

Systematic Review on the Effect of Crohn's Disease Exclusion Diet (CDED) among Children with Crohn's Disease

Edwina Raj; Naresh Bhatt; Kayal Vizhi
Ninette Deborrah R; Aishwarya M S; Prerana Srivastav

Aster CMI Hospital, Bengaluru, India
WGSMA, MAHE (Manipal Academy of Higher Education)

Abstract

Crohn's disease is a chronic inflammatory bowel disease increasingly diagnosed in children and adolescents worldwide. Nutritional status, growth, pubertal development and quality of life in pediatric Crohn's disease gets impacted. Nutritional therapy has become an important part of disease management due to the adverse effects of long-term corticosteroid and immunosuppressive therapy. The Crohn's Disease Exclusion Diet (CDED), usually in combination with Partial Enteral Nutrition (PEN), has emerged as a promising dietary therapy for induction and maintenance of remission in pediatric Crohn's disease. The present literature review is an evaluation of the impact of CDED on pediatric Crohn's disease using data from published clinical trials, observational studies, review articles, and case series from 2014 to 2024. Several studies have shown that CDED with PEN results in clinical remission, reduction of inflammatory markers such as C-reactive protein (CRP) and fecal calprotectin, improvement of serum albumin levels and nutritional status. CDED was better tolerated than exclusive enteral nutrition (EEN) and showed better adherence, better weight gain and better quality of life due to the presence of selected whole foods. Several studies also showed favorable results in patients who had received biologic therapy or failed biologics. The review also emphasizes CDED's role in modulating gut microbiota, improving intestinal permeability, and reducing intestinal inflammation by eliminating processed foods and saturated fats that are associated with dysbiosis. International evidence overwhelmingly

supports the use of CDED in pediatric Crohn's disease; however, Indian literature on CDED is extremely sparse and a solitary research study. An Indian study focused on Exclusive Enteral Nutrition and not on exclusion diets. Hence, there is a need for large Indian studies to validate efficacy, biochemical outcomes, adherence and sustainability among Indian pediatric population.

Keywords:

Crohn's Disease; Crohn's Disease Exclusion Diet (CDED); Partial Enteral Nutrition (PEN); Pediatric Crohn's Disease; Nutritional Therapy; Exclusive Enteral Nutrition (EEN); Clinical Remission; Inflammatory Bowel Disease (IBD); Gut Microbiota; Pediatric Nutrition

Introduction

Crohn's disease is a chronic relapsing inflammatory bowel disease that can affect any site in the gastrointestinal tract. The incidence of Crohn's disease in children has increased markedly over the last few decades. In children, the disease affects not only gastrointestinal health but also growth, nutritional status, bone health, pubertal development, and psychological well-being (Ruemmele et al., 2014).

The classic treatment is based mainly on corticosteroids, immunomodulators and biologic agents such as infliximab and adalimumab. However, corticosteroid therapy is associated with growth retardation and bone mineralization impairment in children and biologics carry a high cost, risk of infections and loss of response over time (Lee et al., 2015). Therefore, nutritional therapy is becoming increasingly important in the

management of pediatric disease.

Traditionally, enteral nutrition (EN) has been recommended as the first line of nutritional therapy to induce remission in pediatric Crohn's disease. While EEN is effective, compliance is often low because children must consume only liquid formulas for several weeks (Day & Lopez, 2015).

To overcome these limitations the Crohn's Disease Exclusion Diet (CDED) was developed. CDED is a structured dietary therapy based on exclusion of dietary components thought to have a negative impact on gut microbiota, intestinal permeability and mucosal immunity. The diet restricts processed foods, food additives and emulsifiers, maltodextrins, processed foods with gluten and excess saturated fats but includes selected natural foods and Partial Enteral Nutrition (PEN) (Sigall-Boneh et al, 2014).

