Nutrición Hospitalaria

Nutr Hosp. 2014;29(3):537-546
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original / *Pediatría*

PRESENT; PREScription of Enteral Nutrition in pediaTric Crohn's disease in Spain

Victor Manuel Navas-López[1], Javier Martín-de-Carpi[2], Oscar Segarra[3], José Ignacio García-Burriel[4], Juan José Díaz-Martín[5], Alejandro Rodríguez[6], Enrique Medina[7], Mercedes Juste[8]; on behalf of the PRESENT Working Group of SEGHNP (Sociedad Española de Gastroenterología Hepatología y Nutrición Pediátrica)

[1]Pediatric Gastroenterology and Nutrition Unit. H Materno. Málaga. [2]H. Sant Joan de Deu. Barcelona. [3]H. Vall de Hebrón. Barcelona. [4]Complexo Hospitalario Universitario de Vigo. [5]Hospital Universitario Central de Asturias. [6]Hospital Universitario Virgen del Rocío. Sevilla. [7]Hospital Doce de Octubre. Madrid. [8]Hospital Clínico Universitario San Juan de Alicante. Spain.

Abstract

Objectives: **Exclusive enteral nutrition (EEN) is one of the therapeutic strategies used to induce remission in pediatric Crohn's disease (CD). Although its use is recommended in clinical practice guidelines and consensus documents, the frequency of this practice in Spain is unknown.**

Methods: **A 70-item questionnaire (PRESENT: PREScription of Enteral Nutrition in pediaTric Crohn's disease in Spain) was drafted and distributed through the SEGHNP (Spanish Society for Pediatric Gastroenterology, Hepatology and Nutrition) e-mail list.**

Results: **We received information from 51 Pediatric Gastroenterology Units. Of the 287 patients newly diagnosed with CD in 2011-2012 at these centres (139 in 2011, 148 in 2012), 182 (63%) received EEN (58% in 2011 and 68% in 2012). 26% of the patients who received EEN in the period studied (64/246) did so during relapses. All the physicians (100%) who responded to the questionnaire believe that EEN is effective in inducing clinical remission in mild to moderate CD. However, 24.5% of respondents never use EEN during relapses. The enteral formulas used most often used were polymeric formulas specific for CD (70.6%) and the preferred administration route was oral, with 60.8% using flavouring and 9.3% allowing a variable percentage of calories in the form of other foods. 65% use 5-ASA together with EEN, 69% use antibiotics and 95% immunomodulators (thiopurines). The duration of EEN tends to be 8 weeks (47.1%), and transition to regular diet was achieved sequentially over a variable period of time. Regarding barriers and limiting factors for the use of EEN, those most frequently reported include lack of acceptance by the patient and/or family (71%), lack of time and/or ancillary staff (69%) and difficulty in convincing the patient and/or family of the suitability of treatment (43%).**

Correspondence: Víctor Manuel Navas-López.
Pediatric Gastroenterology and Nutrition Unit.
Hospital Materno Infantil.
Avda. Arroyo de los Ángeles, s/n.
29011 Málaga. Spain.
E-mail: victor.navas@gmail.com

Recibido: 31-X-2013.
1.ª Revisión: 1-XII-2013.
Aceptado: 1-XII-2013.

PRESENT; PRESCRIPCIÓN DE NUTRICIÓN ENTERAL EN LA ENFERMEDAD DE CROHN PEDIÁTRICA EN ESPAÑA

Resumen

Objetivos: **La nutrición enteral exclusiva (NEE) es una de las estrategias terapéuticas empleadas para inducir la remisión en niños con enfermedad de Crohn (EC). Pese a que la NEE se recomienda en las guías de práctica clínica y en los documentos de consenso, la frecuencia real de su empleo en España es desconocida.**

Métodos: **Encuesta compuesta por 70-items (PRESENT: PREScription of Enteral Nutrition in pediaTric Crohn's disease in Spain) que se distribuyó a través de la lista de distribución de Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (SEGHNP).**

Resultados: **Se recibieron los datos de 51 unidades de Gastroenterología Pediátrica del territorio español. De los 287 pacientes recién diagnosticados de EC durante los años 2011-12 en esos centros (139 en 2011 y 148 en 20212), 182 (63%) recibieron NEE (58% en 2011 y 68% en 2012). El 26% de los pacientes que recibieron NEE estaban en recaída. Todos los facultativos que respondieron pensaban que la NEE es efectiva para inducir la remisión clínica en los brotes leves-moderados. El 24,5% no emplean la NEE durante las recaídas. Las formulas enterales empleadas más frecuentemente fueron las específicas para EC (70,6%), la vía oral fue la más utilizada, el 60,8% utilizaron saborizantes y el 9,8% de las unidades permitían un porcentaje variable de calorías en forma de otros alimentos durante el periodo de NEE. El 65% emplearon 5-ASA junto con la NEE, el 69% antibióticos y hasta un 95% inmunomoduladores. La duración de la NEE fue de 8 semanas en el 47,1% de los casos, la transición hacia una dieta normal se realizó de forma secuencial. En relación a las barreras y factores limitantes encontrados por los respondedores para instaurar la NEE destacaban la falta de aceptación por el paciente y/o la familia (71%), falta de tiempo o de personal auxiliar (69%) y la dificultad para convencer al paciente o su familia de la idoneidad del tratamiento (43%).**

