Use of Enteral Nutrition for the Control of Intestinal Inflammation in Pediatric Crohn Disease

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ABSTRACT

Exclusive enteral nutrition is an effective yet often underused therapy for the induction of remission in pediatric Crohn disease. The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition formed the Enteral Nutrition Working Group to review the use of enteral nutrition therapy in pediatric Crohn disease. The group was composed of 5 pediatric gastroenterologists and 1 pediatric nutritionist, all with an interest and/or expertise in exclusive enteral nutrition. Specific attention was placed upon review of the evidence for efficacy of therapy, assessment of the variations in care, identification of barriers to its widespread use, and compilation of the necessary components for a successful program. The present guideline is intended to aid physicians in developing an enteral nutrition therapy program and potentially promote its use.

Key Words: exclusive enteral nutrition, intestinal inflammation, pediatric Crohn disease

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E nteral nutritional (EN) therapy using liquid formulas (elemental, semielemental, or polymeric) is often used in the management of pediatric Crohn disease (CD). This therapy is usually administered in 2 ways:

1. As exclusive enteral nutrition (EEN)—provided as the sole dietary source, being used as primary medical therapy to induce remission
2. As partial enteral nutrition (PEN)—given in addition to a normal diet, with the primary goal to improve nutritional status or to maintain remission

The North American Society For Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) has published a clinical statement on the role of PEN to improve nutritional status in CD (1). The potential benefits of EEN as a therapeutic option in CD were first documented in case reports and series in the 1970s (2–5). Reduction of symptoms was also observed in patients with CD receiving parenteral nutritional therapy for bowel rest while awaiting surgical resection (6). In 1984, O'Morain et al (7) published a controlled trial demonstrating the benefit of an elemental diet on the induction of remission. Subsequent to this, many researchers have explored the relation between EN and control of inflammation in CD. There is presently strong evidence supporting the use of EEN for induction of remission in pediatric CD. In 2006, both the European Society for Clinical Nutrition and Metabolism (8) and the working group of the Japanese Society for Pediatric Gastroenterology, Hepatology, and Nutrition (9) independently published guidelines recommending that EN be considered as the first-line induction therapy in children with CD, followed in 2010 by similar conclusions by the Inflammatory Bowel Disease (IBD) Working Group of the British Society of Paediatric Gastroenterology, Hepatology, and Nutrition (10).

Despite the evidence, nutritional therapy has not been universally adopted. Levine et al (11) reported that 62% of European pediatric gastroenterologists regularly used EEN compared with 4% of their North American colleagues. Furthermore, treatment protocols used for induction of remission, including type of formula, route of administration, and duration of induction therapy, vary widely (12,13). Even greater diversity seems to be present for maintenance therapy protocols (14–16).

In deference to the wide variability in the use of EN as a primary therapy for CD and the variation in protocols used, the NASPGHAN IBD committee formed the Enteral Nutrition Working Group (ENWG) to review the present medical literature surrounding these issues. Specific attention was placed upon review of the evidence for efficacy of therapy, assessment of the variations in care, identification of barriers to its widespread use, and compilation of the necessary components for a successful program. It was hoped that in doing so, many of the barriers to the implementation of EN in children with CD would be explored and strategies would be presented to aid physicians in developing an EN therapy program.

METHODS

The ENWG was established by the IBD committee of NASPGHAN. Working group members were selected from the

IBD committee with invitations extended to several participants outside the committee who had an interest and expertise in this area. The group members were selected to provide a range in regard to practice jurisdiction (Australia, Canada, United States) and academic and nonacademic practice. The group membership consisted of 5 pediatric gastroenterologists and 1 pediatric nutritionist with expertise in the management of CD. Issues of relevance were first identified through group discussion. Individual topics were distributed to subgroups mandated to review the literature and develop draft summaries. These drafts were subsequently distributed among the full working group for further discussion and revision. Searches were conducted on PubMed (*www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed*). Articles were evaluated using the Oxford Centre for Evidence-based Medicine Levels of Evidence (*www.cebm.net*). Using the Oxford Grades of Recommendation Match 2009 (*www.cebm.net*), the quality of evidence of each of the recommendations made by the committee was determined. Note was made of topics with a paucity of evidence.

