



ORIGINAL ARTICLE

## Exclusive enteral nutrition continues to be first line therapy for pediatric Crohn's disease in the era of biologics<sup>☆</sup>



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### KEYWORDS

Inflammatory bowel disease;  
Crohn's disease;  
Exclusive enteral nutrition;  
Calprotectin

### Abstract

**Background:** Exclusive enteral nutrition (EEN) has been shown to be more effective than corticosteroids in achieving mucosal healing without having their side effects.

**Objectives:** To determine the efficacy of EEN in terms of inducing clinical remission in newly diagnosed CD children and to study the efficacy of this therapeutic approach in improving the degree of intestinal mucosa inflammation.

**Materials and methods:** The medical records of patients with newly diagnosed Crohn's disease treated with EEN were reviewed retrospectively. The degree of mucosal inflammation was assessed by fecal calprotectin (FC). Remission was defined as a PCDAI < 10.

**Results:** Forty patients (24 males) were included, the age at diagnosis was  $11.6 \pm 3.6$  years. Of the 34 patients who completed the EEN period, 32 (94% per-protocol analysis) achieved clinical remission. This percentage fell to 80% in the intention-to-treat analysis. The compliance rate was 95%. Duration of EEN was 6.42 weeks (IQR 6.0–8.14). FC was significantly higher in patients with moderate and severe disease. Median baseline FC levels (680 µg/g) decreased significantly to 218 µg/g ( $p < 0.0001$ ) after EEN. We found a statistically significant correlation between FC and PCDAI ( $\rho = 0.727$ ;  $p < 0.0001$ ). Early use of thiopurines (<8 weeks) vs. subsequent use was not associated with better outcome during the follow-up.

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**Conclusions:** EEN administered for 6–8 weeks is effective for inducing clinical remission and decreasing the degree of mucosal inflammation. We did not find differences in terms of maintenance of remission in patients treated early with thiopurines.

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## PALABRAS CLAVE

Enfermedad inflamatoria intestinal; Enfermedad de Crohn; Nutrición enteral exclusiva; Calprotectina

## La nutrición enteral exclusiva continúa siendo el tratamiento de primera línea en la enfermedad de Crohn pediátrica en la era de los biológicos

### Resumen

**Introducción:** La nutrición enteral exclusiva (NEE) ha demostrado ser más efectiva que los esteroides para alcanzar la curación mucosa sin sus efectos secundarios.

**Objetivos:** Determinar la eficacia de la NEE para inducir la remisión clínica y mejorar el grado de inflamación mucosa en pacientes con EC durante su primer brote.

**Material y métodos:** Revisión de las historias clínicas de pacientes con EC tratados con NEE durante su primer brote. El grado de inflamación mucosa se estimó mediante la calprotectina fecal (CF). Se definió remisión como PCDAI < 10.

**Resultados:** Se incluyeron 40 pacientes (24 varones) con una edad al diagnóstico de  $11,6 \pm 3,6$  años. La duración de la NEE fue de 6,42 semanas (RIQ 6,0–8,14). De los 34 pacientes que completaron el período de NEE, 32 (94% en el análisis por protocolo) alcanzaron la remisión clínica. Este porcentaje descendió al 80% en el análisis por intención de tratar. La tasa de cumplimiento fue del 95%. Los valores de CF fueron significativamente más altos en pacientes con brotes moderados y graves. La CF basal fue de  $680 \mu\text{g/g}$  y descendió de forma significativa a  $218 \mu\text{g/g}$  al final del periodo de NEE ( $p < 0,0001$ ). Hubo correlación estadísticamente significativa entre CF y PCDAI ( $\rho = 0,727$ ;  $p < 0,0001$ ). La introducción precoz del tratamiento con tiopurinas (antes de las 8 semanas) no se asoció a una mejor evolución durante el seguimiento.

**Conclusiones:** La NEE administrada durante 6–8 semanas es efectiva para inducir la remisión clínica y mejorar el grado de inflamación mucosa. No encontramos diferencias en términos de mantenimiento de la remisión en pacientes tratados precozmente con tiopurinas.

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## Introduction

Crohn's disease (CD) is an idiopathic chronic inflammatory disorder. The natural course of Crohn's disease is characterized by flare-ups alternated with periods of remission. Controlling intestinal inflammation is crucial for preventing progressive intestinal damage and the appearance of complications.<sup>1</sup>

The incidence of CD in children and adolescents is approximately 3 cases/100,000 inhabitants (range 1–8/100,000 inhab.) and this has increased in Spain and Europe during the last decade.<sup>2</sup> Up to 20% of CD patients are diagnosed before the age of 18 years. There are differences in the form of onset, natural course, and treatment regimens between adults and children. Another key difference is delayed growth, up to 46% of children and adolescents diagnosed with CD had a decrease in their growth rate before the onset of any other symptoms, and only 12% had a normal growth rate at the time of diagnosis.<sup>3</sup> This is not only found at diagnosis, it has a variable prevalence during follow-up.<sup>4</sup> It is also important to remember that a chronic disease appearing during childhood is associated

with considerable psychological morbidity that may influence personal relationships, psychosexual development, scholastic achievements and adherence to treatment.

There are a wide range of therapeutic objectives that need to be achieved in active disease; these include control of inflammation, mucosal healing, modifying disease progression, preventing the adverse effects of treatment and guaranteeing suitable growth and development.<sup>5,6</sup> Exclusive enteral nutrition (EEN) has been shown to be more effective than corticosteroids, without their side effects, in achieving mucosal and transmural remission, a situation that determines better prognosis in the following years, lower hospitalization rate and less use of biological drugs.<sup>7–11</sup>

Calprotectin is a calcium-binding protein with antimicrobial properties. Calprotectin is released from the cytoplasm of activated neutrophils, and the fecal levels increase in bowel inflammation.<sup>12</sup> Fecal calprotectin (FC) values have been correlated with endoscopic scores in adults and children with IBD. It is a non-invasive biomarker with high sensitivity and specificity that enables monitoring of inflammatory activity and prediction of clinical relapse.<sup>12–17</sup>

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