Conclusiones: **La frecuencia de empleo de la NEE en pacientes con EC es similar a la de otros cuestionarios europeos. Se precisan herramientas y recursos que faciliten**

Conclusions: **EEN use rates are similar to those of other European questionnaires. Tools that facilitate acceptance by the patient and family are needed. Increasing the time dedicated to this therapeutic modality is likewise important. Given the disparity of criteria for indicating treatment with EEN, it would be useful to have widely accepted clinical practice guidelines or protocols that facilitate the decision to use it.**

(Nutr Hosp. 2014;29:537-546)

DOI:10.3305/NH.2014.29.3.7184

Keywords: *Exclusive enteral nutrition. Pediatric Chron's disease. Pediatric inflammatory bowel disease. Survey. Prescription.*

la aceptación por parte del paciente y de su familia así como disponer de más tiempo a dedicar para instaurar esta modalidad terapéutica. Dada la disparidad de criterios para la indicación de la EEN, sería útil disponer de guías de práctica clínica ampliamente aceptadas o protocolos que facilitan la decisión de utilizarla.

(Nutr Hosp. 2014;29:537-546)

DOI:10.3305/NH.2014.29.3.7184

Palabras clave: *Nutrición enteral exclusiva. Enfermedad de Crohn pediátrica. Enfermedad inflamatoria intestinal pediátrica. Encuesta. Prescripción.*

Introduction

Exclusive enteral nutrition (EEN) has been shown to be more effective than corticosteroids inducing mucosal healing in children with Crohn's disease (CD), without the side effects.[1-3] Although its use in pediatric CD is recommended in clinical practice guidelines[4] and consensus documents, the frequency of this practice in Spain, where the incidence of inflammatory bowel disease (IBD) has been on the rise in recent years,[5] is unknown. The aim of this study was to investigate the frequency and characteristics of the use of EEN in pediatric gastroenterology units in Spain through the use of a questionnaire prepared for this purpose.

Materials and methods

The questionnaire was based on other published[6-9] studies, together with other previously unpublished items. The study was conducted by the IBD working group of the Spanish Society for Pediatric Gastroenterology, Hepatology and Nutrition (SEGHNP) and supported by the SEGHNP. All Pediatric Gastroenterology Units in Spain were contacted but participation was, of course, voluntary. Although not all Pediatric Gastroenterology Units have included their patients, all of the reference hospitals across Spain have participated.

The questionnaire (PRESENT: **PRES**cription of **E**nteral **N**utrition in pedia**T**ric Crohn's disease in Spain) sent out consisted of 70 items that include general aspects of IBD and specific aspects of EEN for pediatric CD (Appendix II). The period for receiving the questionnaires was from May 2012 until January 2013. All questionnaires were reviewed and the authors were contacted personally if any errors were detected or if any items were not completed in order to request the pertinent clarifications.

Statistical analysis

The qualitative variables are expressed as a percentage. The chi-square test was used to contrast variables. Values of $p < 0.05$ were considered to be statistically significant.

Ethical considerations

The study was approved by the Ethic's Committee of the first author's center, as representative of the rest of the hospitals. The authors do not have conflicts of interest.

Results

Data were received from 51 Pediatric Gastroenterology Units distributed across Spain. During the 2011-2012 period, 287 cases of CD were newly diagnosed (139 in 2011 and 148 in 2012) at these units; 246 received treatment with EEN in these two years, 182 (63.4%) patients as first-line therapy and 64 during relapses. All the patients who received EEN during relapses had responded previously to EEN at the onset of the disease. The frequency of EEN use as first-line therapy increased from 58% (81/139) in 2011 to 68% (101/148) in 2012 ($p = 0.08$).

Efficacy of EEN to induce remission

With regard to newly diagnosed CD, all those polled believe that EEN is effective in inducing clinical remission, having likewise verified such efficacy at some point. Ninety-six point one per cent (96.1%) maintained that it enables mucosal healing and 84.3%, histological remission. Of the 36 units that had performed endoscopy after EEN, 17 (47.2%) reported mucosal healing and 15 (41.6%) histological remission in some case. In response to whether EEN is effective in relapses, 83.4% contended that it induces clinical remission, 80.4% mucosal healing and 74.5% histological remission. Seventy-six point five per cent (76.5%) use or have used EEN in relapses, having confirmed clinical remission and endoscopic and histological remission in up to 69.2% and 36% of patients, respectively.