Issues in Pediatric CD

Pediatric CD exerts an adverse effect on growth and nutritional state. At presentation, up to 46% of children exhibit linear growth impairment (17) and 85% have lost weight (18). Suboptimal growth may continue despite therapy leading to permanent deficits in final adult height (19). Inflammation, malnutrition, and corticosteroid therapy are important etiological factors for growth impairment in pediatric IBD. Furthermore, concern is increasing about the adverse effects of corticosteroids on growth, bone mineral density, and lack of mucosal healing (20–22). Recent evidence also cites an association of corticosteroid use with an increased incidence of serious or opportunistic infections, especially when used in conjunction with biological therapy (23,24).

Mechanisms of Efficacy of EEN in Pediatric CD

The mechanism of action of EEN for the induction of remission remains conjectural. Hypotheses have included elimination of dietary antigen uptake, overall nutritional repletion, correction of intestinal permeability, diminution of intestinal synthesis of inflammatory mediators via reduction in dietary fat, and provision of important micronutrients to the diseased intestine (25,26). Altered gut microflora is a putative pathogenic mechanism for the mucosal inflammation in CD (27). EEN has been shown to exert both a change in gut microflora and an anti-inflammatory effect (25,28). Children treated with an enteral polymeric diet revealed profound modification of the fecal microflora during and after EEN, suggesting this as a putative mechanism for the induction of remission consequent to EN (25). More detailed discussions about potential mechanisms of action are available in several review articles (29,30).

Evidence for Use of EEN in Pediatric CD

Induction of Remission in Newly Diagnosed Patients

Studies have shown that EEN induces remission in up to 85% of children with newly diagnosed CD (31–35). In the most recent Cochrane review comparing efficacy of induction between corticosteroids and EEN, meta-analyses of 6 trials (192 patients received EEN and 160 patients received steroids) yielded a pooled odds ratio of 0.33 (95% confidence interval [CI] 0.21%–0.53%) favoring corticosteroid therapy (36). The studies analyzed contained both adult and pediatric patients; however, many pediatric

trials were excluded from this analysis owing to methodological weakness. The authors mention that a previous abstract (37) and 1 pediatric trial (37 children randomized, 19 received exclusive polymeric formula, 18 received corticosteroids) (34) both favor EEN over corticosteroids. These pediatric trials, along with a pediatric meta-analysis (38) consisting of 5 randomized controlled trials involving 147 children, which determined that EEN and corticosteroids were equally effective (pooled relative risk 0.95, 95% CI 0.67%–1.34%), may suggest that the benefits of EEN differ in children from adults with a more favorable effect in children. Additionally, a meta-analysis of pooled data from 4 randomized controlled trials in 144 children found no significant difference in remission rates at 8 to 10 weeks between EEN and corticosteroids (relative risk 0.97, 95% CI 0.7%–1.4%, random effects model) (39). Day et al (32) cited intolerance to the formula and inadequate volume as possible reasons why some patients did not achieve remission.

Induction of Remission for Exacerbations

Several studies have explored the effect of EEN in controlling disease exacerbations. In small studies by Seidman et al (31) and Day et al (32) that included children with recurrent disease, at least half of the children receiving EEN entered remission (5/10 and 7/12 patients, respectively). Furthermore, many of the children who had failed to achieve remission were still observed to have decreased disease activity and improved nutritional status (32).

Effect of EEN on Mucosal Healing, Growth, and Nutritional Status

Mucosal healing has been documented in children treated with EEN therapy regardless of type of formula. Borrelli et al (34) demonstrated mucosal healing at 10 weeks in 14 of 19 (74%; 95% CI 51%–89%) patients treated with an exclusive polymeric diet versus 6 of 18 (33%; 95% CI 16%–57%) patients treated with corticosteroids ($P < 0.05$). Seven children treated with EEN showed complete healing, whereas none of the children treated with corticosteroids showed complete mucosal healing. Fell et al (40) demonstrated that treating 29 children with 8 weeks of an oral polymeric diet rich in transforming growth factor-β2 was associated with complete clinical remission in 79% of children. Histological healing occurred in 8 cases in the terminal ileum and in 2 cases in the colon. Other studies have also shown lack of mucosal healing with corticosteroids in CD (20,21). The significance of achieving mucosal healing remains to be determined; however, Baert et al (41) showed that complete mucosal healing after 2 years of therapy in adult patients with CD was the only factor that predicted sustained, steroid-free remission 3 and 4 years after therapy was initiated.