CDED was first introduced by Sigall-Boneh et al. (2014) as a feasible alternative to EEN in paediatric Crohn's disease. Since then, multiple studies have shown it to be effective at inducing remission, improving inflammatory markers, promoting weight gain, and improving quality of life in children with Crohn's disease (Levine et al., 2019).

Methodology

This review of literature was conducted to evaluate the effectiveness of the Crohn's Disease Exclusion Diet (CDED) in pediatric Crohn's disease patients.

Relevant literature was gathered from scientific databases such as PubMed, Google Scholar, Scopus, and various journal websites. Studies published between 2005 and 2024 were included. Keywords used in the literature search included "Crohn's Disease Exclusion Diet," "CDED," "Pediatric Crohn's Disease," "Partial Enteral Nutrition," "Exclusive Enteral Nutrition," "Inflammatory Bowel Disease," and "Dietary Therapy in Crohn's Disease." The review covered randomized controlled trials, observational studies, prospective studies, retrospective studies, review articles, and case series that focused on pediatric patients with Crohn's disease treated with CDED alone or with Partial Enteral Nutrition.

Studies that evaluated clinical remission, the Pediatric Crohn's Disease Activity Index

(PCDAI), inflammatory markers like CRP and fecal calprotectin, serum albumin levels, BMI z-scores, growth outcomes, adherence, quality of life, and response to biologic therapy were included.

The collected data were analyzed and organized into themes such as clinical remission, biochemical improvements, nutritional outcomes, gut microbiota changes, comparisons between CDED and EEN, the use of biologics with dietary therapy, and gaps in Indian research.

Review of Literature:

According to Levine et al. (2019), in their randomized controlled trials involving pediatric patients diagnosed with mild to moderate Crohn's disease, the researchers used Crohn's Disease Exclusion Diet (CDED) along with Partial Enteral Nutrition (PEN). As shown by their results, about 75% of those receiving CDED with PEN experienced remission within 6 weeks, with 12 weeks remission being significantly higher in this group compared to that observed among EEN. Also, there was a significant decrease in CRP and fecal calprotectin in the blood. It should be noted that fecal calprotectin levels dropped significantly to values far below 1000 µg/g from values over 1000 µg/g at the beginning of the research. Moreover, serum albumin concentration increased and nutrition status improved in general terms. Adherence and tolerance in these groups were noticeably improved because the use of this diet allowed eating some whole foods.

Sigall-Boneh et al. (2014) described one of the first cases when CDED with partial enteral nutrition was used. It involved 47 children and teenagers with mild-to-moderate Crohn's disease. At the end of the experiment, after six weeks of treatment, more than 70% experienced remission, and a noticeable improvement in PCDAI index values was detected. Moreover, CRP became normal, which confirmed the reduction of inflammation in the intestine and improvement in compliance compared with EEN.

In Niseteo et al. (2022), CDED along with PEN was tested in comparison with Exclusive Enteral Nutrition. The results showed similar effectiveness in treating the condition but greater patient acceptance and better nutritional recovery. The participants of this

group experienced a decrease in inflammatory indicators and improved serum albumin concentration. The reason for the improvement in nutritional status is associated with increased adherence to the therapeutic regimen due to the ability to eat whole foods and overcome the negative psychological aspect of EEN treatment.

The article by Boneh et al. (2017) is dedicated to assessing the effect of CDED on patients who did not respond well to biological therapy (infliximab and adalimumab). According to the study results, the use of the proposed method resulted in remission even in these cases and significantly decreased both CRP and disease activity indices.

The mechanisms, implementation strategies, and future directions of CDED have been described in a thorough review by Sigall Boneh et al. (2024). Specifically, the authors state that the elimination of processed foods, emulsifiers, maltodextrins, carrageenan, and high amounts of saturated fats can help restore gut microbial homeostasis and increase intestinal impermeability. Additionally, CDED was identified as a therapeutic option for mucosal healing.

In their review, Urlep et al. (2023) evaluated modified CDED based on Partial Enteral Nutrition in pediatric patients with active Crohn's disease. Significant decreases in PCDAI scores, CRP levels, and fecal calprotectin, as well as increases in serum albumin were found to be associated with improved nutritional status.