Table I
Indications for EEN according to disease characteristics

Newly diagnosed *vs.* exacerbations	76.5% only use EEN in newly diagnosed CD patients, not during relapses. 66.7% of those who use EEN in relapses only do so if the patient responded previously to EEN.
Behaviour[+]	43% indicate EEN only in cases of inflammatory phenotype (B1, non-stricturing, non-penentrating).
Location[+]	37.3% only use EEN when only the ileum (L1) or ileum and colon (L3) are affected. 62.7% use EEN regardless of disease location and 31.4% do not use EEN when upper gastrointestinal tract (L4a or L4b) is affected. 50% do not use it in cases with extraintestinal manifestations.
PCDAI[*]	6% only in mild disease, 41.1% in mild to moderate disease and 52.9% regardless of disease severity.
Perianal disease	70.6% use EEN to induce remission in cases of mild perianal manifestations (fissures or skin tags) or in cases of previously drained abscess.
Age	70.6% use it regardless of age and 16.7% do not use it in patients under the age of 3.
Other factors	62.7% only indicate EEN if the patient and their family are collaborative. 25.5% indicate it as the only therapeutic option. Delayed growth contributes to the prescription of EEN in 96.1% of subjects polled.

[+]According to Paris classification of IBD[10].
[*]Pediatric Crohn's Disease Activity Index[11].

Indications for EEN

Table I shows the results for EEN indications.

Comparative analysis of the indications for EEN according to patient treated in units that providing follow-up to a high number of patients (> 50 patients/year) or a small number (< 50) revealed no significant differences.

Specific aspects of EEN

The most common response with regard to the duration of EEN was 8 weeks, chosen by 47.1% of the respondents, followed by 6-8 weeks (22.5%), 6 weeks (19.6%) and others (7.8%). None of those polled use it for periods under 6 weeks or greater than 12 weeks. The oral administration route was preferred in all cases, with nasogastric-feeding only being used when taking enteral formula by mouth was not possible. The response time to assess the efficacy of EEN was 2-3 weeks in 21.6%, 2-4 weeks in 18.4%, 3-4 weeks in 17.6% and 2 weeks in 15.7% of subjects polled.

Regarding which enteral formula was used, in 70.6% of the cases (36/51) polymeric formulas specific for IBD were used, enriched with TGF-β (Modulen IBD® or Resource IBD®); 29.4% indicated other formulas different from the specific ones (flavoured normal- or hypercaloric polymeric formulas or flavoured elemental formulas). The choice of formula was mainly influenced by factors such as taste, cost, availability, nutritional composition, evidence and experience. Table II shows that the most frequent reason for indicating specific formulas was their composition, with particular reference to TGF-β. In the group that used other formulas, 100% declared that there was no evidence that formulas made specifically for IBD were superior to standard polymeric formulas, and that the EEN itself is responsible for the patients' improvement; such effect cannot be specifically attributed to any of the ingredients.

Another aspect we wished to enquire about involved liquids, foods and amount of calories the pa-

Table II
Reasons for choosing the enteral formula

Reason(s)	*IBD-specific enteral formulas (n = 36)*	*Other enteral formulas (n = 15)*	*p*
Composition	58%	7%	0.0001
Availability	50%	0%	0.0001
Evidence	42%	100%	0.0001
Experience	28%	7%	0.079
Taste	17%	53%	0.012
Compliance	14%	53%	0.006
Specificity of the formula	8%	0%	0.234
Use of flavouring	6%	0%	0.336
Cost	3%	20%	0.046

Table III
Combination of EEN with pharmacological treatment

Drug	*Always*	*Sometimes*	*Never*	*I don't know*	*No answered*
Oral 5-ASA preparations	20%	45%	31%	2%	2%
Topical 5-ASA preparations	0%	27%	67%	4%	2%
Antibiotics	2%	67%	27%	2%	2%
Thiopurines	71%	24%	4%	0%	1%
Steroids	2%	18%	78%	0%	2%
anti-TNF	0%	35%	59%	4%	2%

tients were allowed to eat during the EEN treatment period; 90.2% answered only water and the remaining 9.8% indicated between 5-20% of all the calories estimated in the day. At all the centres, the physician in charge of the patient participates in the decision about the formula to be administered. Of subjects polled, 60.8% allow the use of flavouring; of these, 48.4% mention the flavouring provided by Nestlé Nutrition (with banana or strawberry flavour), 22.6% cocoa powder, 3.2% syrups of different flavours and 25.8% a variety of the aforementioned. Once the induction period has been completed, 94.2% progress to a normal diet in the following 2-4 weeks (7.6% follow their own protocol and the remaining 92.4% do not follow any protocols) and 5.8% change to a normal diet quickly, with no specific order when introducing the food groups.

After the induction period, 88.4% provides systematic enteral formula supplementation to all patients during a variable time period that depends on several factors (adherence, nutritional state, etc.). The majority of units opt to supplement with 20-30% of the total calories, which tend to range from 500-750 ml, depending on the patient. The remaining 11.6% only supplement if required for nutritional recovery.

Combination of EEN with pharmacological treatment

Regarding the drugs used concomitantly during the induction of remission with EEN, the results reported by respondents are found in table III.

Professionals involved in the administration of EEN and follow-up

The professionals involved in assessing and indicating therapeutic support via EEN vary according to centre (table IV).

The physician is solely responsible for the follow-up of these patients in 80.4% of the cases. In 9.8% the physician works with a dietician, in 5.8% with a nurse, in 2% with a nurse and psychologist and in the remaining 2% with a nurse, dietician and psychologist. Follow-up is primarily done via telephone and outpatient visits (74.6%) or exclusively by visits (25.4%). The frequency with which the patient is contacted during nutritional treatment is weekly in 56.3% of the centres, fortnightly in 33.3%, monthly in 6.3% and variable in the remaining 4.1%.

