficacy comparable to corticosteroids while simultaneously having a more favorable impact on growth and mucosal healing (Torres et al., 2017).

The CDED diet, discussed in detail in subsequent chapters, represents a promising therapeutic alternative to EEN in both pediatric and adult patients with mild to moderately active CD. Despite advances in pharmacotherapy, approximately 50% of CD patients require at least one surgical intervention within the first 10 years of disease (Rieder et al., 2016). Indications include: intestinal obstruction, fistulas refractory to conservative treatment, abscesses unresponsive to drainage, and lack of response to pharmacological therapy. It should be emphasized that surgical resection is not a curative treatment – the disease recurs in more than half of operated patients within 5 years of the procedure. Surgical treatment thus constitutes a complementary element to pharmacotherapy and dietary interventions within a comprehensive therapeutic strategy.

2. Role of Diet in the Pathogenesis of Crohn's Disease

The Western diet, characterized by high consumption of saturated fats, simple sugars, and highly processed foods, is recognized as a significant risk factor for the development of Crohn's disease (Hou et al., 2011; Khalili et al., 2018).

Studies have shown that food additives, such as emulsifiers, can disrupt the intestinal mucus layer, increase bacterial adhesion to the epithelium, and induce inflammation (Lewis & Abreu, 2017). The gut microbiota plays a key role in maintaining organismal homeostasis. In CD patients, decreased microbial diversity and a reduction in the number of anti-inflammatory bacteria are observed (Sokol et al., 2017).

Diet directly influences microbiota composition by providing substrates for bacteria and modulating the intestinal environment (Khalili et al., 2018). Exclusive enteral nutrition (EEN) is recognized as an effective method of remission induction, particularly in children (Lewis & Abreu, 2017). Despite high efficacy, its use is limited by low patient acceptance and difficulties in long-term adherence.

From a clinical perspective, EEN demonstrates particular benefits in children with CD complicated by growth disturbances – one of the significant extraintestinal complications described in section 1.2. Through improvement of nutritional status, reduction of pro-inflammatory cytokine levels (IL-6, TNF-α), and normalization of the IGF-1 axis, EEN can partially restore normal growth rate (Torres et al., 2017). In clinical studies, EEN induces clinical remission assessed by the PCDAI (Pediatric Crohn's Disease Activity Index) in 74–83% of children after 6–8 weeks of treatment, with simultaneous achievement of mucosal healing in approximately 75–80% of patients (Lewis & Abreu, 2017).

In adults, EEN efficacy is comparable (remission in 60–79%), however therapy adherence is only 40–60%, which significantly limits its practical application in this age group. Among the diets used in CD, the Specific Carbohydrate Diet (SCD), low-FODMAP diet, Mediterranean diet, and CDED stand out. Among these, CDED has gained particular attention due to its efficacy and better tolerability (Niseteo et al., 2022).

The SCD (Specific Carbohydrate Diet) eliminates complex polysaccharides and disaccharides, limiting the substrate for fermentation by pathogenic microbiota. It may alleviate clinical symptoms of CD, however data from randomized controlled trials confirming its impact on mucosal healing are lacking (Khalili et al., 2018).

The low-FODMAP diet (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) demonstrates efficacy primarily in reducing functional symptoms – such as abdominal pain and bloating – which in some CD patients occur independently of inflammatory activity. The Mediterranean diet, rich in omega-3 fatty acids, fiber, and polyphenols, shows anti-inflammatory effects and may support gut microbiota diversity, though its role in CD requires further research (Zhang et al., 2024).

Against the background of the diets mentioned, CDED stands out as the only diet developed with specific pathophysiological mechanisms of CD in mind – reducing exposure to certain dietary antigens that exacerbate inflammation and intestinal dysbiosis. The CDED was developed as an elimination strategy aimed at reducing pro-inflammatory factors and improving intestinal barrier function and microbiota (Levine et al., 2019).