Scarallo et al. (2021) critically analyzed the clinical usefulness of CDED as an intervention in the management of pediatric Crohn's disease. The authors revealed a higher tolerance and adherence to CDED compared to EEN due to the consumption of common foods. An improvement in the nutritional status and inflammatory symptoms indicated the beneficial effects of CDED on the quality of treatment.

Scarallo et al. (2021) concluded that an individually prescribed dietary therapy combined with multidisciplinary approaches significantly increased adherence to CDED and improved patients' quality of life since selected regular foods are allowed to be consumed. This conclusion is essential because it underlines the need for personalized dietary counseling when

planning a therapy for pediatric Crohn's disease.

In their study, Svolos et al. (2019) evaluated a food-based dietary intervention with an attempt to mimic the effects of EEN on inflammatory parameters. It was revealed that CDED resulted in a preferable composition of gut microbiota and a reduced level of inflammation, which supported the underlying mechanism of exclusion diets for the management of Crohn's disease.

As Day and Lopez (2015) stated, nutritional therapy, especially EEN, should be used to treat pediatric Crohn's disease. It helps to achieve proper growth of children, to eliminate nutritional deficits, and reduce intestinal inflammation in the absence of corticosteroids.

Sharma et al. (2020) studied the application of Exclusive Enteral Nutrition (EEN) to Indian patients with Crohn's disease and found decreased levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), along with improved clinical remission. While the focus of this research was on EEN, the article showed the increased importance of the nutritional approach to treating Crohn's disease among Indian patients. At the same time, the applicability of the enteral nutrition protocol in Indian healthcare institutions regardless of dietary and socioeconomic issues was proved.

Vadlapudi et al. (2024) reviewed a randomized pilot trial involving 21 children suffering from Crohn's disease and undergoing biologic treatment but showing ascending levels of fecal calprotectin and staying clinically asymptomatic. Children using CDED plus Pens (PEN) showed higher efficacy of treatment and required fewer doses of biologic drugs than the children having a regular diet. The article emphasized that besides ensuring proper nutrition and growth for children

with Crohn's disease, the nutritional therapy can also be used to lower their inflammatory response and alleviate the severity of symptoms.

Verburgt et al. discussed the current situation with the usage of diets to treat Crohn's disease among children, specifying several important diet-based therapies like EEN, PEN, CDED, and CD-TREAT. According to Verburgt et al., EEN has been shown to have high efficacy but is often limited by low adherence rates,

while PEN and CDED can be viewed as preferable alternatives for daily clinical practices. Besides, Verburgt et al. noted that nutritional therapies in addition to alleviating symptoms might positively affect barrier function, inflammatory processes, and microbial diversity.

The article by Levine et al. (2020) focused on the connection between dietary habits, gut microbiota, and mucosal immunity in people suffering from inflammatory bowel disease.

Moreover, Levine et al. mentioned the possibility of applying dietary approaches like CDED to achieve better disease outcomes, along with medication therapy. At the same time, Levine et al. assessed how various dietary ingredients might cause intestinal inflammation.

Table: Summary Of Selected Studies On Cded In Paediatric Crohn's Disease

Author & Year	Study Design	Population	Main Finding	Biochemical Parameter	Biologics
Levine et al., 2019	Randomized controlled trial	Children with mild–moderate CD	CDED + PEN achieved sustained remission and better adherence than EEN	↓ CRP, ↓ fecal calprotectin, ↑ albumin	Not specified
Sigall-Boneh et al., 2014	Prospective study	Children and young adults with CD	~70% achieved remission with CDED + PEN	↓ PCDAI, normalized CRP	Not specified
Niseteo et al., 2022	Comparative study	Pediatric CD patients	Modified CDED comparable to EEN with better weight gain and adherence	↑ albumin, ↓ inflammatory markers	Not specified
Boneh et al., 2017	Observational study	CD patients failing biologics	CDED induced remission despite poor biologic response	↓ CRP, ↓ disease activity	Patients on infliximab/ adalimumab