Table IV
Professionals involved in the indication of EEN

	Always	*Sometimes*	*Never*
Nurse	47%	22%	31%
Dietician	22%	16%	62%
Psychologist	4%	37%	59%
Physician	100%	0%	0%

Assessment of response to EEN

The PCDAI was the most frequent index used (98%) followed by the wPCDAI.[12] Regarding the biochemical parameters to assess response after EEN, 100% use complete blood count (CBC) and albumin, 98% erythrocyte sedimentation rate (ESR), 78% faecal calprotectin, 35% C-reactive protein (CRP), 22% iron metabolism, and 8% fibrinogen and procalcitonin (PCT); 70.6% use endoscopy and 66.7% use radiological tests to assess the response to treatment.

Advantages and disadvantages of EEN

The results regarding advantages and disadvantages with EEN are shown in table V.

Difficulties

Multiple choice questions were used to explore the objections or difficulties reported by the professionals for establishing EEN; 14% of the respondents reported no difficulties, 36% only one difficulty, another 36% reported two difficulties and up to 14%, more than three difficulties (table VI).

Table V
Advantages and disadvantages of EEN

Advantages		*Disadvantages*	
Absence of side effects	80%	Maintenance and compliance difficulties. Motivation	80%
Clinical and histological remission (mucosal healing)	75%	Dietary considerations (monotonous, high volume to ingest, flavour)	30%
Improvement of nutritional parameters, growth and sexual maturity	61%	Requires closer follow-up than other treatments. Frequent check-ups	22%
Prevents the use of corticosteroids	29%	Slow improvement of symptoms	12%
Safety	10%	Altered quality of life (QoL)	12%
Outpatient setting	4%	Prolonged time period	10%
Update vaccination schedule	4%	Price	10%
Easy prescription	4%	Not useful in exclusively colonic or perianal disease	4%

Table VI
Difficulties found for establishing EEN

Lack of acceptance by the patient and/or family	71%
Lack of time and/or ancillary staff (dieticians, nutritionists, psychologists, etc.) to collaborate in the follow-up and support of these patients	69%
Difficulty convincing the patient and/or family of treatment suitability	43%
Budgetary limitations	10%
Difficulty using alternatives to the oral route at my centre (NG tube, gastrostomy)	8%
Difficulties in prescription and administration of the nutrition by the hospital (logistics)	2%
I do not believe in the benefits of mono-therapy EEN to induce remission	0%

Discussion

Although EEN has been proven to be beneficial in the treatment of pediatric CD, there are some questions that remain unanswered. We had access to data from different surveys regarding the use of this therapeutic modality in the United States, Canada, Europe, Israel and Australia,[6-9,13] (table VII) but we did not know the real situation regarding EEN use in Spain.

The use of EEN is widespread in Spain, since all of the respondents confirm regular use of EEN, at a rate much higher than that published by other authors (table VII). Although the studies shown in table 7 have been published recently, much of the data were collected before a meta-analysis regarding the efficacy of EEN was published. Nevertheless, it is true that series with the greater number of patients and better design are subsequent to 2005, when the best evidence for EEN in the treatment of CD was published. One of the possible reasons for this difference in use may be related to the fact that the Spanish National Healthcare System subsidizes enteral formulas for the treatment of CD. This is a key factor, since EEN has been shown to be superior to steroids in achieving mucosal healing,[1,2,14] a situation that determines better prognosis in the following years, lower hospitalisation rate and less use of biological drugs.[15]

Despite the fact that the efficacy of EEN for controlling CD relapses is 50%,[14,16] and even if there is not remission, there is a decrease in inflammatory activity and an improvement in nutritional state, only 24.5% use EEN in this scenario, which is likely conditioned by the difficulty for re-establishing and maintaining the EEN again for another 6-8 week period.

Initial studies revealed that EEN was less effective than steroids in exclusively colonic CD,[17] although this

Table VII
Published surveys about use of EEN in CD

Study	*USA*	*Europe*	*Canada*	*Israel*	*Australia*	*Asia-Pacific*	*All data*
Levine et al[6]	4.3%	61.8%	36%	19.2%	–	–	–
Steward et al[7]	9%	–	32%	–	–	–	–
Gråfors et al[8]	–	65%[A]	–	–	–	–	–
Whitten et al[9B]	100%	92%	–	–	–	75%	89%
Day et al[12]	–	–	–	–	38%	–	–

[A]Only data from Sweden.
[B]USA 2 units; Asia-Pacific 8 units; UK 16 units; Europe 9 units.

was not corroborated by later studies.[18,19] This is an important issue because 37.3% of the respondents do not use EEN in this clinical setting on the basis of their own previous experience. In our opinion, more studies along these lines are needed to clarify the real response according to disease extension.