Although the effect of EEN on weight gain appears to be variable (34,37,42,43), the positive effect of EEN compared with corticosteroids upon linear growth is clearly established to occur even within 10 weeks to 6 months (44). Newby et al (44) reported on studies by Sanderson et al (43) (15 children) and Thomas et al (45) (24 children), which showed that height velocity standard deviation scores were significantly increased in the enteral feeding group compared with the corticosteroid group at 6 months ($P < 0.05$). Body composition is also shown to improve with EEN. These favorable effects of nutrition may occur in the absence of mucosal healing. Even in clinically stable adolescents with CD, EEN promotes anabolism by suppressing proteolysis and increasing protein synthesis (46,47).

PEN Versus EEN for Induction of Remission

Initial studies evaluating EN used formulae as the sole dietary intake, with exclusion of all other foods. The only published study to consider the need for complete exclusion of normal diet was a recent randomized clinical study conducted in the United Kingdom, in which 24 children were administered standard EEN and 26 children were given 50% of their energy as formula and 50% as normal food (48). The EEN group had a remission rate of 42%, which was almost 3-fold greater than that of the partial EN group (15%) ($P < 0.035$). Despite this, some pediatric units do allow the addition of various foods in addition to EEN (49). One group has reported (unpublished data) that allowing 10% of energy intake as conventional foods does not appear to decrease the efficacy of EN as induction therapy. Because of a lack of published data, no definite recommendation can be made on the efficacy of this approach.

Influence of Formula Composition

Although elemental or semielemental formula was initially used in EEN, available data does not show any significant difference in outcome based on the type of formula used (34,50) or any advantage to additives such as glutamine (51). A meta-analysis of 10 trials (334 adult patients) did not reveal any difference in efficacy between elemental and nonelemental formulations (odds ratio 1.10; 95% CI 0.69%–1.75%) (36). Polymeric formulas are generally less expensive and have better taste characteristics, permitting oral administration in many children. Moreover, the use of polymeric formula may be associated with better weight gain than an elemental diet (52). Because the use of a nasogastric (NG) tube to administer feeds may be associated with perceived negative feelings toward EEN, polymeric formula may facilitate increased acceptance and use of enteral therapy (53,54).

Influence of Disease Location

Whether EEN provides a better outcome in colonic or small bowel disease is unclear, although some evidence tends to favor EEN in small bowel disease rather than in active colonic disease (55). Afzal et al (55) have shown that isolated colonic disease does not respond to EEN as well as ileocolonic or ileal disease (11/12 patients with ileal disease achieved remission, 32/39 with ileocolonic disease achieved remission, 7/ 14 with isolated colonic disease achieved remission, $P = 0.021$). Other investigators have not shown support for this (10/13 patients with isolated small bowel disease achieved remission at 4 weeks compared with 15/19 patients with isolated colonic disease, $P = 0.88$) (56). The meta-analysis by Zachos et al (36) was unable to make definitive conclusions on this aspect because of a lack of power. Until the importance of disease location on response to EEN is definitively delineated, it would seem reasonable to consider its use for all patients with CD.

Refeeding Syndrome

EEN is an extremely safe therapy; however, rare cases of refeeding syndrome have been reported in children and adolescents with IBD (57–59). Refeeding syndrome is a condition characterized by fluid shifts and electrolyte abnormalities (hypophosphatemia, hypokalemia) that may occur when a profoundly malnourished patient receives enteral nutritional rehabilitation. If a child is significantly malnourished (eg, body mass index z score < -1.5) and is being treated with EEN, then an initial period of hospitalization and monitoring and treatment for refeeding syndrome (daily electrolytes, gradual refeeding, phosphate supplementation) should be considered.

