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Case Report

Cyclic Exclusive Enteral Nutrition as an Alternative to Medical Maintenance in Crohn Disease—A Case Report

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Abstract

We present a case report of an 11-year-old girl diagnosed with Crohn's Disease and managed with maintenance cyclic exclusive enteral nutrition with satisfactory long-term biochemical and symptomatic control.

Keywords

Cyclic exclusive enteral nutrition; Crohn's disease; inflammatory bowel disease

1. Introduction

Crohn Disease (CD) is one type of inflammatory bowel disease (IBD): it is characterized by active and chronic inflammation affecting any part of the gastrointestinal tract in a patchy fashion [1]. Diagnosis of CD is based on a combination of endoscopic, histologic and imaging assessments.

Though the precise etiology of CD is unknown, it is believed to result from an interplay of genetic susceptibility with immune, bacterial, and environmental factors (such as diet) [2]. After diagnosis, the treatment of CD involves induction and then ongoing maintenance of remission with the treatment of flares.

Exclusive Enteral Nutrition (EEN) was first used to manage CD in the 1970s, following observations that patients treated with elemental formula while awaiting surgery had significant improvement in their symptoms [3]. EEN was subsequently validated as a suitable therapy and is now advocated as the first-line therapy for induction of remission in children with active CD by European and North American organizations [4-6]. Although various protocols have been described, generally, EEN involves 6-8 weeks of a diet comprised solely of nutritionally complete drinks with no other food intake [6]. The efficacy of EEN is not adversely impacted by the availability or choice of formulae selected for treatment [7]. EEN is well-documented to lead to an equivalent or superior remission rate (typically around 80%) compared to remission rates with corticosteroids without significant side effects. Furthermore, EEN positively affects linear growth, an essential issue in children with CD.

Though regularly used as an induction treatment, ongoing use of a nutritional enteral formula for maintenance of remission, such as maintenance of enteral nutrition (MEN) or cyclic EEN, is described less frequently. This report highlights the case of a 15-year-old girl diagnosed with CD managed with cyclic EEN with consequent long-term clinical and biochemical remission.

2. Case Report

This girl was diagnosed in 2019 at 11 years of age after presenting with two months of diarrhea, hematochezia, periumbilical abdominal pain, and 5 kg weight loss (15% total body weight). Weight was 32.70 kg (z-score -0.67), height 146.8 cm (z score 0.03) with a body-mass index (BMI) of 15.38 (z-score -1.06). She had no significant past medical history but did have a family history of CD (maternal aunt). The only finding on the initial assessment was mild right iliac fossa tenderness.

Initial investigations showed thrombocytosis (platelets 473 × 10 g/L), with C-reactive protein of 22 mg/L and ESR of 18 mm/hr. She had hypoalbuminaemia (27 g/L) and a markedly raised fecal calprotectin level (>1000 ug/g). Given her presenting features and these initial results, she proceeded to have an endoscopic assessment with a view to a likely diagnosis of IBD. Endoscopically, there were non-bleeding gastric erosions and multiple discontinuous aphthoid ulcers involving the terminal ileum and colon (with relative rectal sparing). Histology showed mild active gastritis, ileitis, and colitis with granulomata, which were consistent with CD. Magnetic resonance enterography did not show any definite small bowel abnormality.

She was initiated on EEN with a target volume of 1600 ml daily using standard polymeric formulae (Ensure, Abbott, Auckland, New Zealand (NZ)). During the 8-week course of EEN, she had prompt and complete resolution of all symptoms and gained 3.8 kg overall. Repeat testing at the end of EEN showed calprotectin 69 ug/g, CRP <3 mg/L, ESR 2 mm/hr, and albumin 39 g/L.

She was then managed with maintenance enteral nutrition (MEN), comprising 600-800 ml of polymeric formula daily with 2-3 meals of standard foods. Subsequently, she has continued a four-week cycle with MEN for three weeks, followed by one week of EEN. Other than a two-week course of metronidazole (to manage a mild change in symptoms four months after diagnosis), she has remained in clinical and biochemical remission for more than four years with this cycling regimen alone. Over this time, systemic inflammatory markers (CRP, ESR, and albumin) have remained normal,

and calprotectin levels have been repeatedly less than 150 ug/g. Furthermore, she has had no gastrointestinal or extra-intestinal manifestations of IBD and has had satisfactory growth (most recent parameters: weight 57.10 kg, height 165.5 cm, BMI 19.15 z-score -0.29). She has had normal pubertal development and no disruption to normal daily activities throughout observation.

This child's medical and nutritional management was monitored regularly in a multidisciplinary pediatric IBD clinic as per international consensus guidelines [8, 9]. This clinic comprises the pediatric gastroenterologist, the gastroenterology registrar, the paediatric dietitian and the clinical nurse specialist. This child was reviewed more frequently after her initial diagnosis, decreasing to monthly and then three-monthly reviews as disease activity remained stable. Within this setting, the dietitian monitored her anthropometry and nutritional adequacy, and clinical recommendations were suggested based on the assessment to ensure optimal nutrition and growth. Furthermore, annual nutritional screening blood test were also completed.

3. Discussion

EEN has been well-validated and supported as an effective and safe therapy for remission induction in individuals with active CD [10]. However, the role of ongoing administration of enteral formulae after a course of EEN to maintain remission has not been established.