Regarding the enteral formula used, there are two clearly differentiated groups: those who use specific formulas for IBD (Resource IBD® or Modulen IBD®) as it contains TGF-β and due to the motivating effect of taking a formula adapted to a specific disease, and another group that sustains, as made clear by the studies published, that there are no differences between formulas,[20-23] attributing the improvement experienced by patients to the EEN and the administration conditions and not to any of their components. Another factor is compliance, which seems to be superior in the case of flavoured polymeric formulas. One reason for the 3% of survey respondents who used specific formulas for IBD patients was the price although the average price of a specific formula for IBD in Spain is 17 €/1,000 kcal, similar to non-specific pediatric normocaloric formulas; slightly more expensive than pediatric hypercaloric formulas (14,6 €/1,000 kcal) and more expensive than adults hypercaloric (9.3 €/1,000 kcal) and normocaloric (9,7 €/1,000 kcal) formulas.

The optimal method for introducing normal diet after EEN has not been established, and there is no data to suggest that progressing to a hypoallergenic diet, gradual or sudden introduction of diet following EEN influence the maintenance of remission.[9,24]

The majority of respondents identified various difficulties in re-establishing diet, despite having no doubts about the efficacy of EEN. Almost three-quarters of those polled consider the lack of acceptance by the patient and/or family to be the main difficulty in establishing EEN. A more proactive attitude in the professional involved might have led to higher acceptance rates; not initially offering any other therapeutic option could also be considered a valid approach.

Added to this preliminary difficulty is the second most frequent barrier: lack of time and/or ancillary staff (dieticians, nutritionists, psychologists, etc.) to help in the follow-up and support of these patients. In our opinion, this greatly conditions prescription since, unlike steroids, EEN patients require a lot of motivation to achieve their goals and must be followed-up more frequently and closely.

Our study is the first of its kind to be conducted in Spain. The data were collected over a short period of time, at a time when the evidence regarding the beneficial effects of EEN is on the rise.

A limitation of all surveys is the fact that results reflect the opinions of a selected population, pediatric gastroenterologists, who usually use EEN, willing to participate in the study.

To summarize, 8 weeks of EEN is the most frequent therapeutic option in newly diagnosed CD children in Spain. Formulas made specifically for IBD are used the most. The advantages of EEN compared to other therapeutic modalities are mucosal healing without side effects. The difficulties most frequently found were lack of acceptance by the patient and/or family and lack of time and/or ancillary staff to help in the follow-up and support of these patients.

Tools to facilitate acceptance by the patient and family are needed. Increasing the time dedicated to this therapeutic modality is likewise important. Given the disparity of criteria for indicating treatment with EEN, it would be useful to have widely accepted clinical practice guidelines or protocols that facilitate the decision to start with EEN.

Appendix I

The following investigators participated in the PRESENT study:

Masiques Mas ML(Hospital General de Granollers Barcelona), Guallarte Alias MP (Corporació Sanitaria Universitaria Parc Tauli Sabadell), Donat Aliaga E (Hospital Universitario La Fe Valencia), Sánchez Sánchez C(Hospital General Universitario Gregorio Marañón), Martínez Gómez MJ (Hospital Universitario Niño Jesús de Madrid), Pociello Almiñana N (Hospital Arnau de Vilanova de Lleida), Barrio Torres J (Hospital Universitario de Fuenlabrada Madrid), Pérez Parras MA (Complejo Hospitalario de Jaén), Argüelles Martin F (Hospital Universitario Virgen Macarena Sevilla), García Martín M (Hospital Universitario Virgen Macarena Sevilla), Rivero de la Rosa MC (Hospital Universitario Virgen Macarena Sevilla), Arévalo Garrido A (Complejo Hospitalario de Jaén), Sánchez Valverde-Visus F (Complejo Hospitalario de Navarra, Pamplona), López Ruzafa E (Hospital Universitario Torrecárdenas, Almería), Rodríguez Salas M (Hospital Universitario Reina Sofía, Córdoba), García Blanca JA (Hospital Universitario Puerta del Mar Cádiz), Galera Martínez R (Hospital Universitario Torrecárdenas, Almería), Suarez Cortina L (Hospital Ramón y Cajal de Madrid), Cortes Mora P (Hospital Universitario Santa Lucía de Cartagena), Rosell Camps A (Hospital Universitario Son Espases, Mallorca), Navalón Rubio M (Hospital Universitario Virgen de la Arrixaca, Murcia), Irastorza Terradillos I (Hospital Universitario Cruces, Bilbao), Ros Arnal I (Hospital Infantil Miguel Servet, Zaragoza), Ramos Boluda E (Hospital Universitario La Paz, Madrid), Gutiérrez Junquera C (Hospital Universitario Puerta de Hierro-Majadahonda, Madrid), Leis Trabazo R (Hospital Clínico Universitario de Santiago, Santiago de Compostela), Bartolomé Porro JM (Complejo Asistencial de Palencia), Peña Quintana L (Hospital Materno-Infantil. Las Palmas de Gran Canaria), Balmaseda Serrano E (Hospital General Universitario de Albacete), Solar Boga A (Complejo Hospitalario Universitario A Coruña), Moreno Álvarez A (Complejo Hospitalario Universitario A Co-