Duration of Therapy

The duration of EEN therapy varies substantially across published reports (29,39), from 3 to 12 weeks. A recent survey of a number of pediatric centers across North America, Europe, and Asia also demonstrated a wide variance in the duration of EEN regimens (49). The average duration in the units surveyed was 8.5 ± 1.7 weeks, with a range from <6 weeks to >12 weeks. The majority of units (81%) used a 6- to 8-week period of EEN.

Two other surveys of individual pediatric gastroenterologists have been conducted in North America (59) and Australasia (60). These illustrate similar conclusions, with most using 6 to 8 weeks of EEN as a standard. Eleven of 12 doctors in Australasia and 46% of North American physicians used EEN for this time period. Interestingly, however, 25% of the North American gastroenterologists used EEN for >8 weeks (with some using >12 weeks). The time period of EEN may be seen as a compromise between ensuring adequate compliance and optimization of benefits. Undoubtedly, the variation and lack of consistency add to the confusion surrounding EEN. As a group, we recommend a period of at least 8 weeks, acknowledging the potential that a longer course of up to 12 weeks may have increased efficacy and be indicated in certain settings. Further research is required to determine the optimal duration of EEN as induction therapy in CD.

In addition, several studies suggest that although initial benefits are noted on the inflammatory state and nutritional status during the first couple of weeks of therapy, further improvements continue during the following weeks. The time to achieve clinical remission appears variable. Inflammatory markers improve in as little as 1 week, (28) and time to remission has been reported within as few as 11 days to 2.5 weeks (39). Unfortunately, data examining the range of time to remission are lacking, and it is likely that some patients require a longer period than 2.5 weeks to achieve remission. As a group, we suggest that upon initiating EEN, patients be given a period of at least 3 to 4 weeks to allow for observation as to whether this therapy will be effective. If no improvement is seen during that time, then a change in treatment plan may be warranted; however, continued administration may yield benefits even in those who have not responded within this time frame. The success of longer duration of therapy to decrease recurrence rate remains to be substantiated.

Route of Administration

For induction, EEN may be administered orally or with a nasogastric (NG) tube. It is unclear whether one method is superior to the other. Oral feedings are common in Australia, the United Kingdom, and some US centers. The advantages of oral administration include the lower costs and complexity that are associated with NG tubes and pumps; however, poor palatability may limit acceptance.

Reintroduction of Food

Another aspect of EEN is the resumption of normal diet at the end of the period of exclusive formula. Different approaches to the reintroduction of normal diet include the gradual introduction of food quantity while formula volume decreases to the use of a low-allergen diet in which new foods are introduced every 2 days (27,61). No clear data support a hypoallergenic diet approach. The approach of introducing a meal every 2 to 3 days while

gradually reducing the volume of formula appears to be a reasonable compromise among compliance, efficacy, and tolerance by children and adolescents. The 2010 UK guidelines suggested cautious reintroduction for 1 to 3 weeks dependent on patient symptoms while weaning EN (10).

Concomitant Medications

EEN induction has been used as monotherapy or with medications such as mesalamine, 6-mercaptopurine/azathioprine, methotrexate, and infliximab (9,13). The superiority of one approach over the other is unknown. Despite whether concomitant medications are used for induction therapy, it is vital that a transition plan toward maintenance therapy be formulated as EEN therapy nears completion. In this regard, consideration is often given to initiation of immunomodulators as maintenance medications. Others have considered ongoing maintenance therapy with EN (discussed below).

Maintenance of Remission

PEN Regimens

Numerous reports have considered and evaluated the role of PEN in the maintenance of remission and prevention of relapse. In addition to prolonging remission, such an approach may delay the requirement for further therapy (eg, steroids) and optimize growth and nutrition. Such a therapeutic strategy may also be used in combination with maintenance medical therapy, but may be limited by compliance. Such programs have been provided in various forms: overnight NG feeds in conjunction with normal daytime eating, short bursts of NG feeds every few months, or as oral supplements in addition to oral eating throughout the day.