Ongoing nutritional intervention as a sole intervention to maintain remission has predominantly been considered as MEN, defined as ongoing enteral formulae (typically <35% of daily required caloric intake) in addition to standard foods. MEN can be delivered through the day as oral drinks, or overnight via a nasogastric tube [11]. MEN can be differentiated from other terms such as supplementary enteral nutrition (where the goal is to boost caloric intake or to be given alongside other medical therapies) or partial enteral nutrition (PEN) (defined as between 30-50% of a child's estimated energy requirements) [10].

In one report, Konno et al. [12] retrospectively assessed the long-term effectiveness of MEN in association with aminosalicylates in 58 children with CD. The combination of MEN and aminosalicylates (without other therapies) was effective at maintaining remission, with relapse rates of 12% at 1 year, 27% at 2 years, and 48% at 5 years. Only six (10%) of the 58 patients required intestinal surgery during observation.

Wilschanski et al. [13] showed prolongation of remission and improved linear growth with overnight enteral formulae in conjunction with an unrestricted daytime diet. A group of 65 children who had completed EEN to induce remission chose to have either overnight nasogastric supplemental feeds with an oligopeptide or amino acid formula 4-5 nights per week or an unrestricted diet without supplementary feeds. The children who received overnight feeds had lower relapse rates than those whi did not at 6 months (17% versus 79%) and 12 months (43% vs 79%). In addition, when the mean height velocity data was compared between groups (the year preceding treatment compared with the year following treatment), data showed the supplemental group had superior growth velocity (mean of 2.9 cm/year vs 0.4 cm/year).

A recent systematic review with meta-analysis evaluated the outcomes of MEN in individuals with CD [14]. The data arising from the eight studies with 429 patients (adult and pediatric studies) showed that clinical relapse was lower at 6-24 months in those receiving nutritional therapy than in those not receiving nutritional therapy (Risk Ratio (RR) 0.67, 0.54-0.82, Number Needed to Treat

(NNT) 5). In this evaluation, nutritional intervention also resulted in a higher rate of clinical remission at 6 to 12 months (67% vs 48%, RR 1.32).

Although these data suggest potential benefits, the most recent European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines recommend that MEN should be used only in a select group of children with mild CD not receiving maintenance medication [4]. Furthermore, the European Society for Clinical Nutrition and Metabolism (ESPEN) does not support the use of MEN for children with CD to prolong remission [5].

An alternative approach for ongoing nutritional support to maintain remission is cyclic EEN. Belli et al. [15] demonstrated the potential efficacy of this approach in eight children with CD. These children were given EEN (with an elemental formula) for one month every four months over a year. The outcomes were compared to the children's progress over the preceding 12 months and that of four age-matched controls on standard treatment. The use of cyclic EEN in this group resulted in less cumulative prednisone use (22.1 mg/kg/yr vs. 78.9 mg/kg/yr), enhanced linear growth (mean height gain of 7cm/yr vs. 1.7cm/yr), and weight gains (mean of 6.9 kg/yr vs 2.7 kg/yr). Disease activity scores were also improved in the children who received cyclic EEN (Crohn disease activity index of 63 ± 13.4 in the cyclic EEN group v 128.8 ± 23.5 in the control group). This improvement occurred after the first course of EEN and persisted thereafter. Despite the small numbers in the study, this showed the promise of cyclic EEN for improving growth failure in children with CD, a significant complication of the disease process affecting 15-40% of children by enhancing nutrition and decreasing exposure to growth stunting medications such as prednisone. [16].

The advantages of this therapeutic strategy include delaying or preventing the escalation of medical therapies, avoiding potential medication-related side effects, and the ongoing optimization of a child's nutritional intake to avoid growth failure [12, 17, 18]. Potential disadvantages include the development of avoidant/restrictive food intake disorder (ARFID) or other disordered eating patterns and the importance of adherence.

Furthermore, while some children may have difficulty coping with their CD overall, and CD is associated with increased rates of anxiety or depression, EEN can also be a psychologically challenging process for some children [19]. Adherence and the consequent efficacy of EEN in children are optimized by providing adequate support systems and regular reviews or encouragement [19]. One report showed that the adherence of young adults to a course of EEN can be related to the individual's motivation to complete treatment and a conscientious personality [20]. Comparatively, pediatric studies show high rates of adherence to EEN, suggesting that children struggle less with motivation when adhering to dietary treatment.

The girl described in the current report was very motivated and had significant family support. Furthermore, she was reviewed regularly at planned outpatient appointments and had opportunities to communicate with the team between appointments. Together, these factors likely enabled her to adhere to this dietary regimen.

One potential risk of any nutritional intervention would be the development of nutritional deficiencies, mainly if such an intervention were not managed and monitored carefully. Nutritional deficiencies are well recognized in the setting of IBD in children [21, 22]. These risks were mitigated using a complete nutritional product in the current case. Furthermore, the current patient has had regular dietetic, clinical, and micronutrient monitoring and annual dietary screening.

In conclusion, this case report suggests a role for cyclic EEN as a potential maintenance regimen for appropriate individuals with CD. This approach may provide long-term remission without other

maintenance therapies. However, further observational data and prospective evaluations are required to provide clear guidelines for patient selection, optimization of this approach, and complete delineation of the benefits and risks of this approach.

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Written informed consent has been obtained from the patient to publish this report. Due to the nature of the report, formal ethical review was not required (as per local institutional guidelines). ASD's research activities are supported by Cure Kids.

Author Contributions

MGB: Writing – original draft, formal analysis, writing – review and editing. SCB: Conceptualization, writing – review and editing. ASD: Methodology, writing – review and editing, overall supervision. All authors have read and approved the published version of the manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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