CDED excludes products with documented impact on gut microbiota and the mucosal barrier: wheat, animal dairy, fatty meat, highly processed products, and certain emulsifiers. Instead, specific proteins (chicken breast, eggs), vegetables, fruits, and olive oil are recommended – products with prebiotic and anti-inflammatory properties. The diet proceeds in three phases corresponding to clinical stages: Phase 1 (weeks 1–6) constitutes

the most intensive elimination phase – 50% of calories come from specific solid foods, and 50% from partial enteral nutrition (PEN), which allows maintaining adequate nutrient intake while simultaneously modifying the intestinal environment. Phase 2 (weeks 7–12) reduces the PEN contribution to 25%, gradually increasing the variety of solid diet. Phase 3 (from week 13) constitutes the remission maintenance phase, with further expansion of the permitted product range while maintaining the main elimination principles (Levine et al., 2019).

CDED influences the composition of the gut microbiota, increasing the proportion of beneficial bacteria and reducing the number of pro-inflammatory bacteria (Levine et al., 2019). Additionally, it improves intestinal barrier integrity and reduces inflammation, which is reflected in a decrease in inflammatory markers (Szczebułek et al., 2021).

At the microbiological level, CDED increases the representation of bacteria from the Lachnospiraceae and Ruminococcaceae families – producers of short-chain fatty acids (SCFA), including butyrate with immunomodulatory and intestinal epithelium-protective effects. Simultaneously, a reduction in the abundance of adherent-invasive Escherichia coli (AIEC) strains is observed – bacteria pathogenetically associated with CD and detected particularly frequently in patients with the NOD2/CARD15 genotype (Sokol et al., 2017). At the structural level, CDED improves the expression of tight junction proteins (occludin, claudin-1), which directly translates into improved intestinal barrier integrity and reduced translocation of bacterial antigens to the lamina propria of the mucosa – a key mechanism sustaining transmural inflammation (Levine et al., 2019). At the immunological level, the diet leads to a reduction in IL-6, IL-1β, and TNF-α levels and normalization of Th1/Th17 axis activity, which clinically correlates with a decrease in CDAI, normalization of CRP, and reduction in fecal calprotectin levels – markers used to assess disease activity and monitor treatment response (Szczebułek et al., 2021).

Clinical studies have shown that CDED, particularly in combination with partial enteral nutrition (PEN), can lead to clinical remission in a significant proportion of patients (Levine et al., 2019; Szczebułek et al., 2021).

The key evidence for CDED efficacy is the randomized controlled trial by Levine et al. (2019), conducted in a pediatric population (n=74, age 4–18 years) with active CD (PCDAI ≥10). Clinical remission (PCDAI <10) at week 6 was achieved in 75.6% of patients in the CDED+PEN group versus 45.1% in the EEN group (p=0.01). Also clinically significant was the durability of remission: at week 12, this effect was maintained in 75.6%

vs 56.9% of patients in the CDED+PEN and EEN groups respectively. CRP normalization (<0.5 mg/dL) was achieved in 66% of patients in the CDED+PEN group compared to 44% in the EEN group. These results indicate that CDED is not only effective but also demonstrates superior clinical outcomes for children compared to the previously used EEN.

In the adult population, the study by Szczebułek et al. (2021) demonstrated that CDED induces clinical remission (CDAI <150) in 76.9% of patients with moderately active CD. Clinical response (CDAI reduction ≥70 points) was achieved in 80.8% of participants. Furthermore, in patients achieving remission, a statistically significant reduction in fecal calprotectin was observed – suggesting decreased mucosal inflammatory activity, which has significant clinical importance as a marker of treatment response. These results indicate that CDED is not merely a symptomatic diet, but demonstrates a real impact on biological markers of CD activity in both children (PCDAI, CRP) and adults (CDAI, calprotectin).

Chronic disease such as CD can limit physical activity through fatigue, malnutrition, and inflammation. An appropriate diet can improve physical capacity and support recovery (Zhang et al., 2024).