Sigall Boneh et al., 2024	Review article	Pediatric and adult CD	CDED may improve mucosal healing and gut microbiota	Discussed inflammatory pathways	Adjunct role discussed
Urlep et al., 2023	Clinical study	Children with active CD	Modified CDED + PEN improved disease activity and nutrition	↓ PCDAI, ↓ CRP, ↓ fecal calprotectin, ↑ albumin	Not specified

Scarallo et al., 2021	Review/case series	Pediatric CD	Better adherence and tolerance to CDED than EEN	Nutritional improvement	Not specified
Svolos et al., 2019	Pilot dietary intervention study	Children with CD	Food-based diet reduced inflammation and altered microbiota favorably	Reduced inflammatory response	Not specified
Day & Lopez, 2015	Review article	Pediatric CD	Nutritional therapy supports growth and reduces inflammation	General inflammatory improvement	Not specified
Sharma et al., 2020	Clinical study	Indian CD patients	EEN improved remission and inflammatory status	↓ CRP, ↓ ESR	Not specified
Vadlapudi et al., 2024	Editorial/commentary	Children with CD on biologics	CDED + PEN reduced inflammation and biologic escalation	↓ fecal calprotectin, ↓ inflammatory markers	Reduced need for biologic intensification
Verburg et al., 2021	Review article	Pediatric CD	EEN effective; CDED and PEN more feasible long term	Improved gut barrier and inflammation discussed	Not specified
Levine et al., 2020	Review article	IBD patients	Excluding processed foods may improve remission maintenance	Gut microbiota and inflammation modulation	Not specified

Discussion

From the studies reviewed in this paper, it can be concluded that nutritional therapy continues gaining more importance as a treatment option in pediatric Crohn's disease with special focus on CDED in combination with PEN. Several studies show that the use of CDED in combination with PEN is effective in inducing and maintaining remission and also results in better compliance compared to EEN (Levine et al., 2019; Sigall-Boneh et al., 2014). Reductions in markers of inflammation, namely C-reactive protein (CRP), erythrocyte

sedimentation rate (ESR), and fecal calprotectin, have been observed (Urlep et al., 2023).

A large share of research highlights practical benefits of using CDED as opposed to EEN. Since

CDED allows consumption of selective whole foods, it contributes to greater patient compliance, higher quality of life, and positive nutrition effects like weight gain, increased serum albumin concentration, and improved BMI z-score (Niseteo et al., 2022; Scarallo et al., 2021). Moreover, some studies

suggest that CDED influences gut flora and helps to decrease inflammation by eliminating processed food and additives from diet (Svolos et al., 2019; Levine et al., 2020). It has also been hypothesized that CDED could act as adjunctive therapy with biologics due to potential reduction in inflammation caused by Crohn's disease (Boneh et al., 2017; Vadlapudi et al., 2024).

Although there is some internationally produced evidence in favor of CDED, there is a lack of Indian-based studies dealing with this issue. Based on the available literature, most Indian studies concentrate on the effectiveness of EEN (Sharma et al., 2020). Therefore, further Indian-based research should be carried out on the effectiveness of CDED.

Conclusion

There is strong support in the literature for the use of the Crohn's Disease Exclusion Diet and Partial Enteral Nutrition in managing pediatric Crohn's disease. Research showed that the CDED induced remission, decreased the levels of inflammatory markers, improved the nutritional status of children, and improved adherence to treatment. In comparison to EEN, CDED is more flexible as it allows children to consume selective whole foods. Furthermore, the diet has proven to be effective for children who were under biologic medications, which would indicate the role of CDED in the improvement of gut microbiota balance. While the international literature on CDED has been growing recently, there have been very few studies in India. Thus, future research in India in relation to the CDED is needed to determine its effectiveness, biochemical results, adherence, and sustainability.

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