Two Canadian groups have considered the first 2 approaches. A report from the Hospital for Sick Children, Toronto, described 28 children provided with elemental formula delivered overnight by an NG tube while consuming a normal diet in the daytime compared with 19 children in whom EEN successfully induced remission but who opted to discontinue nocturnal elemental feedings (14). At 12 months, 43% (12/28) of patients receiving nocturnal elemental feedings had relapsed compared with 79% (15/19) who had discontinued supplemental elemental feedings ($P < 0.02$). Investigators from Quebec used an alternate approach in another cohort of 8 children with CD and growth failure (15). These children received periods of NG elemental formula (70% of energy requirements) for 1 of 4 months during a 1-year period. Significant height and weight gains, decrease in the Crohn's Disease Activity Index, and decrease in prednisone use were noted.

Several studies from Japan have also evaluated the role(s) of PEN in adult populations. One study included 51 patients with CD in remission, who were randomized to receive half of their energy as elemental formula with normal diet (26 patients) or to have an unrestricted normal diet (with no additional supplements) (25 patients) for up to 24 months (16). Remission had previously been induced by EEN, parenteral nutrition, surgical resection, or corticosteroids. During the period of observation, the relapse rate of the treatment group was almost half of the free-diet group (34.6% vs 64.0%; multivariate hazard ratio 0.40, 95% CI 0.16%–0.98%). The study was halted before the end of the planned study period, as the interim analyses had shown benefit for the use of formula and the investigators deemed it to be inappropriate to continue allocation to a free-diet group. Of note, all of the patients in both groups received concomitant mesalazine and 6 in each group received 50 mg/day of azathioprine.

A Japanese study assessed the effect of EN on recurrence in adult patients postresection for ileal or ileocolonic CD (62). Forty adult patients were allocated to receive either continuous EN administered via NG at nighttime with a lowfat daytime diet for >12 months or a standard diet. The 20 patients who received overnight feeds had rates of endoscopic disease recurrence of 25% after 6 months and 30% after 12 months. In contrast, the group who had a standard diet had recurrence rates of 40% and 70% at the same 2 time points ($P = 0.027$ at 12 months). All of the patients in both groups received mesalazine (Pentasa, 3000 mg/day) during the entire study. No patients received corticosteroids, immunosuppressive drugs, or infliximab before symptoms recurred.

Another Japanese study evaluated PEN to prevent postoperative recurrence (63). A group of adults (n = 24) who received at least 1200 kcal/day of polymeric or elemental formula for 12 months after resection were shown to have a much lower risk of disease recurrence than a control group (n = 16) who were not given PEN ($P = 0.017$). 5-Aminosalicylic acid at doses ranging from 1500 to 2250 mg was administered to 14 patients; however, none of the patients received concomitant corticosteroids or thiopurines (6-mercaptopurine or azathioprine) after surgery. When administered in patients after bowel surgery, PEN reduced the cumulative rate of postoperative recurrence especially in patients with penetrating-type disease ($P = 0.005$) and those without colitis ($P = 0.051$).

Barriers to Use

Levine et al (11) measured significant variations in the use of EEN in a transatlantic survey of 167 physicians from the United States, Canada, western Europe, and Israel. Although 4% of North American pediatric gastroenterologists use EEN regularly, 62% of European practitioners reported regular use. The present study did not consider the reasons behind these practice differences.

Recently, 2 studies have evaluated attitudes to EEN and use of EEN in North America (326 respondents) (59) and Australia (21 respondents) (60). North American pediatric gastroenterologists (n = 326) reported that concerns about adherence were the main disadvantage of EEN and provided a barrier to wider usage. Australian respondents also commented that adherence was a concern but cited other issues including cost and resource demands. Both of these surveys noted that experience with EEN during gastroenterology training related to present use and confidence with EEN.

Presently, no studies have assessed factors influencing patient or parent acceptance. The above 2 surveys (59,60) examined physician attitudes but did not fully consider parental or family factors. Personal experience has identified concerns about the adverse effects of corticosteroids as favorably influencing acceptance of EEN. The expense of EEN, concerns about giving up conventional foods, poor palatability of formulas, and fear of tube feedings have been cited as reasons for patient and/or parental refusal of EEN.