ruña), Eizaguirre Arocena FJ (Hospital Universitario Donostia, San Sebastián), Botija Arcos G (Hospital Universitario Fundación Alcorcón, Madrid), Lorenzo Garrido H (Hospital Universitario de Basurto), Armas Ramos H (Hospital Universitario de Canarias, Tenerife), Reyes Abreu G (Hospital Universitario de Canarias, Tenerife), López Casado MA (Hospital Materno Infantil Virgen de las Nieves, Granada), Salcedo Lobato E (Hospital Universitario de Getafe, Madrid), Rodríguez Martínez C (Hospital Vega Baja, Orihuela, Alicante), Ortigosa del Castillo L (Hospital Universitario Nuestra Señora de la Candelaria, Tenerife), Alberto R (Hospital Universitario Nuestra Señora de la Candelaria, Tenerife), Torres Peral R (Hospital Universitario de Salamanca), Martín Martínez B (Hospital de Terrasa), López MJ (Hospital de Terrasa), García Casales Z (Hospital de Txangorritxu, Araba), Chicano Marín FJ (Hospital Universitario Los Arcos del Mar Menor, Murcia), Pérez-Moneo Agapito B (Hospital Infanta Leonor, Madrid), Barros García P (Hospital San Pedro de Alcántara, Cáceres), Marugán de Miguelsanz JM (Hospital Clínico Universitario de Valladolid), Calvo Romero C (Hospital Clínico Universitario de Valladolid), Manzano Infante MJ (Instituto Hispalense de Pediatría Sevilla), Rodríguez Herrera A (Instituto Hispalense de Pediatría Sevilla).

Appendix II

Questionnaire on the use of exclusive enteral nutrition as treatment in Crohn's disease

A. General information about patients with IBD on follow-up in your Unit

1. How many patients with inflammatory bowel disease (IBD) do you currently have on follow-up in your unit?
2. How many of them are diagnosed with Crohn's disease (CD)?
3. How many were diagnosed in 2011?
4. How many of the patients with CD were treated in 2011 with EEN?
5. How many of these were recently diagnosed?

B. Exclusive Enteral Nutrition (EEN) in newly diagnosed CD patients

6. Do you **think** that EEN is effective in inducing **clinical** remission in CD patients?
7. Do you **think** that EEN is effective in inducing **endoscopic** remission in CD patients?
8. Do you **think** that EEN is effective in inducing **histological** remission in CD patients?
9. Do you **use** EEN in newly diagnosed CD patients?
10. Have you **verified** whether EEN is effective in inducing **clinical** remission in CD patients?
11. Have you **verified** whether EEN is effective in inducing **endoscopic** remission in CD patients?
12. Have you **verified** whether EEN is effective in inducing **histological** remission in CD patients?

C. Exclusive Enteral Nutrition (EEN) during CD relapses

13. Do you **think** that EEN is effective in inducing **clinical** remission in CD patients?
14. Do you **think** that EEN is effective in inducing **endoscopic** remission in CD patients?
15. Do you **think** that EEN is effective in inducing **histological** remission in CD patients?
16. Do you **use** EEN during relapses?
17. Have you **verified** whether EEN is effective in inducing **clinical** remission in CD patients?
18. Have you **verified** whether EEN is effective in inducing **endoscopic** remission in CD patients?
19. Have you **verified** whether EEN is effective in inducing **histological** remission in CD patients?

D. Indications and contraindications of EEN in CD

Question	*T*	*F*
20. I only use EEN in newly diagnosed patients, not in relapses		
21. I use EEN in relapses only if there was a previous response to EEN		
22. The location of the disease influences my indication for EEN.		
23. I only use it in cases when the ileum (L1) or ileum and colon (L3) are affected.		
24. I do not use EEN in exclusively colonic disease (L2).		
25. I do not use EEN if the upper digestive tract (duodenum, oesophagus) is affected (L4).		
26. I do not use EEN in perianal disease regardless of the perianal manifestations (fissures, fistulas, tags, abscesses, etc.).		
27. I do use EEN if the perianal disease is in the form of fissures or tags or if there is a correctly drained abscess		
28. I do not use EEN if the perianal disease is in the form of fistulas or abscesses even if correctly drained.		
29. I use EEN regardless of the phenotype (inflammatory, stricturing or penetrating)		
30. I only use EEN in inflammatory phenotypes		
31. I only use EEN in inflammatory and penetrating phenotypes		
32. I only use EEN in inflammatory and stricturing phenotypes		
33. I use the PCDAI to estimate the severity		
34. I use EEN in all CD patients, regardless of severity		

Appendix II *(cont.)*
Questionnaire on the use of exclusive enteral nutrition as treatment in Crohn's disease

Question	*T*	*F*
35. I only indicate EEN in mild disease		
36. I only indicate EEN in moderate disease		
37. I only indicate EEN in severe disease		
38. I only indicate EEN in mild to moderate disease		
39. I only indicate EEN in moderate to severe disease		
40. For severe disease, in addition to the PCDAI, I consider other factors when deciding whether or not to use EEN, such as: general status is affected, significant weight loss, prolonged symptoms, diagnostic delay, significant puberty delay, and also if there is upper digestive tract involvement.		
41. If the patient has a severe disease and presents one or several of the factors from the previous question I DO NOT indicate EEN.		
42. I consider age as a factor when indicating EEN.		
43. I use EEN regardless of patient age.		
44. I do not use EEN in children under the age of 2-3 years.		
45. I only use EEN starting at a determined age.		
46. I only use EEN if I observe that the patient and their family are collaborative.		
47. I indicate EEN and "make them" collaborative, providing no other options.		
48. I do not use EEN in cases of extraintestinal manifestation.		
49. Delay in weight or growth contributes to whether I indicate EEN.		