From a clinical perspective, CDED carries significant practical implications for different groups of CD patients. In the pediatric population, CDED offers the opportunity to induce remission without the need for corticosteroids – drugs with documented negative effects on growth and bone density. The possibility of avoiding or delaying steroid therapy is particularly valuable in children with the inflammatory phenotype of CD. At the same time, by supporting growth and correcting protein-calorie deficiencies, CDED addresses one of the key extraintestinal complications of CD – growth disturbances occurring in 15–40% of children with this disease (Torres et al., 2017).

In adult patients, CDED has potential as a bridge method before initiating or optimizing pharmacotherapy, as well as an element of remission maintenance. The improvement of nutritional status resulting from CDED use can have a direct impact on the efficacy of concurrently administered biological agents – malnutrition is an independent risk factor for poorer response to biologics and higher frequency of postoperative complications (Rieder et al., 2016). Improvement of body composition, reduction of tissue inflammation, and rebuilding of energy reserves directly translate into higher exercise tolerance and quality of life for patients (Zhang et al., 2024).

In clinical practice, CDED should be implemented in a multidisciplinary model, involving a gastroenterologist, clinical dietitian, and – in the case of pediatric patients – a

pediatrician. Monitoring of efficacy should be based on clinical assessment (CDAI/HBI in adults, PCDAI in children) and measurements of inflammatory markers: CRP and fecal calprotectin. Standardization of monitoring protocols is necessary for comparability of results between centers and for implementing the diet in daily practice as an element of comprehensive CD treatment.

Clinical Evidence

The Levine et al. (2019) study constitutes the key clinical evidence confirming the efficacy of the CDED in the treatment of Crohn's disease in children. In a randomized controlled trial involving 74 children with active CD, CDED combined with partial enteral nutrition (PEN) was compared with exclusive enteral nutrition (EEN). Clinical remission assessed by the PCDAI score (<10 points) at week 6 of treatment was achieved in 75.6% of patients in the CDED+PEN group versus 45.1% in the EEN group (p=0.01). Remission was maintained at week 12 in 75.6% versus 56.9% of patients, and CRP normalization (<0.5 mg/dL) occurred in 66% versus 44% of subjects. The authors conclude that CDED combined with PEN is a more effective and better-tolerated method of remission induction than EEN, thus representing a breakthrough in the dietary approach in pediatric CD.

Szczebułek et al. (2021) conducted a prospective observational study evaluating the efficacy of CDED in remission induction in adult patients with active CD. Of 26 adult participants with a mean baseline CDAI of 265 points, clinical remission (CDAI <150) was achieved in 76.9% of patients, and clinical response (CDAI reduction ≥70 points) was recorded in 80.8% of subjects after 12 weeks of dietary treatment. An important finding was the statistically significant reduction in fecal calprotectin concentration (on average from 623 to 198 μg/g), confirming a reduction in inflammation at the mucosal level. The study demonstrated that CDED is not only an effective symptomatic approach, but actually modifies the biological markers of disease activity, which extends its potential applications beyond the pediatric population.

The narrative review by Niseteo et al. (2022), dedicated to dietary interventions in inflammatory bowel disease with particular emphasis on CDED, demonstrated a significant advantage of this diet in terms of patient adherence compared to EEN (adherence approximately 80–90% vs 40–60%). Analysis of available clinical studies confirmed that

CDED achieves comparable or higher efficacy in remission induction than EEN while simultaneously demonstrating significantly better patient acceptance. The authors conclude that CDED – as the first elimination diet developed with specific pathophysiological mechanisms of CD in mind – constitutes a practical and evidence-based alternative to EEN in both pediatric and adult populations, and should be considered as the first line of dietary treatment in patients with mild to moderate CD activity.

Zhang et al. (2024), reviewing current evidence on the role of diet in inflammatory bowel disease, identified CDED as one of the best-documented dietary interventions in CD. The authors emphasize that despite the promising results of available studies, the impact of CDED on hard endpoints – such as mucosal healing, avoidance of pharmacotherapy escalation, and hospitalization and surgery rates – remains insufficiently documented. They conclude that further long-term randomized controlled trials with adequate statistical power are needed, which would allow for determining the place of CDED in standard CD treatment guidelines and enable its individualization based on disease phenotype and patient microbiota profile.