Two studies have considered the effect of EEN upon quality of life (QOL). The IMPACT II questionnaire was used to define QOL scores in 26 children being treated with 8 weeks of EEN (64). QOL scores improved in 24 of the 26 children during this time, with QOL scores correlating closely with disease activity ($r = 0.67$). A second study evaluated psychological well-being and attitudes to therapy of 30 children; half were managed with EEN via NG tube and half with corticosteroids (54). A formal QOL questionnaire was not used by these investigators. Although some aspects of the results favored EEN over steroids, the main conclusions of the present study were in regard to the disruption of daily

life secondary to EEN and the difficulties encountered by changing diet in this way.

Required Resources

To promote success, EEN programs must have the necessary supports. At present, no published studies delineate the optimal resources. Discussions held with centers with more extensive experience that use EEN highlight several issues. Attitudes among health care staff that promote the use of EEN and the center's experience appear to play a large role. Most programs have available dedicated dieticians who perform critical roles to determine appropriate nutrient intake and in administration of the program. Nursing support with experience in administering and teaching care of tube feedings and use of the feeding pumps is necessary for those who are unable to tolerate oral formula. Access to psychological support is important for many patients, both in regard to their disease in general and particularly with the issues around EEN. This support may help tremendously with overcoming resistance to restricting conventional foods and accepting EEN. The costs of many of the formulas are high and may not be covered by the relevant health system.

Unfortunately, many patients do not have health insurance and for those who do, many plans do not cover the costs of EEN. In some jurisdictions, coverage may be obtained if formula is delivered by a tube, either NG or gastrostomy tube. The high cost is likely to be a negative influence on the use of this therapy. The rate of nonadherence is unknown.

Practical Considerations

It is important that the health care provider clearly present the benefits of EEN as induction therapy to the patient and his or her family, highlighting the efficacy of EEN to induce remission, its effect on mucosal healing and linear growth, and the avoidance of significant corticosteroid adverse effects. Once a decision is made to proceed to EEN, a number of items need to be considered including the determination of energy, method of administration, and expectations around the duration of therapy.

Prescription of daily volumes of formula is based upon the child's estimated energy requirement. The estimated energy requirement can be calculated using the Schofield equation (65), which estimates basal metabolic rate from weight (other energy prediction equations such as the Food and Agriculture Organization/World Health Organization/United Nations University [1985] energy recommendations (66), Oxford (67), and dietary reference intakes estimated energy equations [2002] (68) can be used). Hill et al (69) determined that the Schofield equation best predicted the measured resting energy expenditure in pediatric patients with IBD (3–18 years) and suggested that it be used when measured resting energy expenditure could not be obtained (Table 1). Actual body weight or ideal body weight for height (height for chronological age) should be used in the equation depending on whether the child is of an appropriate weight or underweight for height. An activity factor should be added, based upon the child's usual activity level. This will provide a goal volume that can be considered as a minimum daily volume. After commencement of EEN, the child's nutritional status needs to be re-evaluated regularly and adjusted as required. Hunger and/or poor weight gain are common indications to increase the prescribed daily volume. In general, most children require 120% of reference nutrient intake. In addition to meeting energy requirements, it is important to ensure that the child's fluid requirements are sufficient. Total fluid intake is not necessarily met by ingestion of formula alone, and the deficit must be made up by consuming water.

Once energy and fluid requirements are calculated, decisions on the type of formula and route of ingestion are determined. As stated, polymeric, semielemental, and elemental formulas appear equivalent in regard to efficacy in controlling inflammation. Choice of formula used is often influenced in part by cost and route of administration. Generally, the polymeric formulas are significantly less expensive. Polymeric formulas are more palatable and therefore may be better suited if the oral route is chosen. Furthermore, as previously discussed, significant practice variations exist regarding the use of oral supplementation and flavoring agents (ie, syrups) when using EEN as induction therapy. Some providers allow the supplementation of foods (eg, hard candy, gum), whereas others do not; however, because of a paucity of data, no recommendation can be made on the practice of allowing such supplementation.