E. Specific aspects of EEN

50. What is the standard duration of EEN at your unit? (days, weeks, months)

51. Do you ever prolong EEN more than 12 weeks? Specify.

52. Which type of formula do you tend to use for EEN?
    a) Modulen IBD
    b) Resource IBD
    c) Other Polymeric Formula. Specify:
    d) Semi-elemental Formula. Specify:
    e) Elemental Formula. Specify:

53. What are your reasons for using this type of formula? (cost, taste, composition, availability, scientific evidence, etc.).

54. Does the physician participate in the decision on which formula to administer as EEN for Crohn's disease?

55. What is the most frequent route of administration? Rate as 1, 2 or 3, with 1 being the most frequent:
    Oral NG tube Gastrostomy

56. What do you allow the patients to eat or drink during the EEN period? Specify the % of daily calories.

57. Do you use flavouring? Specify the type (cocoa powder, syrups, etc.)

F. EEN as maintenance therapy

58. How do you effect progression from EEN to normal diet? Do you follow any clinical practice guidelines or protocols?

59. Once the EEN period has been completed, do you prescribe the formula as a supplement? If so, how much do you prescribe and for how long? The quantity can be expressed in ml or in % of daily calories.

G. Drugs used during EEN in newly diagnosed CD patients

60. If you tend to use adjuvant therapy with EEN in newly diagnosed CD patients, specify which, and the frequency of use. Mark with an X

	Always	*Sometimes*	*Never*	*I don't know*
Oral 5-ASA				
Topical 5-ASA				
Steroids				
Antibiotics				
Immunomodulators				
Anti-TNF				

Appendix II *(cont.)*
Questionnaire on the use of exclusive enteral nutrition as treatment in Crohn's disease

H. Professionals involved in the administration of EEN

61. Which of these healthcare professionals is routinely involved in the administration of EEN at your centre?

	Always	*Sometimes*	*Never*	*I don't know*
Nurse				
Dietician				
Psichologist				
Physician				

I. Follow-up protocol

62. Who performs the follow-up of these patients at your centre? (physician, nurse, dietician, other):
63. Which method do you use for the follow-up of these patients? (telephone, email, visit to clinic, etc.)
64. With what frequency do you contact the patient?

J. Assesment of response to treatment

65. How to you assess response to treatment?

	Always	*Sometimes*	*Never*	*I don't know*
Symptoms				
Lab tests				
Endoscopy				
Radiology				

– Symptoms: do you use any scores? Which?
– Tests: specify the parameters you use (CRP, PCT, Calprotectin, Lactoferrin, orosomucoid, others)
– Endoscopy
– Radiology (mark those that correspond)
  - Ultrasound
  - MR
  - Barium enema transit time

K. Advantages and disadvantages of EEN

66. Advantages	67. Disadvantages

L. Limiting factors for the use of EEN

68. Which of the following factors do you consider to be limiting at your Unit for an improved/greater use of EEN. Circle:
  a) Lack of time and/or ancillary staff (dieticians, nutritionists, psychologists, etc.) to help in the follow-up and support of these patients.
  b) Difficulties in prescription and administration of the nutrition by the hospital (logistics).
  c) Budgetary limitations.
  d) Difficulty convincing the patient and/or family of the treatment suitability.
  e) Lack of acceptance by the patient and/or family.
  f) Difficulty using alternatives to the oral route at my centre (NG tube, gastrostomy).
  g) I do not believe in the benefits of mono-therapy EEN to induce remission.
  h) Others:

M. Greather use of EEN

69. What type of information or material would you like to have available in order to use EEN more regularly?

N. Comments (70)

References

1. Heuschkel RB, Menache CC, Megerian JT, Baird AE. Enteral nutrition and corticosteroids in the treatment of acute Crohn's disease in children. *J Pediatr Gastroenterol Nutr* 2000; 31 (1): 8-15.
2. Dziechciarz P, Horvath A, Shamir R, Szajewska H. Meta-analysis: enteral nutrition in active Crohn's disease in children. *Aliment Pharmacol Ther* 2007; 26 (6): 795-806.
3. Day AS, Whitten KE, Sidler M, Lemberg DA. Systematic review: nutritional therapy in paediatric Crohn's disease. *Aliment Pharmacol Ther* 2008; 27 (4): 293-307.
4. Critch J, Day AS, Otley A, King-Moore C, Teitelbaum JE, Shashidhar H; NASPGHAN IBD Committee. Use of enteral nutrition for the control of intestinal inflammation in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr* 2012; 54 (2): 298-305.
5. Martín-de-Carpi J, Rodríguez A, Ramos E, Jiménez S, Martínez-Gómez MJ, Medina E; on behalf of the SPIRIT-IBD Working Group of SEGHNP (Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica). Increasing incidence of pediatric inflammatory bowel disease in Spain (1996-2009): The SPIRIT registry. *Inflamm Bowel Dis* 2013; 19 (1): 73-80.
6. Levine A, Milo T, Buller H, Markowitz J. Consensus and controversy in the management of pediatric Crohn disease: an international survey. *J Pediatr Gastroenterol Nutr* 2003; 36: 464-9.
7. Stewart M, Day AS, Otley A. Physician attitudes and practices of enteral nutrition as primary treatment of paediatric Crohn disease in North America. *J Pediatr Gastroenterol Nutr* 2011; 52 (1): 38-42.
8. Gråfors JM, Casswall TH. Exclusive enteral nutrition in the treatment of children with Crohn's disease in Sweden: a questionnaire survey. *Acta Paediatr* 2011; 100 (7): 1018-22.
9. Whitten KE, Rogers P, Ooi CY, Day AS. International survey of enteral nutrition protocols used in children with Crohn's disease. *J Dig Dis* 2012; 13 (2): 107-12.
10. Levine A, Griffiths A, Markowitz J, Wilson DC, Turner D, Russell RK et al. Pediatric modification of the Montreal classification for inflammatory bowel disease: the Paris classification. *Inflamm Bowel Dis* 2011; 17 (6): 1314-21.
11. Hyams J, Markowitz J, Otley A, Rosh J, Mack D, Bousvaros A et al. Pediatric Inflammatory Bowel Disease Collaborative Research Group. Evaluation of the pediatric crohn disease activity index: a prospective multicenter experience. *J Pediatr Gastroenterol Nutr* 2005; 41 (4): 416-21.
12. Turner D, Griffiths AM, Walters TD, Seah T, Markowitz J, Pfefferkorn M et al. Mathematical weighting of the pediatric Crohn's disease activity index (PCDAI) and comparison with its other short versions. *Inflamm Bowel Dis* 2012; 18 (1): 55-62.
13. Day AS, Stephenson T, Stewart M, Otley AR. Exclusive enteral nutrition for children with Crohn's disease: use in Australia and attitudes of Australian paediatric gastroenterologists. *J Paediatr Child Health* 2009; 45 (6): 337-41.
14. Borrelli O, Cordischi L, Cirulli M, Paganelli M, Labalestra V, Uccini S et al. Polymeric diet alone versus corticosteroids in the treatment of active pediatric Crohn's disease: a randomized controlled open-label trial. *Clin Gastroenterol Hepatol* 2006; 4 (6): 744-53.
15. Grover Z, Muir R, Lewindon P. Exclusive enteral nutrition induces early clinical, mucosal and transmural remission in paediatric Crohn's disease. *J Gastroenterol* 2013. In press.
16. Seidman E, Griffiths A, Jones A, Issenman R. Semi-elemental (S-E) diet *versus* prednisone in pediatric Crohn's disease. *Gastroenterology* 1994; 104 (4 Pt 2): A778.
17. Afzal NA, Davies S, Paintin M, Arnaud-Battandier F, Walker-Smith JA, Murch S et al. Colonic Crohn's disease in children does not respond well to treatment with enteral nutrition if the ileum is not involved. *Dig Dis Sci* 2005; 50: 1471-5.
18. Buchanan E, Gaunt WW, Cardigan T, Garrick V, McGrogan P, Russell RK. The use of exclusive enteral nutrition for induction of remission in children with Crohn's disease demonstrates that disease phenotype does not influence clinical remission. *Aliment Pharmacol Ther* 2009; 30 (5): 501-7.
19. Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst Rev* 2007;CD000542.
20. Khoshoo V, Reifen R, Neuman MG, Griffiths A, Pencharz PB. Effect of low- and high-fat, peptide-based diets on body composition and disease activity in adolescents with active Crohn's disease. *JPEN J Parenter Enteral Nutr* 1996; 20 (6): 401-5.
21. Rodrigues AF, Johnson T, Davies P, Murphy MS. Does polymeric formula improve adherence to liquid diet therapy in children with active Crohn's disease? *Arch Dis Child* 2007; 92: 767-70.
22. Akobeng AK, Miller V, Stanton J, Elbadri AM, Thomas AG. Double-blind randomized controlled trial of glutamine-enriched polymeric diet in the treatment of active Crohn's disease. *J Pediatr Gastroenterol Nutr* 2000; 30 (1): 78-84.
23. Ludvigsson JF, Krantz M, Bodin L, Stenhammar L, Lindquist B. Elemental versus polymeric enteral nutrition in paediatric Crohn's disease: a multicentre randomized controlled trial. *Acta Paediatr* 2004; 93 (3): 327-35.
24. Day AS, Whitten KE, Lemberg DA, Clarkson C, Vitug-Sales M, Jackson R, Bohane TD. Exclusive enteral feeding as primary therapy for Crohn's disease in Australian children and adolescents: a feasible and effective approach. *J Gastroenterol Hepatol* 2006; 21 (10): 1609-14.