Sigall Boneh et al. (2017) conducted a multicenter cohort study evaluating the efficacy of CDED in patients with active CD who had failed biological therapy. In a study involving 34 children and adults with biologic-refractory CD, clinical remission after 6 weeks of dietary treatment was achieved in 61.8% of participants, and clinical response in 73.5% of subjects. Of particular significance, in 5 out of 6 patients qualified for surgical intervention, the application of CDED made it possible to avoid surgery. The results suggest that CDED may constitute an effective rescue strategy in patients with CD refractory to standard and biological therapy, opening new therapeutic possibilities in this particularly challenging group of patients (Sigall Boneh et al., 2017).

Limitations of Current Evidence

Despite promising results, the CDED requires strict adherence to its principles and specialist supervision. Furthermore, long-term studies evaluating its efficacy are lacking (Niseteo et al., 2022). One of the key limitations of available studies is the small number of randomized controlled trials (RCTs) evaluating the efficacy of CDED. The majority of published studies are based on observational or single-arm studies, which significantly

reduces the strength of clinical evidence. Randomized trials, such as the Levine et al. (2019) study, included relatively small patient groups (several dozen subjects per arm), which substantially limits the statistical power of the results and the possibility of generalizing them to a broader CD patient population.

Another significant limitation is the short observation period in most available studies, which generally does not exceed 12 weeks. Such a short follow-up period makes it impossible to evaluate the long-term efficacy of the diet and its impact on mucosal healing – a parameter considered one of the most important endpoints in modern CD treatment. To date, none of the published studies has assessed the impact of CDED on mucosal healing in endoscopy or on histological parameters, which constitutes a significant gap in the current evidence base.

Studies on CDED also lack standardized endpoints and efficacy assessment methods. The use of different disease activity scales (CDAI, HBI, PCDAI) and different definitions of remission and treatment response makes it difficult to compare results between studies. Furthermore, dietary adherence in real-world conditions – outside the controlled environment of clinical trials – may be considerably more difficult due to the dietary requirements of the diet, its costs, and the limited availability of recommended products. Data on actual patient adherence in outpatient settings remain insufficient.

Previous studies mainly focused on the inflammatory (luminal) phenotype of CD, leaving a gap in knowledge regarding the efficacy of CDED in patients with stricturing or penetrating phenotypes. Data from studies evaluating combined use of CDED with biological treatment are also lacking – which is particularly important in the context of the increasingly widespread use of biological therapies in CD. Finally, many observational studies are subject to selection bias – participants are primarily motivated and well-cooperating patients, which may overestimate the observed effects of dietary intervention relative to the general patient population.

Clinical Implications

Crohn's Disease Exclusion Diet (CDED) is supported by growing clinical evidence, including randomized controlled trials and systematic reviews, demonstrating its effectiveness in inducing and maintaining remission in mild-to-moderate Crohn's disease.

The strongest evidence exists in pediatric populations, while emerging data confirm its utility in adults. Despite promising outcomes, further large-scale, standardized randomized trials are required to fully establish its role in clinical guidelines.

Authors' Contributions

Conceptualization was done by Agnieszka Przybyłowska; methodology by Agnieszka Przybyłowska and Agnieszka Piechowicz; software by Sylwia Bryksy; checking by Hanna Tymchenko; formal analysis by Aleksandra Marciszewska; investigation by Martyna Świątecka; resources by Jakub Kaźmierczyk; data curation by Jakub Jopek; writing-rough preparation by Michał Popczyk; writing-review and editing by Ewa Buczkowska; visualization by Agnieszka Przybyłowska and Agnieszka Piechowicz; supervision by Sylwia Bryksy; project administration by Jakub Jopek; All authors have read and agreed with the published version of the manuscript.

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