It remains unclear whether the delivery of EEN is improved by oral or by tube method. Oral feedings are typically taken by at least 3 or 4 portions throughout the day, with additional water offered as desired. The child should aim to progressively increase the volume taken each day, so that the full volume is achieved by day 3 or 4. In addition, a plan for the introduction of NG feedings should be outlined in the event that oral ingestion is unsuccessful.

TABLE 1. Equations for predicting REE and BMR (kcal/day) in children from 3 to 18 years old

Source	Sex, age range, y	Equation
Schofield et al (65)	Female, 3–10	$BMR = (16.97 \times Wt) + (161.8 \times Ht) + 371.2$
	Male, 3–10	$BMR = (19.6 \times Wt) + (130.3 \times Ht) + 414.9$
	Female, 10–18	$BMR = (8.365 \times Wt) + (465 \times Ht) + 200$
	Male, 10–18	$BMR = (16.25 \times Wt) + (137.2 \times Ht) + 515.5$
FAO/WHO/UNU (66)	Female, 3–10	$REE = (22.5 \times Wt) + 499$
	Male, 3–10	$REE = (22.7 \times Wt) + 495$
	Female, 10–18	$REE = (12.2 \times Wt) + 746$
	Male, 10–18	$REE = (17.5 \times Wt) + 651$
Oxford (67)	Female, 3–10	$BMR = (15.9 \times Wt) + (210 \times Ht) + 349$
	Male, 3–10	$BMR = (15.1 \times Wt) + (74.2 \times Ht) + 306$
	Female, 10–18	$BMR = (9.4 \times Wt) + (249 \times Ht) + 462$
	Male, 10–18	$BMR = (15.6 \times Wt) + (266 \times Ht) + 299$

BMR = basal metabolic rates; FAO = Food and Agriculture Organization; Ht = length in meters; REE = resting energy expenditure; UNU = United Nations University; WHO = World Health Organization; Wt = body weight in kilograms.

NG tube feedings can be used, with the advantage that patients do not develop taste fatigue. This may be an option especially when longer periods of EEN are recommended. Options for NG tubes include having the patient or caregiver learn to place the tube each night or for a long-term tube to be placed for several weeks. NG feedings can largely be administered overnight to minimize the effect on the patient's daily routine, although it is common for the infusion to extend into the awake hours. In addition, pumps are available that can be carried in a backpack to allow mobility during daytime administration. Typically, when initiating tube feedings, start at $^1/_2$ volume and increase to full volume for 1 to 2 days. Initiate feeds at half the hourly goal rate. For instance, if goal feed is 100 mL/hour × 20 hours/day, start feeds at 50 mL/hour and progress by increasing 10 mL/hour for 3 to 6 hours depending on the severity of disease and level of tolerance expected. It should take 24 to 36 hours to reach goal feeds. Encourage the child to drink water during NG feed progression to ensure maintenance fluid requirements are met. Further increases in tube feeding rate may be required if the child complains of hunger. In such a case, one can consider increasing the rate by 5 mL/hour each day until complaints of hunger have subsided. Typically, tube feeding is designed to meet minimum fluid and entire nutritional requirements; however, some units allow the child to drink a specified volume of clear fluids (eg, Popsicles, soup broth) in addition to the formula. Variations in practice allowing additional clear fluids are likely related to whether EEN is delivered orally or via NG tube. With the former, it would be important not to promote the intake of other liquids/foods, which may result in decreased overall intake of the formula on a daily basis, whereas for patients receiving EEN delivered via NG, oral supplementation with clear fluids may be one way to help promote compliance and ensure that adequate fluids are ingested.

The necessary teaching and support for patients receiving EEN must be available. With tube feeding, the patient and family must be taught how to care for the tube, including how to check for proper tube placement, flush tubes, and troubleshoot if tubes should become blocked. Clear instructions about operation of the feeding pump and the daily cleaning routine for the formula bags must be given. Teaching generally is provided by an experienced nurse, although videos may be helpful.

A system must be in place to determine how the patient is going to accept delivery of the required formula and supplies. Families instituting NG tube feedings need to be aware of all of the supplies required such as tubing, bags (small, large, or both), stethoscope, syringes, and feeding pump. Issues of cost are important to address because this tends to be a relatively expensive intervention. Expenses are borne in various ways, in some by government programs and others as health insurance coverage. Unfortunately, many patients have no financial support to aid with the costs. The use of polymeric formulas may help to keep the expenses lower.

Upon commencement of EEN, ways to integrate the period of EEN into the family setting should be considered and discussed. This may include changing family routines or avoiding favorite meals during this time. In addition, the family should be aware of effective ways to reintegrate the child into the classroom and to participate in most sports and classroom activities with minimal disruption. Parents are encouraged to meet with teachers, the principal, and any other individuals to outline the reason for EEN and what, if anything, is required to be done at school. This open approach helps ensure that the child receives support and acceptance at school. Parents and child are encouraged to speak to the child's class to address questions and concerns. Visits by the IBD nurse to the school or direct communication with school staff may help facilitate this.

The child's progress should be monitored closely, especially during the initial 2 weeks. Regular telephone contact and/or clinic visits with the team are important to document response, to demonstrate changes in weight, to assess adherence, to ensure that the child is not hungry or overfull, and to troubleshoot and address any difficulties. This follow-up may provide the family a sense of security and aid adherence.

For patients using NG feedings who decide to continue with its long-term use, the insertion of a gastrostomy tube is an option. The use of gastrostomy tubes in children with CD is a safe intervention. Israel et al (70) reviewed their experience with gastrostomy tubes in 16 children with CD who received PEN. Of these, 2 had endoscopic evidence of gastroduodenal CD and 6 had microscopic chronic gastritis. Minor complications included external leakage, discomfort, and local wound infection in 5 patients. Thirteen patients had the gastrostomy tube removed at the time of publication. Twelve had prompt and complete healing of the gastrostomy site. One developed a small gastrocutaneous fistula, which required suturing for successful closure.

SUMMARY

In summary, EEN offers an alternative to corticosteroids to induce remission in pediatric CD and should be supported as a first-line induction therapy in pediatric CD, regardless of active disease location. Although the precise mechanism(s) of action remains unclear, EN has a beneficial effect on growth and nutritional status as well as markers of inflammation and the promotion of mucosal healing. Furthermore, the use of EEN will avoid the significant adverse effects of corticosteroids. The ongoing use of PEN may be especially beneficial in children displaying growth and pubertal delay. The mechanism of action of EEN remains conjectural and further research is required to determine the mechanism of action and optimal use of this therapy.

Comments

1. EEN is an effective induction therapy in newly diagnosed (level 1a, grade A) and active CD (level 2b, grade C).
2. EEN has an improved adverse-effect profile over corticosteroids (level 1a, grade A).
3. EEN has been shown to promote mucosal healing (level 1b, grade A) and has beneficial effect on linear growth (level 2b, grade A).
4. Elemental, semielemental, and polymeric formulas have similar efficacy in the induction of remission in pediatric CD (level 1b, grade A).
5. For induction, published studies support a period of at least 8 weeks of EEN (level 1a, grade A), but there may exist benefits for longer durations of up to 12 weeks in some individuals (level 5, grade D).
6. Ongoing use of PEN in conjunction with other therapeutic strategies may be especially beneficial in children with stunting and pubertal delay (level 5, grade D).
7. The optimal components of a successful EEN program have not been determined. It is the opinion of the Enteral Nutrition Working Group that programs incorporating the coordinated services of a nurse and dietitian in addition to medical staff have a greater chance of success. Some children and their families may also require access to social work and/or psychological supports (level 5, grade D).
8. Because poor exposure to EEN during fellowship training has been cited as a factor in decreased use, we urge that EEN be promoted during training (level 5, grade D).

9. The wide variation in many aspects of enteral therapy highlights the need for further research to evaluate the determinants of optimal care. Furthermore, research into understanding the mechanism(s) by which EN induces remission in CD could well lead to a greater understanding of the biological and environmental determinants for disease pathogenesis (level 5, grade D).

10. EN is an expensive intervention. Physicians caring for patients with pediatric CD need to advocate for the costs of nutritional care programs to be covered by private health insurance plans and/or government (level 5, grade D).

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